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Wild Running and Switch-Off Behavior Elicited by Electrical Stimulation of the Inferior Colliculus: Effect of Anticonvulsant Drugs

ABDALLAH BAGRI, GUY SANDNER AND GEORGES DI SCALA

L.N.B.C., Centre de Neurochimie du C.N.R.S. 5, rue Blaise Pascal F-67084 Strasbourg Cedex, France

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BAGRI, A., G. SANDNER AND G. DI SCALA. *Wild running and switch-off behavior elicited by electrical stimulation of the inferior colliculus: Effect of anticonvulsant drugs.* PHARMACOL BIOCHEM BEHAV **39**(3) 683–688, 1991.—The behavioral and motivational effects of electrical stimulation of the inferior colliculus (IC) were investigated. Electrical stimulations of either the dorsal part or ventral part of the IC both elicited wild running (WR). Nevertheless, the ventral part was found more sensitive than the dorsal part, as lower intensities were needed to elicit WR. Moreover, WR differed depending on the part of the IC stimulated. It stopped as soon as the stimulation was switched off when the ventral IC was stimulated, whereas it further persisted in a poststimulus WR when the dorsal IC was stimulated. This poststimulus WR was abolished by anticonvulsant drugs such as diazepam, phenytoin or sodium valproate. In an operant escape conditioning paradigm (switch-off test), only stimulation of the ventral IC readily sustained switch-off learning. Dorsal IC stimulations did not, possibly because of the poststimulus enduring effects of the stimulation, as evidenced by poststimulus WR. Indeed, the anticonvulsant drugs which abolished this poststimulus WR also permitted switch-off of dorsal IC stimulations. It is concluded that electrical stimulations of the IC (dorsal or ventral) elicit aversive effects and that WR elicited either by ventral or dorsal stimulation may represent the overt expression of these aversive effects.

Electrical brain stimulation Inferior colliculus Wild running Switch-off behavior Epilepsy Aversion Diazepam Phenytoin Sodium valproate

WILD running behavior characterizes the initial step of audiogenic seizures in the rat [see for review (11)]. The inferior colliculus (IC) is known to play a key role in the audiogenic seizure susceptibility and the elicitation of wild running (WR). Thus audiogenic seizure susceptibility has been attributed to an alteration of the GABAergic neurotransmission within the IC (9,17), and, indeed, microinjections of a GABA A antagonist, bicuculline methiodide, into the IC induced a susceptibility to audiogenic seizures in normal rats (3). Besides, direct activation of the IC by electrical stimulations was shown to elicit WR and seizures (2,12).

Behavioral reactions similar to WR, namely running and jumping, have been reported during electrical stimulations of other mesencephalic structures such as the periaqueductal gray (PAG), the superior colliculus (SC) and the cuneiform nucleus (CN) (6, 20–22). In several instances, it has been shown that these behavioral reactions were the overt expression of an aversive state. Thus electrical stimulation of the PAG, the SC, or the CN supported operant escape learning in a switch-off situation (5, 6, 14, 15, 20–22). Despite the similarity of the behavioral effects of IC stimulations with effects of the stimulation of these structures, no systematic study exists that tested if the electrical stimulation of the IC induces aversive effects.

In the present study, we have analyzed the behavioral and motivational effects of electrical stimulation of the IC. More precisely, we have verified that WR is elicited by electrical stimulation of the dorsal IC, as described previously (12). Since bicuculline microinjection into the ventral IC, another means to excite the neuronal substrate, elicited WR as well (1), we furthermore assessed the effects of a stimulation applied to the ventral IC. Since dorsal IC stimulation-induced WR had been related to a paroxystic activity (12), we tested the effects of three anticonvulsant drugs on WR. Furthermore, since WR was similar to those behavioral responses related to aversion, we assessed the putative aversive effects of electrical stimulation of the dorsal and ventral parts of the IC in a switch-off paradigm. These putative aversive effects were further studied in the presence of anticonvulsant drugs.

METHOD

Animals and Surgery

Forty-one male Wistar rats weighing 250–300 g at the beginning of the experiment were used. They were kept on a 12/12-h dark/light cycle and housed in individual cages with food and water supplied ad lib.

