



Chronic solvent-induced encephalopathy: European consensus of neuropsychological characteristics, assessment, and guidelines for diagnostics[☆]

Evelien van Valen^{a,*}, Christoph van Thriel^b, Ritva Akila^c, Linda Nordling Nilson^d, Rita Bast-Pettersen^e, Markku Sainio^c, Frank van Dijk^f, Gert van der Laan^a, Maarten Verberk^f, Ellie Wekking^{a,g}

^a Netherlands Center for Occupational Diseases, Coronel Institute of Occupational Health, Academic Medical Center, University of Amsterdam, The Netherlands

^b Leibniz Research Center for Working Environment and Human Factors, Dortmund, Germany

^c The Centre of Expertise for Human Factors at Work, Finnish Institute of Occupational Health, Helsinki, Finland

^d Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, University of Gothenburg, Gothenburg, Sweden

^e National Institute of Occupational Health, Oslo, Norway

^f Coronel Institute of Occupational Health, Academic Medical Center, University of Amsterdam, The Netherlands

^g Dijke en Duin, Center for Mental Health Care, Department of Neuropsychology, Castricum, The Netherlands

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ABSTRACT

Introduction: The presence of neuropsychological impairment is a hallmark of chronic solvent-induced encephalopathy (CSE), and using clinical neuropsychological procedures to generate a valid assessment of the condition is crucial for its diagnosis. The goals of this consensus document are to provide updated knowledge of the neuropsychological characteristics of CSE and to provide internationally acceptable guidelines for using neuropsychological assessments in the process of diagnosing patients who are suspected of having CSE.

Materials and methods: A European working group that was composed of experts in the field of the clinical diagnosis of CSE met at several round-table meetings and prepared this report. The first section of the consensus paper addresses a review of the relevant literature that was published between 1985 and March 2012. The second section addresses recommendations for the clinical neuropsychological assessment of patients who are suspected of having CSE.

Results: The literature review indicates that the most common neuropsychological impairments in CSE patients are within the domains of attention, particularly the speed of information processing, memory, and motor performance. It appears that the influence of CSE on memory processes mainly involves immediate recall and generally involves verbal, visual and visuospatial material.

In the second section, six recommendations are presented regarding important functional domains for the neuropsychological diagnostic process of CSE that relate to the evaluation of neuropsychological impairment, the assessment and evaluation of symptoms, differential diagnostic considerations, the reliability and validity of neuropsychological test results, and the retesting of patients.

Discussion and conclusions: These recommendations will contribute to the improvement of the process for accurately diagnosing CSE, better counselling for CSE patients, the comparability of epidemiological data between countries, and finally, by raising awareness, these recommendations will contribute to combating the adverse health effects of occupational exposure to solvents.

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1. Introduction

Long-term occupational exposure to organic solvents may result in a brain syndrome known as chronic solvent-induced

encephalopathy (CSE). During the 1970s and 1980s, there was growing awareness of a consistent pattern of symptoms and complaints that were reported by workers that were related to long-term solvent exposure, especially in Nordic countries. Since then, a large number of researchers have shown evidence of impaired neuropsychological performance in workers who are exposed to solvents (e.g., Arlien-Søborg et al., 1979; Hänninen, 1988; Meyer-Baron et al., 2008).

Structural neurotoxicity was confirmed in both animal (Korbo et al., 1996; Nielsen et al., 2006) and in vitro studies (McDermott et al., 2007) for several individual solvents. A recent overview of the neuronal effects of solvent abuse (Yücel et al., 2008) showed

[☆] Working group: Belgium: Lode Godderis, Rita Verachtert, Mineke Viaene; Czech Republic: Pavel Urban; France: Dominique Chouaniere; Germany: Lilo Altman, Christoph Lang, Helmut Lilienthal, Monika Meyer-Baron, Axel Muttray, Andreas Seeber, Wolfgang Zschiesche; Italy: Elisa Albini, Roberto Lucchini; Sweden: Kai Österberg; The Netherlands: Moniek van Hout.

* Corresponding author. Tel.: +31 20 5665308.

E-mail address: e.vanvalen@amc.uva.nl (E. van Valen).

that severe central nervous system dysfunction and diffuse structural damage in the cerebral white matter in periventricular/subcortical regions of the brain are present in solvent abusers but that the solvent concentrations in these cases generally exceeded those in occupational settings by a wide margin. The neurotoxic mechanism that underlies the influence of organic solvents on the central nervous system is not yet fully understood (Ridgway et al., 2003). In some CSE cases, neuroradiology and functional imaging have been used to demonstrate mild cortical atrophy (Mikkelsen et al., 1988; Keski-Säntti et al., 2009; Haut et al., 2006) and effects in dopamine-mediated frontostriatal circuits (Visser et al., 2008).

