A Study on the Effect of Lead on Event-Related Potentials among Lead-Exposed Workers

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Abstract: Objectives: In order to clarify the effect of lead on higher cerebral functions, lead-exposed workers (Pb group) and controls were examined for event-related potentials. Subjects and Methods: Fourteen lead-exposed workers with a mean age of 57.1 yr (SD=4.27, range 48–64; lead concentration of whole blood ranged from 33 to 106 µg/dl with a mean of 58.6 and SD 28.6 µg/dl) and 19 age-matched control workers with a mean age of 57.3 yr (SD=4.80, range 48–65) were examined. Visual P300 was recorded by button pushing to the target image (minute checkerboard pattern, 20%), and the NO-GO potential by no button pushing to the target image (same as above, 50%). Results: Latencies of P300 in the Pb group (475 ± 46.0 ms) were significantly delayed compared with those in controls (407 ± 42.4 ms, p<0.01 by Student’s t test). Amplitudes of the NO-GO potential in the Pb group (4.59 ± 2.04 µV) significantly increased compared with those in the controls (3.18 ± 1.41 µV, p<0.05). Conclusion: The finding suggests that lead exposure affects high cerebral functions of cognition and attention, but is unclear in suppression of movement.

Key words: Lead-exposed workers, Visually stimulated P300, NO-GO potential, Latency

Introduction

The effects of lead on the central nervous system (CNS) of humans have been studied by many researchers with various methods. Of importance among them are electrophysiological methods such as electroencephalography (EEG), evoked potentials (EP) and event-related potentials (ERP). Studies on occupational effects on P300, most common ERP, with the conventional auditory oddball task have been conducted for many years1–9). Traditional P300 is followed by P300 with visual stimulation (V-P300) introduced by Couchense10). The latency of V-P300 prolonged about 100 msec and its amplitude increases about 20–30% compared with P300, but the basic characteristics of cognition and attention in the high cerebral functions and the generator of V-P300 are similar to those of P30011). In the occupational exposure to toxic chemicals, workers are often exposed to machine noise too, which may cause hearing loss. Since the hearing loss may affect the effective stimulation sound level of P300 measurement by means of auditory stimulation, the effect of noise exposure should be excluded from ERP measurement. Accordingly, V-P300 measurement avoiding auditory disturbance due to occupational noise exposure may be useful in evaluating the toxic effect of lead exposure among workers in the presence of noise exposure. Solliway et al. observed that latencies of the N2 and P300 components of visual event-related potentials among 21 individuals occupationally exposed to lead with PbB ranging from 29 to 53 µg/dl were significantly longer than those of 40 controls with a mean PbB of 7.7 µg/dl10). They also observed that both the N2 and P300 latencies significantly correlated with the blood lead levels of the subjects, and the P300 latency correlated with the concentration of delta-aminolevulinic acid (delta-
ALA) in urine.

Lead poisoning has been found to cause hyper-activity in children\(^\text{12}\), which may be explained as insufficient control of suppression. Gemba\(^\text{13}\) reported on NO-GO potential (NOGO-P) which is observed at the prefrontal and frontal area of the scalp by visual stimulation of colour discrimination. This potential is considered to be related to the suppression of hand movement (No-go) in button pushing. Consequently, we tried to apply NOGO-P using visual stimulation as an indicator of the suppression function in lead-exposed workers.

In this study, we employed V-P300 and NOGO-P measurement in order to clarify the effect of lead on the higher functions of the CNS.

**Subjects and Methods**

**Subjects**

The subjects were 14 lead-exposed workers (Pb group) with a mean age of 57.1 yr (SD, 4.27 yr; range, 48–64) and with a duration of exposure to lead averaging 26.8 yr (Table 1). There were five lead-copper metal casters, four lead-base paint manufacturers, three lead casters and two lead smelters. They were not suffering from diseases or injuries which might have affected the CNS function, had no past or current exposure to neurotoxicants except for lead, did not smoke 40 or more cigarettes a day and did not consume more than 80 ml of alcohol a day. This information was obtained from anamnesis and periodic health examination records. Seventeen normal controls were included in the study with the same criteria as for the lead-exposed workers. Information on their health was obtained by the same methods. Their ages were matched to within 2 yr of those of lead-exposed workers and averaged 57.9 yr (SD, 5.18 yr; range, 48–65) (Table 1). Their job titles are clerk (n=7), driver (n=6) and pensioner (n=4).

