Electroencephalographic studies on petrol intoxication: comparison between nonleaded and leaded white petrol

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Saito, K. (1973). British Journal of Industrial Medicine, 30, 352-358. Electroencephalographic studies on petrol intoxication: comparison between nonleaded and leaded white petrol. The effect of nonleaded and leaded petrol on the brains of rats was studied electroencephalographically. Bipolar electrodes were implanted on the brain surface between the frontal and occipital lobes of the left hemisphere. The rats were divided into two groups and were given by intraperitoneal injection 1 ml of either nonleaded white petrol (WP) or leaded petrol (LP) containing 1 000 ppm of tetraethyl lead per 100 g body weight. The electrocorticogram was observed for 10 days and the lead content of the brain, liver, and kidney was estimated.

The rats injected with leaded petrol showed excessive tension and excitement by the sixth or seventh day, and their body weight had diminished significantly by 10 days. One to three days after both LP and WP injection, the δ, θ, and α waves decreased significantly but the electrocorticogram from six or seven days after LP injection showed marked α and θ waves. The lead content in organs of the LP group was far greater than in those of the WP group and a correlation between the electrocorticogram and lead content was recognized.

The composition of petrol presents an important problem because of air pollution due to lead and photochemical substances contained in exhaust gases from motor vehicles (Hirschler and Gilbert, 1964; Konopinski and Upham, 1967; Colucci, Begeman, and Kumler, 1969; Kobayashi, Hori, and Tsuchiya, 1970; Pierrard, 1972). Their effects on the population (Hofreuter, Catcott, Keenan, and Xintaras, 1961; Hyuga et al., 1970) have become a serious matter. We have previously reported on the toxicity and lead content of commercially available regular petrol and high octane petrol in relation to the survival rate of rats and their electrocorticograms (ECoG) (Saito, Inai, and Takakuwa, 1972). Petrol is largely composed of n-heptane and n-hexane and contains more than 10 kinds of hydrocarbons such as n-octane, n-decane, toluene, and xylene. Its toxicity is, therefore, complicated by this composition and the mixing rate of alkyl lead. Tetraethyl lead is a liquid and is fat-soluble; it is therefore much more toxic than inorganic lead. We have experienced this intoxication in Japan (Asada, 1953; Yamaga et al., 1959). Although the toxicity of tetraethyl lead per se is not a general environmental problem, it is very important for us, who specialize in environmental health, to be familiar with the toxicity of tetraethyl lead and petrol.

In this experiment a comparison was made between
Materials and methods

The skulls of 19 white male Wistar rats, weighing 330 to 453 g and aged 7 months, were drilled under Nembutal-ether anaesthesia about 3 mm from the left side of the sagittal suture at points 1-3 mm above and below the coronary suture. Bipolar electrodes, having a small socket for a transistor and with a silver globular tip 0-7 mm in diameter to protect the cortex from injury, were implanted on the surface of the brain about 3 mm apart over the frontal and occipital lobes of the left hemisphere. The electrodes were attached on the skull permanently with dental cement. The rats were divided into two groups, one containing 12 rats and the other seven. The former group was given white petrol only (WP) and the latter group white petrol containing 1000 ppm lead (LP); in both groups the petrol was injected into the abdominal cavity in a dose of 1 ml/100 g body weight. The tetraethyl lead content of the petrol (LP) was 1-0 mol/l, that is, 16-5 mg/kg body weight of rat. The LD₅₀ value for tetraethyl lead is 13-2 to 18-0 mg/kg (Cremer, 1965).

The observations were made one month after recovery from the implant operation. The ECoG was recorded one day before and 1, 2, 3, 4, 5, 7, and 10 days after injection respectively. It was measured under normal conditions in an electrically shielded chamber with a 13-channel electroencephalograph and ECoG frequency analyzer (Nihon Kohden Model ME 132B and 4B). The primary trace, the ongoing activity in the ECoG (δ wave 2-4 Hz, θ wave 4-8 Hz, α wave 8-13 Hz, β₁ wave 13-20 Hz, β₂ wave 20-30 Hz), and each 10-second integral value of these waves were averaged for 5 to 10 minutes of a recording.