CSE usually develops gradually in conjunction with ongoing exposure to organic solvents. A minimum of more than 10 years of substantial everyday exposure to solvents at work is regarded as a requirement for developing CSE (DGUV, 2010; Keski-Säntti et al., 2010; Mikkelsen et al., 1988; Vaene et al., 2001). However, CSE may also be encountered in cases of very high exposure over a shorter period of time. Initial symptoms of CSE are usually reported before the cessation of exposure to a solvent, and they generally do not progress after the cessation of exposure (van Valen et al., 2009). In patients who are referred for diagnosis and treatment of CSE, the assessment of past individual lifetime exposure to neurotoxic solvents is crucial in the diagnostic process, although the retrospective estimation of exposure potentially being liable to substantial errors must be taken into consideration (Burstyn and Kromhout, 2002; Tielemans et al., 1999).

Due to the non-specific clinical picture of CSE as a condition that affects cognition and emotion in ways that essentially overlap the damage profiles of other neurological and psychiatric diseases and the potential errors in the estimation of relevant solvent exposure, the clinical diagnosis of CSE requires a multidisciplinary team. This multidisciplinary team generally includes a neurologist, an occupational physician, an occupational hygienist and a neuropsychologist. Practitioners of other disciplines, such as a psychiatrist or toxicologist, may also be consulted. The assessment includes collecting the exposure and medical histories of the patient along with the patient's symptoms and their course in relation to the patient's exposure and medical histories, the detection of the presence of neurological signs of CSE, and the measurement of the quantity and quality of neuropsychological impairment in relation to other causes that affect mental abilities. The team works together to reach a consensus regarding the probability of CSE relative to alternative causes of health complaints, which are usually other diseases.

To aid in the diagnostic process, previous working groups have provided classification systems for determining the character and severity of CSE: a WHO report (WHO, 1985) and a workshop that took place in Raleigh, NC (Baker and Seppäläinen, 1986). A schematic overview of both classification systems can be found in Table 1. In 1997, a paper by White and Proctor (1997) provided knowledge about CSE to a wider clinical community, but there are still no uniform criteria that are in use for characterising CSE in both epidemiological studies and patient evaluation (van der Hoek et al., 2000, 2001).

The diagnosis of CSE depends largely on the results of a neuropsychological assessment that objectively evaluates the cognitive impairment of the patient. It is supposed that the impairment has been caused by the permanent dysfunction of frontostriatal brain circuits (Visser et al., 2008) resulting from chronic exposure to neurotoxic solvents. More than two decades of experience with the neuropsychological aspects of the evaluation of CSE in Europe are now being used in an effort to elaborate on the existing classification systems with the aim of developing more distinct and practical guidelines for the diagnosis of CSE on the basis of neuropsychological test results.

There are two main aims of this paper: (1) to provide updated knowledge about the neuropsychological characteristics of CSE and (2) to provide guidelines for the use of neuropsychological assessment in the process of diagnosing patients who are suspected of having CSE. The development of a standardised approach to the neuropsychological assessment of CSE will facilitate both the diagnostic evaluation of individual CSE patients and the international comparability of clinical and epidemiological studies of CSE patients.

The first section of this paper includes a review of the scientific literature regarding the neuropsychological characteristics of CSE that focuses on the articles that were published after the WHO and Raleigh workshops. The second section of this paper includes the guidelines for the neuropsychological assessment of CSE that have been suggested by the consensus of the group.

2. Methods

2.1. Method for obtaining updated knowledge regarding neuropsychological characteristics of CSE

To describe the neuropsychological characteristics of CSE, two relevant and important sources of data must be considered: data from epidemiological studies of solvent-exposed workers and data from patient studies. Both sources have advantages and disadvantages in terms of the information about CSE that they provide.

Epidemiological information about exposed workers has the advantage that subjects may not have been selected on the basis of various signs and symptoms prior to the start of a study. The disadvantage of this approach is that in countries where the exposure levels are relatively low, only a few workers with signs and symptoms that are moderate-to-severe will be found, partly because most workers with moderate-to-severe symptoms will have left their jobs and partly because exposure to organic solvents has declined in many jobs in the last few decades (Caldwell et al., 2000). Many workers have only been exposed to solvents for a few years, which is in contrast to, for example, retired workers, who are not often included in studies of populations of workers. It is often difficult to discriminate between acute and chronic solvent effects in those studies because the workers have seldom been out of a situation in which there is solvent exposure for a sufficiently long interval prior to testing.

Data from patients who have been diagnosed with CSE have the advantage that the included populations can be compared, and data from this type of study group have immediate relevance for clinical assessment protocols. Furthermore, symptoms are more severe in these patient groups, and thus, they are easier to describe, and workers who drop out of a given population of workers due to illnesses or retirement can be included in a patient group. However, clinical studies are subject to referral- and investigator biases; the pattern of emerging patient characteristics is often influenced by the signs and symptoms that are used as the criteria for referral and by the signs and symptoms that are considered 'characteristic' in labelling a patient as having CSE by the investigator, which in turn influence the choice of tests that are used and the questions that are asked.

Data from epidemiological studies of solvent-exposed workers on neuropsychological characteristics were reviewed in recent meta-analysis of Meyer-Baron et al. (2008), and the findings of this analysis are described in the results section of this paper.

No reviews regarding the neuropsychological characteristics of CSE are available. Reviews by Baker (1994) and Mikkelsen (1997), which cover some of the same studies, are primarily concerned with exposed workers, and not with patients. Therefore, to provide an update to the knowledge about the neuropsychological

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