We have also found orellanine, orellinine and orelline in methanol extracts of another species – the *Cortinarius speciossimus* mushroom. Using the procedure described for orellanine we isolated from this fungus a substance with chromatographic and spectroscopic properties were identical with those of orellanine from *Cortinarius orellanus*.

Recently, Caddy et al. have reported[11,12] the isolation from *Cortinarius speciossimus* of a fluorescent toxin cortinarine A and its derivative, probably nontoxic substance, cortinarine C for which they suggested a polypeptide structure. It is interesting that cortinarine A, like orellanine, underwent decomposition at 270 °C, yielding a yellow product.

Although the total synthesis of orellanine has not been achieved, some model compounds prepared in our laboratory with structural features resembling those of orellanine and orelline (4,4′-dihydroxy-2,2′-bipyridyl and its bis N-oxide, 3,3′-dihydroxy-2,2′-bipyridyl, 3,4-dihydroxypyridine and 2-(2′-hydroxyphenyl)-pyridine-N-oxide) showed many similarities in chemical and spectroscopic properties[9,13] to the natural products.

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The role of the substantia nigra on the rage reaction elicited by hypothalamic stimulation, in the cat[1]

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Summary. The effects of substantia nigra stimulation on the rage reaction evoked by hypothalamic activation were studied. The reference value of the rage reaction was the latency of the hissing, which was constant in all animals when hypothalamic stimulation was performed with the same parameters. Simultaneous activation of substantia nigra and hypothalamus determined a significant decrease in hissing latency. The influence of the substantia nigra on the affective components of the aggressive behavior is underlined.
Key words. Striatal system; aggressive behavior; ventromedial hypothalamus; rage reaction; hissing.

Electrical stimulation of specific points within the hypothalamus of the cat may induce two forms of aggressive behavior: a quiet biting, predatory type of attack, which is preferentially directed at a rat, with no signs of autonomic participation[3] and a typical rage reaction with mydriasis, piloerection, snarling and showing of the teeth, which culminates in hissing[4–6]. It has been shown that the striatal system participates in the control of aggressive behavior: On the one hand, caudate nucleus stimulation inhibits both rage and attack display[7,8]; on the other hand, lesions of the striatal pathways to and from the substantia nigra at the level of the medial forebrain bundle result in a contralateral loss of patterned reflexes, which mediate attack behavior in the cat[9]. In this paper the effects of substantia nigra stimulation on the rage reaction elicited by hypothalamic activation will be considered.

Material and methods. The experiments were performed on five cats with chronically implanted electrodes. After general anesthesia (pentobarbital 50 mg/kg i.p.) the animals were placed on a stereotaxic apparatus (DKI 1404) and pairs of stainless steel wires (1–1.5 interelectrode distance, 25–50 μm tip) were implanted bilaterally in the ventromedial hypothalamic nucleus (A 9–12, L 1–2, H 4–5) and in the substantia nigra (pars compacta) (A 3–4, L 4–5, H 5–6)[10]. The animals, 6–8 days after surgery were subjected to experimental sessions in a behavioral cage (70 × 70 × 100 cm, inside dimensions). Both hypothalamus and substantia nigra were stimulated unilaterally and the side of the hypothalamic stimulation was chosen in relation to the lower threshold for the appearance of the behavioral response. The hypothalamus was stimulated with trains varying between 15–20 sec, 30–60 c/sec, 0.1–1 msec and with progressively higher current values (0.2–0.6 mA) until the complete affective display appeared and culminated in the hissing. The interval between the beginning of the hypothalamic stimu-

Effects of substantia nigra stimulation on hissing latency

Cat No.	Control sec[a]	Substantia nigra sec[a]	%[b]	t
1	8.16 ± 0.93	5.87 ± 0.57	28.06	3.17*
2	11.05 ± 1.29	6.92 ± 0.45	37.37	4.36*
3	10.07 ± 1.36	6.47 ± 0.33	35.75	4.04*
4	9.35 ± 0.92	4.55 ± 0.20	51.33	7.16**
5	11.08 ± 1.01	5.58 ± 0.30	49.64	6.29**

