Available online at www.sciencedirect.com
SCIENCE DIRECT®
Neurotoxicology and Teratology 26 (2004) 131–137
NEUROTOXICOLOGY AND TERATOLOGY
www.elsevier.com/locate/neutera

Brief communication

Simultaneous changes of the spontaneous and stimulus-evoked cortical activity in rats acutely treated with mercuric chloride

László Pecze, András Papp*, László Nagymajtényi

Department of Public Health, University of Szeged, H-6720 Szeged, Dóm tér 10., Hungary

Received 1 July 2003; received in revised form 1 July 2003; accepted 17 July 2003

Abstract

In earlier studies of our laboratory and in several other reports, alterations in the electrical activity of the cortex of experimental animals on subchronic mercury (Hg) administration were described. In the present work, simultaneous changes in the spontaneous and stimulus-evoked cortical activity elicited by acute administration of inorganic Hg were evaluated with the aim of finding any correlation of the two, possibly giving insight into the mechanism of the alterations. In young adult male Wistar rats, spontaneous cortical, as well as stimulus-evoked cortical and peripheral nervous activity was recorded, before and after acute administration of 3.5 and 7.0 mg/kg Hg^{2+} ip. The effects of Hg^{2+} appeared within 10 min and most became significant over 3 h. On the cortex, slowed spontaneous activity, as well as increased amplitude and latency of the evoked potentials (EPs) was seen, and in the periphery, decreased nerve conduction velocity. These alterations seemed to be consistent with a separate cortical and peripheral axonal effect of Hg.

Keywords: Inorganic mercury; Electrocorticogram; Evoked potential; Rat

1. Introduction

Mercury—traditionally an occupational risk factor, but present nowadays in various elements of the environment due to human activity—is one of the heavy metals known to be harmful for the nervous system.

The neurotoxic effects of mercury (Hg) in humans are variable, from neuromuscular disorders [21] to abnormalities of the higher nervous functions [44]. In occupational exposure to inorganic Hg, alterations of the cortical electrical activity have been reported, both in form of slowed electroencephalogram (EEG) [34], as amplitude increase of the somatosensory evoked potential (EP) [26] and delayed waves in the brainstem auditory EP [11].

In animal experiments, the neurotoxic effect of Hg has been described at several levels of organisation. At the molecular level, Hg—in both inorganic and organic form—was found to affect a range of ion channels in the peripheral and central nervous system [40]. Calcium homeostasis, an important factor of normal neuronal function, was also disturbed by Hg^{2+} [9], via interfering with Ca uptake of the endoplasmic reticulum [15]. Elevated level of the transmitters noradrenaline [17], and dopamine and serotonin [24] were observed in rats treated with Hg^{2+}. Ligand binding of muscarinic receptors was inhibited by Hg compounds in rat cortical neuronal membranes in vitro [6]. At the level of organs, damage to motor axons by mercuric chloride was described [32].

Inorganic salts of Hg are generally supposed to have low penetration across the blood–brain barrier [2]. It has been observed, however, that the barrier itself is damaged as soon as 1 h after administration of an Hg dose comparable to ours (6 mg/kg ip [41]). Using up to 10 mg/kg $HgCl_2$ ip [30] Hg deposits in cortical and spinal neurons of rats were observed. Likewise, deposited Hg was found in the postmortem dissected brains of miners exposed to inorganic Hg [22].

Earlier studies of our group were aimed at Hg effects on the cortical activity. In rats with subchronic $HgCl_2$ treatment (0.4 and 1.6 mg Hg^{2+}/kg, five times a week per os, 4 to 12 weeks), alterations in the spontaneous [10] and stimulus-evoked [33,38] cortical activity were found. It has remained unclear, however, how alterations in different forms of macroscopic activity are related among each other and

* Corresponding author. Tel.: +36-62-545119; fax: +36-62-545120.
E-mail address: ppp@puhe.szote.u-szeged.hu (A. Papp).

