section 3

Psychological Treatment of CTE
Psychological treatment of patients with chronic toxic encephalopathy: lessons from studies of chronic fatigue and whiplash

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Abstract

Background: Chronic toxic encephalopathy (CTE), which can result from long-term exposure to organic solvents, is characterised by problems of attention and memory, fatigue, and affective symptoms. There is little experience with (neuro)psychological treatment in this patient group. We reviewed treatment outcome studies of CTE and comparable syndromes, namely, chronic whiplash associated disorder (WAD) and chronic fatigue syndrome (CFS), with a view to providing recommendations for the psychological treatment of patients with CTE.

Methods: PubMed and PsychLIT were systematically searched and reference lists of retrieved articles were studied. The articles were classified according to study design and level of evidence.

Results: The studies of CFS provided high-level evidence for the effectiveness of cognitive-behaviour therapy (CBT) in challenging dysfunctional cognitions regarding the effectiveness of rest and in stimulating graded activity. The studies of WAD were methodologically weaker, and most evaluated a combination of CBT and graded activity training. There was some evidence that changing fatigue- or pain-related behaviours may result in cognitive improvement. Two uncontrolled studies of CTE evaluated cognitive rehabilitation techniques but yielded inconsistent findings.

Conclusions: CBT techniques focusing on changing illness attributions and on stimulating graded activity might be useful for patients with CTE, diminishing fatigue-related problems of concentration and memory. Future studies should evaluate whether cognitive deficits of CTE patients as a result of neurotoxic effects of exposure should be treated by cognitive rehabilitation.

Introduction

Organic solvents are widely used in industry, in paints, glues, coatings, and degreasing agents, and many of these solvents have neurotoxic properties. Occupations “at risk” are for example painters, spray-painters, offset-printers, and carpet-layers. In the last decades, numerous epidemiological studies of the effects of long-term occupational exposure to organic solvents on cognitive functions and personality have been published, showing group differences in subjective symptoms and performance on various neuropsychological tests between workers.
exposed or not to organic solvents. Several studies showed a dose-response relationship between symptoms and exposure [1]. Yet only a small proportion of chronically exposed workers develop chronic toxic encephalopathy (CTE). This syndrome is characterised by cognitive disturbances in concentration and memory functioning, and by non-specific neurasthenic symptoms such as fatigue, headache, lability of affect, irritability, and difficulties in impulse control [2, 3].

The pathophysiological mechanisms underlying CTE are still unclear. The results of neurological and neuro-imaging examinations are usually normal, so the diagnosis often cannot be supported by “objective” neurological data. Thus CTE is diagnosed by the exclusion of other causes, based on consensus by a multidisciplinary diagnostic team. Two international working groups have proposed slightly different diagnostic criteria for CTE [4, 5], but neither set of criteria appears to be widely used in clinical practice [6, 7]. Neuropsychological assessment is the cornerstone for identifying the subtle and otherwise difficult to detect neurobehavioural consequences of exposure, but has methodological weaknesses, such as the lack of control over variables (for example, suboptimal performance or malingering and social expectancy effects). Many patients are engaged in litigation procedures, and the problems of aggravation of symptoms and underachievement on neuropsychological tests are often not addressed [7, 8].

Perhaps as a consequence of these diagnostic problems, the diagnosis CTE is not universally accepted in clinical practice. This often leads patients to feel that their medical practitioners or their social environment do not take their problems seriously. Moreover, possibly because they want to prove that their symptoms are real, many patients insist on a purely somatic explanation for their complaints. Even the possibility that psychosocial aspects may influence their complaints and the course of their disorder may be threatening to them. These issues complicate the diagnostic process, but may also have consequences for treatment. Despite the complexity and controversy of diagnosis, it is a fact that many patients present with incapacitating complaints and ask for treatment.

The objective of this review was to establish evidence-based recommendations for psychological treatment or cognitive rehabilitation for CTE patients. However, an initial search showed there to be very few studies of psychological treatment for patients with CTE [9, 10, 11, 12], and so we extended our search to include outcome studies for syndromes characterised by a comparable symptom cluster of problems in attention and memory, fatigue, and affective symptoms. The chronic whiplash associated disorder (WAD) and chronic fatigue syndrome (CFS) share with CTE the same symptom complex, the lack of objective evidence (laboratory, neurological, or neuropsychological) to support the diagnosis, and the lack of universal acceptance by clinicians (See table 1). The cognitive complaints of CTE patients can be seen as the result of an interaction
between neurotoxic effects of exposure, individual coping capabilities and psychosocial support.

