NeuroToxicology 59 (2017) 263–269

Contents lists available at ScienceDirect

NeuroToxicology

Full length article

Neurotoxic impact of mercury on the central nervous system evaluated by neuropsychological tests and on the autonomic nervous system evaluated by dynamic pupillometry

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ARTICLE INFO

Article history:
Received 30 October 2015
Received in revised form 9 April 2016
Accepted 11 April 2016
Available online 16 April 2016

Keywords:
Mercury
Cognitive functions
Autonomic nervous system
Pupillometry

ABSTRACT

Mercury vapor is highly toxic to the human body. The present study aimed to investigate the occurrence of neuropsychological dysfunction in former workers of fluorescent lamps factories that were exposed to mercury vapor (years after cessation of exposure), diagnosed with chronic mercurialism, and to investigate the effects of such exposure on the Autonomic Nervous System (ANS) using the non-invasive method of dynamic pupillometry. The exposed group and a control group matched by age and educational level were evaluated by the Beck Depression Inventory and with the computerized neuropsychological battery CANTABeclipse – subtests of working memory (Spatial Span), spatial memory (Spatial Recognition Memory), visual memory (Pattern Recognition Memory) and action planning (Stockings of Cambridge). The ANS was assessed by dynamic pupillometry, which provides information on the operation on both the sympathetic and parasympathetic functions. Depression scores were significantly higher among the former workers when compared with the control group. The exposed group also showed significantly worse performance in most of the cognitive functions assessed. In the dynamic pupillometry test, former workers showed significantly lower response than the control group in the sympathetic response parameter (time of 75% of pupillary recovery at 10 cd/m^2 luminance).

Our study found indications that are suggestive of cognitive deficits and losses in sympathetic autonomic activity among patients occupationally exposed to mercury vapor.

1. Introduction

Metallic mercury is used in chemical industrial applications, by manufacturers of products such as fluorescent lamps, batteries, and thermometers, and also by health professionals such as dentists in the preparation of dental amalgam (Manahan, 1992). Mercury vapor is highly toxic to the human body and can remain in the atmosphere for weeks. In addition, it is highly soluble and easily penetrates the pulmonary alveoli, blood-brain barrier and placenta (Azevedo, 2003). Even after the end of exposure, mercury continues to cause harm to the body. In addition, it was found that the effects might be irreversible (Zachi et al., 2008).

Mercury is especially toxic to the Central Nervous System (CNS). Several studies suggest that individuals who were exposed to mercury vapor do have cognitive impairments (Smith et al., 1983; Soleo et al., 1990; Liang et al., 1993; Ellingsen et al., 2001), mostly in memory, attention and psychomotor functioning. However, not all studies have found changes in the same parameters (Ellingsen et al., 2001; Meyer-Baron et al., 2002).

Losses related to cognitive functions (Zachi et al., 2007; Zachi et al., 2008; Barboni et al., 2009) were found in subjects with ceased exposure. Furthermore, studies with individuals who died more than ten years after the end of exposure found high concentration of metal deposits in brain tissues (Hargreaves et al., 1988; Kosta et al., 1975).

As well as the CNS, the Autonomic Nervous System (ANS) is highly affected by mercury exposure. Symptoms such as pain, heart hate variability, paresthesia and hypotonia, mostly found in children exposed to the metal (Appenzeller and Oribe, 1997), indicate the presence of mercury effects on the ANS. Mercury exposure is associated with increased blood pressure and decreased heart rate variability (Vupputuri et al., 2005; Valera et al., 2009). Studies show the relationship between prenatal

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http://dx.doi.org/10.1016/j.neuro.2016.04.010
0161-813X/

exposure to mercury and decline in heart rate variability in children from 7 to 14 years old (Sorensen et al., 1999; Oka et al., 2002; Grandjean et al., 2004; Murata et al., 2006). Furthermore, the negative impact of mercury (in this case, in its organic form) on heart rate variability has been demonstrated in a study from Japan, in which a group of subjects followed for 14 weeks a diet rich in tuna and swordfish (with high concentrations of mercury) (Yaginuma-Sakurai et al., 2009). Another negative association was found between mercury and heart rate variability in a population living near industrial areas in Korea (Lim et al., 2009).