0892-0362/$ – see front matter © 2003 Elsevier Inc. All rights reserved.
doi:10.1016/S0892-0362(03)00092-8

how they are derived from the above-mentioned neuronal or subneuronal effects of Hg. Increased spontaneous cortical activity, together with depressed EPs, as seen in our earlier work, was a reasonable constellation (see Discussion), but was established by group comparison (treated vs. control), that is, indirectly. In the present work, by measuring the

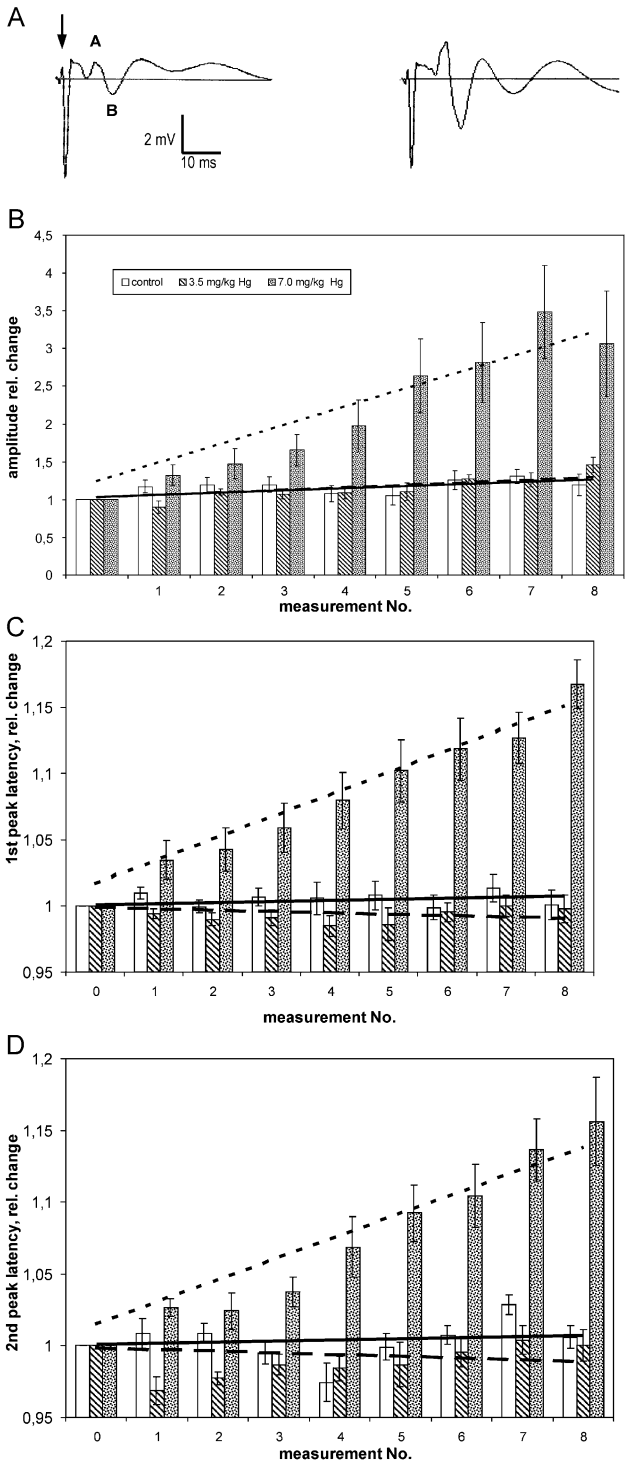

Fig. 1. Somatosensory cortical responses evoked by whisker stimulation and the time trend of the Hg^{2+}-induced changes. (A) Original records of the EP corresponding to the pre-treatment state (0th measurement, left) and 160 min after treatment (8th measurement, right). The amplitude was measured between the two main peaks (A and B) and the latencies, between the stimulus artefact (arrow) and A or B. (B–D) Time trend of the peak-to-peak amplitude (B), 1st peak latency (C) and 2nd peak latency (D) of the cortical evoked potential. Abscissa: Time in 20 min increments from the administration of $HgCl_2$, the 0th measurement is the pre-administration average. Ordinate: Relative change of the parameter plotted, unity is the pre-administration average. The bars represent mean ± S.E.M. Linear regression lines fitted by EXCEL.

simultaneous alterations in the spontaneous and stimulus-evoked cortical activity during the effect of acute $HgCl_2$ treatment in rats, our aim was to see in a more direct way if these alterations were correlated and to what extent.

