EFFECTS OF LOCUS COERULEUS STIMULATION ON MURICIDE IN OLFATORY BULBECTOMIZED AND RAPHE LESIONED RATS

Tsuneyuki YAMAMOTO, Shigenobu SHIBATA and Showa UEKI
Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan
Accepted May 25, 1982

Abstract—In order to elucidate the role of central monoamines in muricide of the rat, the effects of electrical stimulation of the locus coeruleus (LC) were investigated on two types of muricide induced by olfactory bulbectomy (OB rats) and midbrain raphe lesions (raphe rats). Muricide was inhibited in 71.4% of the OB rats by bilateral LC stimulation and in 26.7% by unilateral stimulation. Even in the rat in which muricide was not inhibited following LC stimulation, muricide was almost invariably suppressed by LC stimulation after pretreatment with pargyline. The antimuricidal effect of LC stimulation was partially blocked by administration of propranolol, but not by phenoxybenzamine. In contrast, muricide was inhibited by bilateral LC stimulation in 44.4% of the raphe rats, but this effect was not potentiated by pretreatment with pargyline. On the other hand, muricide was not significantly inhibited by either dorsal raphe or medial raphe stimulation in any OB rats. These results suggest that noradrenaline plays a more important role in inhibiting muricide in OB rats than in raphe rats.

Muricide is well known to be induced in rats by regional brain lesions (1–3), administration of Δ9-tetrahydrocannabinol (4, 5), and long-term isolation (6). It is postulated that the serotonergic system plays a role in the inhibition of muricide, the basis for this being the following points: [1] muricide is produced by lesions of the midbrain raphe nuclei (3, 7), areas containing 5-HT cell bodies, and administration of agents such as 5,7-dihydroxytryptamine (8) or p-chlorophenylalanine (9) that decrease the activity of 5-HT neurons; conversely, [2] muricide is inhibited by administration of the 5-HT precursor 5-hydroxytryptophan and 5-HT receptor agonists (10, 11). Recently, it was also demonstrated that muricide induced by long-term isolation was inhibited by electrical stimulation of the dorsal raphe nuclei (12).

On the other hand, some experiments have suggested that brain catecholamines play an inhibitory role in muricide. These hypotheses are based on the following facts: [1] the occurrence of muricide was related with a decrease in brain noradrenaline (NA) contents (13, 14), [2] drugs which increased the activity of catecholaminergic neurons selectively inhibited muricide (15–17), and [3] dorsal NA bundle lesions highly facilitated muricide (18). Furthermore, Leaf et al. (14) postulated that the adrenergic system in the amygdala, which was known to have an important role in regulating muricide (19), played an inhibitory role since NA administered directly into the amygdala inhibited muricide. However, these results are not
entirely consistent with the other reported results (20, 21). Namely, intrahypothalamic 6-hydroxydopamine suppressed predatory aggression with a reduction of the concentration of NA (22).

In addition, muricidal rats showed higher forebrain levels of NA and higher turnover rate for NA than non-killer rats (23). One of the reasons for the discrepancy in these experimental results may be the differences in the underlying mechanism leading to muricide depending on the method of induction. So far, no experiments have been reported that have focussed on the qualitative difference in various types of muricide induced by different methods.

The present study was designed to investigate the effects of electrical stimulation of the locus coeruleus (LC), containing NA cell bodies, on muricide induced by either olfactory bulbectomy or raphe nuclei lesions and to elucidate whether the NA neurons participate differently in the two types of muricide. Furthermore, the study was undertaken to examine the effects of electrical stimulation of the raphe nuclei on muricide induced by olfactory bulbectomy. In this experiment, regional functions of the raphe nuclei were also investigated by examining separately the effect of stimulation to either the dorsal or medial raphe nucleus.

MATERIALS AND METHODS

Animal: Experiments were carried out on male Wistar King A strain rats, weighing approximately 180–250 g at the start of experimentation, supplied by the Kyushu University Institute of Laboratory Animals. Although this strain has a low incidence of spontaneous killer rats, only non-killer rats were used.

The animals were housed in individual cages (20×21×17 cm) with wire-mesh walls throughout the experimental period and were given food and water ad lib. These animals were maintained at a room temperature of 22±1°C and on a 12 hr light-dark schedule with lights off at 19:00. All tests were performed between 10:00 and 16:00.