At the end of a 10-day experimental period, the rats were decapitated, and it was confirmed histologically that the electrodes were on the surface of the cortex. At the same time the brain, liver, and kidney were taken out. Lead contained in these organs was extracted with APDC MIBK after wet-ashing with sulphuric and nitric acids and determined by atomic absorption spectrophotometry (Hitachi Model 207).

Results

Clinical symptoms

The rats in the electrically shielded chamber before administration of petrol were restless at first, walked up and down the length of the chamber, and tried to rub off the lead wires fitted on the head and to climb up the side wall of the chamber. In about 10 minutes they settled down, and the ECoG was recorded without fluctuation. One to four days after petrol injection the rats showed slowing of movements, a crouching posture, and absence of reaction to stimuli. Walking movements appeared from five days after injection. One to four days after petrol injection behaviour such as crouching was more noticeable in the LP group than in the WP group.

After the fifth day from petrol injection, the rats in the WP group gradually approached their pre-injection state, but the rats in the LP group showed excessive tension, excitement, anxiety, and sensitivity to stimuli such as sudden noise and movement. These abnormal states reached a climax at seven or eight days after LP injection. After the tenth day from injection, the rats quietened down from excitement.

Changes in body weight

The body weights of the rats in both groups before petrol injection are shown in Table 1. The average body weight of the WP group before injection was 389-4 g and that of the LP group 396-4 g. The body weight 10 days after petrol injection was 351.8 g in the WP group and 298.0 g in the LP group. The body weights of both groups decreased significantly compared to their original weights. Decrease of body weight in the LP group was more significant compared to that in the WP group.

<table>
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<th>Before injection</th>
<th>10 days after injection</th>
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<tr>
<td>WG</td>
<td>389-4 ± 13-5</td>
<td>351-8 ± 10-81</td>
<td>−37-6 ± 3-5²</td>
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<tr>
<td>LG</td>
<td>396-4 ± 13-1</td>
<td>298-0 ± 24-3³</td>
<td>−98-4 ± 15-5²</td>
</tr>
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</table>

Mean ± SE ²Change significant at 10% level ³Change significant at 5% level ⁴Change significant at 1% level

body weight of the WP group before injection was 389-4 g and that of the LP group 396-4 g. The body weight 10 days after petrol injection was 351.8 g in the WP group and 298.0 g in the LP group. The body weights of both groups decreased significantly compared to their original weights. Decrease of body weight in the LP group was more significant compared to that in the WP group.

ECoG before and after petrol injection

The control ECoG before injection showed a dominant θ wave and marked α and δ waves, and the amplitudes of these waves ranged from 50 to 150 microvolts. An ECoG after WP injection showed decreases in the δ, θ, α, and β₁ waves. The β₂ wave was inclined to increase, and the rats showed a state of slow motion and a crouching posture at this time. The α waves of rats in the LP group increased markedly and dominantly seven days after LP injection (Fig. 1). At this time the rats showed excessive excitement and tension. This progression is shown in Tables 2 and 3 and in Figure 2. In comparison with the control ECoG, only the α wave decreased significantly one, two, and three days after WP injection (p < 0.05), but from four days after WP injection no significant changes were shown. One to three days after LP injection there was a significant decrease of the δ and
FIG. 1. ECoG changes in rats injected with leaded petrol (LP); before injection and 1, 3, 5, 7, and 10 days after injection: primary trace, ongoing activities of δ, θ, α, β₁, β₂, and the integral values for 10 seconds.

θ waves as well as a significant increase of the α wave at seven days and the θ wave at 10 days after LP injection (p < 0.05). Significant differences were observed when changes of these waves in the WP group were compared with those in the LP group (p < 0.05). At 10 days after LP injection only the θ wave showed a significant change.

