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Endogenous Brain Norepinephrine Levels Following Bilateral Olfactory Bulb Ablation[1]

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CAIRNCROSS, K. D., S. P. M. SCHOFIELD AND J. R. BASSETT. *Endogenous brain norepinephrine levels following bilateral olfactory bulb ablation.* PHARMAC. BIOCHEM. BEHAV. 3(3) 425–427, 1975. – Changes in endogenous norepinephrine (NE) levels after bilateral olfactory bulb section have been found to occur in the rat brain. Since olfactory tract projections are confined to the ventral adrenergic pathway, and this pathway projects to the pyriform cortex, it was decided to examine the distribution of endogenous NE between the pyriform cortex and the remaining neocortex. It was demonstrated that significant reductions in NE content occurred in both brain regions, although the greater reduction occurred in the pyriform cortex. There were no significant changes in hypothalamic NE. It is concluded that sensory deprivation plus olfactory system damage induce specific changes in central function, which relate to noradrenergic pathways.

Olfactory bulb Norepinephrine Pyriform cortex Cerebral cortex Hypothalamus

FOLLOWING bilateral olfactory bulb ablation pronounced changes occur in the behavioral response of rats to aversive stimuli [4,12]. It has been established also that this surgical procedure induces marked pathological and biochemical changes in olfactory projection systems to the olfactory cortex. In particular there occurs a degeneration in primary olfactory neurones passing to the pyriform cortex [14] which is accompanied by a reduction in endogenous brain norepinephrine (NE) in the telencephalon [15]. King and Cairncross [10] suggested therefore that the anatomical and physiological evidence implicated the cerebral cortex as the functional centre in the changed response to the aversive stimulus.

In view of these observations it was important to ascertain whether surgical interference with the afferent olfactory pathways produced a nonspecific reduction of NE in the cortex, or whether the change in endogenous NE concentration related only to cortical olfactory projection areas. Such a question related to observations by Ungerstedt [17] and Livett [11] regarding the differentiation of central ascending NE pathways into dorsal and ventral components. The ventral components, arising primarily from the medulla and pons, ascend in the mesencephalic reticular formation to the diencephalon and have a significant collateral projection to the limbic system [17].

The dorsal norepinephrine pathway originates in the brain stem, and forms a separate bundle at the origin of the Pontine nucleus. These axons ascend within the medial forebrain bundle and terminate in the thalamus, whence projections pass to the telencephalic cortical regions. The two ascending pathways may be considered therefore to subserve different functions. The dorsal bundle co-ordinates telencephalic cortical activity through diffuse post-thalamic projections; the ventral pathway through diencephalic and limbic function could modify the autonomic and endocrine components of behavior [13].

This paper describes experiments undertaken to ascertain whether the observed reduction in endogenous NE levels relate to the whole cortex, or whether the reduction is prescribed to olfactory projection areas.

METHOD

Animals

Experimentally naive male Wistar rats (Macquarie strain 100–130 days old were used in all experiments. The animals were housed singly in conditions of constant temperature and humidity and subjected to a reverse light cycle (light 8 p.m. – 8 a.m.) beginning fourteen days prior to the surgical procedures.

Procedure

Surgery. Rats were treated preoperatively with 120,000 units of Bicillin and were anaesthetised with an injection of

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TABLE 1

EFFECT OF OLFACTORY BULB ABLATION ON THE NE CONTENT OF VARIOUS REGIONS OF THE RAT BRAIN

Procedure		Norepinephrine (μg/g tissue) mean ± S.D.* Hypothalamus	Pyriform Cortex	Neocortex
Sham operated	(10)†	1.060 ± 0.179	0.301 ± 0.030	0.229 ± 0.030
Bilateral ablation	(7)	1.042 ± 0.101	0.228 ± 0.021	0.193 ± 0.013
p‡		>0.080	<0.001	<0.01

*Standard deviation
†Number of animals/group
‡p calculated using unpaired t test; $p = 0.05$ is significant.