Although we found a sufficient number of studies evaluating the effectiveness of psychological treatment, we found no data concerning cognitive rehabilitation programmes, even though most patients with WAD [16] or CFS [17] complain of impaired cognitive function. Therefore we briefly refer to other available data on cognitive rehabilitation for patients with memory or attention problems.

Table 1

<table>
<thead>
<tr>
<th>Chronic Toxic Encephalopathy (WHO criteria) [4]</th>
<th>Chronic Fatigue Syndrome (CDC and Oxford criteria) [13, 14]</th>
<th>Chronic Whiplash Syndrome (Quebec Task Force) [15]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnostic Criteria</strong></td>
<td></td>
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</tr>
<tr>
<td>• Psychological and cognitive symptoms</td>
<td>• Debilitating fatigue present for at least six months</td>
<td>• Acceleration-deceleration mechanism of energy transfer to the neck, which may result from rear-end car accidents</td>
</tr>
<tr>
<td>• Verified exposure to neurotoxic solvents</td>
<td>• Affects physical, cognitive and psychological functioning</td>
<td>• A variety of physical, cognitive and psychological complaints present for at least six months</td>
</tr>
<tr>
<td>• Other organic diseases and primary psychiatric diseases reasonably well excluded</td>
<td>• Not been caused by any other identifiable clinical (medical or psychiatric) condition</td>
<td></td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Impaired memory</td>
<td>• Fatigue</td>
<td>• Impaired memory</td>
</tr>
<tr>
<td>• Concentration problems</td>
<td>• Impaired memory</td>
<td>• Concentration problems</td>
</tr>
<tr>
<td>• Fatigue</td>
<td>• Concentration problems</td>
<td>• Neck and shoulder pain</td>
</tr>
<tr>
<td>• Headache</td>
<td>• Tender lymph nodes</td>
<td>• Dizziness</td>
</tr>
<tr>
<td>• Irritability</td>
<td>• Muscle and joint pain</td>
<td>• Tinnitus</td>
</tr>
<tr>
<td>• Emotional lability</td>
<td>• Headache</td>
<td>• Headache</td>
</tr>
<tr>
<td>• Loss of initiative</td>
<td>• Unrefreshing sleep</td>
<td>• Visual problems</td>
</tr>
<tr>
<td></td>
<td>• Postexertional malaise</td>
<td>• Emotional lability</td>
</tr>
</tbody>
</table>

Non symptom associations
Lack of objective data to support diagnosis
Diagnosis of exclusion based on a working case definition
Syndrome under debate
Method

A systematic search for studies of outcomes of psychological treatment and cognitive rehabilitation for people with CTE, CFS, and WAD was performed, using the databases PubMed (National Library of Medicine, USA) and PsychLIT, from inception to June 2000. The search was updated through August 2002, using PubMed. The following combination of key words was used: (Whiplash OR Chronic Fatigue Syndrome OR Chronic Toxic Encephalopathy) AND (Psychological Treatment OR Rehabilitation OR Remediation OR Training OR Cognitive Therapy OR Psychotherapy). References in the retrieved articles were also examined.

Articles were included if they met the following criteria: the study had to be an original treatment evaluation study, providing empirical data concerning (neuro)-psychological treatment of adult patients with CTE, CFS, or WAD. Two of the authors independently performed the selection process. This resulted in a 100% agreement. For the selected studies, we focused on the following issues: syndrome, study design, theory regarding aetiology, subject characteristics, treatment methods, individual or group treatment, outcome measures, results, and recommendations for clinical practice. The articles were classified according to their study design and level of evidence. Randomised controlled trials were classified as “quality A evidence”, case-control studies without randomization as “quality B evidence”, clinical series of cases without controls as “quality C evidence”, and case reports based on single cases as “quality D evidence”. Case reports are not described in detail in this review.

