NeuroToxicology 33 (2012) 742–752

Contents lists available at SciVerse ScienceDirect

NeuroToxicology

XINC 2011 – Full Papers

Decision rules for assessment of chronic solvent-induced encephalopathy: Results in 2370 patients

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ARTICLE INFO

Article history:
Received 10 December 2011
Received in revised form 9 June 2012
Accepted 13 June 2012
Available online 18 June 2012

Keywords:
Chronic solvent-induced encephalopathy
Solvent
Toxic encephalopathy
Diagnosis
Cognitive
Neuropsychology
Neurotoxicology

ABSTRACT

For the diagnosis of patients suspected of chronic solvent-induced encephalopathy (CSE), it would be helpful if the applied cognitive tests show a characteristic profile of impairment in this disease. We investigated the existence of such a profile. In 1997–2006 two expert teams in The Netherlands systematically examined 2370 patients referred for evaluation of suspected CSE. The procedure included two selection steps: (1) intake interview, using criteria of exposure, development of symptoms and absence of non-solvent causes, and (2) seven tests of the computerized Neurobehavioural Evaluation System (NES). Patients showing negligible impairments were considered free from CSE and were not further examined. The third step comprised a neuropsychological, neurological and exposure evaluation. Explicit decision rules for the diagnosis of CSE were developed, including a minimum score for cognitive impairment summarizing 25 cognitive tests. These rules were retroactively applied to 563 patients, comprising 513 patients who had regularly completed all diagnostic steps and a sample of 50 out of the approximately 450 patients with negligible impairments on the NES, who were fully examined. The data from this sample were extrapolated to the original number of 450. In the combined population of 963 patients, a calculated 301 patients were given the diagnosis 'Solely CSE', 242 'CSE and other disease', 158 'Other Disease' and 262 'No (known) disease'. In the Solely CSE patients, the most impaired tests regarded Verbal Fluency & -Similarities, Motor Speed and Simple Attention. A profile of test results that might support the identification of patients with CSE amongst the other referred patients, was not found. The diverging results of related cognitive tests indicate that the use of a core test battery is needed to improve comparability. We consider the decision rules as a step towards a more objective assessment of CSE.

1. Introduction

Long-term exposure to organic solvents may cause a chronic encephalopathy, often labelled chronic solvent-induced encephalopathy (CSE), if the exposure has been sufficiently high and enduring. According to World Health Organization (WHO, 1985) the most common symptoms are 'increased fatigue, bad memory, concentration difficulties and personality changes'. In 1985, diagnostic criteria and two international classifications for CSE have been introduced. The WHO (1985) diagnostic criteria require: '(a) a verified exposure to neurotoxic solvents; (b) a clinical picture of organic nervous system damage with typical subjective symptoms and (c) objective findings in clinical and auxiliary examinations, and (d) other organic diseases and primary psychiatric diseases reasonably well excluded'. WHO classifies the effects of solvents on the central nervous system in three stages: 'organic affective syndrome' (type I), 'mild chronic toxic encephalopathy' (type II), and 'severe chronic toxic encephalopathy' (type III). Somewhat differently, the Raleigh classification (Baker and Seppäläinen, 1986) recognizes four stages: 'symptoms only' (type 1), 'sustained personality or mood change' (type 2A), 'impairment of intellectual function' (type 2B), and 'dementia' (type 3).

The Diagnostic and Statistical Manual (DSM-IV-TR, American Psychiatric Association, 2000) mentions '292.82 inhalant-induced

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0161-813X/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuro.2012.06.005

persisting dementia' and '292.84 inhalant-induced mood disorder'. The International Classification of Diseases (ICD-10, WHO, 2007) mentions F 18.7 'mental and behavioural disorders due to use of volatile solvents; residual and late-onset psychotic disorder'. Although CSE is included in the European Union list of Occupational Diseases (European Commission, 2003), diverging protocols are used for the diagnosis (Van der Hoek et al., 2001).

The article 'chronic solvent-induced encephalopathy: European consensus of neuropsychological assessment, characteristics, and guidelines for diagnostics' published by a European Consensus Group (Van Valen et al., 2012) includes a literature review of 19 articles on neuropsychological impairments in patients diagnosed with CSE. The utility of these articles is limited due to unspecific diagnostic criteria, a wide variety of tests that are used, small sample sizes and questionable reference data. A widely acceptable standardized diagnostic approach for CSE, including a quantifying diagnostic protocol for cognitive impairment, may contribute to better patient care, comparability of incidences, and support a policy for disease compensation and prevention, especially in places where solvent exposure is still high. A standardized approach may also facilitate evaluation of exposure–response relationships, e.g. in cohort studies. In the absence of a gold standard that specifies detailed criteria for the diagnosis of CSE, such an approach inevitably must be a consensus product such as developed by the European Consensus Group for the neuropsychological aspects of CSE.

