NeuroToxicology 32 (2011) 916–922

Contents lists available at ScienceDirect

NeuroToxicology

Prevalence of psychiatric disorders in patients with chronic solvent induced encephalopathy (CSE)

Ieke Visser [a,*], Elizabeth M. Wekking [b], Angela G.E.M. de Boer [c], Elisabeth A. de Joode [d], Moniek S.E. van Hout [e], Saskia van Dorsselaer [f], Henricus G. Ruhé [a], Jochanan Huijser [g], Gert van der Laan [b], Frank J.H. van Dijk [c], Aart H. Schene [a]

[a] Program for Mood Disorders, Department of Psychiatry, Academic Medical Center, Amsterdam, The Netherlands
[b] Netherlands Centre for Occupational Diseases, Academic Medical Center, Amsterdam, The Netherlands
[c] Coronel Institute of Occupational Health, Academic Medical Center, Amsterdam, The Netherlands
[d] Department of Psychiatry and Neuropsychology, University of Maastricht, Maastricht, The Netherlands
[e] Department of Psychology, Medical Spectre Twente, Enschede, The Netherlands
[f] Trimbos Institute, Utrecht, The Netherlands
[g] Arkin, Amsterdam, The Netherlands

ARTICLE INFO

Article history:
Received 2 November 2010
Accepted 6 May 2011
Available online 13 May 2011

Keywords:
Chronic solvent induced encephalopathy
Prevalence rates
Psychiatric disorders
DSM IV
Occupational health

ABSTRACT

Introduction: Long term occupational exposure to organic solvents may induce chronic solvent-induced encephalopathy (CSE), characterized by mild to severe cognitive impairment, generally seen as the key diagnostic feature. Psychiatric disorders are often diagnosed in subjects with CSE, but were never studied in more detail. This study was designed to establish the prevalence rates of DSM IV mood, anxiety, and alcohol and substance related disorders in patients with CSE.
Materials and methods: In CSE, $n = 203$ (consecutively recruited between 2002 and 2005), defined according to the criteria of the World Health Organisation (WHO), one month prevalence rates of DSM IV mood, anxiety, and life time alcohol/substance related disorders were assessed using the Structured Clinical Interview for DSM IV disorders (SCID). These prevalences were compared with those from an age and gender matched community sample ($n = 3212$) while controlling for insufficient neuropsychological test effort.
Results: In CSE, prevalence rates for major depressive disorder ($n = 36$, relative risk (RR) = 7.4), dysthymia ($n = 15$, RR = 6.0), panic disorders ($n = 18$, RR = 7.1), agoraphobia ($n = 7$, RR = 5.5) and generalized anxiety disorder ($n = 19$, RR = 15.8) were increased. Reduced prevalence rates were found for alcohol related disorders ($n = 21$, RR = 0.3). Insufficient neuropsychological test effort was not associated with increased prevalence rates of DSM IV disorders in subjects suspected of CSE.
Discussion and conclusions: In conclusion, in this first large scale study in patients with CSE, prevalence rates of DSM IV mood and anxiety disorders were elevated as compared with those in the general community, while the prevalence rates of alcohol related disorders were reduced. Further study must determine whether CSE, and mood and anxiety disorders, share a same, solvent induced, neurobiological pathway, supporting the use of a more inclusive diagnostic approach. Additionally, randomised controlled trials are needed for the urgent issue of how to treat mood and anxiety disorders in CSE patients effectively.

1. Introduction

Worldwide, numerous workers are exposed to organic solvents for the duration of many years which may induce chronic solvent-induced encephalopathy (CSE), also described as chronic toxic encephalopathy (CTE) (White and Proctor, 1997). The United Kingdom's Health and Safety Executive estimated that 8% of the working population regularly uses organic solvents (UK HSE, 1988). In the United States nine million workers are exposed to solvents, representing 3.7% of the general population (US DHHS, 1987).

In 1985 the World Health Organisation (WHO) formulated diagnostic criteria for CSE: (a) a verified exposure to neurotoxic organic solvents in adequate temporal relationship with the onset

* Corresponding author at: Program for Mood Disorders, Department of Psychiatry, Academic Medical Center, Meibergdreef 5, 1105 AZ Amsterdam, The Netherlands. Tel.: +31 20 8913638; fax: +31 20 8913701.
E-mail address: i.visser@amc.uva.nl (I. Visser).

0161-813X/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuro.2011.05.001

of symptoms, (b) a clinical picture of organic nervous system damage with typical subjective symptoms, like memory and attentional complaints, depressed mood, irritability, sleep disturbances and fatigue, (c) objective impairments, like memory and attentional deficits assessed by standardised neuropsychological tests, and (d) the exclusion of primary organic, or primary psychiatric syndromes (WHO, 1985). According to the WHO, CSE can be classified into three types: organic affective syndrome (type I), mild chronic toxic encephalopathy (type II) and severe chronic toxic encephalopathy (type III). In addition, the Raleigh classification proposes four types of CTE: symptoms only (type 1), sustained personality or mood change (type 2A), impairment of intellectual functioning (type 2B) and dementia (type 3) (Baker and Seppalainen, 1986). The WHO type 1 and Raleigh type 1 and 2A encompass the same subjective symptoms. The WHO type II and Raleigh type 2b imply objective evidence of attention and memory deficit as well as decreased psychomotor function that are generally considered as the key diagnostic criteria for CSE.