Results

Retrieval of articles

Using the keywords, 324 articles were retrieved from the Pubmed database. Thirty articles were selected after initial review of the title and summary. After a more detailed review eight more articles were excluded because they appeared not to be treatment outcome studies or did not evaluate psychological treatment methods. Three studies were identified as follow-up studies of already selected studies [18, 19, 20]. A PsychLIT search revealed an additional 73 articles, 12 of which met inclusion criteria and were included for further evaluation. No other articles were extracted from the reference lists. Of the selected 34 studies, 24 studies evaluated interventions for subjects with CFS, 5 studies focused on subjects with WAD and 5 studies on subjects with
Table 2. Summary of outcome studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Level of evidence</th>
<th>Treatment</th>
<th>No. Of Patients/ Controls</th>
<th>Follow-up, in months</th>
<th>Outcome Measure/ Significant Effects</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronic Toxic Encephalopathy (CTE)</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Engel et al., 2000</td>
<td>C</td>
<td>Rel</td>
<td>8 / 0</td>
<td>None</td>
<td>Neuroph, PS</td>
<td>No follow-up results</td>
</tr>
<tr>
<td>Abjornsson et al., 1998 / Lindgren et al., 1997</td>
<td>C</td>
<td>GrT(C-Rehab), PRT</td>
<td>14 / 0</td>
<td>6 and 84</td>
<td>PatSat, Neuroph, PS, Cogn, Work</td>
<td>At 7-yr patients show increased social interaction, decreased psychological distress, but no difference with a comparable not treated group</td>
</tr>
<tr>
<td>Jensen et al., 1985</td>
<td>C</td>
<td>C-Rehab</td>
<td>11 / 0</td>
<td>10</td>
<td>PS, Cogn</td>
<td>(Neuropsychological tests not specified)</td>
</tr>
<tr>
<td><strong>Chronic Whiplash</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dijkstra &amp; Mesch, 1997</td>
<td>B</td>
<td>MD Rehab: CBT</td>
<td>25 / 25</td>
<td>None</td>
<td>PS, Cogn, Work</td>
<td>“Cognitive problems of whiplash patients result from pain”</td>
</tr>
<tr>
<td>Vendrig et al., 2000</td>
<td>C</td>
<td>MD Rehab: GE, CBT</td>
<td>26 / 0</td>
<td>6</td>
<td>PH, PS, Work, Med</td>
<td>Combination of subjective and objective measures</td>
</tr>
<tr>
<td>Heikkila et al., 1998</td>
<td>C</td>
<td>MD Rehab: GE, CBT</td>
<td>73 (40 whip)</td>
<td>24</td>
<td>PS, QOL, Work</td>
<td>Variables from social environment, QOL and coping resources predicted treatment outcome</td>
</tr>
<tr>
<td>Soderlund &amp; Lindberg, 2001</td>
<td>D</td>
<td>CBT, GE</td>
<td>3 / 0</td>
<td>None</td>
<td>PS, PH</td>
<td>“Functional behavioural analyses can be useful in physiotherapy” for assessment and planning of treatment</td>
</tr>
<tr>
<td>Vendrig, 1997</td>
<td>D</td>
<td>CBT</td>
<td>1 / 0</td>
<td>None</td>
<td>PS</td>
<td>Detailed description of treatment</td>
</tr>
<tr>
<td><strong>Chronic Fatigue Syndrome (CFS)</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ridsdale et al., 2001</td>
<td>A</td>
<td>CBT versus Counseling</td>
<td>80 / 80</td>
<td>3</td>
<td>PatSat, PH, PS, QOL</td>
<td>Only 45 of 160 patients met criteria for CFS. Positive changes in both groups, no differences between groups, except CBT group more satisfied</td>
</tr>
<tr>
<td>Prins et al., 2001</td>
<td>A</td>
<td>CBT, support groups</td>
<td>93-94 / 91</td>
<td>6</td>
<td>PH, PS, QOL</td>
<td>Passive activity pattern and focusing on bodily symptoms predicted less improvement</td>
</tr>
<tr>
<td>Powell et al., 2001</td>
<td>A</td>
<td>GE, patient education 3 treatment conditions</td>
<td>37, 39, 38 / 34</td>
<td>8</td>
<td>PH, PS, QOL</td>
<td>Short intervention can also be effective</td>
</tr>
<tr>
<td>Soederberg &amp; Evengard, 2001</td>
<td>A</td>
<td>GrT(non-directive)</td>
<td>7 / 7</td>
<td>None</td>
<td>PatSat, PH, PS, QOL</td>
<td>Focus was non-directive. No focus on increasing activities Sharing experiences was most important. Wish that therapist is more active</td>
</tr>
<tr>
<td>Study</td>
<td>Setting</td>
