Neuropharmacology, 1976, 15, 91–97. Pergamon Press. Printed in Gt. Britain.

ROLE OF SUPERIOR COLLICULUS SEROTONIN IN THE GROOMING BEHAVIOUR OF CATS

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Summary— The present study provides evidence that a serotonergic system in the superior colliculus is involved in the regulation of grooming behaviour. Significant decreases in tryptophan hydroxylase activity and serotonin content were found in the superior colliculi of cats with pontile lesions and frontal neocortical lesions, which display a dissociation of appetitive and consummatory grooming behaviours. Neither tryptophan hydroxylase activity nor serotonin content were significantly changed in thyroidectomized cats, which display the same abnormal grooming behaviour. 5-Hydroxytryptophan administration or monoamine oxidase inhibition plus tryptophan administration abolished the abnormal grooming behaviour in each of the three groups of cats, suggesting that the change in a serotonergic system is a critical aspect of the abnormal behaviour in cats with pontile lesions and frontal neocortical lesions, and that a serotonergic system may also be involved in the genesis of the abnormal grooming behaviour in thyroidectomized cats. Functional inactivation of the serotonergic system by lysergic acid diethylamide administration or by serotonin receptor blockade did not induce the abnormal grooming behaviour in normal cats, indicating that other factors are involved in the genesis of the abnormal behaviour. Previous studies indicated that glucocorticoids are the other critical factor. Thus, a serotonergic system in the superior colliculi, operating at some level of glucocorticoid function, is involved in the integration of appetitive and consummatory grooming behaviours. These data provide the first demonstration of the biological mechanisms underlying the integration of the appetitive (learned) and consummatory (unlearned) components of instinctive behaviour.

An abnormal grooming behaviour, consisting of a dissociation of the appetitive and consummatory components of the behavioural sequence following tactile stimulation of the body surface, occurs in cats with pontile lesions (RANDALL, 1964), cats with frontal neocortical lesions (TRULSON, NICOLAY and RANDALL, 1975) and in thyroidectomized cats (TRULSON, 1974). The appetitive and consummatory components of grooming behaviour normally occur in a well-integrated sequence, but during the abnormal behavioural state tactile stimulation of the cat's body surface elicits a consummatory grooming bite, lick, or scratch (the type of response elicited is a response normally used to groom the region of the body surface that is tactually stimulated) which appears immediately and is not directed to the body surface. Since the consummatory response occurs without the appetitive or orienting behaviour that normally precedes it, the behaviour is non-functional. The dissociated grooming behaviour is of theoretical interest because it provides a model for studying the anatomical and biochemical bases of the classical appetitive–consummatory behavioural dichotomy of SHERRINGTON (1906) and CRAIG (1918). Also, grooming behaviour is important because it maintains a health boundary required for homeostasis and, therefore, for life itself. Another interesting aspect is the rhythmical nature of the behavioural abnormality: the percentage of the body surface from which the grooming fragments can be elicited varies with the seasons of the year (RANDALL and PARSONS, 1972).

Systemic administration of 5-hydroxytryptophan (5-HTP), the immediate precursor of the putative neurotransmitter serotonin (5-HT) in the central nervous system, abolishes the abnormal grooming behaviour in cats with pontile lesions (TRULSON and RANDALL, 1973) and in thyroidectomized cats (TRULSON, 1974). Microinjections of 5-HTP or 5-HT into the superior colliculus (but not other brain regions) also abolishes the abnormal behaviour in cats with pontile lesions (TRULSON and RANDALL, 1973), indicating that a defect in the serotonergic system in the superior colliculus may be an essential condition for the abnormal grooming behaviour. Pharmacological depletion of 5-HT does not induce the abnormal behaviour in normal cats (TRULSON and RANDALL, 1973; TRULSON *et al.*, 1975), indicating that other factors may be involved. Another critical factor appears to be glucocorticoids, since adrenalectomized cats administered a 5-HT-depleting drug, *p*-chlorophenylalanine (*p*-CPA), display the abnormal grooming behaviour (RANDALL, ELBIN and SWENSON, 1974). The present study further specifies the biological bases for the integration of appetitive and consummatory grooming behaviours in the cat.