Surgery: The animals were anesthetized with sodium pentobarbital (40 mg/kg, i.p.) and placed on a stereotaxic instrument. For olfactory bulbectomy, after a suitable hole was made in the skull just above the olfactory bulb, the dura was cut, and the main olfactory bulb was bilaterally removed by suctioning.

Lesions of the midbrain raphe nuclei were carried out by inserting a monopolar electrode of 0.4 mm diameter, made of insulated stainless steel wire, with placement according to the rat brain atlas of König and Klippel (24) and applying a direct current of 3 mA for 15 sec to both the dorsal (frontal plane [F]: 0.16, lateral plane [L]: 0, horizontal plane [H]: 1.0) and medial (F: 0.16, L: 0, H: −2.5) raphe nuclei.

After olfactory bulbectomy (OB rat) or raphe lesions (raphe rat), each rat was immediately housed in an individual cage. On the 5th and 7th day after surgery, muricide tests were conducted for a 15 min period. Only rats which exhibited muricide on both of these days were selected for use in the chronic implantation of stimulation electrodes at either the LC or raphe nuclei. According to the stereotaxic coordinates of König and Klippel, bipolar stainless steel electrodes (tip diameter, 0.2 mm; uninsulated length, 0.2 mm; polar distance, 0.8 mm) for electrical stimulation were implanted bilaterally into the LC (posterior: 1.5, lateral: 1.2, ventral: 7.0 deep from the skull). For the raphe nuclei, identical electrodes were chronically implanted at either the dorsal or medial raphe in the same manner. In each case, the electrode was stereotaxically inserted into the brain at a 15° angle from L: 1.5 for the dorsal raphe and 20° angle from L: 2.9 for the medial raphe in order to produce electrical stimulation on each raphe nuclei separately and to avoid
damage to the sagittal venous sinus as much as possible.

Electrical stimulation of LC or raphe: The electrical brain stimulation was started at least 7 days after surgery. The killer rats were stimulated while in their individual cages using an electric stimulator (MSE-40, Nihon Kohden). Electrical stimulation of the LC or raphe nuclei with square pulses (5–10 Hz, 0.5 msec, 5V) were applied for 5–10 min. In conjunction with these experiments, the effects of phenoxybenzamine and propranolol on the response induced by LC stimulation were also examined. In these experiments, LC stimulation was applied for 2 min at 5, 15, 30, 45, 60, 90, and 120 min after drug administration.

Measurement of muricide and hyperemotionality: In the muricide test, the number of rats which exhibited muricide within 90 sec after introduction of a mouse into the home cage was determined after electrical brain stimulation. Other hyperemotionality of rats was measured by scoring the emotional responses to [1] air blowing on the back (startle response) and [2] a rod presented in front of the snout (attack response). These responses were graded as follows: score 0, no reaction; score 1, slight; score 2, moderate; score 3, marked; score 4, extreme response.

Drugs: The drugs used in this study were phenoxybenzamine hydrochloride (20 mg/kg), propranolol (20 mg/kg), and pargyline (10 mg/kg). These drugs were intraperitoneally administered in a volume of 0.2 ml/100 g body weight.

After termination of the experiment, all rats were sacrificed, and the heads were perfused with saline and 10% formalin. Thereafter, 60–60 μm sections of brains were prepared and stained with cresyl violet to verify the locations of the inserted electrodes. The results from rats whose electrodes were not located in the proper positions were omitted from the data analysis.

RESULTS

Figure 1 shows representative locations of the electrode tips in the locus coeruleus (LC), the dorsal raphe (d-R), and the medial raphe nuclei (m-R).

In the non-electrical stimulation state, the OB rats (N=14) exhibited muricide within 19.9±10.9 (average±S.D.) sec when a mouse was placed in the rat’s home cage. Muricide in the OB rats was significantly inhibited 30 sec after bilateral LC stimulation (P<0.01, Fisher’s exact probability test, Fig. 2). At this time, for rats (N=8) in which muricide was not inhibited, the killing latency tended to be

