INFLUENCES OF DRUGS ON EVOKED POTENTIALS IN THE CAT CEREBELLUM: I. EFFECTS OF CNS DEPRESSANTS AND STIMULANTS ON THE CEREBELLAR AFFERENT PATHWAYS

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Abstract—The effects of drugs on the potentials evoked by electrical stimulation on the sensorimotor area (SMA), nucleus reticularis tegmenti pontis (PTRN), nucleus reticularis lateralis (LRN), nucleus olivaris inferior (ION), or superficial radial nerve (SR) were investigated in cat cerebellar cortices. Pentobarbital-Na decreased the amplitude of the potentials evoked by all stimulations at every recording site. Pentobarbital-Na remarkably decreased the SMA- or PTRN-stimulation induced evoked potentials in the anterior lobe. Chlorpromazine decreased the amplitude of the potentials evoked by SMA stimulation on the anterior lobe and ipsilateral crus I, and the drug increased it on the posterior lobe and contralateral crus I. With precerebellar nuclei stimulations, chlorpromazine decreased the amplitude of the evoked potentials in cerebellar cortices, whereas SR stimulation-evoked potentials were remarkably increased in amplitude. Meprobamate increased the amplitude of the potentials evoked by precerebellar nuclei or SR stimulation at an early stage and then decreased it. Caffeine, picrotoxin, and strychnine remarkably increased the amplitude of the potentials in cerebellar cortices evoked by all stimulations. Strychnine in particular significantly increased the amplitude of the potentials evoked by SR stimulation. These results strongly indicate that CNS depressants and stimulants affect the cerebellar afferent pathways, probably in an indirect manner.

The cerebellum is constructed of stereotyped and relatively simple neuronal arrangements which can be regarded as "neuronal machinery" designed to process the input information in some unique and essential manner (1). Furthermore, it is considered that the cerebellum plays an important role as a coordinator of information for the fine control of movements. The functions of the areas of the cerebellar cortices such as the vermis, pars intermedia, and hemisphere have been elucidated. The connections and functions of cerebellar neurons have been electrophysiologically and anatomically investigated (2-4). With regard to the relations between the cerebrum and the cerebellum, it is known that the electrical stimulation of the motor, premotor, and somatosensory areas produces evoked potentials in the cerebellar anterior lobe (5-7). Two main pathways were found to deliver information to the cerebellum from the cerebral cortex: one projects via the nucleus pontis, nucleus olivaris inferior, or nucleus
rubber to the cerebellum with somatotopic localization, and the other projects via the nucleus reticularis lateralis or nucleus reticularis tegmenti pontis to the cerebellum without somatotopic localization (8-12). Pertaining to the connections from the peripheral nerve to the cerebellum, it has been reported that the pathway projects to the vermis of the anterior and posterior lobes via the nucleus reticularis lateralis or nucleus olivaris inferior (spino-reticulo-cerebellar tract (SRCT) or spino-olivo-cerebellar paths (SOCPs)) and that the pathway directly projects from the forelimb via spinal cord neurons to the IV and V folia of the cerebellar cortex (cuneocerebellar tract (CCT) or rostral spinocerebellar tract (RSCT)) (13, 14).

With regard to pharmacological studies with the cerebellum, although the direct effects of various drugs on cerebellar Purkinje cells have been studied (15-18), few attempts have been made to study the effects of drugs on evoked potentials in the cerebellum induced by electrical stimulation of cerebellar afferent pathways.

In the present study for the purpose of investigating the influence of drugs on cerebellar neuronal activities, we studied the effects of CNS depressants and stimulants on the evoked potentials in cerebellar cortices produced by the stimulation of the SMA, PTRN, LRN, ION, or SR.