The rats were anesthetized with a mixture of ketamine (125 mg/kg, IP) and diazepam (3 mg/kg, IP). A twisted pair of enameled nichrome wires (125 μm in diameter) was implanted bilaterally into each inferior colliculus. The tips of the wires in each pair were vertically separated by 1.5 to 2 mm. For the

lower electrode, the following coordinates were used, the lambda serving as reference for every plane: AP: −0.2, ML: 1.8, DV: 6.0 mm. Two frontal and two occipital stainless steel screws anchored a microconnector to the skull by means of dental cement. One of the pins of the microconnector was connected with one of the screws (ground wire). Each of the remaining pins was connected with an implanted electrode.

Stimulation Procedures and Behavioral Measurements

Parametric study for the elicitation of WR. This experiment was performed with a group of 17 rats. One week after surgery, each rat was placed into an experimental area limited by a cylindric transparent wall made of Plexiglas (60 cm in diameter and 100 cm high). One of the electrodes was connected to a stimulator delivering a continuous train of negative pulses (duration: 0.5 ms). The stimulating intensity was continuously monitored on an oscilloscope across a 100 kohm resistor included in the stimulation circuit. In a subgroup of 8 rats, the threshold intensities for the elicitation of WR by stimulation of the ventrally located electrodes were determined. The interpulse interval (IPI) was set to 20 ms, and the initial intensity was set to 20 μA. The stimulation train was applied during 10 s, then switched off during 30 s, then increased by a 25-μA step and applied again and so on until WR occurred (with a cutoff intensity of 400 μA). The threshold intensity necessary for the elicitation of WR as well as the duration of the latter were recorded. In the remaining 9 rats, a similar procedure was used for electrodes located dorsally. Since WR elicited outlasted the end of the stimulation, the effect of varying the IPI on the duration of the poststimulus WR was studied at threshold. The IPIs (10, 20, 30 and 40 ms) were tested in a random sequence, and the use of two differing IPIs was separated by a 48-hour rest period.

Effect of anticonvulsant drugs on the duration of WR. Six rats were used to evaluate the effects of anticonvulsant drugs on the duration of poststimulus WR elicited by stimulation of dorsal IC. The threshold intensity was determined at an IPI = 20 ms. The duration of the poststimulus WR was recorded at threshold before and 10 minutes after the administration of diazepam (1 mg/kg), phenytoin (30 mg/kg), valproic acid (200 mg/kg), and vehicle (saline). At least 48 hours separated two consecutive randomized pharmacological treatments. A control without any injection was available from the parametric study described before.

Switch-Off Training and Measurement

Parametric study of the switch-off response. Among the 18 remaining rats, 10 were selected that showed stimulation elicited WR from a pair of ipsilateral electrodes (dorsal and ventral). Each rat took part in a shaping session. During this session, the rat was first allowed to habituate to the test cage for 10 min. The front wall of that cage comprised a lever connected to a computer. A press of the lever switched off the intracerebral stimulation for 15 s (switch-off test). The IPI was set at 20 ms. The stimulation intensity was initially set to 20 μA, then it was increased by 5-μA steps until WR occurred. The rat was progressively shaped to press the lever. Any one of the four electrodes was used randomly for switch-off shaping.

After the end of the shaping period, one electrode sustaining switch-off behavior was selected for switch-off training. The rat was then submitted daily to two training sessions for one week.

After this switch-off training period, the rat was submitted to a switch-off measurement session. The stimulation pulse train applied to the electrode used for training was driven by a computer which also recorded the switch-off latency according to a procedure previously described (4). The salient feature of this system is the fact that the computer: 1) selects an IPI value randomly chosen within a range predetermined by the experimenter, 2) sets on the electrical stimulation at this IPI, 3) switches off the stimulation when the rat presses the lever, and 4) records the switch-off latency (SOL), i.e., the time elapsed between the onset of the stimulation and its offset by the rat. Fifty SOL were recorded during each measurement session.

Following the switch-off measurement sessions, transfer of switch-off learning to the other electrodes was tested. The transfer test was preceded by a 10-min warming up period during which the rat was allowed to switch off the stimulation applied to the electrode used for the switch-off training. Then the stimulation was commutated to another electrode, and the rat was directly submitted to a measurement session.

