Notes

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Effects of centrally Acting Drugs on Cerebellar and Cerebral Electroencephalogram in Young Chickens

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The nature and origin of the cerebellar electrical activity induced by epileptogenics have been well investigated in mammals.[2-4] The cerebellar electroencephalogram (EEG) in chicks was recently reported.[5] However, there are no published pharmacological reports on chick cerebellar EEG experiments, although cerebral EEG studies in chicks have been done by many authors from both physiological[6,7] and pharmacological[8-10] aspects. In the present study, an experiment was made to examine the chick cerebellar and cerebral responses induced by drugs and research a clue to the action of a neurotoxic substance, lyoniol-A.

Material and Method

The experiments were performed on male young chicks (Golden neck strain, weighing 40—80 g) ranging in age from 3 to 14 days after hatching. Animals were fixed on the self-made stereotaxic apparatus, immobilized by gallamine triethiodide and artificially ventilated. The recording electrodes were made from insect pins insulated except for approximately 0.5 mm of the tips. The electrodes fixed to a plastic plate were implanted through the skull on the surface of cerebral and cerebellar cortices (Fig. 1). EEG recordings were done by Nihon-kohden RM-150 polygraph. In some experiments, EEGs were recorded without gallamine and under restraint. Several control experiments were included in each series. The body temperature was maintained constant using an infrared lamp. Drugs were dissolved in 0.9% saline, and injected into the jugular vein through a cannula except for the intraperitoneal injection of chloralose.

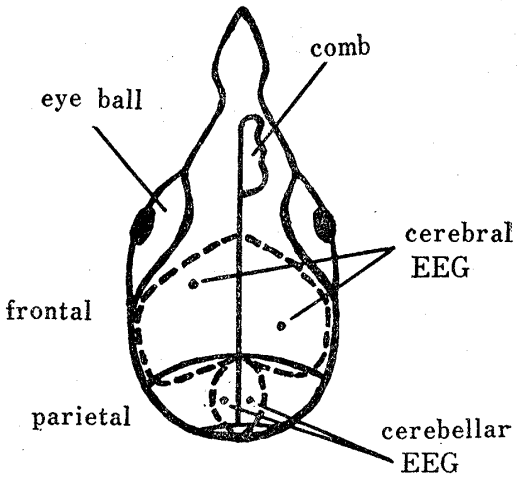

Fig. 1. Dorsal View of the Head of a Young Chick

Dotted lines represent the projected outline of the brain.

Result and Discussion

Spontaneous EEG patterns of gallamine-immobilized chicks were characterized by low amplitude (5—15 μV) fast waves in the cerebellum and waves with amplitude of approxi-

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mately 100 μv in the cerebrum. Without gallamine and under restraint, cerebral EEG patterns were almost the same as those of gallamine-immobilized chicks, and when the chick closed its eyes EEG patterns with high amplitude appeared in the cerebrum as reported by Ookawa, *et al.*[6]

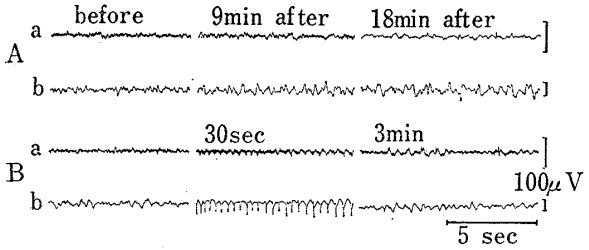

Fig. 2. Electroencephalographic Responses induced by Chloralose and Strychnine in Young Chicks

a) cerebellar EEG pattern
b) cerebral EEG pattern
A: chloralose 60 mg/kg, *i.p.*, B: strychnine nitrate 1.0 mg/kg, *i.v.*

Following the injection of chloralose (60 mg/kg, *i.p.*), cerebral EEG patterns were changed to high amplitude slow waves, whereas no changes in cerebellar EEG patterns could be found. Approximately 20 min later, cerebral EEG patterns with higher amplitude appeared and fast wave components of cerebellar EEG disappeared (Fig. 2A).

Strychnine nitrate (1.0 mg/kg, *i.v.*) caused a reduction of amplitude followed by convulsive waves in cerebellar and cerebral structures (Fig. 2B). The increase of mean frequency was remarkable in the cerebellum. Even after convulsive waves disappeared in the cerebrum,spike-like patterns in the cerebellum remained unchanged (Fig. 2B). Following the injection of pentylenetetrazol (30 mg/kg, *i.v.*) EEG patterns in the cerebellum were changed at the same time as those in the cerebrum (Fig. 3A). Marossero, *et al.*[11] found in cats that pentylenetetrazol (100 mg/kg, *i.v.*), while inducing the well-known change in cortical activity, evoked the