Fig. 1. Photograph of coronal sections showing the stimulating electrodes within the locus coeruleus (A), the dorsal raphe (B), and the medial raphe nuclei (C).
delayed to 36.5±12.6 sec. The inhibition of muricide by LC stimulation was increased with a prolonged stimulation period. At 9 min after starting stimulation, muricide disappeared in 71.4% of the OB rats. In addition, the killing latency for killer rats tended to be delayed compared to the latency found in the non-stimulated state. At 30 sec after cessation of LC stimulation, muricide appeared in 71.4% of the OB rats (P<0.05); and the killing latency was shortened to 23.8±11.7 sec (Fig. 2). At 10 min after the cessation of stimulation, muricide recovered in 78.6% of the OB rats, except for 2 of them in which inhibition of muricide persisted up to 30 min after the cessation of stimulation. Five days after the completion of the above experiment, pargyline 10 mg/kg i.p. was administered to 3 rats in which muricide was not inhibited by LC stimulation at any time. This dose of pargyline alone did not inhibit muricide. At 45 min after administration of pargyline, bilateral LC stimulation (10 Hz, 5V, 0.5 msec) inhibited muricide in all OB rats. However, when the stimulation electrodes were located inferior or posterior to the LC or in the lobus anterior of the cerebellum, the inhibition of muricide was not found in any animals and not changed even by the pargyline pretreatment (N=6).

On the other hand, unilateral LC stimulation inhibited muricide in 2 out of 15 OB rats 30 sec after starting the stimulation (Fig. 3). At this time, the killing latency for killer rats was
Table 1. Effects of midbrain raphe stimulation on muricide in OB rats

| Time during electrical stimulation | Inhibition of muricide | Killing latency (sec) | Inhibition of muricide | Killing latency (sec) | Inhibition of muricide | Killing latency (sec) | Inhibition of muricide | Killing latency (sec) |
|----------------------------------|------------------------|----------------------|------------------------|----------------------|------------------------|----------------------|------------------------|----------------------|
| 0                                | 0/8                    | 18.5±13.6            | 0/5                    | 27.5±18.1            | 0/9                    | 15.4±3.1             | 0/8                    | 19.6±9.4             |
| 30 sec                           | 1/8                    | 250±13.5             | 1/5                    | 25.0±14.1            | 0/9                    | 163±8.4              | 0/8                    | 220±13.3             |
| 2 min                            | 1/8                    | 22.9±13.8            | 1/5                    | 29.8±2.4             | 1/9                    | 16.8±6.0             | 0/8                    | 18.3±10.9             |
| 5 min                            | 2/8                    | 25.0±18.1            | 1/5                    | 25.6±15.1            | 1/9                    | 15.9±4.2             | 0/8                    | 22.4±13.6             |

Raphe stimulation was given for a 5 min period. The muricide test was performed 30 sec, 2 min and 5 min after initiation of stimulation.
20.7±18.4 sec, not differing from that found in the control state, 17.1±8.5 sec. At 9 min after initiation of the stimulation, only 4 of 15 animals showed an inhibition of muricide (Fig. 3). Eight rats which exhibited no inhibition of muricide upon unilateral LC stimulation were given unilateral stimulation at 45 min after administration of pargyline in a dose of 10 mg/kg i.p. Thirty sec after initiation of unilateral LC stimulation, muricide was inhibited in 6 of 8 OB rats. Of 6 animals which exhibited inhibition of muricide, 3 showed no aggressive behavior; but each of the other 2 tried to attack a mouse. These effects abated gradually after cessation of the stimulation. Ten min after the stimulation was stopped, muricide was observed in all animals (Fig. 3).

Table 1 shows the effect of m-R or d-R stimulation on muricide in OB rats. Muricide was inhibited by m-R stimulation (5-10 Hz, 5 V, 0.5 msec) in only 1 of 8 OB rats after 30 sec and 2 min, and in 2 rats after 5 min. At this time, the killing latency was not significantly different from that found in the control state. When m-R stimulation was given after pargyline pretreatment to 5 animals in which muricide had not been inhibited, only one animal showed inhibition of muricide (Table 1). Similarly, d-R stimulation (5-10 Hz, 5 V, 0.5 msec) caused no significant change in the muricide of OB rats, and also no difference in the killing latency at any time (Table 1).

Figure 4 shows the effect of LC stimulation on muricide in raphe rats. The killing latency was 23.6±7.8 sec in raphe rats (N=9) in the control state. At 30 sec after initiation of bilateral LC stimulation (5-10 Hz, 5 V, 0.5 msec), muricide was inhibited in 4 out of 9 raphe rats (Fig. 4). However, the inhibitory effect was not increased with a prolonged stimulation. Furthermore, the killing latency for the rats in which muricide was not inhibited 30 sec after LC stimulation was 24.4±9.3 sec, not differing from that in the control state. A tendency toward a delay of the killing latency in proportion to the stimulation period was not observed.