Switch-off measurement under anticonvulsant drugs. Nine rats among the 10 with the dorsal and the ventral electrodes positive for WR elicitation were treated with diazepam, phenytoin and valproate in a random sequence. Most rats were treated with the three drugs. Ten minutes after an IP administration of one of the drugs, the SOL versus IPI relationship was evaluated for the training electrode. Transfer of switch-off learning to the other electrodes was further tested under pharmacological treatment in other similar measurement sessions.

Histology

On completion of the experiments, the rats were killed by an overdose of pentobarbital and perfused intracardially with NaCl 0.9% followed by 4% formalin. Serial 20-μm brain sections were stained with cresyl violet in order to localize the stimulation sites which were then drawn on the corresponding frontal planes of the atlas of Paxinos and Watson (16).

Data Analysis

For statistical computations, Dixon BMDP software was used (8). One-way analyses of variance were used to assess: 1) the dependence of the threshold intensities on the location of the stimulating electrode (2 levels, dorsal versus ventral), 2) the dependence of the duration of the poststimulus WR on the IPI (4 levels: IPI of 10, 20, 30 and 40 ms), and 3) the dependence of the duration of the poststimulus WR on the nature of the anticonvulsant drug used (4 levels: saline, diazepam, phenytoin and sodium valproate).

For the switch-off measurement, raw data corresponding to 50 IPI obtained during the measurement session were used for data analysis. A semilogarithmic transformation of the SOL versus IPI function yielded a linear relationship. A regression line was computed for each measurement session using a least square criterion. Each regression line was characterized by its slope, its ordinate at the origin and its residual variance. A two-way analysis of variance was used to assess the dependence of the slope of the SOL versus IPI relationship on the drug used (within factor, 3 levels: diazepam, phenytoin and sodium valproate) and on the location of the stimulating electrode (in between factor, 2 levels: dorsal versus ventral).

RESULTS

Elicitation of WR by Electrical Stimulation

Threshold intensities eliciting WR. At lower intensities (just below threshold), the rat stopped its ongoing behavior and showed a freezing attitude as soon as the stimulation was set on. At threshold intensity, the stimulation of the IC elicited wild running (WR) 2 to 7 s after the onset of the stimulation. This

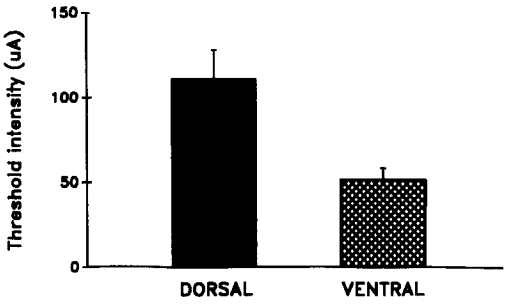

FIG. 1. Mean threshold intensities for the elicitation of WR from dorsal IC sites (filled bargraph) and ventral IC sites (crosshatched bargraph). The interpulse interval (IPI) was set to 20 ms.

WR consisted in fast running, directed ipsilaterally to the stimulation electrode side, which was sometimes interspersed with jumps. For ventral sites, jumps occurred all along the stimulation period. For dorsal ones, jumps occurred only at the beginning of the WR period. The threshold intensity depended on the placement of the stimulating electrode within the IC. Figure 1 shows that threshold intensities for the elicitation of the WR were lower in rats that were stimulated through ventral electrodes than in those stimulated through dorsal ones. A one-way analysis of variance (2 levels: dorsal versus ventral) confirmed that this dorso-ventral difference was significant, $F(1,14)=8.89$, $p<0.05$.

Another dorso-ventral difference was observed: WR elicited by ventral stimulation stopped as soon as the stimulation was switched off, whereas, when elicited by dorsal stimulation, it outlasted the end of the stimulation. The WR that persists after the end of the stimulation has been called the "poststimulus WR" (12). Figure 2A shows that the mean duration of this poststimulus WR did not depend on the interpulse interval: IPI (1/frequency). At an IPI = 20 ms, the mean value of the duration of the poststimulus WR was 7.25 s (SEM = 0.85 s).

Effect of anticonvulsant drugs on the duration of the "poststimulus WR." The effects of three anticonvulsant drugs, diazepam, sodium valproate and phenytoin, on the duration of the poststimulus WR were studied at threshold using an IPI = 20 ms. Under anticonvulsant treatment, WR elicited by dorsal IC stimulation was less explosive, and the duration of the poststimulus WR was shortened. A one-way analysis of variance (4 levels: saline, diazepam, phenytoin, and sodium valproate) showed that the drug effect was significant, $F(3,21)=44.10$, $p<0.0001$. Figure 2B illustrates this result and shows that the effect of diazepam, phenytoin or sodium valproate did not differ from each other.