METHODS

One-hundred and ten adult, male cats (*Felis catus* L.) were housed individually in a room under temperature control (22 ± 1°C) and artificial lighting (lighting schedule synchronized with external lighting).

Surgical procedures

Strict aseptic techniques were followed in all surgical procedures. All cats were anaesthetized by intraperitoneal injection of sodium pentobarbital (35 mg/kg) and administered 3,3-methylethylglutaramide (20 mg/kg) at the completion of surgery.

Seventeen cats received stereotaxic, anodal pontile lesions bilaterally, as previously described (RANDALL, 1964). Twenty six cats received bilateral lesions of the frontal neocortex. The neocortex rostral to the ansate and anterior ectosylvian sulcus and dorsal to the rhinal fissure was removed by aspiration. Eleven cats received sham surgery: the surgical procedure was terminated when the dura was exposed.

Sixteen cats were thyroidectomized using a combination of surgical and radioactive ablation techniques. The thyroid glands were removed, and one pair of parathyroid glands was implanted into a pocket in the sternomastoideus muscle. The cats were provided with a 1% solution of calcium lactate for one week postoperatively. One week after the surgical thyroidectomy each cat received a single intramuscular injection of ^{131}I(1·3 mCi/kg) in order to ablate any accessory thyroid tissue. Six cats received bilateral adrenalectomy according to the method of HOPCROFT (1966). These cats were provided with an electrolyte solution (Vetrad-O, Don Hall Laboratories) for drinking. Because of the occasional occurrence of accessory adrenal tissue, the adrenalectomized cats were tested for the presence of glucocorticoids. Blood and urine samples were collected from adrenalectomized and control cats, and analyzed for 11-hydroxycorticoids using the method of MATTINGLY (1962). Nine cats received sham surgery: incisions were made through the skin and muscle layers as in the endocrine ablation groups, but no glands were removed.

Measurement of abnormal grooming behaviour

A quantitative measure of the degree of the behavioural abnormality was obtained using standard diagrams of the right and left lateral views of a cat containing a grid pattern of dots (see TRULSON *et al.*, 1975, for illustration). Imitation bites (sharply tapping the body surface), licks (gently moving a finger along the body surface), and scratches (actually scratching the body surface) were systematically directed to the cat's entire body surface, and the areas from which each type of consummatory grooming fragment could be elicited were entered on the diagram. The percentage of the body surface from which consummatory grooming fragments could be elicited was calculated by computing the fraction of the total number of dots enclosed within the "responsive areas".

Tryptophan hydroxylase activity

The cats were anaesthetized with sodium pentobarbital (35 mg/kg, i.p.). The brains were removed and dissected on ice according to the method of TRULSON *et al.* (1975), to obtain the superior colliculi, dorsal thalamus, hypothalamus and cerebral neocortex. A cerebellar neocortical tissue sample, consisting of a large portion of the ansiform lobule and small fragments of the paraflocculus, was also obtained. In all cases, bilaterally symmetrical left and right tissue samples were obtained and homogenized together for the tryptophan hydroxylase assays. Tryptophan hydroxylase activity was assayed using the method of GAL and PATTERSON (1973).

5-HT content

The cats were anaesthetized with sodium pentobarbital (35 mg/kg, i.p.). The brains were removed and dissected on ice to obtain the superior colliculi, dorsal thalamus, hypothalamus, cerebral neocortex and cerebellar neocortex, as described above. Serotonin was measured using a modification of the method of BOGDANSKI, PLETSCHER, BRODIE and UDENFRIEND (1956). The tissue samples were weighed and homogenized in 1·5 ml cold 0·1 M HCl containing 0·01% ascorbic acid. The 36,000 *g* supernatant was adjusted to pH 10·0 with anhydrous sodium carbonate and saturated with sodium chloride. After adding 2·5 ml borate buffer (pH 10·0) the 5-HT was extracted into 3·0 ml *n*-butanol. The butanol phase was transferred to centrifuge tubes containing 0·6 ml of 3 M HCl and 10·0 ml purified heptane. The tubes were shaken for 10 min and spun for 5 min, and the organic phase was removed by aspiration. Samples (0·5 ml) of the HCl were transferred to test tubes containing 1·0 ml of 10 M HCl and 0·1 ml of 1% cysteine solution. After adding 0·5 ml of OPT reagent (4 mg of ortho-phthalaldehyde in 100 ml of 10 M HCl) and mixing thoroughly, the tubes were heated in boiling water for 15 min. The reaction mixture was cooled to room temperature and the fluorescence was measured at 480 nm with activation at 360 nm.