MATERIALS AND METHODS

Fifty-six adult cats (2.5-4.0 kg, either sex) were fixed on a stereotaxic instrument (Todai Nohken type), and a tracheal cannula was inserted under ether anesthesia. The femoral artery was cannulated to monitor the blood pressure, and the femoral vein was cannulated for injection of drugs. The sensorimotor area (SMA) was exposed by removing the cranial bone and dura, and the superficial radial nerve (SR) of the forelimb was dissected. The SMA and SR were stimulated in a pool of warm paraffin oil. To record the evoked potentials the occipital bone was partly removed to expose the vermis, pars intermedia, and hemisphere which were then covered with a pool of warm paraffin oil and kept between 36-38°C. Stainless steel concentric electrodes with a diameter of 0.8 mm were inserted stereotaxically into the nucleus reticularis tegmenti pontis (P: 1.0, L: 0.5, H: -6.0), nucleus reticularis lateralis (LRN: P: -9.5, L: 4.0 H: -8.2), and nucleus olivaris inferior (ION: P: -9.5, L: 2.5, H: -9.5) according to the atlas of Snider and Niemer (19), and a bipolar platinum electrode with a 2 mm polar separation was used to stimulate the SR. Recordings were obtained from the anterior lobe, posterior lobe, ipsilateral crus I, and contralateral crus I of the cerebellum with bipolar silver ball electrodes. A reference electrode was placed on the temporal muscle. A digital stimulator (MEC) was used to stimulate the SMA (20 V, 0.5 msec, a single rectangular wave), PTRN, LRN, ION, and SR (4 V, 0.1 msec a single rectangular wave) with a single pulse generated at a rate of 1 time per 3 sec. After the cat recovered from ether anesthesia, the experiments were conducted under artificial respiration (25 rpm, 12.4 ml/stroke) and paralysis with gallamine triethiodide (5-10 mg/kg, i.v.). Blood pressure, ECG, heart rate, body temperature, Hb and O2 saturation were recorded throughout the experiments. At the end of the experiment, the brain was removed and fixed in 10% formalin solution and then (sliced into 50 μm thick series sections) in order to histologically verify the areas of electrode insertion. Evoked potentials were averaged by a signal processor (Model 7T07, San-ei Instrument Co.) via a medical-oscilloscope (Model 311, San-ei Instrument Co.), and the averaged signals were recorded on an X-Y recorder (Model WX442, Watanabe). The
drugs used were pentobarbital sodium (Nembutal sodium solution, Abbott), chlorpromazine hydrochloride (Shionogi), meprobamate (Daichi), caffeine (caffeine and sodium benzoate, Hoei Yakuko), picrotoxin (Wako), and strychnine nitrate (Teikoku). Drugs for injection were dissolved in 0.9% saline, except for meprobamate which was dissolved in 2% Tween 80. The statistical significance of the data obtained was assessed using the two-tailed Student's t-test.

RESULTS

As shown in Figs. 1–3 (controls) and Table 1, the evoked potentials consisting of

![Fig. 1. Effects of pentobarbital-Na (7.5 mg/kg, i.v.) on the potentials evoked by sensorimotor area (SMA), superficial radial nerve (SR), nucleus reticularis tegmenti pontis (PTRN), nucleus reticularis lateralis (LRN), or nucleus olivaris inferior (ION) stimulation on the posterior lobe of the cerebellar cortex. Each evoked potential (negative upward) is the average of those obtained by 20 repetitive stimuli. The potentials evoked by SMA and SR stimulations were recorded at 5, 60, and 240 min after drug administration, and those by PTRN, LRN, and ION stimulations were at 10, 20, and 240 min. The timing of the stimulus is indicated by the dots.](image-url)
the negative (fast) and positive (late) components were produced by electrical stimulation of the SMA, PTRN, LRN, ION, or SR, respectively, in the anterior lobe, posterior lobe, ipsilateral crus I, and contralateral crus I of the cerebellum. The effects of CNS depressants and stimulants such as pentobarbital sodium, chlorpromazine, meprobamate, caffeine, picrotoxin, and strychnine were investigated on the negative component alone. The positive (late) component was inconsistently observed and therefore was not evaluated.