Elicitation of Switch-Off Behavior by Electrical Stimulation of the IC

Elicitation of switch-off behavior by ventral but not by dorsal IC stimulation. Switch-off learning depended on the location of the stimulating electrode. Only stimulation through ventral electrodes sustained switch-off learning. Suprathreshold stimulation of 10 ventrally located sites (in 10 rats) prompted the rats to interrupt the stimulation by pressing the lever. During the first training session, as training progressed to switch-off learning, the jumps and the running tended to disappear, and the rat learned to stay on, or next to, the lever and to press it when being stimulated. The next days, training resulted in a complete disappearance of explosive reactions even at low IPIs (high frequencies). Figure 3 shows a typical switch-off response of a rat stimulated in the ventral IC. At a constant intensity (threshold at IPI = 20 ms), decreasing the IPI (increasing the frequency) prompted the rat to interrupt the stimulation with shorter latencies.

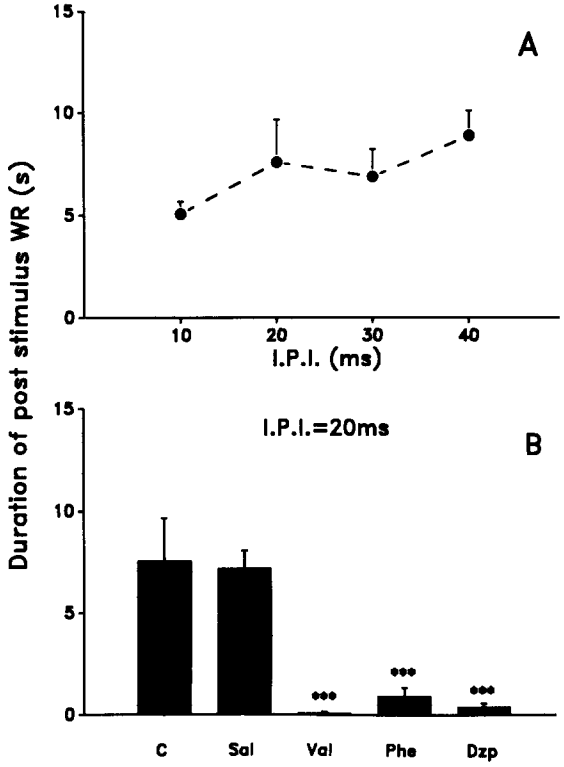

FIG. 2. Effects of varying the IPI (A) or of the pharmacological treatment (B) on the duration of the poststimulus WR elicited by electrical stimulation of dorsal IC sites. The intensity of the stimulation was set at threshold for each IPI used. C: control; Sal: saline; Val: sodium valproate (200 mg/kg); Phe: phenytoin (30 mg/kg); Dzp: diazepam (1 mg/kg).

Using the same method, we could not shape and train the

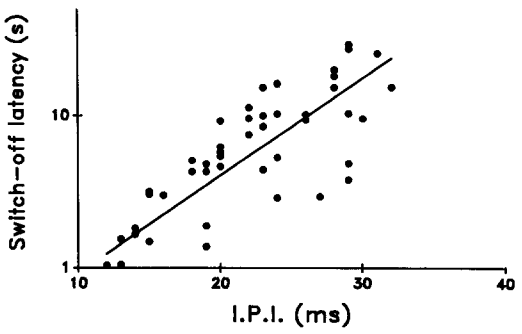

FIG. 3. Typical example of a switch-off response elicited by electrical stimulation of ventral IC sites. A total of 50 switch-off latencies (SOLs) were recorded during a single measurement session. The SOLs were measured as a function of interpulse interval (IPIs). A linear regression line was determined from these SOLs.