Equithesin (8.1 ml nembutal, 60 mg/ml; 1.063 g magnesium sulphate; 18.15 ml propylene glycol; 4.95 ml ethanol; 2.125 g chloral hydrate and made to 50 ml with distilled water) at a dose of 0.33 ml per 100 g body weight I.P. The head of the animal was secured in a stereotaxic instrument and the frontal bone exposed through a midline incision extending 2 cm caudad from the rim of the orbit. Burr holes were drilled through both frontal bones, 2 mm lateral to the frontal suture at a point level with the posterior rim of the orbit. A blunt probe was introduced and the olfactory bulbs sectioned anterior to the frontal lobes, and the olfactory lobe was aspirated. A surgical foam containing 0.1% dequalinium chloride was plugged into the holes, the wound sprinkled with penicillin powder and closed. Sham operated rats underwent the same surgical procedure except that lateral olfactory bulb ablation was not undertaken.

Brain dissection. A period of 28 days was allowed to elapse before the rats were sacrificed by decapitation. This allowed complete Wallerian degeneration and ensured endogenous NE levels were stable [5]. Olfactory bulb ablation was confirmed post mortem as described by King and Cairncross [10].

The brain was removed from the skull and the dissection technique carried out on an ice-cooled plate (4°C). The hypothalamic dissection was as described by Glowinski and Iversen [7]. The cortical dissection was as follows: The ventral surface of the brain was exposed and a transverse section made at the level where the olfactory tubercle joins the cortex. Longitudinal incisions were then made the length of the cortex, lateral to the hypothalamic margins, thus freeing the ventral edges of the pyriform cortex. A third section was made laterally along the rhinal fissure which forms the uppermost border of the pyriform area. The pyriform cortex was then detached from the remaining cortex.

All brain regions were frozen in liquid nitrogen, weighed and stored at −20°C until assayed for NE.

Norepinephrine assay. The NE extracted after the method of Anton and Sayre [1] and assayed spectrofluorimetrically as described by Haggendal [8]. A recovery test of 0.08 μg NE in 0.4N perchloric acid was included in each assay group, and recoveries ranged from 75–90 percent. The NE measured was then corrected for recovery and sample weight and was expressed as μg/g wet tissue.

RESULTS

The effect of olfactory bulb ablation on the endogenous NE content of the hypothalamus, neocortex and pyriform cortex is shown in Table 1. It can be seen that following ablation a significant depletion in the level of endogenous NE occurred in both the pyriform cortex and the neocortex but not in the hypothalamus. The percent reduction in endogenous NE was greater in the pyriform cortex (24.3 percent) than in the neocortex (15.7 percent).

DISCUSSION

The results obtained show that following bilateral olfactory tract section, there is a reduction in NE content of both the pyriform cortex and remaining areas of the telencephalon. The supposition therefore, that the NE reduction might be confined to olfactory projection areas is not valid, and supports the observation that no direct pathway from the olfactory bulb to the pyriform cortex has been demonstrated [14]. The results obtained suggest that following bilateral olfactory tract section there occurs a dysfunction in both the ventral and dorsal ascending noradrenergic pathways. Such a dual dysfunction could be expected to reflect itself in memory and learning processes as well as fixed behavioral patterns, having a diencephalic or mesencephalic origin. This latter presumption is well documented; anosmic animals demonstrate changes in aggressive behavior [3], in mating and maternal behavior [6,9]. Memory and learning are affected also, particularly a deficit has been demonstrated in the learning of avoidance tasks [4, 10, 12]. A decrease in noradrenaline availability has been associated with this condition [10], and drug treatment aimed at overcoming the NE deficit has resulted in rats being able to improve their performance in aversive conditioning [5]. The body of evidence suggests therefore

that sensory deprivation plus tissue damage in the form of olfactory tract ablation induces specific changes in central nervous system function, and that these changes relate probably to NE availability in both ventral and dorsal noradrenergic pathways. This conclusion is supported by the work of Cain [2] who suggests that changes in behavior in the rat are not wholly due to loss of the olfactory sense but also relate to central nervous tissue ablation.

The observation that hypothalamic NE levels are not changed following bilateral olfactory tract ablation substantiates the results of other workers [16] and indicates that the depletion of endogenous NE described is specific to the cortical regions investigated.

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