2. Materials and methods

The experiments were done on adult male Wistar rats (~ 350 g body weight) in groups of eight animals each (7.0 mg/kg Hg^{2+}, 3.5 mg/kg Hg^{2+} and control). In urethane (1000 mg/kg body weight) [3] anaesthesia, the head of the rats was clamped in a stereotaxic frame and the left hemisphere was exposed. Wounds were sprayed with 10% lidocaine and the exposed cortex was covered with warm paraffin oil. After ~ 1-h recovery, silver recording electrodes were placed on the somatosensory projection area of the whiskers (barrel field) [43] and of the tail of the animal. The corresponding peripheral sites (whiskery skin and base of tail) were stimulated by electric pulses (~ 4 V, 0.05 ms, 1 Hz). Recording and evaluation of the electrical activity was PC-based using the NEUROSYS software (Experimetria, UK). The pattern of recording consisted of a 5-min electrocorticogram (ECoG) taken from both areas simultaneously, followed EPs recorded by applying one train of 20 stimuli to each of the peripheral sites. These records were averaged, and the latency and amplitude of EP measured. From the ECoGs, band activity (standard, delta to gamma) [20] was automatically deter-

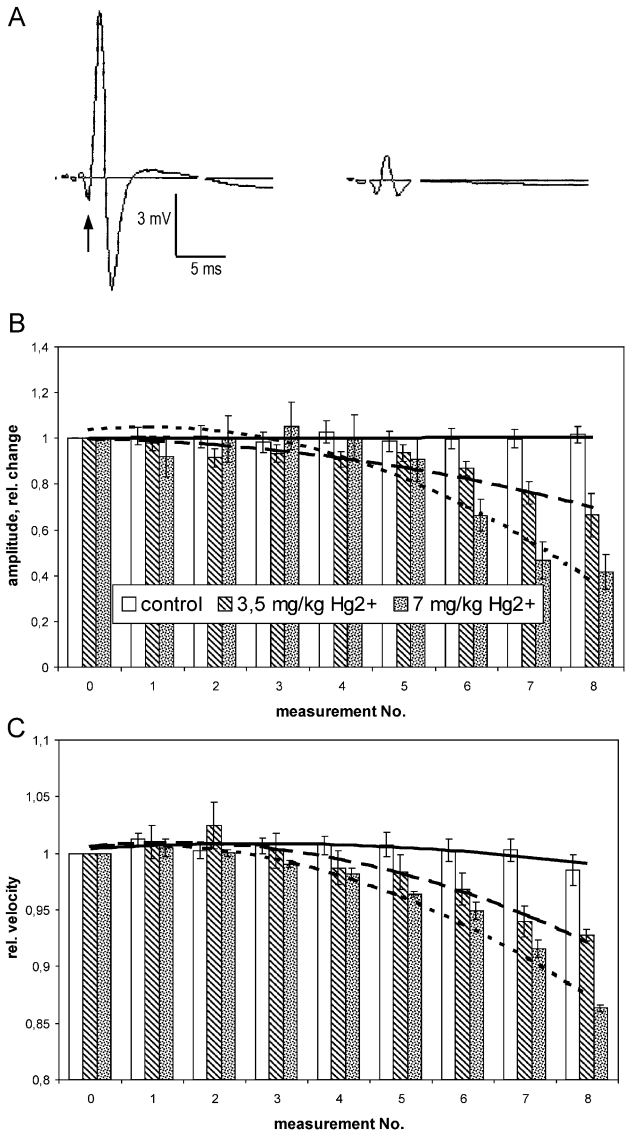

Fig. 2. Tail nerve compound action potentials and the time trend of its changes induced by Hg^{2+}. (A) Original records in pre-treatment state (0th measurement, left) and 160 min after treatment (8th measurement, right). Amplitude (B) was measured between the main peaks. Conduction velocity (C) was based on the onset latency (arrow). (B–C) Time trend of the amplitude and the calculated conduction velocity on Hg^{2+} administration. Plotted as in Fig. 1, except that the fitted curves are of second order.

mined and the so-called ECoG index calculated (relation of the low and high frequencies in the recorded ECoG, delta + theta/beta1 + beta2). During tail stimulation, compound action potential of the tail nerve was also recorded, and its latency and amplitude measured. This pattern was repeated every 20 min. After at least four control records, Hg (7.0 or 3.5 mg/kg Hg^{2+}) was administered ($HgCl_2$ dissolved in distilled water to 1 ml/kg administration volume) via a peritoneal cannula and further eight records were taken (the last one at 160 min after administration). Control rats received the same amount of pure distilled water. The dose of 7.0 mg/kg was chosen on the basis of earlier experiments with different multiples of the dose (1.6 mg/kg), which proved to have a significant effect in subchronic exposure [10,33,38]. The time span of the whole experiment was determined by the general state of the animals, which usually began to deteriorate after ~ 5 h of anaesthesia (judged on the parameters of untreated controls). Consequently, the doses had to be high enough to elicit a clear effect in about 2 h.