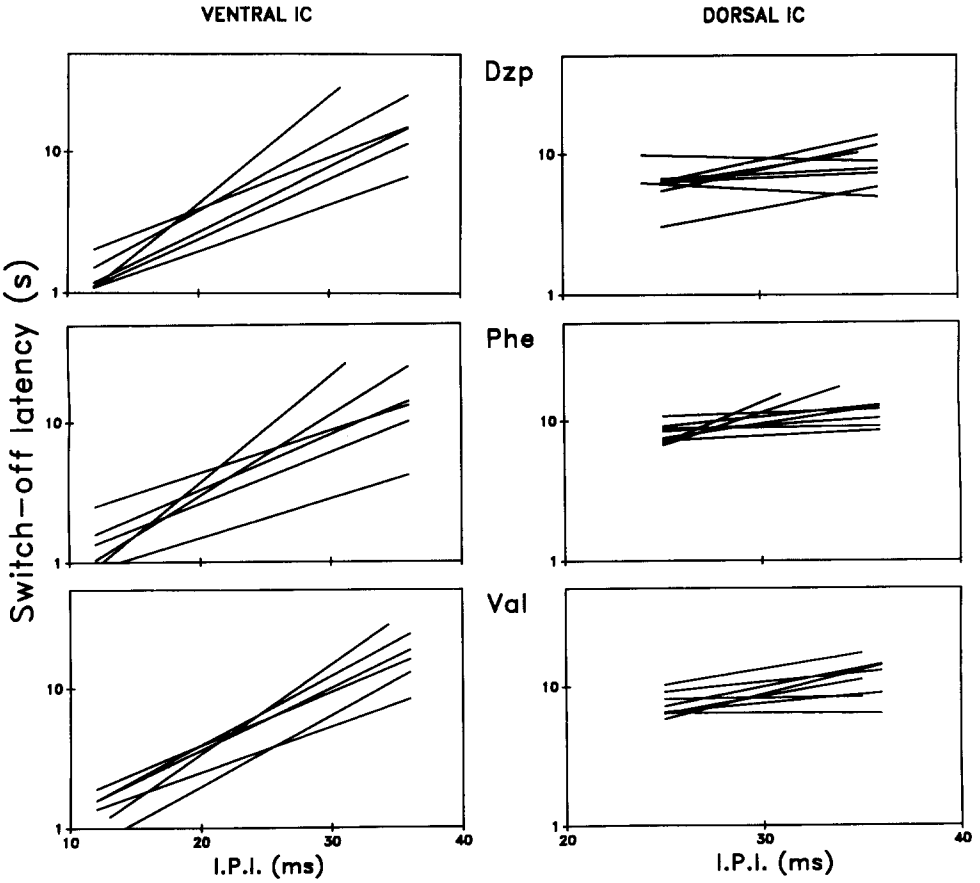

FIG. 4. Comparison of the regression lines of the SOL versus IPI relationship under anticonvulsant drugs. The regression lines were obtained following electrical stimulation of ventral IC sites (3 left graphs) or of dorsal IC sites (3 right graphs). Dzp: diazepam (1 mg/kg); Phe: phenytoin (30 mg/kg); Val: sodium valproate (200 mg/kg).

animals to switch off the stimulation applied to 9 dorsally located sites (in 9 rats). Each threshold intensity stimulation applied to these sites induced WR which outlasted the stimulation.

Transfer of switch-off learning to dorsal sites under anticonvulsant drugs. Once a rat stimulated at a ventrally located site had learned the switch-off behavior, it did not systematically switch off the stimulation at every other site. Thus, when using the contralateral ventral site, it soon switched off the stimulation, but, when a dorsally located site was used, it did not. In contrast, transfer of switch-off learning from a ventral to a dorsal site occurred in all the 9 rats tested following administration of diazepam (1 mg/kg), valproic acid (200 mg/kg) or phenytoin (30 mg/kg).

The switch-off latency (SOL) versus IPI relationship when the stimulation was applied to ventrally located sites (3 left graphs) and dorsally located sites (3 right graphs) obtained under diazepam, phenytoin or sodium valproate are represented in Fig. 4. The slopes of the regression lines were lower for dorsal sites than for ventral sites, whatever the drug used. A two-way analysis of variance (within factor, 3 levels: 3 drugs; in between factor, 2 levels: dorsal versus ventral) showed that the slopes depended on the location of the stimulation site [$F(1,10) = 13.47$, $p<0.01$ for diazepam, $F(1,12) = 5.34$, $p<0.05$ for phenytoin and $F(1,11) = 16.15$, $p<0.01$ for sodium valproate]. The slopes did not depend on the nature of the anticonvulsant used (respectively, mean slope: 0.10, 0.10. 0.11 for diazepam, phenytoin and valproic acid for ventral sites and 0.05, 0.03, 0.04 for dorsal sites). Figure 4 shows also that the range of IPI differed according to the location of the stimulation site (10–40 ms for ventral sites, 25–40 ms for dorsal sites). Decreasing the IPI below 25 ms for dorsal sites resulted in the induction of WR without switch-off behavior.