<td>Design</td>
<td>Treatment</td>
<td>Sample Size</td>
<td>Follow-up</td>
<td>Outcome Measures</td>
</tr>
<tr>
<td>------------------------------</td>
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</tr>
<tr>
<td>Deale et al., 1997</td>
<td>A</td>
<td>CBT versus relaxation</td>
<td>30 / 30</td>
<td>6 (60)</td>
<td>PatSat, PH, PS, QOL</td>
<td>Both groups improved on PS. At 5 year follow-up positive results maintained, but few patients reached normal fatigue scores.</td>
</tr>
<tr>
<td>Sharpe et al., 1996</td>
<td>A</td>
<td>CBT</td>
<td></td>
<td>30 / 30</td>
<td>PH, PS</td>
<td>Only significant effect was a higher QOL for group combining CBT with PhT.</td>
</tr>
<tr>
<td>Lloyd et al., 1993</td>
<td>A</td>
<td>CBT+ PhT, PhT, CBT, Contr</td>
<td>20, 26, 21 / 23</td>
<td>3</td>
<td>PH, PS, QOL, Lab</td>
<td>Work</td>
</tr>
<tr>
<td>Marlin et al., 1998</td>
<td>B</td>
<td>MD-Rehab: CBT, GE, Vocational Therapy, Rel</td>
<td>51 / 20</td>
<td>0 – 12+</td>
<td>PH, PS</td>
<td>Control group was invited, but declined treatment. Follow-up results on only 17 treated patients and 5 controls. Depression group improved on PH and PS. CFS group not improved. CFS patients with high depression improved on PS.</td>
</tr>
<tr>
<td>Friedberg &amp; Knupp, 1994</td>
<td>B</td>
<td>GrTh (CBT)</td>
<td>22 CFS, 22 depression / 22 CFS</td>
<td>None</td>
<td>PH</td>
<td>Dropout 33%. Positive results only for pts regularly attending. No data on possible factors predicting less improvement.</td>
</tr>
<tr>
<td>Essame et al., 1998</td>
<td>C</td>
<td>MD-rehab</td>
<td>19 / 0</td>
<td>12</td>
<td>PH</td>
<td>Six severe cases from Butler’s study (1991) qualitatively described.</td>
</tr>
<tr>
<td>Balter &amp; Unger, 1997</td>
<td>C</td>
<td>GrTh (CBT)</td>
<td>12 / 0</td>
<td>None</td>
<td>PatSat, PS</td>
<td></td>
</tr>
<tr>
<td>Chakler et al., 1996</td>
<td>C</td>
<td>CBT</td>
<td>6 / 0</td>
<td>3</td>
<td>PH, PS, QOL</td>
<td>Only retrospective data.</td>
</tr>
<tr>
<td>Cox &amp; Findley, 1994</td>
<td>C</td>
<td>GE + CBT</td>
<td>28 / 0</td>
<td>6</td>
<td>PH, work</td>
<td>Only retrospective data.</td>
</tr>
<tr>
<td>Butler et al., 1991</td>
<td>C</td>
<td>CBT</td>
<td>50 / 0</td>
<td>3 + 48</td>
<td>PH, PS, QOL</td>
<td>Many invited pts refused therapy. Factors influencing outcome were: treatment resisting effective disorders, and attribution of symptoms to physical causes.</td>
</tr>
<tr>
<td>Bonnet et al., 1995</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hammond, 2001</td>
<td>D</td>
<td>EEG-Biofeedback &amp; self-hypnosis</td>
<td>1 / 0</td>
<td>5, 7, 9</td>
<td>PH, PS</td>
<td>Outcome measures consisted of questionnaires &amp; collaborative inter views with parents.</td>
</tr>
<tr>
<td>Masuda et al., 2001</td>
<td>D</td>
<td>CBT &amp; fasting ther</td>
<td>1 / 0</td>
<td>Lab, PS, PH</td>
<td>Detailed description of treatment rationale and treatment procedure.</td>
<td></td>
</tr>
<tr>
<td>Prins &amp; Bleijenberg, 1999</td>
<td>D</td>
<td>CBT</td>
<td>1 / 0</td>
<td>7, 19</td>
<td>PH, PS, Work</td>
<td>Detailed description of treatment rationale and treatment procedure.</td>
</tr>
<tr>
<td>Powell et al., 1999</td>
<td>D</td>
<td>GE + Patient Education based on CBT</td>
<td>2 / 0</td>
<td>6</td>
<td>PH, PS</td>
<td>In first phase, symptoms and treatment are explained in a physical model, only later in psychological terms.</td>
</tr>
<tr>
<td>Bertangolli &amp; Morris, 1997</td>
<td>D</td>
<td>GrTh (CBT)</td>
<td>1 / 0</td>
<td>None</td>
<td>PH, PS, QOL</td>
<td>Detailed description of treatment procedure for one group member. No data of whole group.</td>
</tr>
<tr>
<td>James &amp; Folen, 1996</td>
<td>D</td>
<td>EEG-Biofeedback</td>
<td>1 / 0</td>
<td>None</td>
<td>Neuroph, PS, Cog</td>
<td>No control over test-retest effects.</td>
</tr>
</tbody>
</table>
CTE. The selected studies are summarised in table 1, describing quality of evidence, treatment method, number of patients, follow-up period in months, outcome measures and significant effects, and some evaluative remarks.

