CHAPTER 1

Introduction
This thesis focuses on the neuropsychological diagnosis and treatment of chronic toxic encephalopathy (CTE), or “painters’ disease”. CTE is characterised by neurasthenic and cognitive complaints associated with chronic exposure to organic solvents. Affected individuals have problems in attention, memory and executive functioning, and experience fatigue, instability of affect and difficulties in impulse control.

Anyone who has worked with organic solvents, occupationally or incidentally in his or her leisure time, will acknowledge that these substances have acute anaesthetic effects. High exposure to such solvents can cause dizziness, drowsiness, numbness, headache and fatigue. With modest exposure these complaints are completely reversible, but extremely high exposure can lead to persistent damage to the nervous system and even to coma or death [1, 2]. Although the effects of acute exposure to organic solvents are well recognised, evidence regarding the neurobehavioural effects of recurrent, frequent exposure to lower doses of organic solvents is far less conclusive.

In the last decades, many epidemiological studies investigated these neurobehavioural effects of chronic solvent exposure. A majority of these studies have reported subclinical neuropsychological effects in group comparisons of exposed versus non-exposed subjects [3], but the psychological pattern of effects observed and the existence of exposure-effect relationships are inconsistent. The wide range of tests and scoring methods used make it difficult to compare study results. Moreover, these results do not provide insight in the effects of solvent exposure on an individual level.

Only a minority of exposed workers develop CTE, but studies of individual susceptibility and genetic predisposition have yielded inconclusive results. In clinical practice it is difficult to establish whether the cognitive and emotional complaints of an individual patient are solvent induced. In 1985, the WHO formulated criteria for the diagnostic classification of CTE, recommending that a core battery of neuropsychological tests be used when diagnosing CTE [4, 5]. However, the international use of these criteria and the choice of the neuropsychological battery are far from uniform [6, 7], and so it is perhaps not surprising that there is not a uniform international picture regarding the clinical presentation and prevalence of CTE.
CTE is a difficult diagnosis to establish. First, it is often very difficult to obtain a reliable exposure history, because data are largely dependent on the patient’s own recall. Secondly, there is usually no significant neurological and neurophysiological impairment [8], and for this reason the diagnosis leans heavily on neuropsychological assessment. While this reflects the increased influence of clinical neuropsychology and neuropsychological methods, it simultaneously reveals some of the weak spots of this discipline [9]. Several factors have to be taken into consideration when interpreting test results, such as the effect of co-existing psychiatric, medical, or neurological disorders, and the difficulty in characterising premorbid status (e.g. premorbid problems in learning and attention), and in investigating the possible interaction between e.g. alcohol abuse and solvent exposure. Moreover, performance on neuropsychological tests can be negatively influenced by affective disorders, pain, somatisation and motivational problems.

The aims of this thesis are to study a controversial issue concerning the diagnosis of CTE and to evaluate a (neuro)psychological treatment programme for patients with diagnosed CTE. The thesis is divided in three sections:

1: Behavioural neurotoxicology
2: Diagnosing CTE
3: Psychological treatment of CTE

The first section (chapter 2) provides a general introduction to behavioural neurotoxicity in a broader context. The acute and chronic neurotoxic effects of organic solvents are described, as are the neurobehavioural effects of exposure to pesticides, heavy metals, carbon monoxide, and alcohol and drugs. Special attention is paid to current theories regarding mechanisms of neurotoxicity.

In the second section, three chapters are devoted to a very controversial issue in the diagnosis of CTE, namely, the influence of insufficient effort on neuropsychological test results. Neuropsychological testing is the cornerstone of the diagnosis, but the results of neuropsychological testing may be invalidated by the intentional or unintentional production of mental symptoms, or aggravation of cognitive problems, resulting in insufficient effort. Insufficient effort may especially be a problem in patients with suspected CTE, because these patients are often involved in litigation or financial compensation procedures and thus may be motivated to aggravate cognitive problems. To put it bluntly, CTE patients may simply exaggerate or fake their complaints in order to receive financial compensation or to obtain early
retirement. However, it is also possible that insufficient effort results from patients focusing on a somatic explanation for their complaints or from a feeling that medical practitioners or their social environment do not take their problems seriously.