Figure 5 shows the actual location of the stimulation sites. The WR which stopped as soon as the stimulation was switched off was elicited from sites located in the ventral part of the IC (7 sites) as well as between the IC and the nucleus cuneiformis (1 site). The WR which outlasted the end of the stimulation was elicited from sites located in the dorsal IC (9 sites used for the parametric study and 6 sites used for the pharmacological study). Eight of the ventral sites positive for elicitation of switch-off behavior were located in the ventral part of the IC. Two other sites were located in the nucleus cuneiformis. The dorsal sites (9 among 10) from which switch-off behavior could not be obtained, except when anticonvulsant drugs were used, were located in the dorsal part of the IC.

DISCUSSION

The present study showed that electrical stimulation of the IC, either ventral or dorsal, elicited wild running (WR). More precisely, the results showed that the threshold intensities for the

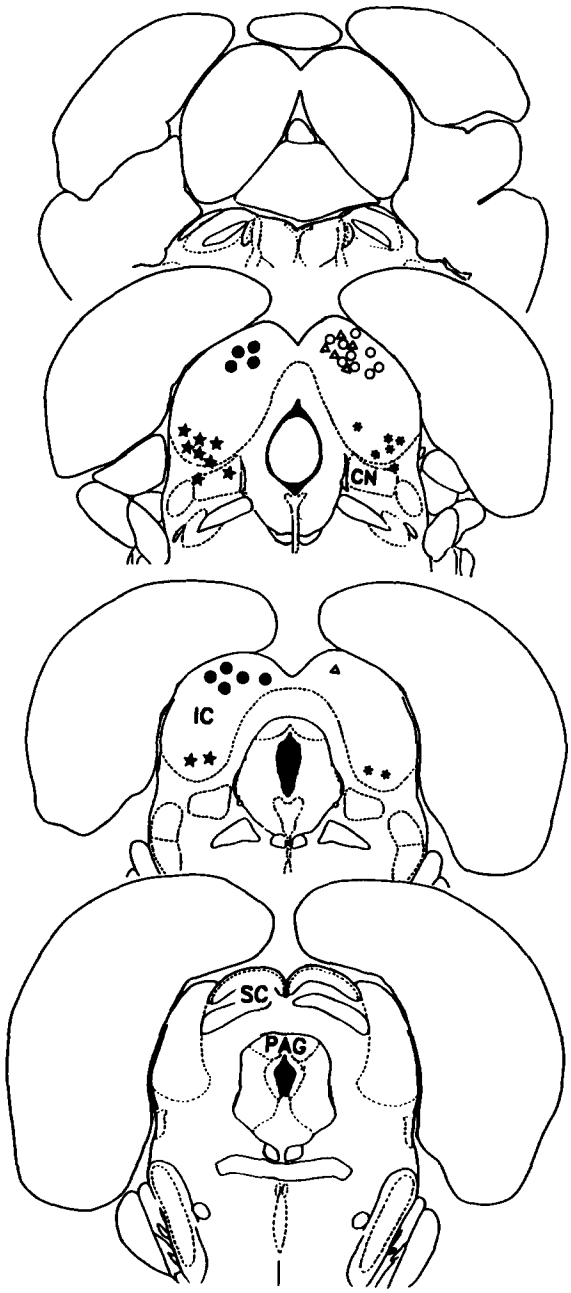

FIG. 5. Location of IC stimulation sites that were used in the behavioral and motivational study. On the left are represented the sites used for switch-off behavior elicitation, and on the right are represented the sites used for WR elicitation. ★: Switch-off behavior. ●: Switch-off behavior only under anticonvulsant treatment. WR which outlasted the end of the stimulation (○: parametric study; △: anticonvulsant treatment). *: WR which stopped as soon as the stimulation was switched off.