The subjects were informed of the objective and the procedure of the study, and gave us their written consent.

<table>
<thead>
<tr>
<th></th>
<th>Lead-exposed workers (n=14)</th>
<th>Controls (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>57.1 ± 4.27 (48–64)</td>
<td>57.9 ± 5.18 (48–65)</td>
</tr>
<tr>
<td>Exposure duration (yr)</td>
<td>26.8 ± 14.7 (6–46)</td>
<td>–</td>
</tr>
<tr>
<td>Lead in whole blood (µg/dl)</td>
<td>58.6 ± 28.6 (33–106)</td>
<td>–</td>
</tr>
</tbody>
</table>

**Methods**

A questionnaire on CNS symptoms was used in the present study. It was composed of four sections including physical symptoms, depressive symptoms, autonomic nervous symptoms and high-function-related symptoms (memory, judgment and thinking).

The examinations were conducted from 10 a.m. to 4 p.m. in order to avoid circadian fluctuations in ERP responses. The subjects were introduced to an electrically shielded box (1.4 m × 1.4 m × 0.7 m) and asked to sit in a chair under slightly dimmed lighting.

**ERP methods:** ERP tests were conducted by Sapphire 4EM electromyography (Medelec Co., UK) and VDO-SC98 visual stimulation system (NEC Medical Systems Co., Japan). Visual stimulation was conducted with a rough and minute checkerboard pattern through a cathode ray tube (CRT) with a duration of 100 ms at a distance of 1 m from the subjects. Both checkerboard patterns were put into the VDO-SC98 system from the Sapphire 4EM via a video camera. In this system, “check size 64” was called the minute checkerboard pattern and “check size 16” was the rough one. “Check size 64” was employed as the target image, and “check size 16” as the non-target image. Needle electrodes were inserted into the scalp subcutaneously at the Cz and Pz positions according to the 10–20 system. Two disk electrodes attached to both ears and connected to each other served as the reference electrodes. A disk electrode attached to Fpz in the 10–20 system served as the ground electrode.

In V-P300 measurement, the intervals between visual stimulations ranged from 2 to 3 s, and about 20% of the visual stimulations were target images. The 40 responses amplified with a band-path of 1.5 Hz to 50 Hz were averaged for 1 s analysis time. The subjects were instructed to push the button when the target image appeared.

In NOGO-P measurement, the intervals between visual stimulations ranged from 5 to 6 s, and about 50% of the visual stimulations were target images. One hundred responses amplified with a band-path of 1.5 Hz to 50 Hz were averaged for 1 s analysis time. The subjects were instructed not to push the button for the target image.
The figure shows typical wave patterns of ERPs of a lead-exposed worker.

**Method of measuring lead in whole blood:** Lead in whole blood (PbB) was applied for evaluation of the lead exposure level. PbB was measured by Kosaka’s method\(^1\). Control subjects were not examined according to anamnesis on occupational history without lead exposure.

**Statistical analysis**

The comparison of latencies and amplitudes of ERPs of the exposed and the controls was done with Student’s \(t\) test. Regression analysis was performed between ERP indicators and PbB in lead-exposed workers by Stat-view (Version 5.0).

**Results**

PbB of lead-exposed workers ranged from 33 to 106 \(\mu g/dl\) with mean of 58.6 and SD 28.6.