Studies have indeed shown that long-term occupational exposure to organic solvents is frequently accompanied by symptoms of depression and anxiety (Morrow et al., 1990, 1993; Condray et al., 2000; Kaukiainen et al., 2004; Bast-Pettersen, 2009). With respect to the diagnostic procedure for CSE, patients with primary psychiatric symptoms, severe enough to be categorized as a syndrome, are excluded during the diagnostic work-up. However, this is usually done using unstructured clinical interviewing. In the two aforementioned classification systems for CSE, mild to moderate psychiatric symptoms are not excluded as these are generally considered to be part of a neurotoxic syndrome after (long term) solvent exposure. These symptoms include depressed mood, irritability, loss of interest, and marked change in personality involving emotional stability, impulse control, and general mood and motivation.

A better understanding and conceptualization of these psychiatric symptoms in CSE is necessary for clinical recognition and implications, such as the development of treatment strategies and, given the recurrent nature of mood and anxiety symptoms, the improvement of prevention. Thus far study designs on psychiatric symptoms after occupational solvent exposure were hampered by several methodological issues. First, prevalence's of psychiatric symptoms, syndromes or disorders have been predominantly described in solvent exposed populations (both referred and non-referred) but without a 'lege artis' diagnostic evaluation for the presence of CSE (Morrow et al., 1990, 1993; Kaukiainen et al., 2004). For the assessments of psychiatric symptoms authors predominantly used self rating scales and questionnaires (Morrow et al., 1990, 1993; Kaukiainen et al., 2004; Nordling Nilson et al., 2010). Thus far, only three studies investigated the presence of DSM IV disorders using structured clinical interviews; one in clinically referred workers (patients) (Morrow et al., 2000), one in exposed workers who were not applying for medical care (Condray et al., 2000), and one in paint manufacturers (Bolla et al., 1990), but no diagnostic evaluation on the presence of CSE was reported in these studies. So, it is unclear whether the psychiatric symptoms seen in patients properly diagnosed with CSE qualify as psychiatric disorders according to the criteria for DSM IV disorders, as assessed with structured clinical interviews. Second, studies were performed in modest sample sizes without the use of appropriate control groups, such as community samples. Third, prevalence rates of DSM IV alcohol and substance related disorders in solvent exposed workers seemed to be within the normal range (Morrow et al., 2000; Condray et al., 2000). These results are unexpected in the light of the usual positive association of mood and anxiety disorders, and comorbid alcohol and substance related disorders in the general population (Reiger et al., 1990). Also, previous studies suggested the presence of alcohol related disorders in house painters (Riise et al., 1995). Fourth, previous studies did not control for an important characteristic of suspected CSE patients: up to forty five percent of solvent exposed patients suspected of CSE display insufficient effort during neuropsychological diagnostic testing, resulting in an exaggeration, consciously or unconsciously, of neuropsychological symptoms. The presence of insufficient effort may be indicative for malingering, thus excluding the diagnosis CSE (van Hout et al., 2003). Insufficient effort was previously shown to be common in similar syndromes with subjective complaints, such as chronic whiplash, chronic fatigue, and post-concussional syndromes (Kessels et al., 2000; Werf et al., 2000; Binder and Rohling, 1996). So, the question is raised whether insufficient effort during neuropsychological diagnostic testing in solvent exposed individuals might be (also) associated with a subjective exaggeration of psychiatric symptoms and, therefore with an overestimation of prevalence rates.

Summarizing, evidence is missing on the prevalence and severity of DSM IV mood, anxiety and alcohol and substance related disorders in solvent exposed workers, systematically diagnosed with CSE according to WHO criteria, using appropriate clinical psychiatric assessment and a community sample as a control group, and controlling for the presence of insufficient effort during the assessment. The aim of our study was twofold: (a) to determine the prevalence of mood, anxiety and alcohol and substance related disorders in patients diagnosed with CSE as compared with a control community sample, and (b) to compare the prevalence rates of mood, anxiety and alcohol and substance related disorders in patients diagnosed with CSE as compared with suspected CSE patients showing insufficient neuropsychological test effort. We hypothesized that the prevalence rates of psychiatric disorders in CSE patients are higher as compared with the prevalence rates in a community sample, and that suspected CSE patients showing insufficient neuropsychological test effort show higher prevalence rates of psychiatric disorders as compared with CSE patients showing sufficient neuropsychological test effort.

2. Methods

2.1. CSE subjects

The study subjects were recruited consecutively between 2002 and 2005 from workers ($n = 912$) suspected of CSE referred by general practitioners, occupational physicians or other medical specialists to the Netherlands Center for Occupational Diseases, a nationwide referral center with a substantial public notice (Fig. 1). Diagnostic evaluations for CSE were performed without charge and without initial purposes of financial compensation (Hoek et al., 2001). In total 433 of the initial 912 subjects were invited for further examination after the first screening on symptoms, exposure and other explanations (Fig. 1). Of these 433 subjects, 351 patients fulfilled the four diagnostic WHO criteria for CSE (WHO, 1985): (a) a verified exposure to neurotoxic organic solvents (volatile hydrocarbon chemicals and their derivates, as well as mixtures) in adequate temporal relationship with the onset of symptoms, (b) a clinical picture of organic nervous system damage with typical subjective symptoms, like memory and attentional complaints, depressed mood, irritability, sleep disturbances and fatigue, (c) objective impairments, like memory and attentional deficits assessed by standardised neuropsychological tests, and (d) the exclusion of primary organic, or primary psychiatric syndromes, after completion of the standardised diagnostic protocol for CSE including extensive physical, neurological, neuropsychological and occupational health examination (Hoek et al., 2000). After written informed consent was obtained, 323 patients were assessed on DSM IV disorders with the