PARALLEL CHANGES OF THE SPONTANEOUS AND STIMULUS-EVOKED CORTICAL ACTIVITY ELICITED BY ACUTE TREATMENT WITH INORGANIC MERCURY IN RATS.

Running head: Changes of cortical activity to acute mercury treatment

KEY WORDS: Mercury, cortex, electrocorticogram, sensory evoked potential, rat

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ABSTRACT: Mercury is known to affect the activity of the nervous system of animals and humans, as indicated by the multitude of neurological signs following e.g. occupational exposure. In animal experiments, heavy metals cause a variety of alterations in the central and peripheral nervous system activity but an explanation as to mechanism of action is missing in a number of cases. The aim of the work presented was to find correlation between the changes of spontaneous cortical activity (electrocorticogram, ECoG) and cortical sensory evoked potentials (EPs) recorded from rats acutely treated with mercuric chloride. Adult male Wistar rats were anesthesized with urethane. Silver recording electrodes were placed on the exposed left somatosensory projection area of the whiskers and of the tail. The corresponding peripheral sites were stimulated by electric pulses. During tail stimulation, compound action potentials of the tail nerve were also recorded. After at least 4 control records, mercury ($HgCl_2$, 7 mg/kg) was administered via a peritoneal cannula and the recording was continued for further ca. 2 hours. In the spontaneous activity, increased activity of the low and decreased activity of the high frequency bands was seen Simultaneously, the amplitude of the EPs increased. On the tail nerve potential, Hg caused an amplitude decrease and a latency increase. Latency increase of the cortical EP and the decrease of nerve conduction velocity evolved simultaneously. The alterations are likely due to some specific, and not to a general toxic, effect of Hg.

INTRODUCTION

Mercury is one of the metals which has been known since the antiquity. Its ongoing production and use (including traditional medicines) resulted in numerous cases of human exposure and intoxication. Today, large populations are being affected first of all by foodborne mercury compounds (ATSDR, 1999).

Humans exposed to Hg show a variety of symptoms from neuromuscular disorders (Kark, 1994) up to abnormalities of the higher nervous functions and changes of personality (Zavariz and Glina, 1992; Grandjean et al, 1997; Dolbec et al, 2000). Alterations of the cortical basal and evoked electrical activity have been described (Tokuomi et al., 1982; Piikivi and Tolonen, 1989; Counter et al 1998).

Dési et al. (1996) and Nagymajtényi et al. (2000) described the alterations of the electrocorticogram (ECoG) in rats following subchronic exposure to inorganic mercury. Changes were also found in the cortical evoked potentials (EPs) (Schulz et al., 1997; Papp et al., 2000). A

comprehensive explanation of the Hg-induced changes in the activity of the cortex is , however, missing, in spite of the numerous data on the effects of Hg^{2+} on ion channels (Sirois and Atchison, 1996), and calcium homeostasis (Denny and Atchison, 1996). The aim of the present work was to find correlation between the changes of ECoG and evoked potentials recorded from rats acutely treated with mercury chloride.

METHODS

The experiments were done on adult male Wistar rats (ca. 350 g b.w.). In urethane (1000 mg/kg b.w.) anesthesia, the head of the rats was clamped in a stereotaxic frame and the left hemisphere was exposed. Silver recording electrodes were placed on the somatosensory projection area of the whiskers (barrel field) and of the tail of the animal. The corresponding peripheral sites (whiskery skin and base of tail) were stimulated by electric pulses (ca. 4 V, 0.05 ms, 1 Hz). The pattern of recording consisted of a five-minute epoch of ECoG taken from both areas simultaneously. Then, EPs were recorded by applying one train of 20 stimuli to each of the peripheral sites. During tail stimulation, compound action potentials of the tail nerve were also recorded. This pattern was repeated every 20 minutes. After 5 control records, mercury ($HgCl_2$, 7 mg/kg) was administered via a peritoneal cannula and the recording was continued for further ca. 2 hours. On the EPs, amplitude and peak latency was measured by hand after automated averaging. Form the ECoG records, band activity was automatically computed and the ECoG index (delta+theta / $beta_1$+$beta_2$) calculated.

RESULTS

Both the spontaneous and the evoked cortical activity were altered by the acute Hg treatment. In the spontaneous cortical activity, a shift to lower frequencies was observed, at both recording sites (projection of the whiskers and the tail, respectively). The effect of Hg on the EP was seen as an increase of the peak-to-peak amplitude and of the latency of the two peaks. These effects were more pronounced on the whiskers projection area. On the tail nerve potential, Hg caused an amplitude decrease and a lower conduction velocity. The alterations of the cortical EP and the spontaneous activity evolved in parallel and were manifest only in animals treated with the higher dose of Hg.