Pupil tests can provide a simple non-invasive method of ANS assessment (Bremner, 2008). Pupil dilation is determined by the contraction of the iris dilator muscle, formed by sympathetic fibers. On the other hand, pupil constriction is determined by the contraction of the pupil sphincter, formed by parasympathetic fibers. The intrinsically photosensitive Retinal Ganglion Cells (ipRGCs), which are melanopsin-containing, contribute to the pupillary light reflex. Studies indicate that pupillometry is useful in the early detection of autonomic dysfunction (Dutsch et al., 2004; Eppens et al., 2006; Smith and Smith, 1999; Ferrari et al., 2010). However, there is a gap in research about the relationship between dynamic parameters of pupillometry and mercury poisoning (and other toxic metals).

Studies report the activation of the ANS during cognitive functioning tasks (Hansen et al., 2009; Mukherjee et al., 2011). The relationship between cognitive and autonomic functions have been the focus of several studies (Collins et al., 2012; Zambotti et al., 2012). In a study with individuals who had mild cognitive impairments, the subjects with more significant autonomic dysfunction had more severe neuropsychological deficits (Collins et al., 2012). The findings indicate that the ANS is associated with cognitive impairment (Musser et al., 2011; Collins et al., 2012; Zambotti et al., 2012). However, most studies used heart rate variability evaluation as an indicator of autonomic dysfunction and made a more general analysis, without differentiating the sympathetic and parasympathetic division of the ANS.

In the present study, we evaluated cognitive functions and the ANS of intoxicated patients, who had been occupationally exposed to mercury vapor in fluorescent lamp factories years after cessation of exposure. They had been occupationally exposed to mercury vapor in fluorescent lamp factories. Finally, we aimed to verify the correlation between the parameters of the pupil test and the neuropsychological performance.

2. Material and methods

2.1. Participants

Thirty-one former workers at fluorescent lamp industries (17 males, 14 females; mean age = 50.13 +7.03) (Table 1) were examined. They were referred by the Occupational Health Service, Medical School of the University of São Paulo, where they had been diagnosed with mercury intoxication, and followed up for several years. These patients had been placed on disability retirement due to health problems related to chronic occupational exposure to mercury vapor. They had been exposed to elemental mercury for an average of 11 (±6.33) years and had been away from the exposure situation for an average of 11.81 (±6.43) years. Age-matched controls (n = 20, 9 males, 11 females), mean age = 49.16 (+7.29) were recruited among relatives of the former workers and the staff from the University of São Paulo (cleaning and maintenance staff). Years of education were similar in both groups – exposed group: 9.58 (+2.49), control group: 8.94(+3.21). The exclusion criteria for both groups were history of alcoholism, drug abuse, smoking, head injury, use of medications that interfere with the activities of the nervous system, IQ less than 80, ophthalmological diseases, ophthalmic surgery. The demographic characteristics of the participants are summarized in Table 1. No significant differences were found between the two groups regarding age or years of formal education.

2.2. Tests and procedures

All subjects signed informed consent. The procedures were approved by the Research Ethics Committees of the Institute of Psychology, University of São Paulo.

The participants filled out a form with information about possible exposure to other neurotoxic substances, their labor history and general medical history, including data on the use of alcohol, drugs, psychotropic and general medications.

A test of malingering – Rey 15-item Memory Test (Schretlen et al., 1991) – was also included, only for exposed patients. We decided to include it because the intentional production of symptoms has been reported in toxic exposure (Greve et al., 2006). Patients may exaggerate or fake their symptoms motivated by secondary gains such as avoiding work or obtaining financial compensation.

We used a computerized battery (CANTABeclipse V3.0) to access cognitive functions (which unlike manual tests provide

Table 1
Demographic characteristics of the participants.

	Exposed Group		Control Group		
Sex	n	M + SD	n	M + SD	*p*
	31		20		
Male	17		9		
Female	14		11		
Age (years)		50.13 (+7.03)		49.16 (+7.29)	0.716
Education level (years)		9.58 (+2.49)		8.94 (+3.21)	0.616
Beck (total score)		23.93 (+0.90)		17.11 (+1.97)	0.001*
IQ		94.03 (+1.20)		94.76 (+2.01)	0.761
Time of Exposure (years)		11.00 (+6.33)		–	
Time of cessation of exposure (years)		11.81 (+6.43)		–	

M = Mean; SD = Standard Deviation; n = number of subjects.