Pharmacological studies

The size of the responsive area was determined for each cat before and after the pharmacological treatments, and these measures were used to evaluate the effects of the various drugs on the abnormal grooming behaviour.

Tryptophan, 5-HTP and p-chlorophenylalanine administration. Five cats with frontal neocortical lesions received a single injection of DL-5-HTP (25 mg/kg i.p., in 0·3% gum tragacanth in physiological saline) and 3 cats with frontal neocortical lesions received a single injection of DL-tryptophan (25 mg/kg, i.p., in the same vehicle). Three cats with frontal neocortical lesions that were displaying few or no grooming fragments (because of spontaneous variations) received *p*-CPA (150 mg/kg per day in gourmet cat food) for 5 consecutive days. Similar pharmacological studies have already been performed in cats with pontile lesions and in thyroidectomized cats (TRULSON and RANDALL, 1973).

Monoamine oxidase inhibition and tryptophan administration. Four cats with pontile lesions received

a single injection of trans-2-phenylcyclopropylamine (5 mg/kg, i.p.) in saline followed 3 hr later by a single injection of L-tryptophan (25 mg/kg, i.p.) in 0·3% gum tragacanth in saline. Four control cats with pontile lesions received a single intraperitoneal injection of 1 ml saline followed 3 hr later by a single injection of 0·3% gum tragacanth in saline (2 ml, i.p.). Groups of cats with frontal neocortical lesions and thyroidectomized cats received the same treatments.

LSD administration. Seven normal cats received a single injection of lysergic acid diethylamide (LSD, 100 μg/kg, i.p.) and were monitored for the abnormal grooming behaviour for 3 hr. The experiment was repeated using 2 lower dosages of LSD (15 μg/kg and 40 μg/kg) and one higher dosage (250 μg/kg). Lysergic acid diethylamine has been shown to inactivate the serotonergic system by acting directly on serotonin-containing cell bodies (AGHAJANIAN, HAIGLER and BLOOM, 1972).

5-HT receptor blocking agents. Five normal cats received a single injection of cinnaserin (10 mg/kg, i.p.) and five normal cats received a single injection of methylsergide (5 mg/kg, i.p.). All cats were monitored for the abnormal grooming behaviour for 3 hr. Both cinnaserin and methylsergide have been shown to be effective 5-HT receptor blockers at these dosages (JACOBS, 1974).

Anatomy

Following dissection of the brains used in the tryptophan hydroxylase and 5-HT assays, the remaining brain parts were placed in formalin for several hours and then washed with water and placed in 70% ethanol. The loci of the frontal neocortical lesions were determined by gross dissection. The brainstems with pontile lesions were dehydrated in a series of ethanols, and infiltrated and embedded in paraplast. Two series of 20 μm transverse sections were obtained at 0·5 mm intervals and stained with cresyl violet and Heidenhain stains. Each lesion was reconstructed in a transverse plane through the maximal extent of the lesion using a projection microscope.

RESULTS

Behaviour

All cats with pontile lesions, frontal neocortical lesions and thyroidectomized cats displayed prominent grooming fragments, while none of the adrenalectomized cats or control cats displayed any of the abnormal grooming behaviour. Longitudinal monitoring of the abnormal behaviour indicated that a peak in the size of the responsive area occurred in the fall of the year in each of the 3 groups of cats that displayed the abnormal behaviour.

Tryptophan hydroxylase activity

Tryptophan hydroxylase activity was significantly decreased in the superior colliculi (−30%) and dorsal thalamus (−25%) in cats with pontile lesions, and in the superior colliculi (−33%) in cats with frontal neocortical lesions (Table 1). No significant changes in tryptophan hydroxylase activity were found in the thyroidectomy or adrenalectomy groups. The 11-hydroxycorticoid levels in adrenalectomized cats were decreased 83% in plasma and 80% in urine.

5-HT content

Serotonin content was significantly decreased in the superior colliculi (−29%) of cats with pontile lesions and in the superior colliculi (−28%) of cats with frontal neocortical lesions. No significant changes in 5-HT content were detected in the thyroidectomy group (Table 2).