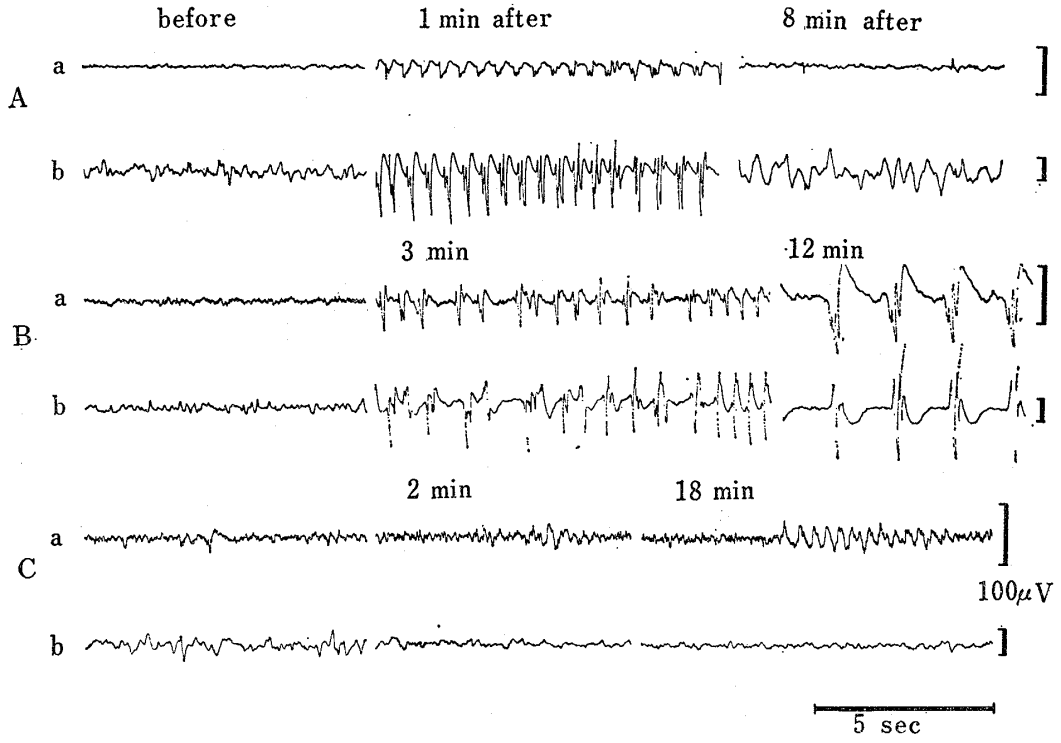

Fig. 3. Electroencephalographic Responses induced by Pentylenetetrazol, Picrotoxin and Lyoniol-A in Young Chicks

a) cerebellar EEG pattern b) cerebral EEG pattern
A: pentylenetetrazol 30 mg/kg, *i.v.*, B: picrotoxin 2.0 mg/kg, *i.v.*, C: lyoniol-A 8.0 mg/kg, *i.v.*

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synchronous change in cerebellar activity. With picrotoxin (2.0 mg/kg, *i.v.*), cerebral EEG patterns with high amplitudes occurred and several min later convulsive waves developed in both structures (Fig. 3B).

We have studied a neurotoxic substance, lyoniol-A,[12a,b] which disturbs motor function of animals and causes a peculiar posture. It seems worthwhile to examine the effect of this substance on the chick cerebellum. Lyoniol-A (8.0 mg/kg, *i.v.*) caused a decrease of amplitude and an increase of mean frequency in the cerebellum and a decrease of amplitude in the cerebrum. Approximately 20 min later, peculiar synchronized patterns developed in the cerebellum although no changes could be found in the cerebrum (Fig. 3C). Without gallamine and under restraint, the low amplitude fast waves induced by lyoniol-A in the cerebrum continued even when the chick closed its eyes, indicating the arousal state of the cerebrum. In our previous study in rats,[12c] lyoniol-A accelerated the EEG arousal patterns in the motor cortex while showing no clear modification of electrical activity in the cerebellum, hippocampus and amygdala. In chicks the cerebellum seems to be more sensitive than the cerebrum in contrast to rats. These results suggest the advantage of employing birds for the study on the drugs which affect the motor function or posture regulation.

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Studies on the Syntheses of Analgesics. XXXIII.[1] Synthesis of N-Methyl-N-[2-(3-methoxyphenyl)-2-phenyl]propylhydrazine (Studies on the Syntheses of Heterocyclic Compounds. CDXCVI.[2])

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In the previous papers, we reported syntheses of ethyl 2-(ω-aminoalkyl)-2-(3-methoxyphenyl)phenylacetates[4] and 1,2,3,4,5,6-hexahydro-2,6-methano-3-methyl-6-phenyl-2,3-benzo[*g*]diazocines,[1] in which one nitrogen was introduced instead of the C_2-carbon of benzomorphan ring, using 1-(3-methoxyphenyl)-1-phenylacetonitrile (III)[5] as a starting material for the purpose of getting the drugs effective to the central nervous system, particularly to analgesic activity. Since the azamorphinan derivative (I),[6] prepared by Kametani, was proved to

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2) Part CDXCV: T. Kametani and K. Fukumoto, *Synthesis*, in press.
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