Temporal trend of the parameters recorded was visualised on "parameter value by time" correlation plots, which indicated the gradual appearance of clear-cut differences between the parameters (amplitude, latency and EEG index) of the control vs. treated groups. Significance of these differences was tested by means of the General Linear Model (GLM) of the SPSS software (SPSS, Chicago, IL, USA), which uses univariate ANOVA to test regression. Group was taken as fixed variable, time as covariate, and the significance of group *and* time effect was observed. For post hoc analysis, LSD was used. Possible correlation between different parameters was tested by generating parameter to parameter plots in EXCEL.

3. Results

Acute treatment with inorganic Hg had a clear effect on the spontaneous and stimulus-evoked cortical activity.

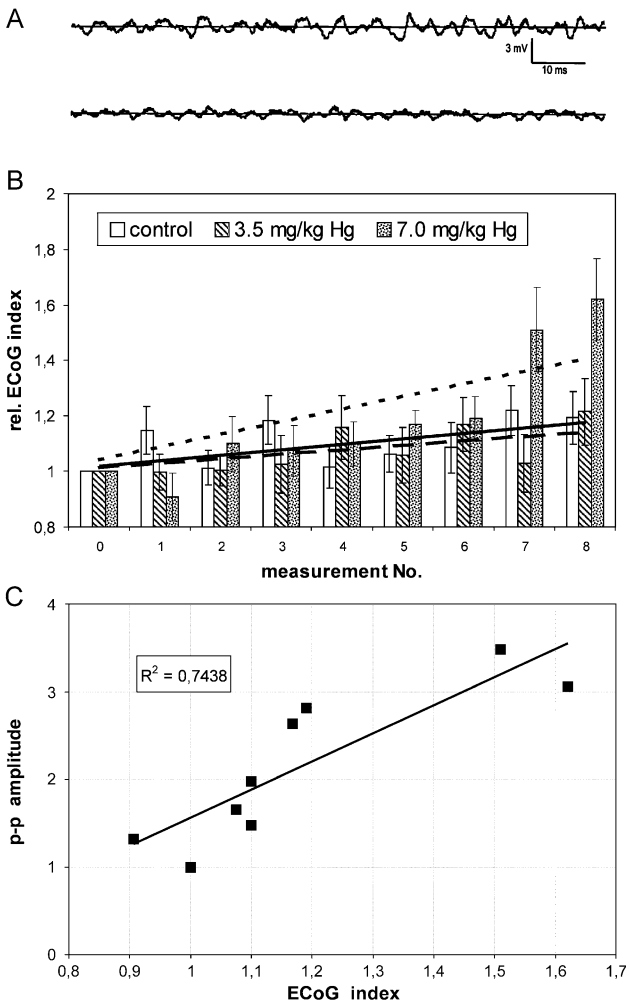

Fig. 3. Records of spontaneous cortical activity and the time trend of the ECoG index on Hg^{2+} administration. (A) Ten-second sections of the ECoG in control (upper trace) and 160 min after 7.0 mg/kg Hg^{2+} administration (lower trace). (B) Time trend of the ECoG index on Hg administration. Plotted as in Fig. 1. (C) Correlation diagram of the ECoG index (abscissa) and the EP amplitude (ordinate). Pre-administration and postadministration absolute values from the 7.0 mg/kg Hg^{2+} group. Linear regression line fitted.