5-HTP, tryptophan and p-CPA administration

Administration of 5-HTP abolished the abnormal grooming behaviour in all cats with frontal neocortical lesions, while administration of tryptophan did not affect the abnormal behaviour in any of the cats. The abnormal behaviour was abolished within 20 to 120 min after 5-HTP administration and reappeared with 24 hr in each case. Administration of *p*-CPA induced the abnormal behaviour in cats with frontal

Table 1. Tryptophan hydroxylase activity (nmol/hr per mg, mean ± S.E.M.) in five brain regions in cats with pontile lesions, cats with frontal neocortical lesions, thyroidectomized cats, adrenalectomized cats and control cats

Group	Superior colliculi	Dorsal thalamus	Hypothalamus	Cerebral neocortex	Cerebellar neocortex
Control (n = 12)	1·01 ± 0·08	0·99 ± 0·07	1·10 ± 0·09	0·33 ± 0·03	0·29 ± 0·02
Pontile lesion (n = 6)	0·71* ± 0·07	0·74* ± 0·08	0·98 ± 0·13	0·38 ± 0·05	0·26 ± 0·04
Frontal neocortical lesion (n = 6)	0·68* ± 0·05	0·81 ± 0·08	1·01 ± 0·17	0·22 ± 0·06	0·21 ± 0·05
Thyroidectomy (n = 6)	0·90 ± 0·08	1·00 ± 0·11	0·94 ± 0·10	0·35 ± 0·04	0·36 ± 0·05
Adrenalectomy (n = 6)	1·13 ± 0·08	1·22 ± 0·13	1·02 ± 0·09	0·41 ± 0·06	0·33 ± 0·04

* Significant change from control ($P < 0·05$, Dunnett's Test).

Table 2. 5-Hydroxytryptamine content (nmol/g, mean ± S.E.M.) in five brain regions in cats with pontile lesions, frontal neocortical lesions, thyroidectomized cats and control cats

Group	Superior colliculi	Dorsal thalamus	Hypothalamus	Cerebral neocortex	Cerebellar neocortex
Control (n = 5)	7·62 ± 0·36	5·83 ± 0·47	7·71 ± 0·20	1·82 ± 0·18	1·28 ± 0·14
Pontile lesion (n = 3)	5·44* ± 0·57	4·80 ± 0·52	6·06 ± 0·50	1·68 ± 0·33	1·54 ± 0·25
Frontal neocortical lesion (n = 3)	5·49* ± 0·43	5·71 ± 0·69	7·22 ± 0·87	1·25 ± 0·43	0·92 ± 0·18
Control† (n = 3)	5·07 ± 0·60	6·70 ± 0·91	6·99 ± 0·55	0·90 ± 0·10	0·93 ± 0·18
Thyroidectomy (n = 3)	4·42 ± 0·43	4·53 ± 0·91	6·53 ± 0·44	0·95 ± 0·13	0·84 ± 0·17

* Significant change from control ($P < 0·05$, Dunnett's Test).

† The thyroidectomized cats and their controls were assayed at a different time of the year than the lesioned cats and their controls, accounting for the difference between the 2 control groups.

neocortical lesions that were not displaying the behaviour because of spontaneous seasonal reversions, while *p*-CPA administration to normal cats did not induce the abnormal grooming behaviour. These results are summarized in Table 3.

Monoamine oxidase inhibition plus tryptophan administration

The size of the responsive area was decreased in all 3 groups of cats that received the monoamine oxidase (MAO) inhibitor after 3 hr, and the remaining grooming fragments were abolished in each group of cats within 1 hr after administration of tryptophan. The abnormal grooming behaviour reappeared within 24 hr in each group of cats (Figs. 1, 2 and 3). When the MAO inhibitor was administered alone, the maximal decrease in the size of the responsive area occurred approximately 3 hr after administration.

Administration of LSD and 5-HT receptor blockers to normal cats

None of the abnormal grooming behaviour was observed in any of the normal cats, neither before treatment nor after the administration of LSD, cinnaserin, or methylsergide.