Unilateral LC stimulation produced an inhibition of muricide in one out of 4 animals 30 sec after starting stimulation (Fig. 4). Potentiation of the muricide inhibition in proportion to the stimulation period was not observed. To 6 (bilateral stimulation, N=3; unilateral stimulation, N=3) of the raphe rats which showed no inhibition of muricide upon LC stimulation, LC stimulation was given after pretreatment with pargyline. In this case, muricide was inhibited in only one raphe rat. The killing latency was not significantly delayed.

Figure 5 shows the effects of phenoxybenzamine and propranolol on the antimuricidal action of bilateral LC stimulation in OB rats. In the control state prior to LC stimulation, the killing latency for OB rats was 19.5±8.0 sec (N=10). In the animals treated with saline, an inhibition of muricide was observed by LC stimulation successively applied for 3 min after saline treatment. The antimuricidal effect of LC stimulation was inhibited in 3 of 6 OB rats 5 min after administration of propranolol at 20 mg/kg i.p. (Fig. 5). This effect lasted up to 60 min after drug treatment. When LC stimulation was not given, all rats exhibited muricide at any time.
Fig. 5. Effects of adrenergic blockers on the muricide inhibition induced by bilateral LC stimulation in OB rats. LC stimulation was applied for 3 min each at the points indicated by arrows after administration of either phentolamine or propranolol. The muricide test for a 1 min period was performed twice, i.e., 30 sec and 2 min after initiation of LC stimulation. The effect of drugs was evaluated as positive when muricide was not suppressed in either of the tests.

during the experimental periods (120 min). Namely, propranolol alone did not produce an inhibition of muricide at any time. On the other hand, phentolamine, 20 mg/kg i.p., did not inhibit the antimuridal effect of LC stimulation in OB rats at any time (Fig. 5).  

**DISCUSSION**

The present study demonstrated that muricide in OB rats was more significantly inhibited by LC stimulation than by raphe stimulation. It has been suggested that brain catecholamines play an inhibitory role in muricide since muricide is [1] specifically inhibited by the drugs which potentiate the activity of catecholaminergic neurons such as tricyclic antidepressants (16) and [2] facilitated by dorsal NA bundle lesions in OB rats (18). Our present results agreed well with these findings.

In contrast to this, some papers have reported that muricide is increased by NA injection into the ventral tegmental area (25) and suppressed by drugs which decrease brain NA such as disulfiram (26), α-methyl-p-tyrosine (27), and 6-hydroxydopamine (22). These reports suggest that NA plays a facilitatory role in muricide.

The authors previously reported that muricide was different between OB rats and raphe rats with respect to its characteristics (3), the responses to various antidepressants (28), and the effect of amygdaloid lesions (29); and it was suggested that the underlying neural mechanism differed depending on the method of inducing muricide. The present study showed that some difference was found in the effect of LC stimulation on muricide between OB rats and raphe rats. Namely, the muricide of OB rats tended to be more markedly inhibited by LC stimulation as compared to that of raphe rats. This is consistent with the fact that the muricide of OB rats is more strongly inhibited by desipramine, among the antidepressants, which has a selective uptake blocking effect of NA rather than of 5-HT (30).

The muricide of OB rats is markedly inhibited by medial amygdaloid lesions (29), and it is also suppressed by microinjection of NA into the medial amygdala (31). The turnover rate of NA in the amygdala is markedly decreased by olfactory bulbectomy in rats (4). Furthermore, the field potential of the amygdala elicited by olfactory bulb stimulation is inhibited by LC stimulation (32). These findings suggest that the antimuridal effect of LC stimulation in OB rats may be attributed to suppressed function in the amygdala caused by NA release. In addition, the inhibitory effect of LC stimulation on muricide was partially antagonized by propranolol but not by phentolamine, suggesting that this effect was caused through adrenergic β-receptor mechanisms.