elicitation of WR were lower in the ventral than in the dorsal part of the IC, indicating that the ventral part is more excitable. Furthermore, the behavioral responses elicited from each of these areas of the IC differed by their temporal characteristics. The WR elicited from the ventral IC stopped as soon as the stimulation was switched off, whereas the WR elicited from the dorsal IC outlasted the end of the stimulation. This result confirms a previous study showing that poststimulus WR was only produced in the dorsal IC (12). WR is considered as the behavioral expression of an epileptic activity of the IC, since at least the poststimulus WR was associated with a paroxysmal activity of the IC and since some anticonvulsant drugs such as phenytoin or sodium valproate abolished it (12). The present results confirmed that these anticonvulsant drugs, but also diazepam, abolished the poststimulus WR. WR elicited by stimulation of the IC resembles the escape behavior elicited by electrical stimulation of the neighboring CN or PAG (7, 20, 22). It is noteworthy that, like in the ventral IC, the behavioral effects are contingent upon the stimulation. Many studies reported that electrical stimulations of these structures induce aversive effects, since stimulated rats perform an operant task to escape the effects of the stimulation (5, 6, 14, 15, 20–22). The second part of our study investigated whether WR elicited by stimulation of the IC resulted from an underlying aversive effect.

Electrical stimulation of the ventral IC induced aversive effects, since rats performed an operant task to escape the effect of the stimulation. Thus properties similar to those of the PAG, the SC and the CN could be attributed to the ventral IC. Even though these areas are located close to each other, the aversive effects elicited from the ventral IC are probably due to the excitation of this substrate, as it could be deduced from the parametric study of the switch-off response. The slopes of the regression lines of the SOL versus IPI relationship obtained with similar methods for the MLR, the PAG (6) or the ventral IC were found to be different. Furthermore, most sites in the ventral IC were at least 0.5 mm away from the PAG or the MLR, a distance longer than the radius of the stimulated area (10).

Switch-off learning could not be elicited from dorsal IC sites, and transfer of switch-off learning from ventral to dorsal IC sites did not occur. It is likely that the occurrence of the poststimulus WR prevented learning of switch-off behavior. It has been shown that, if a delay is put between the operant response and the actual cessation of the aversive stimulation, the switch-off response disappears (13). Thus it is suggested that the poststimulus WR delayed too much the reinforcement to allow association between the press of the lever and the end of the effect of the stimulation. This hypothesis implicitly involves the idea that the poststimulus WR is related to a poststimulus aversive effect of the stimulation. Our results are in favor of this hypothesis, since anticonvulsant drugs which abolished the poststimulus WR permitted transfer of switch-off learning to dorsal IC sites. An alternative interpretation cannot be discarded; electrical stimulation of dorsal IC would induce no aversive effect. The aversive effect induced by stimulations of dorsal IC sites revealed in the presence of diazepam, phenytoin or sodium valproate would be therefore generated by these drugs. However, at least two of the anticonvulsant drugs used here, diazepam and sodium valproate, were shown to have antiaversive effects on switch-off elicited by stimulating the PAG (4).

Under anticonvulsant drugs, the switch-off responses produced by ventral stimulations still differed from those produced by dorsal stimulations. The slopes of the regression lines of the SOL versus IPI relationship for dorsal IC were about horizontal, suggesting that the switch-off response did not depend on the frequency and the strength of the stimulation. In contrast to the ventral IC or the PAG (18), excitation of the dorsal IC at suprathreshold intensities may not induce a gradual behavioral response but rather a maximal constant response. As no similar results could be obtained without pharmacological treatment, it is difficult to attribute this behavioral propriety to neurophysiological mechanisms within the dorsal IC. But we speculate that it probably expresses an all-or-nothing neuronal response to the stimulation. Data available from studies on the PAG indicated a gradual neuronal response to the stimulation (18,19), but the IC

was not yet investigated in similar electrophysiological studies.

In conclusion, the present study shows that aversive effects and epileptic activity can be induced by activating the same neural substrate within the IC. Further studies are, however, needed to investigate if these affective effects and neurological disorders share common neurophysiological mechanisms.