Anatomy

The locus of a typical frontal neocortical lesion is displayed in Figure 4. Figure 5 shows the reconstruction of a transverse section through the maximal extent of a typical pontile lesion. The lesions were located at the level of the paralemniscal and caudal central tegmental fields, extending from the lateral tegmentum to the edge of the brainstem and into the pons.

DISCUSSION

A change in a serotonergic system in the superior colliculi is an essential aspect of the lesion-induced dissociation of appetitive and consummatory grooming behaviours, since tryptophan hydroxylase activity and 5-HT content were decreased in the superior colliculi, and microinjections of 5-HT into the superior colliculi (but not other brain regions) abolished the abnormal behaviour (TRULSON and RANDALL, 1973). The fact that MAO inhibition plus tryptophan administration abolishes the abnormal grooming behaviour is further evidence for a specific involvement of 5-HT. The similar defect in tryptophan hydroxylase and 5-HT in the superior colliculi after pon-

Table 3. Effects of 5-HTP, tryptophan and *p*-CPA administration on the abnormal grooming behaviour in cats with frontal neocortical lesions

Group	Treatment	*n*	Responsive area (% of body surface) Before treatment	After treatment	Level of significance*
Frontal neocortical lesion	5-HTP	5	21 ± 7	0	$P < 0·02$
	tryptophan	3	19 ± 6	20 ± 8	
Frontal neocortical lesion	*p*-CPA	3	4 ± 2	33 ± 10	$P < 0·01$
Normal	*p*-CPA	8	0	0	

* Randomization test for independent samples.

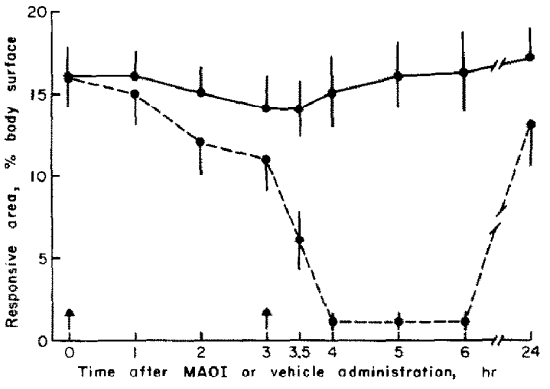

Fig. 1. Effects of MAO inhibitor (MAOI) plus tryptophan (dashed line) and vehicle (solid line) on the abnormal grooming behaviour in cats with pontile lesions. MAO inhibitor or vehicle was administered at zero time and tryptophan or vehicle was administered 3 hr later. Each point represents the mean for 4 cats, and the vertical bars represent standard errors of the mean. The effect of MAO inhibitor plus tryptophan differed significantly from the vehicle effect ($P < 0{\cdot}02$, Randomization test).

tile and frontal neocortical lesions cannot be explained in terms of the interruption of direct projections of serotonergic neurones, since there are no serotonergic cell bodies or fibres of passage in the regions of the lesions (PIN, JONES and JOUVET, 1968), indicating that the change is mediated transneuronally. The serotonergic system that projects to the superior colliculus may receive a facilitatory input from the frontal neocortical and pontile regions, and lesioning these areas would decrease the activity of these neurones. There are direct projections from the frontal neocortex to the serotonin-containing raphe nuclei (BRODAL, WALBERG and TABER, 1960) as well as to the superior colliculus (SPRAGUE, 1963). The

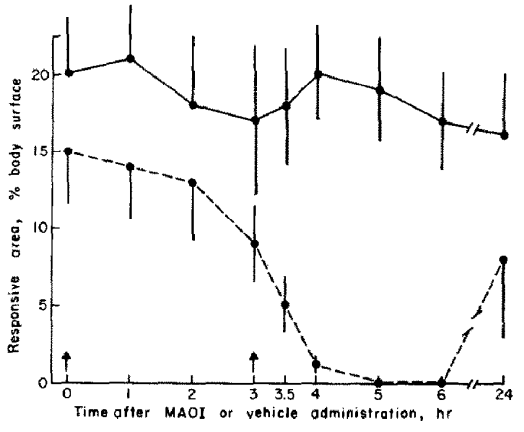

Fig. 2. Effects of MAO inhibitor (MAOI) plus tryptophan (dashed line) and vehicle (solid line) on the abnormal grooming behaviour in cats with frontal neocortical lesions. MAO inhibitor or vehicle was administered at zero time and tryptophan or vehicle was administered 3 hr later. Each point represents the mean for 3 or 4 cats, and the vertical bars represent standard errors of the mean. The effect of MAO inhibitor plus tryptophan differed significantly from the vehicle effect ($P < 0{\cdot}03$, Randomization test).