In order to see if the changes of the ECoG and EPs were due to a common mechanism, correlation diagrams were plotted. As seen in *Fig. 1*, the changes in both parameters of the EPs were in strong correlation with the changes of ECoG.

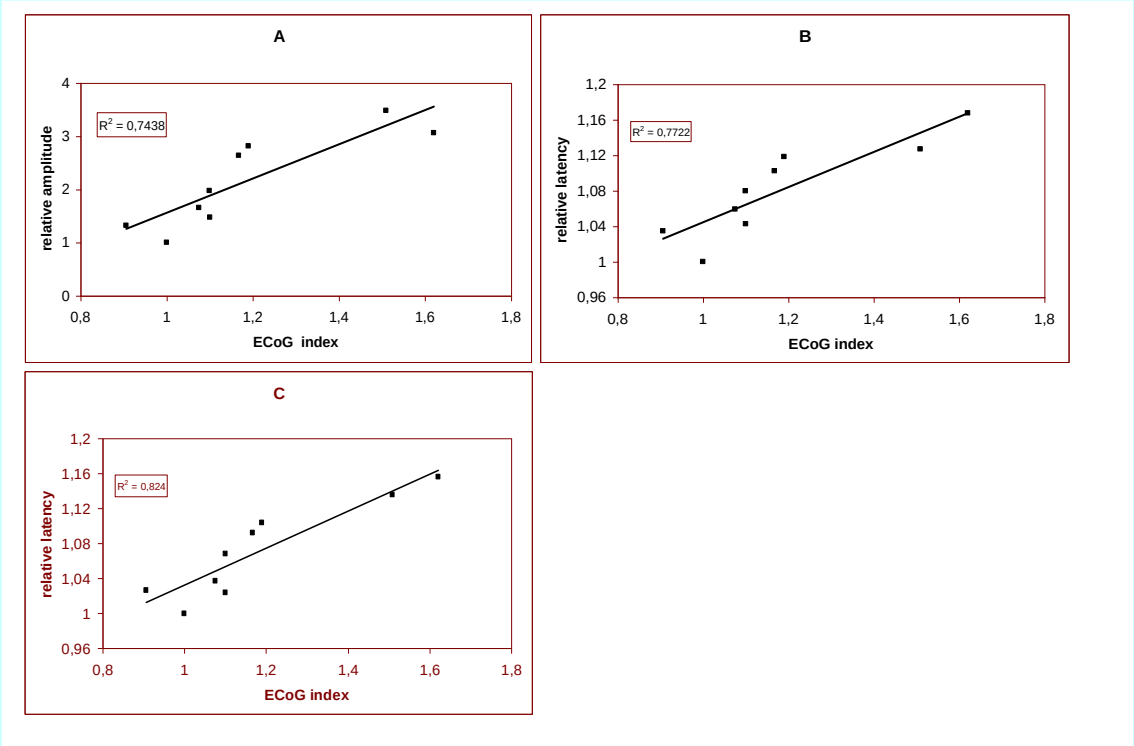

Fig. 1. Correlation diagrams between the ECoG index and the peak-to-peak amplitude (A), 1st peak latency (B) and 2nd peak latency (C) of the evoked potentials recorded from the whisker projection area. Insert: correlation coefficient. Linear regression lines fitted by EXCEL.

DISCUSSION

According to the results, there seems to be a clear correlation between the changes of spontaneous and stimulus-evoked cortical activity recorded from the somatosensory cortex of rats following acute treatment with inorganic mercury. In animal experiments, including those done earlier at our department, different heavy metals caused a variety of alterations in the

central and peripheral nervous system activity (Dési et al, 1996; Schulz et al., 1997; Nagymajtényi et al., 2000). However, there is as yet no comprehensive mechanistic explanation of the alterations observed.

In humans, exposure to various forms of Hg resulted in alterations of the spontaneous and evoked cortical activity. Minamata patients showed somatosensory evoked potentials where one of the wave components was missing. In he same subjects, there was also a sensory cortical atrophy (Tokoumi et al., 1982). Chloralkali workers, subject to long term, low level exposure to inorganic mercury, showed significantly slower rhythms and reduced EEG amplitude (Piikivi and Tolonen, 1989), and altered evoked potentials (Chang et al,, 1995), changes similar to those found by us in rats.

The observed amplitude increase of EPs and the shift of ECoG frequencies correspond to 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). Mercury reduces the activity of choline acetyltransferase (Dwivedi et al, 1980), glial uptake of glutamate (Brookes, 1988) and the sensitivity of GABA receptors (Narahashi et al, 1994), all indicating that components of the neurotransmitter and modulator systems are likely sites of action.

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