In case of the cortical response evoked by whisker stimulation (Fig. 1A), Hg effect was primarily seen on the amplitude. On dosage of 7.0 mg/kg Hg^{2+} ip, there was a clear increase in the response amplitude (before Hg: 1.79 ± 0.18 mV, 160 min after 7.0 mg/kg Hg: 5.48 ± 0.17 mV; group mean ± S.E.M.), which started immediately after administration and developed over the recording period [GLM: $F(2,21) = 60.6$, $P < 0.001$] (Fig. 1B). Dosage with 3.5 mg/kg Hg^{2+} caused only a nonsignificant (LSD: *ns*) increase in the cortical response amplitude. The effect on the latency was less expressed. The peak latency of both main waves of the EP increased significantly (LSD: $P < 0.05$) on dosage of 7.0 mg/kg Hg^{2+} ip (for the 1st peak, before Hg: 10.76 ± 0.14 ms, 160 min after 7.0 mg/kg Hg: 11.94 ± 0.15 ms) but not on 3.5 mg/kg Hg^{2+} ip [GLM: 1st peak: $F(2,21) = 66.3$ $P < 0.001$; 2nd peak: $F(2,21) = 44.0$, $P < 0.001$] (Fig. 1C,D).

The change of the cortical response evoked by stimulation of the tail was similar but less strong. The amplitude increased both in the groups given 3.5 (LSD: *ns*) or 7.0 mg/kg Hg^{2+} [LSD: $P < 0.05$; GLM: $F(2,21) = 15.1$, $P < 0.001$]. The latency times showed no significant change [GLM: $F(2,21) = 2.9$, $P > 0.05$].

On the tail nerve action potential, Hg^{2+} caused an amplitude decrease and a latency increase; the latter corresponding to a slower conduction velocity (Fig. 2). With 7.0 mg/kg Hg^{2+}, a slight, hardly significant increase of the amplitude was seen, followed by gradually evolving clear decrease (before Hg: 3.215 ± 0.30 mV, 160 min after 7.0 mg/kg Hg: 1.331 ± 0.23 mV) which was significant (LSD: $P < 0.05$). The effect of 3.5 mg/kg Hg^{2+} on the amplitude decrease was also significant [GLM: $F(2,21) = 10.0$, $P < 0.001$; LSD: $P < 0.05$ for both doses]. The decrease of the conduction velocity (before Hg: 15.42 ± 0.31 m/s, 160 min after 7.0 mg/kg Hg: 13.26 ± 0.87 m/s) was significant in both treated groups [GLM: $F(2,21) = 17.3$, $P < 0.001$].

Mercury caused a shift to lower frequencies in the spontaneous cortical activity (Fig. 3A) at both recording sites. According to the formula given in Materials and methods, this resulted in increased ECoG index values. As seen in Fig. 3B, there was a slow shift also in the ECoG index of the control animals. Compared to that, the effect of 7.0 mg/kg Hg^{2+} was significant [GLM: $F(2,21) = 4.8$, $P < 0.05$; LSD for high dose: $P < 0.05$] (Fig. 3B). There was a significant [$R^2 = 0.744$, $F(7) = 20.3$, $P < 0.01$] correlation between the alteration of the spontaneous cortical activity (ECoG index) and the EP amplitude. These two alterations evolved in parallel and were manifest only in animals treated with the higher dose of Hg^{2+}, as shown by the correlation diagram (Fig. 3C).

4. Discussion

In the work presented, a clear correlation was demonstrated between the changes of spontaneous cortical activity (ECoG) and cortical sensory EPs recorded from rats acutely treated with inorganic Hg. Following exposure to inorganic Hg compounds, accumulation of Hg within the CNS has been demonstrated [1,22,30], in spite of the tendency of both Hg^{+} and Hg^{2+} to bond to plasma proteins. Time course and amount of Hg accumulation in the rats' brain was not determined in our experiments. Literature data showed that a comparable dose (6 mg/kg $HgCl_2$ ip) affected the blood–brain barrier within 1 h [41] and Hg was deposited in cortical cells in 18 h [16]. Conversion to elementary Hg [13] may have contributed to deposition in the brain.

In animal experiments, including those done earlier at our department [10,33,38], different heavy metals caused a variety of functional changes in the central and peripheral nervous system. However, a comprehensive mechanistic explanation of the alterations seen has been generally missing.