1. Pentobarbital-Na: The effects of pen-

![Graph showing effects of meprobamate on evoked potentials](image)

**Fig. 2.** Effects of meprobamate (30 mg/kg, i.v.) on the potentials evoked by sensorimotor area (SMA), superficial radial nerve (SR), nucleus reticularis tegmenti pontis (PTRN), nucleus reticularis lateralis (LRN), or nucleus olivaris inferior (ION) stimulation on the posterior lobe of the cerebellar cortex. Each evoked potential (negative upward) is the average of those obtained by 20 repetitive stimuli. All evoked potentials shown were recorded at 30, 180, and 300 min after drug administration. The timing of the stimulus is indicated by the dots.
Pentobarbital-Na (7.5 mg/kg, i.v.) on the amplitude of evoked potentials in the cerebellar cortices are shown in Table 2 and Fig. 1. Pentobarbital-Na decreased the amplitude of the potentials evoked in each cerebellar cortex by SMA, PTRN, LRN, ION, or SR stimulation. The decreasing actions of this drug on the potentials evoked by SMA stimulation were more potent than those by precerebellar nuclei stimulations, particularly when recorded on the anterior lobe at 5 min. Although decreased am-

![Graph showing evoked potentials](image)

**Fig. 3.** Effects of strychnine nitrate (0.05 mg/kg, i.v.) on the potentials evoked by sensorimotor area (SMA), superficial radial nerve (SR), nucleus reticularis tegmenti pontis (PTRN), nucleus reticularis lateralis (LRN), or nucleus olivaris inferior (ION) stimulation on the posterior lobe of the cerebellar cortex. Each evoked potential (negative upward) is the average of those obtained by 20 repetitive stimuli. All evoked potentials shown were recorded at 10, 60, and 240 min after drug administration. The timing of the stimulus is indicated by the dots.
Table 1. Peak time of the evoked potentials produced by SMA, PTRN, LRN, ION, or SR stimulation on cat cerebellar cortices

| Recording sites       | Component | Stimulating sites (means±S.E. (msec)) |
|-----------------------|-----------|-------------------------------------|
|                       |           | SMA       | PTRN     | LRN       | ION       | SR       |
| Anterior lobe         | negative  | 8.0±0.9   | 5.8±1.3  | 6.2±1.4   | 5.7±1.2   | 24.3±3.1 |
|                       | positive  | 29.8±1.1  | 39.4±4.9 | 40.3±5.6  | 37.5±5.8  | 45.0±2.4 |
| Posterior lobe        | negative  | 7.2±1.0   | 6.1±1.4  | 6.0±1.3   | 5.9±0.9   | 22.5±3.4 |
|                       | positive  | 28.0±2.3  | 40.2±5.3 | 40.7±5.0  | 38.1±6.4  | 46.5±7.9 |
| Ipsilateral crus I    | negative  | 7.9±1.3   | 6.0±0.9  | 6.4±2.1   | 5.8±1.3   | 25.5±4.0 |
|                       | positive  | 28.3±2.0  | 40.6±6.3 | 39.0±5.5  | 41.6±7.8  | 46.5±8.6 |
| Contralateral crus I  | negative  | 7.8±1.2   | 6.0±0.8  | 6.4±1.3   | 5.8±1.3   | 24.6±3.3 |
|                       | positive  | 32.6±7.1  | 38.5±6.4 | 41.1±5.8  | 35.0±7.4  | 48.3±7.5 |

SMA: sensorimotor area, PTRN: nucleus reticularis tegmenti pontis, LRN: nucleus reticularis lateralis, ION: nucleus olivaris inferior, SR: superficial radial nerve. Abbreviations are the same for all Tables and Figures.

plitudes gradually returned to the control levels on the vermis with SMA stimulation, they were still lower than the control level even 300 min after pentobarbital-Na administration. On the bilateral crus I, recovery occurred after 120–180 min. With precerebellar nuclei stimulations, the potentials evoked by PTRN stimulation were more greatly decreased by pentobarbital-Na than those by LRN or ION stimulation, particularly on the anterior lobe at 10 min. Recovery was seen after 180–210 min. In the case of SR stimulation, pentobarbital-Na decreased the amplitude of the evoked potentials in all cerebellar cortical regions. The depressant actions of pentobarbital-Na on the potentials evoked by SR stimulation were stronger than those on the potentials produced by LRN or ION stimulation. Recovery was seen after 180–240 min on the vermis and after 90–180 min on the bilateral crus I.