Amount of lead in organs and its correlation with the ECoG
The amounts of lead in the brain, liver, and kidney 10 days after WP injection and 10 days after LP injection are shown in Figure 3. The average values and standard errors in microgrammes per gramme wet weight of the WP group 10 days after injection
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FIG. 2. The changes of δ, θ, α, β1, and β2 waves for the 10-day experimental period (mean ± standard error).

were 0.35 ± 0.06 in the brain, 0.54 ± 0.22 in the liver, and 0.38 ± 0.12 in the kidney. Those of the LP group were 7.65 ± 0.78 in the brain, 7.79 ± 1.04 in the liver, 13.89 ± 2.40 in the kidney, and 12.67 ± 1.91 in the blood. The amount of lead in the organs of the WP group was smaller than that of the LP group.
### TABLE 2
AVERAGE INTEGRAL VALUES OF ECoG (µV/10 sec) IN RATS INJECTED WITH 1 ML/100 G BODY WEIGHT OF NONLEADED PETROL

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1Change significant compared to value before injection at 10% level.

### TABLE 3
AVERAGE INTEGRAL VALUES OF ECoG (µV/10 sec) INJECTED WITH 1 ML/100 G BODY WEIGHT OF LEADED PETROL

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1Change significant compared to value before injection at 1% level
2Change significant compared to value before injection at 5% level
3Change significant compared to value before injection at 10% level
The acute toxic symptoms caused by absorption of petrol are headache, dizziness, delusions, drowsiness, anxiety, excitement, staring, delirium, diminution of tendon reflexes, tremor, faintness, nausea, vomiting, abdominal pain, foaming at the mouth, lowering of body temperature, chilliness of the skin, cyanosis, etc. (Patty, 1963). The symptoms of tetraethyl lead poisoning are insomnia, lack of appetite, nausea, vomiting, irritability, restlessness, nervousness, anxiety, tiredness, excessive dreaming, emotional instability, hallucinations, excitement, delirium, etc. (Cassells and Dodds, 1946; Cremer, 1959; Sanders, 1964). We have previously reported the effect of commercially available regular petrol and high octane petrol on rats and indicated that the toxicity of these petroils was greater than that of nonleaded white petrol, and that these results suggested that the toxicity of petrol was greatly complicated by various combinations of three factors—the quantity and quality of the petrol, and the alkyl lead added to it. Almost all of the rats injected with regular petrol and high octane petrol died with acute poisoning in the previous experiment (Saito et al., 1972), but in the present experiment almost none of the rats injected with LP died during the same 10-day experimental period. The most characteristic clinical symptoms of the LP group of rats in this experiment were excessive tension and excitement, anxiety, and sensitivity to stimuli, as also reported by Cremer (1965). In the previous experiment (Saito et al., 1972) the rats injected with regular petrol and high octane petrol showed nystagmus and convulsions of the extremities about two or three days after injection but almost all died three to five days after injection. The dominant basic pattern of the ECoG before injection, especially the δ, θ and α waves, significantly decreased one to three days after LP injection, and the rats showed loss of appetite, no desire for water, ataxia, drowsiness, dullness, crouching, and a lowered body temperature. The diminution of basic pattern and these clinically severe symptoms in the LP group were significantly more pronounced than those in the WP group. From about the sixth or seventh day after injection the rats of the LP group showed excessive tension and excitement but the rats in the WP group did not show such symptoms and approached the control state. These results also indicate that the acute toxicity of LP is greater than that of WP.

The ECoG during excessive tension and excitement from the sixth or seventh day after LP injection showed a remarkable increase of the α and θ waves. The lead content of the brain, liver, and kidney five days after LP injection was about two to four times that at 10 days after injection (Saito, 1972). Walker and Boyd (1952) and Ermakov and Murashov (1969) reported on the ECoG of a patient poisoned by tetraethyl lead, but they did not suggest by what mechanism the changes in the ECoG were brought about. We suggest that the striking increase of α and θ waves is due to a direct action of triethyl lead, particularly on the brain stem reticular formation. It is known that tetraethyl lead is converted to triethyl lead by the liver and that the triethyl lead enters the brain (Cremer, 1959; Hayakawa, 1972). Whether the changes in electrical activity are a consequence of metabolic disturbances, such as those described by Cremer (1959, 1964, 1965) on glucose and amino acid metabolism, or whether they are due to a direct action on nerve membranes remains unanswered.

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References


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