Ethanol Inhibits Vestibular and Caloric Nystagmus without Affecting Optokinetic Nystagmus in Rabbits

Yoshie MATSUI1,2, Satoshi KASHII2, Masashi SASA1, Shuji TAKAORI1 and Yoshihito HONDA2
Departments of 1Pharmacology and 2Ophthalmology, Faculty of Medicine, Kyoto University, Sakyo-ku, Kyoto 606, Japan
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Abstract—Effects of ethanol on optokinetic, vestibular and caloric nystagmus were investigated in pigmented rabbits to determine whether or not it affects a specific site involved in the induction of various nystagmus. Optokinetic nystagmus was produced by rotation of the drum with vertical stripes at an angular velocity of 0.85°/sec. Vestibular nystagmus was induced by horizontal rotation at an angular velocity of 30°/sec and caloric nystagmus by infusion of cold water into the external meatus. Cumulative injection of ethanol into the auricular vein to doses of 0.1, 0.2, 0.4 and 0.8 g/kg inhibited both vestibular and caloric nystagmus dose-dependently, but did not affect the optokinetic nystagmus. These results suggest that relatively low doses of ethanol mainly act on the peripheral vestibular organ and impair the vestibular function without affecting the optokinetic system.

Acute effects of ethanol on the central nervous system are not uniform; that is, cerebellar Purkinje cells are highly sensitive to ethanol (1, 2), but the visual pathway to the cerebral cortex, including the lateral geniculate nucleus neurons, is not (3). In addition, ethanol inhibits synaptic transmission in the lateral vestibular nucleus neurons, which are monosynaptically activated by vestibular nerve stimulation and mainly project to the spinal cord, but it has little effect on the transmission of the medial vestibular nucleus neurons, which predominantly project to the nuclei innervating the eye muscles (4), although some type I neurons identified by horizontal rotation in the vestibular nuclei are inhibited by ethanol (5).

Ethanol is also known to induce positional and gaze nystagmus (6-9) and inhibit vestibular nystagmus (VN) (10). However, the site in the vestibulo-ocular and optokinetic pathways predominantly affected by ethanol has not been determined. Therefore, we investigated the effects of a low dose of ethanol on VN, optokinetic nystagmus (OKN) and caloric nystagmus (CN).

Materials and Methods

Pigmented rabbits each weighing 2–3 kg were put in a box with the animal's head immobilized by a collar and mouthpiece in a sound-proof room. Horizontal eye movement was recorded by electro-oculography (EOG). The signals amplified by an amplifier (Nihon Kohden: AN-601G) were recorded on a 4-channel recticorder (Nihon Kohden: RJG-4124). The time constant for recording VN and CN was 3.0 and 0.03 sec, respectively. OKN was recorded using amplifiers with DC and the time constant of 0.03 sec.

For recording OKN, the animal was placed in the center of an OKN-drum (1 m in diameter) with black stripes, 1.5 cm in width, at 30° interval along the longitudinal axis. OKN was induced by rotating the drum in a clockwise (CW) or counter-clockwise (CCW) direction at a constant angular velocity of 0.85°/sec. From the DC recording, the amplitude and slow-phase velocity of the nystagmus were measured; and then the gain, which was expressed as a slow phase eye velocity divided by the drum velocity and represented the ability to pursuit the object.
was calculated. The number of OKN was not measured since the occurrence of OKN does not follow the all-or-none law during rotation of the drum at a constant angular velocity. The calculation was done at the steady state of OKN, usually 30 sec after starting the rotation of the drum. For recording VN, the animal was placed on a turntable in a dark room. The VN was elicited by horizontal rotation of the turntable in the CW or CCW direction at a constant angular velocity of 30°/sec for 30 sec. The number and velocity of the rapid phase of both per- and post-rotatory nystagmus (nystagmus seen during the rotation and nystagmus after cessation of the rotation, respectively) were measured before and after injection of ethanol since they are not affected by compensatory eye deviation, which is seen in the direction opposite to that of the rotation. The numbers of per- and post-rotatory nystagmus were counted during the rotation and immediately after cessation of the rotation until the appearance of the final nystagmus, respectively. CN was induced by infusing cold water (20°C, 15 ml) for 10 sec into the left external meatus in a dark room. The number and duration of CN were measured between the initial and final appearance of the nystagmus after caloric stimulation. The amplitude and velocity of the CN were not measured, since these parameters, recorded using a time constant of 3 sec, are greatly affected by body movement, which is sometimes induced by caloric stimulation.

EOG recording was calibrated by eliciting OKN with rotation of the OKN-drum at a velocity of 0.85°/sec in the CW and CCW direction as described by Collewijn (11) who assumed a gain of 1 in the control state. Ethanol (10%, W/V) dissolved in saline was injected at 5-min intervals into the auricular vein to cumulative doses of 0.1, 0.2, 0.4 and 0.8 g/kg, and the eye movements on the EOG were recorded 3 min after each administration. The blood ethanol level was also determined 3 min after administration of each dose of ethanol by gas chromatography in 4 rabbits.

Results

Blood ethanol level: Blood ethanol level increased in a dose-dependent manner and reached 0.15% after the administration of 0.8 g/kg (Fig. 1).

Calibration: To test the reliability of the method of calibrating EOG, the eye was held at the tendon of the lateral rectus muscle and then artificially moved 5 mm, which corresponds to approximately 15° (12) to the lateral side while recording the eye movements on the EOG. There were no differences between the calibration after ethanol ad-

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Fig. 1. Blood ethanol level (%) following intravenous administration of a cumulative doses of ethanol. Blood samples were collected 3 min after each administration. The level is expressed as means±S.E. n=4.