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REFERENCES

1. Bagri, A.; Di Scala, G.; Sandner, G. Wild running elicited by microinjection of bicuculline or morphine into the inferior colliculus of rats: Lack of effect of periaqueductal gray and superior colliculus lesions. Pharmacol. Biochem. Behav.; submitted.
2. Bagri, A.; Di Scala, G.; Sandner, G. Wild running, seizures and aversion elicited by electrical stimulation of the inferior colliculus. Eur. J. Neurosci. 3(Suppl.):2207; 1990.
3. Bagri, A.; Sandner, G.; Di Scala, G. Effects of unilateral microinjections of GABAergic drugs into the inferior colliculus on auditory evoked potentials and on audiogenic seizure susceptibility. Exp. Neurol. 104:82–87; 1989.
4. Bovier, P.; Broekkamp, L. E.; Lloyd, K. G. Enhancing GABAergic transmission reverses the aversive state in rats induced by electrical stimulation of the periaqueductal gray region. Brain Res. 248: 313–320; 1982.
5. Delgado, J. M. R.; Roberts, W. W.; Miller, N. Learning motivated by electrical stimulation of the brain. Am. J. Physiol. 179:587–593; 1954.
6. Depoortere, R.; Sandner, G.; Di Scala, G. Aversion elicited by electrical stimulation of the mesencephalic locomotor region. Physiol. Behav. 47:561–567; 1990.
7. Depoortere, R.; Di Scala, G.; Sandner, G. Treadmill locomotion and aversive effects induced by electrical stimulation of the mesencephalic locomotor region in the rat. Brain Res. Bull. 25:723–727; 1990.
8. Dixon, N. J. BMDP statistical software. Los Angeles: University of California Press; 1981.
9. Faingold, C. L.; Gehlbach, G.; Caspary, D. M. Decreased effectiveness of GABA-mediated inhibition in the inferior colliculus of the genetically epilepsy-prone rat. Exp. Neurol. 93:145–159; 1986.
10. Fouriezos, G.; Wise, R. A. Current-distance relation for rewarding brain stimulation. Behav. Brain Res. 14:85–89; 1984.
11. Jobe, P. C. Pharmacology of audiogenic seizures. In: Brown, R. D.; Daignealt, E. A., eds. The pharmacology of hearing: Experimental and clinical bases. New York: Wiley Interscience; 1981:304–319.
12. McCown, T. J.; Greenwood, R. S.; Frye, G. D.; Breese, G. R. Electrically elicited seizures from the inferior colliculus: A potential site for the genesis of epilepsy? Exp. Neurol. 86:527–542; 1984.
13. Maeda, H.; Nakao, H. Delayed reinforcement of switch-off behavior and amygdaloid lesions in cats. Physiol. Behav. 36:339–342; 1985.
14. Olds, M. E.; Olds, J. Approach-escape interaction in rat brain. Am. J. Physiol. 203:808–810; 1962.
15. Olds, J.; Peretz, B. A motivational analysis of the reticular activating system. Electroencephalogr. Clin. Neurophysiol. 12:445–454; 1960.
16. Paxinos, G.; Watson, G. The rat brain in stereotaxic coordinates. Sydney: Academic Press; 1982.
17. Roberts, R. C.; Ribak, C. E.; Oerthel, W. H. Increased numbers of GABAergic neurons occur in the inferior colliculus of an audiogenic model of genetic epilepsy. Brain Res. 361:324–338; 1985.
18. Sander, G.; Schmitt, P.; Karli, P. Central gray and medial hypothalamic stimulation: Correlation between escape behavior and unit activity. Brain Res. 170:459–474; 1979.
19. Sandner, G.; Schmitt, P.; Karli, P. Effect of medial hypothalamic stimulation inducing both escape and approach on unit activity in rat mesencephalon. Physiol. Behav. 29:269–274; 1982.
20. Sandner, G.; Schmitt, P.; Karli, P. Mapping of jumping, rearing, squealing and switch-off behavior elicited by periaqueductal gray stimulation in the rat. Physiol. Behav. 39:333–339; 1987.
21. Schmitt, P.; Eclancher, F.; Karli, P. Etude des systèmes de renforcement négatif et de renforcement positif au niveau de la substance grise centrale chez le rat. Physiol. Behav. 12:271–279; 1974.
22. Schmitt, P.; Sandner, G.; Karli, P. Escape and approach induced by brain stimulation: A parametric analysis. Behav. Brain Res. 2:49–79; 1981.