This paper intends to supply information relevant for the diagnostic evaluation of patients referred for suspected CSE. Since 1997, two collaborating centers in the Netherlands have systematically evaluated these patients. Here we report the experience that was obtained by the analysis of the database containing data from 2370 patients in the years 1997–2006. Because of the initially large number of referred patients and the limited resources, the diagnostic procedure comprised three consecutive steps, each excluding patients not meeting criteria for CSE. In the present paper, the patients who successfully completed all three steps, were given a summary score of cognitive impairment (CogImp) based on 25 cognitive tests.

We investigated the following questions:

(1) Do patients diagnosed as having CSE, show a cognitive profile that discerns them from the other patients referred for assessment of CSE?

By 'profile' is meant the pattern of scores of the individual tests or functional (sub)domains. Under this study question, two subsidiary questions were asked: (a) do CSE patients have a different profile compared to healthy subjects? and (b) does a profile in CSE patients discern them from the other patients referred for assessment of CSE? While the first question is relevant especially for health surveillance of exposed workers, the second one is important for centers where patients suspected of CSE are referred to. This study focuses on the existence of a profile that supports the correct classification of patients with CSE among the total group referred for assessment of CSE. To this end the patients are classified into four diagnostic groups using criteria of exposure and effect irrespective of a profile; consecutively we investigate whether the patients with solely CSE have a specific profile of impairments compared to the patients with no known disease or with another disease.

(2) What is the contribution of the individual cognitive tests to the summary CogImp score?

As the sensitivity of the tests to detect impairments, e.g. due to CSE, may differ, a test battery with sensitive tests will label more patients as having CSE compared to an insensitive test battery.

2. Methods

2.1. Patients

From 1997 till 2006, 2370 patients (mean age 47 yrs, 96% male) were referred to the two diagnostic teams for evaluation of possible CSE, most of them by their general practitioner (54%) or occupational physician (23%). At intake, 42% were still working, the majority being exposed to solvents, 20% were on long-term sick leave and 23% received a permanent disability pension. The most prevalent occupations were housepainter (29%), printer (11%), car sprayer (11%) and industrial painter (8%). An estimated 95% of the patients was of Dutch origin.

2.2. Diagnostic protocol

In step-1 a specialist in occupational medicine or neurology assessed the symptoms, and the medical and occupational history by means of a semi-structured interview. To enter step-2 the patient had to have: (1) at least five years of solvent exposure to amounts presumed to be sufficient for CSE or, in the case of apparent very high concentration, a shorter period sufficed (see Section 2.3.2). (2) Symptoms of impairment of memory or attention that fit in time with respect to exposure. (3) No evident other explanation for the symptoms; to this end also a set of blood tests was done to exclude metabolic causes: analysis of hemoglobin, electrolytes, thyroid stimulating hormone, glucose, calcium, folate, vitamins B_1 and B_{12} and leukocyte count. If an abnormality appeared, the patient was referred for regular diagnostic and therapeutic work-up. If the symptoms remained after treatment, the patient was allowed to step-2.

In step-2, the patient completed the self-report questionnaire 'Neurotoxic Symptom Checklist-60' (NSC-60, Hooisma et al., 1994) and eight tests of the Dutch adaptation of the computer-based Neurobehavioural Evaluation System-2 (NES2, duration approx. 1 h). Table 1 shows the NES and the other tests applied in this study, categorized in (sub)domains. The NES vocabulary score (a proxy for pre-morbid intelligence) was used only to adjust[3] the results of the other seven NES tests, to which ratings were assigned as described in Section 2.3.1. Patients were invited to enter step-3 if the average score of the seven NES ratings was above 0.15. Patients with a lower score were diagnosed as presumably not having CSE; they were not further examined.

Step-3 comprised (1) a semi-structured interview by a neuropsychologist and the completion of 18 cognitive tests and of the TOMM and ASTM tests to detect insufficient effort (Table 1). Also the Symptoms Checklist SCL-90 (Arrindell and Ettema, 1986) was completed, which is the Dutch adaptation of the SCL-90 (Derogatis, 1975),[4] (2) a neurological and physical examination by a neurologist, and (3) the assessment of an exposure index by an occupational hygienist.

Finally a team consisting of the specialist in occupational medicine, neuropsychologist, neurologist and occupational hygienist decided on the diagnosis. Decision rules for the diagnoses were developed over the course of the 10-year study and these rules were applied retroactively using historical data in the patient's database.

2.3. Decision rules for the diagnosis

For the diagnosis of CSE (Fig. 1) we required (1) cognitive impairment assessed by tests covering nine cognitive subdomains, (2) sufficient exposure to solvents that is not outweighed by competing causes, and (3) symptoms of impairment of memory or attention, assessed by questionnaire and fitting in time with