Type of study: quality of evidence

Nine studies were classified as randomised controlled trials providing quality A evidence. All of these studies concerned the treatment of patients with CFS [21, 22, 23, 24, 25, 26, 27, 28, 29]. The two articles by Sharpe were based on the same study group, as were two studies of Deale. Deale presented 5-year follow-up results on her study [20]. Three studies provided quality B evidence: one study concerned patients with WAD [30], and two studies concerned patients with CFS [31, 32]. There were eleven quality C studies. Two studies concerned WAD [33, 34], and five CFS [35, 36, 37, 38, 39]. Bonner presented 4-year follow-up results of Butler’s study [18]. All four studies concerning CTE were uncontrolled clinical case studies [9, 10, 11, 12]. The articles of Abjornsson and Lindgren were based on the same study group. In 1998 Abjornsson and co-workers presented 7-year follow-up results of their study [19]. Eight studies provided quality D evidence. Six studies concerned CFS patients [40, 41, 42, 43, 44, 45], and two studies evaluated treatment of WAD [46, 47].

Theory regarding aetiology

Most studies of CFS were based more or less implicitly on a multifactorial theoretical model for the aetiology and persistence of symptoms. According to this model, the severity and course of
Symptoms are seen as resulting from a complex interaction between a variety of physiological, behavioural, emotional, and cognitive factors. Focusing on bodily symptoms, low physical activity and a low sense of control contribute to increasing severity of fatigue and functional impairment [26, 43]. Symptoms of CFS are seen as the result of a vicious cycle of inactivity resulting in deconditioning followed by unmodulated attempts to resume activity that result in an exacerbation of symptoms [29, 41, 48].

The studies of chronic whiplash complaints also made use of a cognitive model to explain the perpetuation of symptoms. According to this model, inappropriate cognitions about pain lead to reduced physical activity and may result in the so-called “disuse syndrome”, resulting in somatic dysfunction. The experience of disability in social life and work situations may intensify stress reactions, sleep problems, and depressive symptoms, and can lead to more inappropriate coping behaviour. The result is a vicious circle leading to inactivity, social isolation and increased pain, and problems in memory and concentration.

The studies of CTE seemed to express a multicausal point of view, although authors did not specify an elaborate causal model. Symptoms of CTE were seen to be the sum of the direct effects of solvents on the nervous system and the indirect effects related to the individual’s previous experience of psychological distress and his or her current life situation [10, 11, 49]. Engel stressed the influence of the ability to cope with stress on the symptoms of CTE [12].

The implication of these theoretical models of CFS, CWS and CTE is that treatment should be focused on the interaction between somatic, behavioural, emotional, and cognitive factors.

Treatment methods

Based on these multifactorial causal models, the most frequently evaluated treatment method was individual cognitive behaviour therapy (CBT). In CBT, the patient’s dysfunctional attitudes and beliefs perpetuating the symptoms are identified and explained. Fatigue- or pain-related cognitions are challenged in order to diminish somatic attributions, to improve sense of control over symptoms, and to facilitate a change in behaviour. An important feature of CBT for patients with CWS or CFS is the challenging of dysfunctional beliefs regarding the effectiveness of rest. Patients are advised to gradually increase their level of activity, by pacing their activities and finding a balance between rest and effort.

A second treatment method, which can be named “CBT+”, was mostly used for whiplash
patients. In this approach CBT is combined with actual physical training according to the principle of “graded activity”. Other treatment methods, evaluated only in a single study, were focused group therapy for CFS [29] and relaxation-meditation training for CTE [12]. EEG biofeedback for CFS was described in two case studies [40, 45].