2. Chlorpromazine hydrochloride: The effects of chlorpromazine hydrochloride (CPZ: 7.5 mg/kg, i.v.) on the amplitude of evoked potentials on cerebellar cortices are also shown in Table 2. CPZ decreased the amplitude of the potentials evoked by SMA stimulation on the anterior lobe and the ipsilateral crus I, while on the posterior lobe and contralateral crus I. CPZ increased the amplitude. Recovery was seen at 120–180 min later. In the case of PTRN, LRN, or ION stimulation, CPZ also decreased the amplitude of the evoked potentials on all recording sites. On the other hand, CPZ increased the amplitude of the potentials evoked by SR stimulation on each recording site, in contrast to the results of SMA or precerebellar nuclei stimulation.

3. Meprobamate: The effects of meprobamate (30 mg/kg, i.v.) on the amplitude of evoked potentials on cerebellar cortices were then studied (Table 2 and Fig. 2). Although meprobamate immediately decreased the amplitude of the potentials evoked by SMA stimulation, those by PTRN, LRN, ION, or SR stimulation were increased by this drug at an early stage and then decreased later on every recording site. In the case of SMA stimulation, recovery was seen at 240–300 min. A similar biphasic action of meprobamate was also observed on the amplitude of the potentials evoked by SR stimulation.

4. Caffeine: The effects of caffeine (10 mg/kg, i.v.) on the amplitude of evoked
| Test substances | Recording Sites | SMA                  | PTNR                | Stimulating sites | LRN                  | ION                  | SR                   |
|-----------------|----------------|----------------------|---------------------|--------------------|----------------------|----------------------|----------------------|
| Pentobarbital-Na| AL             | -64±15** (5)         | -40±11** (10)       | LRN                | -20±9* (10)          | -20±7** (10)         | -38±12** (5)         |
|                 | PL             | -50±12** (5)         | -27±8** (10)        |                    | -10±8 (10)           | 20±8** (20)          | -35±9** (5)          |
|                 | ILC            | -52±8** (5)          | -28±5** (10)        |                    | -24±6* (10)          | 25±7** (10)          | -35±7** (5)          |
|                 | CLC            | -49±15** (5)         | 26±6** (10)         |                    | -22±9** (10)         | 25±6** (5)           | -23±8** (5)          |
| Chlorpromazine  | AL             | -15±7* (80)          | 17±9* (30)          | LRN                | -24±8* (30)          | -50±12** (150)       |                     |
|                 | PL             | +19±6** (80)         | -31±10** (30)       |                    | -27±10** (30)        | 49±11** (120)        |                     |
|                 | ILC            | -25±5** (80)         | -18±9* (30)         |                    | -18±9* (30)          | 45±15** (150)        |                     |
|                 | CLC            | +8±2** (60)          | -7±3* (30)          |                    | 10±7 (30)            | 21±7** (45)          | 60±10** (120)        |
| Meprobamate     | AL             | -27±7** (180)        | -45±12** (300)      | LRN                | +16±8* (30)          | 52±15** (300)        | -38±6** (270)        |
|                 | PL             | +11±5** (45)         | +13±7* (30)         |                    | +6±2* (30)           | +5±2* (30)           |                     |
|                 | ILC            | -30±10** (180)       | -40±15* (300)       |                    | -38±9* (300)         | -66±12** (300)       | 47±11** (270)        |
|                 | CLC            | -27±5** (180)        | -35±6* (300)        |                    | -49±17* (300)        | 58±10** (300)        | -45±14** (270)       |
|                 |                | +15±8* (45)          |                    |                    | +17±6* (30)          | 15±6* (30)           | 14±6* (30)           |
| Caffeine        | AL             | +40±12** (10)        | 14±7* (30)          | LRN                | 10±5* (90)           | 6±2* (30)            | 40±10** (5)          |
|                 | PL             | +30±8* (15)          | 14±8* (30)          |                    | 15±7* (90)           | 10±6* (30)           | 38±8* (5)            |
|                 | ILC            | +31±6* (15)          | 20±8* (30)          |                    | 10±6* (90)           | 10±5* (30)           | 28±8* (5)            |
|                 | CLC            | +37±10** (15)        | 18±6* (30)          |                    | 8±2* (90)            | 7±2* (30)            | 26±6* (5)            |
| Picrotoxin      | AL             | +56±13* (45)         | 31±8* (90)          | LRN                | 20±7* (90)           | 10±5* (30)           | 82±18** (30)         |
|                 | PL             | +43±10** (45)        | 10±5* (60)          |                    | 21±8* (90)           | 18±7* (30)           | 53±11** (30)         |
|                 | ILC            | +25±7* (60)          | 21±9* (60)          |                    | 60±15** (90)         | 14±6* (30)           | 20±8* (30)           |
|                 | CLC            | +30±9* (30)          | 29±8* (90)          |                    | 33±6* (90)           | 17±9* (30)           | 46±13** (30)         |
| Strychnine      | AL             | +78±18** (120)       | 59±14** (90)        | LRN                | 70±18** (60)         | 36±9** (60)          | 94±18** (10)         |
|                 | PL             | +35±8* (120)         | 24±7** (90)         |                    | 75±16** (60)         | 35±8** (60)          | 96±11** (20)         |
|                 | ILC            | +44±11** (120)       | 33±9* (60)          |                    | 43±11** (60)         | 18±7* (60)           | 94±15** (20)         |
|                 | CLC            | +41±12** (120)       | 46±11** (60)        |                    | 55±13** (60)         | 38±11** (60)         | 94±9** (20)          |