Apart from this, it is suggested that brain 5-HT also plays an inhibitory role in muricide
since administration of drugs causing a decrease in brain 5-HT such as p-chlorophenylalanine and 5,7-dihydroxytryptamine and raphe nuclei lesions can induce muricide; and conversely, administration of the precursor of 5-HT inhibits muricide. Because electrical stimulation of the raphe nuclei markedly increased brain 5-HIAA (33, 34), raphe stimulation was expected to inhibit muricide. Puciliowski recently reported that muricide induced by isolation housing was markedly inhibited by electrical stimulation of the dorsal raphe nucleus but not by medial raphe stimulation (35). However, as shown in our present results, muricide of OB rats was not significantly changed either by d-R or by m-R stimulation. The reasons for this discrepancy between Puciliowski’s results and ours may be due to the difference in the methods of inducing muricide. Our present finding suggests that brain 5-HT plays a minor role, if any, in the muricide exhibited by OB rats. This is supported by the fact that [1] the muricide of OB rats is more strongly inhibited by drugs which activate the noradrenergic neuron than by serotonergic drugs (28) and that [2] a microinjection of 5-HT into the amygdala does not inhibit muricide (31). However, neither a d-R lesion nor a m-R lesion alone significantly induces muricide (3). In view of this finding, concurrent stimulation of both d-R and m-R may display an inhibition of muricide, although neither d-R nor m-R stimulation alone can suppress it. In any case, since muricide varies in the mechanism of its occurrence and in its characteristics depending upon the method of induction, stimulation of the LC and raphe nuclei may produce different effects on different types of muricide.

Acknowledgements: This investigation was supported by a Grant-in-Aid for Encouragement of Young Scientists and a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture in Japan and partly supported by a Grant for Neurotropic Drug Research from the Fujisawa Pharm., Co. Ltd., Osaka, Japan.

REFERENCES

1) Malick, J.B.: A behavioral comparison of three lesion-induced models of aggression in the rat. Physiol. Behav. 5, 679–681 (1970)

2) Ueki, S., Nurimoto, S. and Ogawa, N.: Characteristics in emotional behavior of the rat with bilateral olfactory bulb ablations. Folia psychiat. neurol. jap. 26, 227–237 (1972)

3) Yamamoto, T. and Ueki, S.: Characteristics in aggressive behavior induced by midbrain raphe lesions in rats. Physiol. Behav. 19, 105–110 (1977)

4) Valzelli, L.: Drugs and aggressiveness. Advances in Pharmacology 5, 79–108 (1967)

5) Ueki, S., Fujiwara, M. and Ogawa, N.: Mouse-killing behavior (muricide) induced by J1-tetrahydrocannabinol in rats. Physiol. Behav. 9, 558–567 (1972)

6) Valzelli, L. and Garattini, S.: Biochemical and behavioral changes induced by isolation in rats. Neupharmacology 11, 17–22 (1972)

7) Grant, L.D., Cosicina, D.V., Grossman, S.P. and Freedman, D.X.: Muricide after serotonin depleting lesions of midbrain raphe nuclei. Pharmacol. Biochem. Behav. 1, 77–80 (1973)

8) Pexinos, G. and Atrens, D.M.: 5,7-Dihydroxytryptamine lesions: Effects on body weight, irritability and muricide. Aggress. Behav. 3, 107–118 (1977)

9) Sheard, M.H.: The effect of p-chlorophenylalanine on behavior in rats. Relation to brain serotonin and 5-hydroxyindole acetic acid. Brain Res. 15, 524–528 (1969)

10) Kulkarni, A.S.: Muricidal block produced by 5-hydroxytryptophan and various drugs. Life Sci. 7, 125–128 (1968)

11) DiChiara, G.D., Camba, R. and Spano, P.F.: Evidence for inhibition by brain serotonin of mouse-killing behavior in rats. Nature 223, 272–273 (1971)

12) Kostowski, W., Puciliowski, O. and Plaznik, A.: Effect of stimulation of brain serotonergic system on mouse-killing behavior in rats. Physiol. Behav. 25, 161–165 (1980)

13) Banerjee, U.: Modification of the isolation-induced abnormal behavior in male Wistar rats by destructive manipulation of the central monoaminergic system. Behav. Biol. 11, 573–579 (1974)
14) Leaf, R.C., Lerner, L. and Horovitz, Z.P.: The role of the amygdala in the pharmacological and endocrinological manipulation of aggression. In Aggressive Behavior, Edited by Garattini, S. and Sigg, E.B., p. 120–131, Excerpta Medica, Amsterdam (1969)