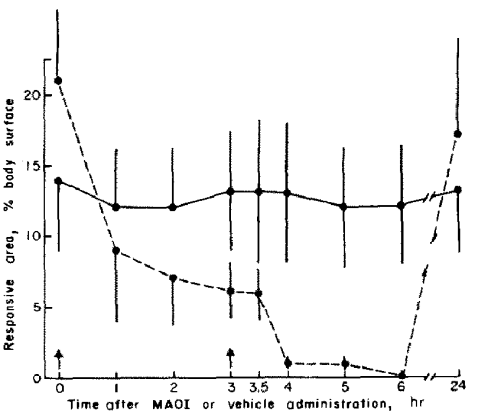

Fig. 3. Effects of MAO inhibitor (MAOI) plus tryptophan (dashed line) and vehicle (solid line) on the abnormal grooming behaviour in thyroidectomized cats. MAO inhibitor or vehicle was administered at zero time and tryptophan or vehicle was administered 3 hr later. Each point represents the mean for 3 or 4 cats, and the vertical bars represent standard errors of the mean. The effect of MAO inhibitor plus tryptophan differed significantly from the vehicle effect ($P < 0{\cdot}03$, Randomization test).

pontile lesion also interrupts fibres to the superior colliculus (ALTMAN and CARPENTER, 1961), and several studies indicate that neurones in the region of the pontile lesion project to the raphe nuclei (e.g. BRODAL *et al.*, 1960; SCHEIBEL and SCHEIBEL, 1958).

Several studies have reported a positive correlation between nerve impulse flow and neurotransmitter synthesis. For example, LSD, which decreases the discharge rate of serotonergic neurones by acting directly on the cell body (AGHAJANIAN *et al.*, 1972), leads to a decrease in 5-HT synthesis and turnover (FREEDMAN and BOGGAN, 1973). Similarly, section of monoamine fibre systems leads to an immediate change in 5-HT synthesis rates (CARLSSON, BEDARD, LINDQVIST and MAGNUSSON, 1972). Since the pontile and frontal neocortical lesions in the present study do not directly interrupt serotonergic neurones, the

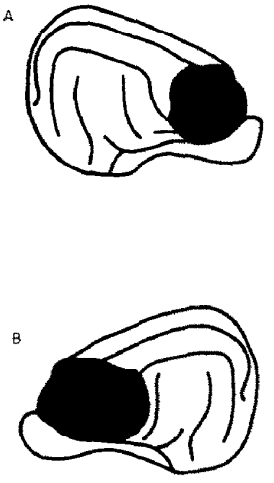

Fig. 4. Diagrammatic representation of right (A) and left (B) cerebral hemispheres displaying the locus of a typical frontal neocortical lesion.

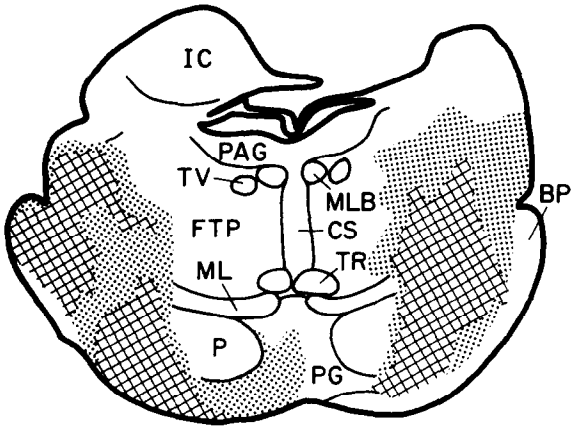

Fig. 5. A reconstruction of a transverse section through the maximal extent of a typical pontile lesion. Cross-hatching indicates total degeneration and stippling indicates partial degeneration. The abbreviations and nomenclature are from BERMAN (1968): BP, brachium pontis; CS, superior central nucleus; FTP, paralemniscal tegmental field; IC, inferior colliculus; ML, medial lemniscus; MLB, medial longitudinal bundle; P, pyramidal tract; PAG, periaqueductal gray; PG, pontine gray; TR, tegmental reticular nucleus; TV, ventral tegmental nucleus.

change in 5-HT metabolism seen in the superior colliculus is evidently a secondary change due to a decrease in nerve impulse flow.