Fig. 2. The calibration of eye movement after administration of ethanol as compared with that before the drug administration. The dotted line shows the control level before the drug administration. Each point indicates a mean±S.E., n=3.
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Fig. 3. Effects of ethanol on optokinetic nystagmus (OKN) and vestibular nystagmus (VN). a: The OKN-drum was rotated in the clockwise (CW) or counterclockwise (CCW) direction at a constant angular velocity of 0.85°/sec. b: VN was induced by rotating the turntable at a constant angular velocity of 30°/sec in the CW and CCW direction in the horizontal plane as shown on the upper line. In all nystagmograms, an upward deflection indicates the right direction.

ministration and that before the administration (Fig. 2). When 0.8 g/kg of ethanol was administered, the calibration was 99±3.2% (S.E., n=3) of that before the drug administration. Therefore, the calibration obtained before ethanol administration was also used after the administration.

OKN: When the drum was rotated, OKN was induced with a rapid phase in the direction opposite to that of drum rotation. There were no alterations in OKN with ethanol up to 0.8 g/kg in 7 of the 8 animals (Fig. 3). In the remaining animal, OKN was inhibited with ethanol at 0.8 g/kg, although it was unaffected by the drug up to 0.4 g/kg. The mean amplitude and gain of OKN were not inhibited by ethanol up to 0.8 g/kg, although 0.2 g/kg of ethanol increased the gain of OKN without any effects on the amplitude (Fig. 4).

VN: VN during rotation in a horizontal plane was induced with a rapid phase in the same direction as that of the rotation; and immediately after abruptly stopping the rotation, VN was produced with a rapid phase in the opposite direction to that of the rotation. Intravenous administration of ethanol dose-dependently inhibited VN in all 4 animals examined (Fig. 3). When ethanol (0.8 g/kg) was applied, per- and post-rotatory VN were completely blocked in 3 and all 4 animals examined, respectively, although only slight
per-rotatory VN was elicited in the remaining animal. The mean number and velocity of the rapid phase VN including both per- and post-rotatory VN were dose-dependently decreased (Fig. 5). However, compensatory eye deviation in the direction opposite to that of the rotation of the turntable was still observed in all 4 animals even with 0.8 g/kg of ethanol. When 0.8 g/kg of ethanol was given, the mean deviations during and after the rotation were 11.50° (7.77°–14.35°) and 12.01° (7.36°–16.10°), respectively.

**CN:** When cold water was infused into the left external meatus, the rapid phase of the nystagmus was in the right direction (contralateral to the infusion site) (Fig. 6). CN was dose-dependently inhibited by ethanol at doses up to 0.8 g/kg in all 4 animals tested. Ethanol also dose-dependently decreased the mean duration and number of CN (Fig. 7). However, OKN was not affected by ethanol up to 0.8 g/kg in 4 animals, although CN was completely inhibited in these animals by the administration of 0.8 g/kg of ethanol.

**Discussion**

The blood level of ethanol increased linearly with the increase in cumulative dose administered. Under these conditions, VN induced by the horizontal rotation was inhibited when the amount of infused ethanol...
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Fig. 7. Effects of ethanol on the duration and number of caloric nystagmus. Each point indicates a % mean±S.E. (n=4) when the control value before ethanol administration is expressed as 100%.

*P<0.05, **P<0.01, as compared with the control.

exceeded 0.1 g/kg and was completely blocked by 0.8 g/kg of ethanol. These results agree with those obtained in humans (10) and rabbits (13), although the blood level of ethanol was not measured in those studies. The caloric response to ethanol was similar to that with rotation-induced nystagmus; the caloric response was inhibited by 0.2 g/kg of ethanol. The inhibition of CN has also been observed in humans (7), although the blood level of the drug has not been determined. It is noteworthy that VN and CN were respectively inhibited by a blood ethanol level as low as 0.02 and 0.04%, concentrations which do not induce remarkable psychomotor function (14). By contrast, OKN was not affected by administration of ethanol up to 0.8 g/kg, which resulted in a blood level of 0.15%. This blood level of ethanol induces ataxia, but OKN can still be produced. In rabbits, impulses from the retina pass through the subcortical (extrageniculate) pathway; that is, they pass through the nucleus of the optic tract and the nucleus reticularis tegmenti pontis (15-18) to the vestibular nuclei. On the other hand, rotational and caloric stimuli excite hair cells in the semicircular canal, and the resultant impulses arrive at the same vestibular nuclei as optokinetic impulses. These impulses caused by optokinetic and vestibular stimuli enter the same ascending pathway to the nuclei innervating eye muscles via the vestibular nuclei (19, 20). Therefore, our findings that a low dose of ethanol inhibits VN and CN suggest that ethanol predominantly acts on the peripheral vestibular organs such as hair cells. However, at higher doses over 0.4 g/kg, ethanol simultaneously inhibits the lateral vestibular nucleus neurons, which project to the spinal cord and contribute to control of the body balance, as reported previously (16, 21). In contrast to our finding that ethanol did not affect OKN in rabbits, Schroeder observed an inhibition of OKN by ethanol in man (10). Human OKN exhibited two patterns: foveal and full-field OKN, which result from a cortical and subcortical mechanism, respectively (22), while the rabbit shows only full-field OKN (11). Therefore, foveal OKN in man may be affected by ethanol via action on the cortical areas.

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