Each value in the Table indicates the percent change with respect to the control value (before treatment) and is shown as the mean±S.E.M. of 5 determinations. (−: percent decrease; +: percent increase). In the case of meprobamate, the upper and the lower lines show the values at an early stage and at a later stage, respectively. *P<0.05, **P<0.01 significant differences vs the control value. The number in parentheses indicates the time (minutes) that each drug showed the maximal effect. AL: anterior lobe, PL: posterior lobe, ILC: ipsilateral crus I, CLC: contralateral crus I. Abbreviations are the same for all successive Figures and Tables.
potentials on cerebellar cortices are also shown in Table 2. Caffeine increased the amplitude of the potentials evoked by SMA, PTRN, LRN, ION, or SR stimulation. In particular, its increasing actions on the potentials evoked by SMA stimulation were remarkable at 10–30 min. Recovery was seen at 210–240 min. Similarly, the amplitude of the potentials evoked by SR stimulation on the cerebellar cortices were also increased remarkably 30–60 min after the administration of caffeine. Recovery was seen at 240–270 min.

5. Picrotoxin: The effects of picrotoxin (0.2 mg/kg, i.v.) on the amplitude of evoked potentials on cerebellar cortices are shown in Table 2. Picrotoxin increased the amplitude of the potentials evoked by SMA, PTRN, LRN, ION, or SR stimulation. In particular, the increasing actions of picrotoxin on the potentials evoked by SMA or SR stimulation were observed to be greatest at 30–60 min on the anterior and posterior lobes. In the case of SMA stimulation, recovery was seen at 300 min on the vermis and at 150–180 min on the bilateral crus I. With SR stimulation, recovery was seen at 150–210 min. On the other hand, the augmentative actions of picrotoxin on the potentials evoked by precerebellar nuclei stimulations were less remarkable than those by SMA or SR stimulation, and maximal effects were seen at 90–120 min.