It seems surprising that there are no studies evaluating cognitive rehabilitation, given that patients with whiplash injuries or CFS frequently report memory and concentration problems. Only the few studies concerning patients with CTE used techniques from cognitive rehabilitation, but these were uncontrolled clinical case series. The patient group of Abjornsson and Lindgren received cognitive rehabilitation consisting of memory training and general cognitive activation. Because other studies of cognitive rehabilitation were not found, we refer to a thorough review by Cicerone [50], who evaluated 655 treatment studies of cognitive rehabilitation for patients with traumatic brain injury and stroke. Cicerone classified selected studies according to their methodological strength. Recommendations for clinical practice were given in four categories: “practice standards”, “practice guidelines”, “practice options”, and “not recommended”. Compensatory memory training was recommended as a “practice standard” for mild memory impairments. Attention training was advised as a “practice guideline” and should focus on complex tasks that require selective or divided attention. Techniques relying on repeated exercise and practice without the development of compensatory methods and/or without extensive involvement of a therapist were not recommended.

Effects of treatments
Chronic Fatigue syndrome

Seven studies were classified as randomised controlled studies. We only refer to these quality A studies. Price and Couper [51] and Reid [13] review three of these studies [21, 22, 23]. All seven studies, except Soederberg [29] are reviewed by Whiting [14].

Except Lloyd’s study [21], all studies used UK (Oxford) or US-CDC criteria for CFS. Both sets of diagnostic criteria require the presence of severe fatigue with a definite onset and lasting for more than six months, substantial functional impairment, and fatigue not being the result of an organic disease. However, the British criteria demand impairment of mental functioning, whereas the US criteria require several physical symptoms. The Australian criteria used by Lloyd incorporate both neuropsychiatric dysfunction, including impairment in memory and/or
concentration, and immunological abnormalities.

Five studies concerned individual CBT [21, 22, 23, 26, 27], one study described a brief educational programme based on CBT techniques [28], and one study described a group therapy format [29]. Four of the six randomised-controlled studies evaluating CBT suggested that CBT may be superior not only to standard medical care [22, 26, 28], but also to guided support groups [26] and relaxation training [23].

Prins [26] evaluated the effectiveness of CBT by comparing three large groups of outpatients randomly assigned to three therapeutic conditions: CBT, a support group to control for therapist’s attention and treatment expectations and a non-treatment control group to control for spontaneous remission. CBT, consisting of 16 individual one-hour sessions, was more effective than either guided support groups or the natural course in terms of fatigue severity and functional impairment. Support groups were no more effective than the natural course. There was, however, a high dropout rate, especially in the CBT and support groups, possibly because patients expected a medical solution for their complaints and were sceptical about the effectiveness of psychological treatment methods for supposedly somatic complaints. Patients with a “passive activity pattern” and patients with a strong tendency to focus on bodily symptoms improved less than patients without these characteristics.

Deale randomly assigned two groups of CFS patients to 13 individual sessions of CBT or relaxation. At the six-month and 5-year follow-up, significantly more patients who had received CBT rated their symptoms as much or very much improved, met criteria for complete recovery, and were free of relapse. However, there were no significant differences between the groups with regard to self-reported physical functioning, fatigue and general health, and employment status. Poor outcome was significantly associated with taking medical retirement or making a new claim for a disability-related benefit during, but not before, treatment [20, 23].

A study by Powell suggests that even a brief intervention can lead to significant improvement of physical functioning and fatigue [28]. Treatment consisted minimally of two individual treatment sessions and two telephone calls, based on cognitive behavioural principles. Patients in two other treatment conditions received seven additional 30-minute telephone contacts, and seven additional individual 1-hour sessions, respectively. Positive effects were reported for all treatment conditions, compared to controls. There were no significant differences between the three treatment conditions.

Ridsdale [27] randomly assigned 160 patients with complaints of chronic fatigue, of whom 45 patients met formal criteria for CFS, to six sessions of CBT or counseling. Both treatments were provided by trained therapists, the counsellors had a psychodynamic approach. Both
treatments showed positive effects. There was, however, no significant difference between the two treatment conditions on any of the outcome measures.

Lloyd [21] randomly assigned outpatients with CFS to a four-cell trial design in which immunological therapy and psychological treatment in the form of CBT were combined with each other and with clinical course. As in Ridsdale’s study, 6 sessions of CBT were given. The only significant difference between treatment conditions was found for the group receiving both treatments, and consisted of greater improvement in quality of life.