Evoked potentials seem usable to asses CNS functions of a human or animal organism exposed to Hg [23]. In the present study, the amplitude of the cortical-evoked response, on stimulation of the whiskers and of the tail, increased. The latency of the potentials evoked by whisker stimulation also increased significantly, but no significant change of the latency of the EP from the tail was seen. In chloralkali workers subject to low-level long-term exposure to airborne inorganic Hg, changes in different EPs were described [7], which were similar to those found by us in rats (increased latency and amplitude). EEG performed in the same occupational group showed significantly slower rhythms and more attenuated amplitudes than in the EEG of unexposed controls [34]. In five patients with Minamata disease (oral methyl-Hg poisoning), short-latency somatosensory EP studies revealed complete absence of the N20 wave component (while the N9, N11, N13, N14 components were normal). Three of these patients showed marked cortical atrophy localised to the central sulci on CT studies consistent with these results [42]. In case of workers exposed to different forms of Hg (e.g., mercuric oxides and phenyl mercuric acid) it was demonstrated that slowing of the median motor nerve conduction velocities correlated with increased levels of Hg in blood and urine, as well as with increased prevalence of neurological symptoms [25,39]. In our experiments, Hg caused an amplitude decrease and a latency increase of the tail nerve action potential, the latter corresponding to a slower conduction velocity.

The observed amplitude increase of EPs and the shift of ECoG frequencies correspond to a diminished spontaneous activity of the cortex. This is likely due to some specific effect of Hg^{2+} (and not to a general toxic effect on the cortex where both spontaneous and stimulus-evoked activity would probably be reduced). The basal cortical activity is under cholinergic modulation [29], by ACh released from ascending fibres and acting on muscarinic receptors. Inorganic Hg can influence this cholinergic activation by inhibiting choline acetyltransferase [14] and by decreasing agonist binding on the muscarinic cholinoceptors [35], resulting in reduced activating influence acting on the

cortical neurons [12]. Under conditions of decreased spontaneous cortical activity, the amplitude of evoked responses generally increases, as has been described in animals [19] and humans [8,18,36].

The excitatory input producing the cortical EPs is glutamatergic. Uptake of glutamate by astrocytes, a major factor in terminating its excitatory and, potentially, excitotoxic action [28,37], is inhibited by $HgCl_2$ at low doses [4]. This might play a role in central nervous system toxicity of Hg, in general [5,27], and may explain the increase of EPs under acute Hg^{2+} influence as we now have found, and its decrease in subchronic application, as described in our earlier works [31].

Acute exposure of rats to inorganic Hg in the present study was found to affect spontaneous cortical, as well as stimulus-evoked cortical and peripheral nervous activity. The alterations seen seem to be consistent with a separate cortical (slowed spontaneous activity, increased EP amplitudes) and axonal (longer latencies of stimulus-evoked cortical and peripheral waves) effect. This finding indicates the necessity of further studies to elucidate the mechanism and localisation of these effects.

References

[1] M.M. Aposhian, R.M. Maiorino, Z. Xu, H.V. Aposhian, Sodium 2,3-dimercapto-1-propanesulfinate (DMPS) treatment does not redistribute lead or mercury to the brain of rats, Toxicology 109 (1996) 49–55.

[2] M. Aschner, J.L. Aschner, Mercury neurotoxicity: mechanisms of blood–brain barrier transport, Neurosci. Biobehav. Rev. 14 (1990) 169–176.

[3] W.C. Bowman, M.J. Rand, Textbook of Pharmacology, Blackwell Scientific Publications, Oxford, 1980, p. 7,15.

[4] N. Brookes, Specificity and reversibility of the inhibition by $HgCl_2$ of glutamate transport in astrocyte cultures, J. Neurochem. 50 (1988) 1117–1122.

[5] N. Brookes, In vivo evidence for the role of glutamate in the CNS toxicity of mercury, Toxicology 76 (1992) 245–256.

[6] A.F. Castoldi, S.M. Candura, F. Costa, L. Manzo, L.G. Costa, Interaction of mercury compounds with muscarinic receptor subtypes in the rat brain, Neurotoxicology 17 (1996) 735–741.

[7] Y.C. Chang, C.Y. Yeh, J.D. Wang, Subclinical neurotoxicity of mercury vapor revealed by a multimodality evoked potential study of chloralkali workers, Am. J. Ind. Med. 27 (1995) 271–279.