V-P300 and NOGO-P parameters among the Pb group and controls are shown in Table 2. V-P300 latencies of the Pb group (475 ± 46.0 ms) were significantly delayed compared with those of the controls (407 ± 42.4 ms, \(p<0.05\)). V-P300 amplitudes of the Pb group (19.3 ± 10.6 \(\mu V\)) tended to increase compared with those of the controls (16.5 ± 9.76 \(\mu V\)), but the difference was not significant. NOGO-P latencies of the Pb group (150 ± 9.24 ms) were slightly delayed compared with those of the controls (144 ± 15.9 ms), but the difference was not significant. Nevertheless, NOGO-P amplitudes of the Pb group (4.59 ± 2.04 \(\mu V\)) were significantly higher than those of the controls (3.18 ± 1.41 \(\mu V\), \(p<0.05\)).

**Discussion**

In the present study, we observed a significant delay in the latency of V-P300 and an increase in the amplitude of NOGO-P in lead-exposed workers compared with control subjects, but no significant correlation between ERP parameters and PbB was found.

Since Pb300 was observed only in response to the target stimulus, its latency is considered to be a measure of certain selective attention\(^1\) and of stimulus evaluation, one of the cognitive processes. In other words, the latency of Pb300 is a function of the time necessary for stimulus evaluation\(^1\). Since the latency of Pb300 correlates inversely with Digit Span subsets of the Wechsler Adult Intelligence Scale, a measure of recent memory, it is considered to be related to memory\(^1\).

The results of the present study in which we could not

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**Table 2. Latency and amplitude of V-P300 and NOGO-P in the subjects (Mean ± S.D.; Parenthesis, range)**

<table>
<thead>
<tr>
<th></th>
<th>Lead-exposed workers</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>V-P300</td>
<td>(n=14)</td>
<td>(n=16)</td>
</tr>
<tr>
<td>Latency</td>
<td>475 ± 46.0**</td>
<td>407 ± 42.4</td>
</tr>
<tr>
<td>(msec)</td>
<td>(397–590)</td>
<td>(360–468)</td>
</tr>
<tr>
<td>Amplitude</td>
<td>19.3 ± 10.6</td>
<td>16.5 ± 9.76</td>
</tr>
<tr>
<td>((\mu V))</td>
<td>(3.04–40.3)</td>
<td>(3.86–35.0)</td>
</tr>
<tr>
<td>NOGO-P</td>
<td>(n=14)</td>
<td>(n=17)</td>
</tr>
<tr>
<td>Latency</td>
<td>150 ± 9.24</td>
<td>144 ± 15.9</td>
</tr>
<tr>
<td>(msec)</td>
<td>(130–164)</td>
<td>(118–157)</td>
</tr>
<tr>
<td>Amplitude</td>
<td>4.59 ± 2.04*</td>
<td>3.18 ± 1.41</td>
</tr>
<tr>
<td>((\mu V))</td>
<td>(0.979–7.73)</td>
<td>(1.00–6.08)</td>
</tr>
</tbody>
</table>

*: \(p<0.05\) and **: \(p<0.01\) by Student’s \(t\) test. The measurement of V-P300 and NOGO-P of some control subjects was unsuccesful.
measure PbB in controls are partially compatible with Solliway’s observation\(^8\). The significant delay of the latency of V-P300 observed in the present study is considered to reflect changes in high CNS functions including attention, memory and cognition. Consequently, the results of the present study indicate that lead affects the high cerebral functions. Since the V-P300 task is simple and not affected by auditory disturbances in the environment, the measurement of V-P300 may be useful for studies on the CNS effects of occupational exposure to neurotoxicants.

In the present study, we tried to apply NOGO-P as an indicator of the suppression function in lead-exposed workers, but no significant differences were observed between the latencies of NOGO-P in the lead-exposed and control groups. However, the observed increase in the amplitude of NOGO-P in the lead group has unclear physiological significance, and further study of NOGO-P is needed.

Regression analysis between ERP indicators and the PbB level was done, but the results were not significant. It is difficult for us to discuss the correlation because the number of subjects was too small.

In the present preliminary study on the ERP effect among lead-exposed workers, significant delay in the V-P300 latency showed that lead exposure may affect the cerebral high function. We plan to continue investigations on the ERP effects among lead-exposed workers.

**References**