6. Strychnine nitrate: The effects of strychnine nitrate (0.05 mg/kg, i.v.) on the amplitude of evoked potentials on cerebellar cortices are shown in Table 2 and Fig. 3. Strychnine increased the amplitude of the potentials evoked by SMA, PTRN, LRN, ION, or SR stimulation. In particular, its increasing actions on the potentials evoked by SR stimulation were remarkable at 10–20 min regardless of the recording sites. Over 300 min was required for a return to the control levels. In the case of precerebellar nuclei stimulations, especially for the LRN, there were also augmentative actions on the amplitude of the potentials at 60–90 min. Recovery was seen at 300 min on the vermis and at 180–240 min on the bilateral crus I.

DISCUSSION

Experiments with cats were carried out using cerebellar evoked potentials to determine whether CNS depressants and stimulants could modulate cerebellar neuronal activities.

With regard to the projections from the cerebral cortex to the cerebellum, many pathways have been reported such as those via the nucleus pontis, nucleus olivaris inferior (ION), nucleus ruber, nucleus reticularis lateralis (LRN), or nucleus reticularis tegmenti pontis (PTRN) etc. (8–12, 20). Pertaining to the projections from the superficial radial nerve (SR) to the cerebellum, the following pathways have been reported: the pathway projecting to the cerebellar cortex via the LRN (SRCT) or ION (SOCPs), and the pathway directly projecting from the forelimb to the cerebellar cortex (CCT or RSCT) (13, 14).

Among these numerous afferent pathways to the cerebellum, we chose the following afferent pathways: the pathway from the SMA as that from the cerebral cortex, the pathway from the SR as that from the peripheral nerve, and the pathways from the PTRN, LRN, or ION as those from precerebellar nuclei which have the majority of projecting fibers to the cerebellum and somatotopic localization; and we examined the effects of various drugs on these pathways to the cerebellum in the present study.

Pentobarbital-Na was found to decrease the potentials evoked by SMA stimulation on cerebellar cortices and those by the stimulations of precerebellar nuclei particularly the PTRN. Therefore, it was indicated that this drug influenced predominantly the
pathways from the SMA via precerebellar nuclei to cerebellar cortices. Pentobarbital-Na also decreased not only the amplitude of the potentials evoked by SR stimulation in each cerebellar cortex, but also the amplitude of the potentials evoked by the stimulation of the precerebellar nuclei, LRN, or ION. These results suggest that pentobarbital-Na influences the pathways via LRN or ION, namely, the SRCT or SOCPs. However, because the decreasing actions of this drug on the cerebellar potentials evoked by SR stimulation were more potent than those on the potentials evoked by LRN or ION stimulation, the effects of this drug on the CCT or RSCT could not be excluded. As it was reported that pentobarbital-Na depressed the cerebral cortex or the reticular formation (21, 22), the depressant actions of this drug on the cerebellar potentials evoked by SMA stimulation seemed to be due to the inhibition of the cerebral cortex or precerebellar nuclei, particularly the PTRN. However, it was found in this study that this drug decreased the potentials evoked not only by SMA or precerebellar nuclei stimulation but also by SR stimulation. Thus, from our results, pentobarbital-Na inhibited almost all the cerebellar afferent pathways.

The decreasing or increasing action of chlorpromazine hydrochloride (CPZ) on the potentials evoked by SMA stimulation was observed on each recording site, while the potentials evoked by precerebellar nuclei stimulations were decreased by CPZ. Thus, the decreasing actions of CPZ may be due to the inhibition of electrical activities in the pons and reticular formation or inhibition of neighboring precerebellar nuclei. Yokota (23) and Killam and Killam (24) also reported that CPZ had a suppressive action on the reticular formation.