Reviewing these six studies, we can conclude that only Lloyd’s study reported disappointing findings. Ridsdale reported positive effects for both evaluated therapies. That both therapies were equally successful in Ridsdale’s study might be because all therapy was provided by specialised therapists. The seventh study, by Soederberg and not reviewed by Whiting, evaluated a supportive and goal-oriented group therapy format for patients with CFS [29]. Fourteen CFS patients were assigned at random to 10 sessions of group therapy or a waiting-list control condition. Issues were acceptance of the new life situation, setting up realistic levels of ambition, and the relation between achievement/self-esteem and activity/rest. During therapy, the most important recurring themes were exchanging latest medical information about CFS, sharing complaints, and acceptance problems. In this sense therapy might have focused on limiting rather than increasing activity levels. There was no significant change in quality of life after group therapy, and no difference between groups. However, the group size was only seven, which considerably reduces the chance on finding significant effects. Patients reported satisfaction with group therapy. The most valuable aspect for them was the sharing of experiences.

Chronic whiplash syndrome

We found only three studies evaluating psychological treatment of chronic problems after whiplash, none of which was a randomised-controlled study. In all instances, the treatment method evaluated was multidisciplinary “CBT+”: cognitive behavioural techniques combined with physical training according to the principle of graded exercise. Much attention was given to the effects of inappropriate pain behaviour, which leads to diminished physical activity and persistence of pain symptoms. Only one of the studies, by Dijkstra, focused on the cognitive complaints frequently reported by patients with whiplash [30]. This case-control study, written in Dutch, is interesting for its theoretical focus on the aetiology of the cognitive complaints
frequently reported by whiplash patients. Dijkstra summarised studies by Olsnes [52], and Radanov [53], who found comparable results for patients with whiplash or chronic pain on neuropsychological testing. He stated that chronic pain behaviour might explain the low performance on attention tests of both groups of patients. This is consistent with a review by Hart and co-workers, who concluded that numerous studies have demonstrated neuropsychological impairment in patients with chronic pain, particularly on measures assessing attentional capacity, processing speed, and psychomotor speed [54]. Dijkstra evaluated a multidisciplinary behavioural treatment programme, based on behavioural principles, for patients with chronic pain. After treatment there were significant positive changes in pain cognitions and reported pain, psychoneurotic complaints, work status and cognitive performance. Neuropsychological test results did not differ from those of healthy controls.

An uncontrolled study by Vendrig reported positive effects of a multidisciplinary, daily, 4-week treatment programme in a specialist outpatient centre, consisting of graded exercise and CBT [34]. A detailed description of the treatment of one of the patients is given in a case study [43]. Another uncontrolled study, by Heikkila, evaluated the effects of an individualised 6-week multidisciplinary intervention programme, using CBT and graded exercise, in 73 patients with chronic pain [33]. Forty patients had chronic whiplash complaints and 33 patients had back or myofascial pain. At the start of the programme, the patients with whiplash had decreased coping resources and lower quality of life, compared to the patients with myofascial pain. At the 2-year follow-up both groups of patients showed an improved quality of life. Significant increases in coping resources occurred only in the patients with chronic whiplash. However, the improvement on these subjective measures was not reflected by more objective measures like sick absenteeism.

Chronic toxic encephalopathy

The four treatment evaluation studies on CTE were all clinical case series. Lindgren [10] and Abjornsson [11] both evaluated the effects of a 10-week programme consisting of group therapy focusing on emotional and social problems, and cognitive rehabilitation groups focusing on visual imagery and association techniques, combined with sessions with the patients’ relatives. Participants were 14 patients with solvent-induced CTE. Inclusion criteria were more than 10 years of daily exposure to organic solvents, symptoms consistent with brain dysfunction,
no other CNS, somatic, or psychiatric diseases or drug abuse. After the 10-week programme, supportive group sessions were continued once a fortnight until the 6-month follow-up. In this sense it was not a real follow-up. After the 10-week programme, the patients and their partners were very satisfied with the treatment. The number of psychiatric symptoms had decreased significantly. However, at 6-months follow-up there was an increase of symptoms even when compared to the first examination. Affective complaints decreased after treatment and remained lower at follow-up. These complaints were investigated in a structured interview with one of the therapists, which might have biased results. Cognitive complaints decreased immediately after the intervention, but reached original levels at follow-up. There were no significant changes in neuropsychological measures on follow-up except in performance of a paired associate learning test. Only four patients were able to return to work. In a 7-year follow-up study, 13 of the 14 patients were evaluated again [19]. Their results were compared to those of a group of 26 untreated patients with CTE. Treated patients showed an improvement in social interaction and social integration, but no significant differences from untreated patients were found on either these psychosocial or neuropsychological measures.

