

BRIEF COMMUNICATION

Behavioral Effect of Intracerebrally Injected Carbachol on Unrestrained Cats

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DECSI, L. *Behavioral effect of intracerebrally injected carbachol on unrestrained cats.* PHARMAC. BIOCHEM. BEHAV. 2(1) 141–143, 1974. — The rage reaction which can be evoked by carbachol stimulation of the hypothalamus on freely moving cat is not specific for the hypothalamus by far. It can also be elicited by carbachol stimulation of the septal region, thalamus (intralaminary nuclei), central grey matter, red nucleus, caudate nucleus, mesencephalic reticular formation as well as by injecting the drug into the cerebral ventricle. No rage reaction can be evoked by carbachol stimulation of the globus pallidus, putamen, dorsal hippocampus, ventral hippocampus, anterior, basal, central or lateral amygdaloid nucleus and the cerebral white matter. The significance of these findings is discussed.

Carbachol Rage Intracerebral microinjection

DIRECT chemical stimulation of the hypothalamus with carbachol (carbamylcholine) in freely moving cats has been demonstrated to evoke a characteristic emotional-behavioral reaction [2, 3, 4, 7, 11, 12, 13, 14, 16] showing a complex behavioral pattern with definite aggression in some cases, and with fear-like behavior in others. On the basis of the most characteristic and most frequent manifestations, and also for the sake of simplicity, we have termed it a rage reaction. (Whether it is real or sham rage lies beyond the scope of the present discussion.) This reaction to intrahypothalamic carbachol has proved quite a consistent finding and can be evoked from several hypothalamic sites. There are some scattered data in the literature on a similar reaction pattern sometimes observed after injecting cholinomimetics in some other parts of the brain in the course of experiments performed for some other purpose [1, 2, 7, 9, 10, 12, 13]. However, we do not know of any systematic investigations which aimed at mapping the subcortical organization of this reaction pattern not even in terms of gross anatomic localization. Since, however, it is rather improbable that the rage reaction should only involve the hypothalamus, experiments were started in this laboratory a few years ago to elucidate what other subcortical brain structures might participate in the organization of this reaction pattern.

METHOD

The experiments were performed on cats with chron-

ically implanted cannulae and electrodes. For measuring the intensity of the rage reaction we used a method developed by us earlier. This is based on the observation that the manifestations of the rage reaction involve not only the general attitude of the animal, its gross behavior, locomotion, etc., but is also accompanied by characteristic vocalization. Thus we simply recorded the growling and hissing of the animal on magnetic tape and estimated the intensity of the reaction by adding up the times of vocalization during a certain period (generally 20 min) after the injection of carbachol. The general principles of the method used have been described in detail previously [4, 14, 16]. Chemical stimulation was performed by injecting 5 μ l of buffered carbachol solution at pH 7.3, by means of a microinjector in about 30 sec. More than 200 cats were used and a total of 17 various regions studied. The results obtained are summarized in Table 1.

RESULTS

Table 1 shows that the rage reaction can be evoked not only from the hypothalamus but also from the septal region, the non-specific (more exactly, the intralaminary) nuclei of the thalamus, the central grey matter, the red nucleus, the caudate nucleus, the mesencephalic reticular formation, and also by injecting carbachol directly into the cerebral ventricle. It cannot be evoked by carbachol stimulation of the globus pallidus, putamen, ventral and dorsal hippocampal formations, anterior, basal, central or

TABLE 1
POSITIVE AND NEGATIVE RESPONSES TO INTRACEREBRALLY INJECTED CARBACHOL

Regions from which a rage reaction can be elicited by carbachol / 0.62–5 μg /	Regions from which no rage reaction can be elicited by carbachol / up to 20 μg /
Hypothalamus	Globus pallidus
Septal region	Putamen
Thalamus / intralaminar cell group /	Ventral hippocampal formation
Central grey matter	Dorsal hippocampal formation
Red nucleus	Anterior amygdaloid nucleus
Caudate nucleus	Basal amygdaloid nucleus
Mesencephalic reticular formation	Central amygdaloid nucleus
Cerebral ventricle	Lateral amygdaloid nucleus
	White matter

lateral cell groups of the amygdala, and from the white matter (other regions have not yet been investigated).

Thus there can be no doubt that several subcortical areas are implicated in the organization of the rage reaction evoked by cholinergic stimulation of the brain. These areas might as well constitute a functional circuit, cholinergic stimulation of any part of which results in a rage reaction.

The reaction patterns evoked from various areas are not exactly alike. There is some difference in locomotor activity (little in the case of the hypothalamus, much in that of the thalamus or reticular formation), in the accompanying autonomic signs (most marked with hypothalamic stimulation), and also in the frequency and intensity of the attempts to attack any object or small animal put before the cat.

DISCUSSION

The rage reaction is easily abolished by topical pre-treatment with a few micrograms of atropine. In addition, it can be antagonized by local application of a functional antagonist (adrenergic stimulant) and also from some remote parts of the circuit. For instance, the rage reaction evoked by carbachol stimulation of the hypothalamus is abolished by simultaneous beta-adrenergic stimulation of the thalamus, or, the rage reaction evoked by carbachol stimulation of the thalamus is inhibited by simultaneous beta-adrenergic stimulation of the red nucleus [5,6].

Thus, at first sight it seems that we are faced with a

real subcortical functional circuit which might correspond to the gross anatomic organization of the rage reaction pattern. (Its chemical organization is certainly cholinergic and most probably involves muscarinic receptors.) However, the circuit explored by chemical stimulation is not completely identical with that explored by electrical stimulation [8]. For this and for other reasons also an alternative explanation is possible for the behavioral effect of intracerebrally injected carbachol in the cat. Also, considering the rather wide-spread regions from which this reaction can be elicited one might as well be right in assuming the carbachol-induced rage reaction to be a general, not really specific response of the brain to intense cholinergic stimulation of the appropriate subcortical structures. The stimulation may not remain strictly localized since, for instance, excitation of the reticular formation or that of the intralaminar thalamic nuclei will certainly spread over the whole brain. Accordingly, this reaction pattern might also be regarded as the brain's general, non-specific response, nearly always in the same form, to intense intracerebral stimulation (be it chemical or electrical) just like, for instance, the general sympathetic response, the alarm reaction to any kind of appropriate external stimuli.

Experiments are now in progress to elucidate the above-outlined functional circuit (if there be any) more exactly and to find some direct clues as to the more detailed anatomic organization of the affective-emotional reactions evoked by direct chemical stimulation of various brain areas in the waking cat.

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