[8] F. Corletto, A. Gentilomo, A. Rosadini, G.F. Rossi, J. Zattoni, Visual evoked responses during sleep in man, in: W. Cobb, C. Morocutti (Eds.), The Evoked Potentials, Elsevier, Amsterdam, 1967, pp. 61–69.

[9] M.F. Denny, W.D. Atchison, Mercurial-induced alterations in neuronal divalent cation homeostasis, Neurotoxicology 17 (1996) 47–62.

[10] I. Dési, L. Nagymajtényi, H. Schulz, Effect of subchronic mercury exposure on electrocorticogram of rats, Neurotoxicology 17 (1996) 719–724.

[11] G. Discalzi, D. Fabbro, F. Meliga, A. Mocellini, F. Capellaro, Effects of occupational exposure to mercury and lead on brainstem auditory evoked potentials, Int. J. Psychophysiol. 14 (1993) 21–25.

[12] H.C. Dringenberg, C.H. Vanderwolf, Involvement of direct and indirect pathways in electrocorticographic activation, Neurosci. Biobehav. Rev. 22 (1998) 243–257.

[13] J.D. Dunn, T.W. Clarkson, L. Magos, Interaction of ethanol and inorganic mercury: generation of mercury vapor in vivo, J. Pharmacol. Exp. Ther. 216 (1981) 19–23.

[14] C. Dwivedi, R. Raghunathan, B.C. Joshi, H.W. Foster, Effect of mercury compounds on acetylcholin transferase, Res. Commun. Chem. Pathol. Pharmacol. 30 (1980) 381–384.

[15] A.J. Freitas, J.B.T. Rocha, H. Wolosker, D.O.G. Souza, Effects of Hg^{2+} and CH_3Hg^+ on Ca^{2+} fluxes in rat brain synptosomes, Brain Res. 738 (1996) 257–264.

[16] B. Gajkowska, G. Szumanska, R. Gadamski, Ultrastructural alterations of brain cortex in rat following intraperitoneal administration of mercuric chloride, J. Hirnforsch. 33 (1992) 471–476.

[17] S. Gasso, C. Sunol, C. Sanfeliu, E. Rodriguez-Farre, R.M. Cristofol, Pharmacological characterization of the effects of methylmercury and mercuric chloride on spontaneous noradrenaline release from rat hippocampal slices, Life Sci. 67 (2000) 1219–1231.

[18] U. Hegerl, G. Juckel, H.J. Möller, Event related brain potentials as indicators of neurochemical dysfunctions in psychiatric patients, Nervenarzt 67 (1996) 360–368.

[19] A. Herz, F. Fraling, I. Niedner, G. Färber, Pharmacologically induced alterations of cortical and subcortical evoked potentials compared with physiological changes during the awake–sleep cycle in cats, in: W. Cobb, C. Morocutti (Eds.), The Evoked Potentials, Elsevier, Amsterdam, 1967, pp. 165–1976.

[20] E.R. Kandel, J.H. Schwartz, Principles of Neural Science, Elsevier, New York, 1985, pp. 643–644.

[21] R.A.P. Kark, Clinical and neurochemical aspects of inorganic mercury intoxication, in: F.A. de Wolff (Ed.), Handbook of Clinical Neurology, vol. 20, Elsevier, Amsterdam, 1994, pp. 367–411.

[22] L. Kosta, A.R. Byrne, V. Zelenko, Correlation between selenium and mercury in man following exposure to inorganic mercury, Nature 254 (1975) 238–239.

[23] M.K. Lakshmana, T. Desiraju, T.R. Raju, Mercuric chloride-induced alterations of levels of noradrenaline, dopamine, serotonin and acetylcholine esterase activity in different regions of rat brain during postnatal development, Arch. Toxicol. 67 (1993) 422–427.

[24] O. Lamm, H. Pratt, Subclinical effects of exposure to inorganic mercury revealed by somatosensory-evoked potentials, Eur. Neurol. 24 (1985) 237–243.

[25] S.P. Levine, G.D. Cavender, G.D. Langloolf, J.W.E. Albers, Elemental mercury exposure; peripheral neurotoxicity, Br. J. Ind. Med. 39 (1982) 136–139.

[26] F. Lille, P. Hazemann, R. Garnier, S. Dally, Effects of lead and mercury intoxications on evoked potentials, J. Toxicol., Clin. Toxicol. 26 (1988) 103–116.