A study by Engel evaluated the effects of a programme of guided relaxation training combined with meditative stretching [12]. Eight patients with CTE were trained for 8 weeks, three times a week. The training had significant positive effects on the ability to relax physically and mentally, as measured with physiological tests. State anxiety decreased 22% during the training period, but no changes were observed in trait anxiety. Cognitive measures were not evaluated.

Jensen evaluated the effects of memory training in eleven patients with CTE. Memory training was given in groups of two, three, or four patients and consisted of 35-40 1-hour sessions, twice a week, in which patients were trained in visualization techniques as a learning strategy [9]. Unfortunately, the author did not describe which neuropsychological measurements were used, but described results only in neuropsychological domains and categories: same, better, worse. Significant improvement in the learning and memory of verbal material was observed after training and this improvement was still present after 10 months. Patients reported a significant reduction of memory and learning problems.
Discussion

Our search revealed surprisingly few treatment evaluation studies, and no randomised controlled trials, of behavioural treatment for patients with WAD or CTE. There were more high-quality studies of the treatment of CFS. Most high-level studies were published recently, suggesting that the methodological quality of outcome research in this area has improved.

The most elegant randomised controlled studies combine a treatment condition with two control conditions: one condition to control for therapist’s attention and treatment expectations, and a no-treatment control group to control for spontaneous remission. Only one study [26] met these criteria. The majority of evaluation studies used subjective outcome measures to assess the effects of treatment. However, apart from self-report measures, more objective criteria, such as return to work, hours worked, medical consumption, evaluation from peers/partners, and neuropsychological tests are needed.

There is quality A evidence that CBT, combining the challenging of illness attributions and stimulating graded activity, has positive results in patients with CFS and can be advised for clinical practice. The level B/C studies evaluating “CBT+” for patients with chronic whiplash complaints suggest that a combination of CBT and actual graded exercise training, and return-to-work counselling can lead to a better self-evaluation and can increase chances of returning to work. To what extent actual graded exercise can enhance the positive results achieved with CBT remains unanswered. However, two A quality studies of patients with CFS, studies not included in the analysis, showed positive effects of physical graded exercise without psychological treatment [55, 56].

Only two selected studies made use of cognitive rehabilitation methods. They both were C quality studies evaluating the treatment of patients with CTE and provided inconsistent results. However, a thorough review [50] evaluating the effectiveness of cognitive rehabilitation methods provided evidence of the effectiveness of compensatory memory strategy training for patients with traumatic brain injury or stroke. Memory training, consisting of internal compensatory strategies, can be effective for mild memory problems when patients are independent according to daily activities. Training of internal compensatory strategies was advised as practice standard. The therapist must be actively involved to foster insight into cognitive strengths and weaknesses, must develop compensatory strategies, and must facilitate the generalization of skills to real-life situations. However, conditions like traumatic brain injury or stroke imply obvious alterations in brain morphology, which is not true for CTE. To which extent training of cognitive strategies can be effective for CTE patients remains to be evaluated in further studies.
What can be learned for the treatment of CTE patients?

Most patients with CTE, like those with chronic whiplash complaints or CFS, report problems of attention and memory, and neurasthenic complaints such as fatigue, irritability, and somatic complaints. These complaints reflect the sum of the direct effects of solvent exposure on the brain and the indirect effects of individual coping resources, cognitive attributions regarding the illness, and the social support system. The cognitive deficits of patients with CTE, which are directly associated with brain damage, might possibly best be treated by cognitive rehabilitation focused on compensatory memory strategies. Further evaluation studies are clearly needed on this subject. Cognitive complaints, however, may lead to social isolation and decreased activity. Patients are often involved in a struggle for recognition of their complaints and in litigation procedures. Some patients may feel victimised by employers or by a political system that tolerates unhealthy levels of occupational exposure, and also by the way they are treated by doctors and insurance agencies. These feelings may influence their cognitions regarding their problems and their coping resources. For therapy to be successful, the patient’s feelings of victimization must be challenged and the patient has to develop the cognition that he can regain control of his life. Based on studies of CFS and whiplash, we conclude that CBT, which challenges unproductive beliefs regarding the effectiveness of rest and stimulating graded activity, may be effective in patients with CTE. Whether a combination of CBT techniques with actual graded activity training might be more effective needs further research. There is some preliminary evidence that changing fatigue and pain behaviours can diminish fatigue-related problems in memory and concentration.
References