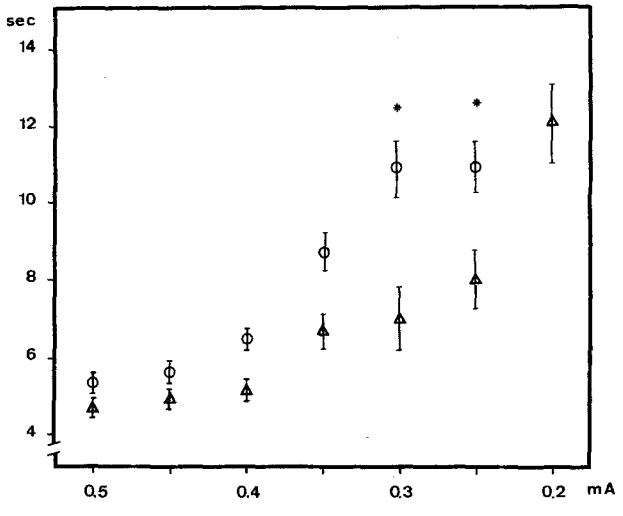
[a] Average ± SD latencies (n = 8) of the hissing in single (hypothalamic alone) and dual (hypothalamic and substantia nigra) stimulations.
[b] Percentage of nigral facilitation.
* $p \leq 0.01$; ** $p \leq 0.001$, Student's t-test.

lation and the appearance of the first hissing was considered as the reference value of the rage reaction and was measured with a stop watch. Hissing latency was constant in all animals if stimulation parameters did not change. Stimulation of the substantia nigra, ipsilateral to the hypothalamus was performed with parameters which determined the appearance of the animal behavioral changes (onset of the head-turning movement). Nigral activation (30–60 c/sec, 0.1–0.5 msec, 0.2–0.4 mA) lasted 4–6 sec and began simultaneously with hypothalamic stimulation. Single (i.e. hypothalamic alone) and dual (i.e. both hypothalamic and nigral) stimulation trials were given in the same session, in which the intertrial interval was maintained constant (10 min). The position of the electrode tips in the ventromedial hypothalamic nucleus and in the substantia nigra (pars compacta) were controlled on serial Nissl sections.

Results and discussion. Electrical stimulation of the cat's hypothalamus, with parameters able to evoke the complete rage reaction, resulted in a behavioral display which culminated in hissing. The animal walked around the cage and showed mydriasis, salivation, piloerection especially down the midline of the back and in the tail, slight retraction of the ears, snarling, growling, showing of the teeth and hissing. Lower stimulus strength and/or frequency determined a weaker affective display without hissing, whereas the increase of the same parameters resulted in a more sustained rage reaction with a greater number of hisses and a corresponding decrease of the hissing latency. The figure (circles) shows an example of the relation between stimulus intensity and hissing latency. In the same animal the development of the rage reaction and the hissing latency did not greatly change when stimulation parameters remained constant.

To study the effects of nigral stimulation on the hissing latency we used specific parameters of hypothalamic activation which induced hissing appearance at almost the same latency (8–11 sec). In these conditions for five animals the mean duration of the hissing latency was 9.94 ± 0.94 sec. When simultaneous stimulation of the hypothalamus and the substantia nigra was performed, it resulted in a decrease of the hissing latency to 5.87 ± 0.37 sec. The table shows that in each animal the results were statistically significant. When hypothalamic stimulation was performed with parameters below the threshold for the appearance of hissing, simultaneous stimulation of the substantia nigra determined its display. However, single stimulation of the substantia nigra never induced the appearance of the rage reaction, even on increasing the strength and the duration of the stimulus (in this case contralateral circling movements appeared). On the other hand when hypothalamic stimulation was performed with parameters which induced hissing latencies between 2 and 5 sec, simultaneous activation of the substantia nigra did not cause a significant decrease of the hissing latency. The figure shows the effects of nigral stimulation on the hissing latency in relation to the intensity of the hypothalamic activation. For each point of the hypothalamic stimulus strength in the abscissa, hissing latency is shown both in single (circles) and dual (triangles) stimulation conditions.

The above results show that substantia nigra stimulation determines a facilitation of the rage reaction obtained in the cat by hypothalamic activation. If, on the one hand, the effect could be considered as nonspecific and related to a greater attentiveness to stimuli, determined by an increase of the nigro-striatal dopaminergic activity[11,12], on the other the observed facilitation of the emotional display could be specifically related to the control exerted by the nigrostriatal system on other behavioral patterns[13]. Moreover, it has been recently suggested that the striatal system may make an important contribution to the specific patterned components of the attack behavior[9]. Our data show that the affective component of the aggressive behavior may also be influenced by the substantia nigra, which might modulate activity in other brain structures (i.e. the amygdaloid nuclei)[14] which contribute more directly to the expression of the rage reaction.



Circles: Relationship between the hissing latency and the hypothalamic (A 10, L 1, H 4.5) stimualtion current (50 c/sec, 15 sec, 0.1 msec) in one cat. Triangles: Effects of simultaneous stimulation (50 c/sec, 5 sec, 0.1 msec, 0.3 mA) of the ipsilateral substantia nigra (pars compacta) (A 3.5, L 4, H 5.5). Each value indicates the average ± SD (n = 8) of the hissing latency. * $p \leq 0.01$, Student's t-test.

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