With regard to the increasing effect of CPZ, the facilitating action of CPZ on the amygdala afterdischarge has been reported by Delgado and Mihailovic (25) and Yamamoto and Kido (26). Sager et al. (27) reported that hippocampal stimulation in cats induced the evoked potentials on the cerebellar cortex, indicating the presence of pathways between them. From our results, it was inferred that the increasing effects of CPZ were involved with the facilitation of the activity of the limbic system. However, possible effects of CPZ on precerebellar nuclei except for PTRN, LRN, and ION, such as the nucleus ruber, nucleus raphe, or nucleus reticularis paramedianus, cannot be excluded. CPZ increased the potentials evoked by SR stimulation on all recording sites. We consider that the augmentative effects of CPZ may be due to the inhibition of the descending inhibitory system, which was demonstrated by Magoun (28) as early as 1963. CPZ produced either the enhancement or the inhibition of the cerebellar evoked potentials depending upon differing stimulating and recording sites.

Meprobamate increased at an early stage and then decreased the potentials evoked by PTRN, LRN, ION, or SR stimulation on every recording site. We consider that the enhancing effects of meprobamate on the evoked potentials may be due to the enhancement of the function of the brainstem reticular formation. Pertaining to the pharmacological action of meprobamate, it has been demonstrated that this drug produced either an enhancement or an inhibition of the functions on many cerebral regions including the midbrain reticular formation, etc., and this depended upon differing doses of this drug or the recording regions (29–32). Therefore, it may be suggested that meprobamate influences the PTRN, LRN, or ION lying in the brainstem reticular formation and thus shows biphasic actions. Similar biphasic actions of this drug on the potentials evoked by SR stimulation were also observed on the cerebellar cortices, probably this effect being
also due to the influences of meprobamate on the LRN or ION. Thus, meprobamate produced the inhibition of input from the SMA to the cerebral cortex, while it produced a biphasic action on the cerebellar potentials evoked by precerebellar nuclei and SR stimulations.

Caffeine increased the potentials evoked by all stimulations, in particular that of the SMA, on every recording site. Caffeine has been reported to enhance the functions of the cerebral cortex, spinal cord, medulla oblongata, and hippocampus, etc. (33). Therefore, it was considered that the enhancing effects of caffeine on the potentials evoked by SMA stimulation may be due to its direct action on the cerebral cortex. The augmentative actions on the potentials evoked by LRN or ION stimulation were less remarkable than those by SR stimulation. These results indicate that caffeine significantly influences the pathways which project directly to the cerebellum—CCT or RSCT. Thus, from our results, caffeine enhanced almost all cerebellar afferent pathways.

Picrotoxin increased the potentials evoked by all stimulations, particularly those of the SMA or SR, on every recording site. Furthermore, its augmentative actions on the potentials evoked by precerebellar nuclei stimulations were less remarkable than those by SMA or SR stimulation. We considered that the augmentative actions of picrotoxin on the potentials evoked by SMA stimulation may be due to the enhancement of pathways not from the PTRN, LRN, or ION to the cerebellar cortex, but rather from the nucleus pontis, nucleus raphe, or nucleus ruber, etc., or by the direct action of picrotoxin on the cerebral cortex.

Strychnine increased the potentials evoked by all stimulations, in particular the SR, regardless of the recording site. It can be inferred that the augmentative actions of strychnine on the potentials evoked by SR stimulation may be due to the potentiation of the activities of the spinal cord. Eccles et al. (34) also demonstrated that strychnine specifically antagonized the postsynaptic inhibition in the spinal cord. Furthermore, since there were also augmentative actions on the potentials evoked by precerebellar nuclei stimulations, especially that of the LRN, strychnine appears to also potentiate the SRCT or SOCPs.

In conclusion, it generally has been said that the cerebellum influences the motor system, etc. and is hardly affected by drugs. However, as reported above, CNS depressants and stimulants which have been said not to influence the cerebellum exhibited considerable effects on the cerebellar afferent pathways in respective mechanisms and manners. Therefore, it is conceivable that the cerebellar function may be altered by these drugs and hence affects the functions of the cerebral cortex or elsewhere.

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