While a change in a serotonergic system in the superior colliculus is an essential condition for the lesion-induced modification in grooming behaviour, this alone is not a sufficient condition to induce the behavioural change. Inactivation of the serotonergic system via LSD administration or by blocking serotonergic receptors did not induce the abnormal grooming behaviour in normal cats. Similarly, attempts to induce the abnormal behaviour in normal cats by depleting or interfering with the synthesis of 5-HT systemically or by microinjections of *p*-CPA locally into the superior colliculi have failed (TRULSON and RANDALL, 1973; TRULSON *et al.*, 1975). The fact that *p*-CPA administration to cats with pontile or frontal neocortical lesions that were not displaying the abnormal grooming behaviour (because of spontaneous reversions) induces the abnormal behaviour, supports the conclusion that another factor is involved, and the fact that *p*-CPA administration induces the same abnormal grooming behaviour in adrenalectomized cats (RANDALL *et al.*, 1974) suggests that the glucocorticoids are the other factor. The glucocorticoids are further implicated in the abnormal grooming state by an inverse relationship between glucocorticoid excretion and size of responsive area found in a longitudinal study (RANDALL and PARSONS, 1972). The fact that administration of glucocorticoids abolishes the abnormal behaviour in cats with frontal neocortical or pontile lesions (TRULSON, 1974) further suggests that the glucocorticoids are the other essential factor.

The finding in the present study that adrenalectomy does not change the activity of tryptophan hydroxylase lends some support to the hypothesis that decreased 5-HT and glucocorticoids are necessary and sufficient conditions for the appearance of the abnormal grooming behaviour. Had decreased tryptophan hydroxylase activity been found in adrenalectomized cats (which lack glucocorticoids but do not display the abnormal behaviour) a third factor may have been indicated. The 11-hydroxycorticoid assays indicated that the cats were completely adrenalectomized. 11-Hydroxycorticoids in adrenalectomized cats measured 17% and 20% of control values in plasma and urine, respectively, and this was probably due to nonspecific fluorescence of plasma and urine. Several studies have reported similar residual fluorescence in plasma and urine in adrenalectomized animals (e.g., SILBER, BUSCH and OSLAPAS, 1958; MATTINGLY, 1962).

The pharmacological studies suggest that the physiological bases of the abnormal grooming behaviour in thyroidectomized cats is similar to that in cats with pontile or frontal neocortical lesions. Administration of MAO inhibitor plus tryptophan, 5-HTP, or glucocorticoids abolishes the abnormal behaviour in all 3 groups of cats and *p*-CPA administration increases the size of the responsive area in all groups (TRULSON and RANDALL, 1973; TRULSON, 1974). Dihydroxyphenylalanine (DOPA) or norepinephrine administration does not significantly change the abnormal behaviour in any of the 3 groups of cats (TRULSON and RANDALL, 1973; RANDALL and TRULSON, 1974; TRULSON, 1974). Lesions of the superior colliculi prevent the occurrence of the abnormal grooming behaviour in thyroidectomized cats (TRULSON, 1974), a result consistent with the finding that lesions of the superior colliculi abolishes the abnormal behaviour in cats with pontile lesions (TRULSON and RANDALL, 1973).

An abnormal rhythm in glucocorticoid excretion has been discovered in thyroidectomized cats (RANDALL, TRULSON and PARSONS, 1975). Therefore, it is definitely established that a glucocorticoid defect exists in thyroidectomized cats, and since glucocorticoid administration abolishes the abnormal grooming behaviour in these cats, this defect is a critical aspect of the behavioural abnormality (RANDALL *et al.*, 1975).