15) Sofia, R.D.: Effects of centrally active drugs on four models of experimentally induced aggression in rodents. Life Sci 8, 705–716 (1969)

16) Ueki, S., Nurimoto, S. and Ogawa, N.: Effects of psychotropic drugs on emotional behavior in rats with limbic lesions with special reference to olfactory bulb ablations. Folia psychiat. neurol. japon. 26, 245–255 (1972)

17) Valzelli, L. and Bernasconi, S.: Psychoactive drug effects on behavioral changes induced by prolonged socio-environmental deprivation in rats. Psychol. Med. 6, 271–276 (1976)

18) Oishi, R. and Ueki, S.: Facilitation of muricide by dorsal norepinephrine bundle lesions in olfactory bulbectomized rats. Pharmacol. Biochem. Behav. 8, 133–136 (1978)

19) Moyer, K.E.: Kinds of aggression and their physiological basis. Commun. Behav. Biol. 2, 65–87 (1968)

20) Salama, A.I. and Goldberg, M.E.: Neurochemical effects of imipramine and amphetamine in aggressive mouse-killing (muricide) rats' Biochem. Pharmacol. 19, 2023–2032 (1970)

21) Banerjee, U.: Modification of the isolation-induced abnormal behavior in male Wistar rats by destructive manipulation of the central monoaminergic systems. Behav. Biol. 11, 573–579 (1974)

22) Jimmerson, D. and Reis, D.J.: Effects of intrahypothalamic 6-hydroxydopamine on predatory aggression in rats. Brain Res. 61, 141–152 (1973)

23) Goldberg, M.E. and Salama, A.I.: Norepinephrine turnover and brain monoamine levels in aggressive mouse-killing rats. Biochem. Pharmacol. 18, 532–534 (1969)

24) König, J.F.R. and Klippel, R.A.: The Rat Brain, A Stereotaxic Atlas of the Forebrain and Lower Parts of the Brain Stem. Williams and Wilkins, Baltimore (1963)

25) Bandler, R.J.: Chemical stimulation of the rat midbrain and aggressive behavior. Nature 229, 222–223 (1971)

26) MacDonnell, M.F. and Fessock, L.: Some effects of ethanol, amphetamine, disulfiram and p-CPA on seizing of prey in feline predatory attack and associated motor pathways. Q.J. Stud. Alcohol. 33, 437–445 (1972)

27) McLain, W.C., III and Powell, D.A.: The effects of α-methylparatyrosine and para-chlorophenylalanine on predatory attack and shock elicited aggression. Newsletter Res. Psychol. 14, 29–31 (1972)

28) Yamamoto, T. and Ueki, S.: Effects of drugs on hyperactivity and aggression induced by raphé lesions in rats. Pharmacol. Biochem. Behav. 9, 821–826 (1978)

29) Shibata, S., Yamamoto, T. and Ueki, S.: Differential effects of medial, central and basolateral amygdaloid lesions on four models of experimentally-induced aggression in rats. Physiol. Behav. 28, 289–294 (1982)

30) Carlson, A., Corrodi, H., Fuxe, K. and Hokfelt, T.: Effect of some antidepressant drugs on the depletion of intraneuronal brain catecholamine stores caused by 4-α-dimethyl-meta-tyrosine. Europ. J. Pharmacol. 5, 367–373 (1969)

31) Watanabe, S., Inoue, M. and Ueki, S.: Effects of psychotropic drugs on mouse-killing behavior in the rat with olfactory bulb ablations. Japan. J. Pharmacol. 29, 493–496 (1979)

32) Oishi, R., Watanabe, S., Ohmori, K., Shibata, S. and Ueki, S.: Effect of stimulation of locus coeruleus on the evoked potential in the amygdala in rats. Japan. J. Pharmacol. 29, 105–111 (1979)

33) Aghajanian, G.K., Rosecrans, J.A. and Sheard, M.H.: Serotonin: Release in the forebrain by stimulation of midbrain raphe. Science 156, 402–403 (1967)

34) Sheard, M.H. and Aghajanian, G.K.: Stimulation of the midbrain raphe: Effect on serotonin metabolism. J. Pharmacol. exp. Ther. 163, 425–430 (1968)

35) Pucilowski, O. and Kostowski, W.: Effects of stimulation of the raphe nuclei on muricide behavior in rats. Pharmacol. Biochem. Behav. 14, Supp. 1, 25–28 (1981)