[27] E. Matyja, J. Albrecht, Ultrastructural evidence that mercuric chloride lowers the threshold for glutamate neurotoxicity in an organotypic culture of rat cerebellum, Neurosci. Lett. 158 (1993) 155–158.

[28] G.J. McBean, P.J. Roberts, Neurotoxicity of L-glutamate and DL threo-3-hydroixyaspartat in the rat striatum, J. Neurochem. 44 (1985) 247–254.

[29] R. Metherate, C.L. Cox, J.H. Ashe, Cellular bases of neocortical activation: modulation of neural oscillations by the nucleus basalis and endogenous acetylcholine, J. Neurosci. 12 (1992) 4701–4711.

[30] B. Möller-Madsen, Localization of mercury in CNS of the rat: II. Intraperitoneal injection of methylmercuric chloride (CH_3HgCl) and mercuric chloride ($HgCl_2$), Toxicol. Appl. Pharmacol. 103 (1990) 303–323.

[31] L. Nagymajtényi, I. Dési, A. Papp, T. Vezér, Neurophysiological changes caused by combined treatment with heavy metals and ethanol in rats, Cent. Eur. J. Occup. Environ. Med. 6 (2000) 217–223.

[32] R. Pamphlett, P. Coote, Entry of low doses of mercury vapor into the nervous system, Neurotoxicology 19 (1998) 39–48.

[33] A. Papp, T. Vezér, L. Nagymajtényi, Possible functional biomarkers among the properties of cortical sensory evoked potentials of rats treated with xenobiotics, J. Physiol. 526 (2000) 161.

[34] L. Piikivi, U. Tolonen, EEG findings in chloralkali workers subjected to

low long term exposure to mercury vapour, Br. J. Ind. Med. 46 (1989) 370–375.
[35] B. Rajanna, C.S. Chetty, S. Rajanna, E. Hall, S. Fail, P.R. Yallapragada, Interaction of metals with muscarinic cholinoceptor and adrenoceptor binding, and agonist-stimulated inositol phospholipid hydrolysis in rat brain, Comp. Biochem. Physiol. 116C (1997) 111–116.
[36] N. Rémond, V. Lesévre, Variations in average visual evoked potential as a function of the alpha rhythm phase (Autostimulation), in: W. Cobb, C. Morocutti (Eds.), The Evoked Potentials, Elsevier, Amsterdam, 1967, pp. 42–52.
[37] M.B. Robinson, S. Djalu, J.R. Buchhalter, Inhibition of glutamate uptake with L-*trans* pyrrolidine 2,4 dicarboxylate potentiates glutamate toxicity in primary hippocampal cultures, J. Neurochem. 61 (1993) 2099–2103.
[38] H. Schulz, L. Nagymajtényi, A. Papp, I. Dési, Behavioural and neurophysiological consequences of subchronic mercury exposure in rats, Cent. Eur. J. Occup. Environ. Med. 3 (1997) 210–223.
[39] R. Singer, J.A. Valciukas, K.D. Rosenman, Peripheral nerve toxicity in workers exposed to inorganic mercury compounds, Arch. Environ. Health 42 (1987) 181–184.
[40] Y.E. Sirois, W.D. Atchison, Effects of mercurials on ligand- and voltage-gated ion channels: a review, Neurotoxicology 17 (1996) 63–84.
[41] G. Szumanska, R. Gadamski, J. Albrecht, Changes of the Na/K ATPase activity in the cerebral cortical microvessels of rat after single intraperitoneal administration of mercuric chloride: histochemical demonstration with light and electron microscopy, Acta Neuropathol. 86 (1993) 65–70.
[42] H. Tokoumi, M. Uchimo, S. Imamura, Minamata disease (organic mercury poisoning) neuroradiologic and electrophysiologic studies, Neurology 32 (1982) 1369–1375.
[43] D.J. Tracey, P.M. Waite, Somatosensory system, in: G. Paxinos (Ed.), The Rat Nervous System, vol. 2, Academic Press, San Diego, 1995, pp. 689–704.
[44] C. Zavariz, D.M.R. Glina, Neurophysiological clinical assessment of workers in an electric lamp factory exposed to metallic mercury, Rev. Saude Publica 26 (1992) 356–365.