Surprisingly, while the use of detection tests of insufficient effort is advocated when diagnosing CTE [9,10], there are no data on the prevalence of insufficient effort in patients with suspected CTE. If insufficient effort is indeed a problem, the cognitive profile of CTE established in earlier studies of the cognitive problems of patients with CTE may not be valid.

Chapter 3 provides new data on the prevalence of insufficient effort in a large patient group with suspected CTE. In this nation-wide study, all patients referred to one of the two Dutch Solvent-Teams for evaluation of CTE were administered two tests for the detection of malingering, the Amsterdam Short Term Memory Test (ASTM) and the Test of Memory Malingering (TOMM).

Psychological tests are usually developed to predict aspects of human behaviour. However, predictive validity cannot be assessed when it comes to insufficient effort, because there is no gold standard to determine with certainty whether or not a patient is exerting suboptimal effort. We can however study construct validity - whether a test really measures what it intends to measure. Construct validity can be demonstrated if test performance correlates with that of other tests intended to measure the same construct, if it correlates with extraneous (non-test) indicators of the construct, and if it does not correlate with variables that are unrelated to the construct.

Chapter 4 presents a construct validity study of eight indices of insufficient effort in a nation-wide patient group referred with suspected CTE: the ASTM, the TOMM, and six indicators of insufficient effort from conventional neuropsychological tests (CVLT, Warrington Recognition Memory Test for Faces (RMT), Trail Making Test, and Digit Span Difference Score). The inter-relationships and relationships with external non-psychological variables, such as litigation and financial compensation, and severity and duration of exposure to organic solvents, were analysed.

The study presented in Chapter 5, the last chapter of this section, was performed to try to answer the intriguing question whether subjects with suspected CTE still show neuropsychological disturbances and psychological complaints if alternative explanations for their poor performance, including insufficient effort, are carefully ruled out. This study also investigates possible relations between exposure duration and severity on the one hand and psychological complaints and neuropsychological deficits on the other.

The third section of this thesis is devoted to the psychological treatment of patients with CTE.
When developing a treatment programme for patients with a specific diagnosis, it is wise to build upon previous studies evaluating treatment effects. Unfortunately, only a few studies have evaluated psychological treatment for patients with CTE, and all of these studies were clinical case series. There is a need for randomised control studies [7]. The systematic review presented in chapter 6 describes the results of treatment outcome studies of syndromes characterised by controversy and a similar symptom complex, namely, the chronic whiplash syndrome and chronic fatigue syndrome. The results of this review were used in designing a new psychological treatment programme for CTE patients.

Chapter 7 describes the results of a randomised controlled evaluation study of a (neuro) psychological treatment programme developed for patients with diagnosed CTE. The treatment rationale was based on the finding that follow-up studies on CTE have not demonstrated a consistent relationship between neuropsychological or neurophysiological recovery and the subjective health condition of the patient [11]. The prognosis of CTE is influenced not only by the severity of cognitive problems, but also by personality characteristics and individual coping styles, social support systems and the socio-economic situation of the patient. Our treatment programme was focused on the interrelatedness of cognitive, psychosocial, and personality factors. We evaluated a newly designed psychological rehabilitation program of 16 (2 X 8) sessions consisting of eight group sessions based on cognitive behavioural principles focusing on coping with the psychological and psychosocial implications of the syndrome, and eight sessions, partly group, partly individual, focusing on cognitive strategies to compensate for memory and attention problems. Patients in the treatment groups were compared to waiting list controls to control for spontaneous recovery and test-retest effects.

Chapter 8, finally, presents a general discussion of the most important findings of this study.

This thesis is the result of the collaborative effort and work of the two Dutch National Solvent Teams, two multidisciplinary centres for the assessment, treatment, and research of chronic toxic encephalopathy. The teams are located in Enschede (Medical Spectrum Twente) and Amsterdam (Academic Medical Centre). The Solvent Team Project is funded by the Health Care Insurance Board, Amstelveen, the Netherlands.
References


section 1

Behavioural Neurotoxicology