The fact that either 5-HTP or MAO inhibition plus tryptophan (but not DOPA) administration abolishes the abnormal grooming behaviour in thyroidectomized cats suggests that thyroid hormones may affect serotonergic neurones. However, neither tryptophan hydroxylase activity nor 5-HT content were significantly decreased in thyroidectomized cats in the present study. Several recent studies have indicated that thyroid hormones affect the sensitivity of monoamine receptors in the CNS (ENGSTROM, SVENSSON and WALDECK, 1974; GREEN and GRAHAME-SMITH, 1974). Thus, the defect in the serotonergic system following thyroidectomy may be a decrease in receptor sensitivity. We conclude that there is a common mechanism for the mediation of the abnormal grooming behaviour (involving the serotonergic system, glu-

cocorticoids and the superior colliculus) in cats with pontile lesions, frontal neocortical lesions, and in thyroidectomized cats.

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REFERENCES

AGHAJANIAN, G. K., HAIGLER, H. J. and BLOOM, F. E. (1972). Lysergic acid diethylamide and serotonin: direct actions on serotonin-containing neurons in rat brain. *Life Sci.* **11:** 615–622.

ALTMAN, J. and CARPENTER, M. B. (1961). Fiber projections of the superior colliculus in the cat. *J. comp. Neurol.* **116:** 157–177.

BERMAN, A. L. (1968). *The Brain Stem of the Cat: A Cyto-Architectonic Atlas with Stereotaxic Coordinates.* The University of Wisconsin Press, Madison.

BOGDANSKI, D. F., PLETSCHER, A., BRODIE, B. B. and UDENFRIEND, S. (1956). Identification and assay of serotonin in brain. *J. Pharmac. exp. Ther.* **117:** 244–251.

BRODAL, A., WALBERG, F. and TABER, E. (1960). The raphe nuclei of the brain stem in the cat. III. Afferent connections. *J. comp. Neurol.* **114:** 261–279.

CARLSSON, A., BEDARD, P., LINDQVIST, M. and MAGNUSSON, T. (1972). Influence of nerve-impulse flow on the synthesis and metabolism of 5-hydroxytryptamine in the central nervous system. *Biochem. Soc. Symp.* **36:** 17–32.

CRAIG, W. (1918). Appetities and aversions as constituents of instincts. *Biol. Bull.* **34:** 91–107.

ENGSTROM, G., SVENSSON, T. H. and WALDECK, B. (1974). Thyroxine and brain catecholamines: increased transmitter synthesis and increased receptor sensitivity. *Brain Res.* **77:** 471–483.

FREEDMAN, D. X. and BOGGAN, W. O. (1974). Brain serotonin metabolism after tolerance dosage of LSD. *Adv. Biochem. Psychopharmac.* **10:** 151–157.

GAL, E. M. and PATTERSON, K. (1973). Rapid nonisotopic assay of tryptophan-5-hydroxylase activity in tissues. *Analyt. Biochem.* **52:** 625–629.

GREEN, A. R. and GRAHAME-SMITH, D. G. (1974). TRH potentiates behavioural changes following increased brain 5-hydroxytryptamine accumulation in rats. *Nature, Lond.* **251:** 524–526.

HOPCROFT, S. (1966). A technique for the simultaneous bilateral removal of the adrenal glands in guinea pigs, using a new type of safe anesthetic. *Exp. Med. Surg.* **24:** 12–19.

JACOBS, B. L. (1974). Evidence for the functional interaction of two central neurotransmitters. *Psychopharmacologia* **39:** 81–86.

MATTINGLY, D. (1962). A simple fluorimetric method for the estimation of free 11-hydroxycorticoids in human plasma. *J. clin. Path.* **15:** 374–379.

PIN, C., JONES, B. and JOUVET, M. (1968). Topographie des neurones monoaminergiques du tronc cerebral du chat: etude par histofluorescence. *C. r. Séanc. Soc. Biol.* **162:** 2136–2141.

RANDALL, W. (1964). The behaviour of cats (*Felis catus* L.) with lesions in the caudal midbrain region. *Behaviour* **23:** 107–139.

RANDALL, W., ELBIN, J. and SWENSON, R. (1974). Biochemical changes involved in a lesion-induced behaviour in the cat. *J. comp. physiol. Psychol.* **86:** 747–750.

RANDALL, W. and PARSONS, V. (1972). Rhythmic dysfunctions in 11-hydroxycorticoid excretion after midbrain lesions and their relationship to an abnormal grooming behaviour in cats. *J. Interdiscipl. Cycle Res.* **3:** 3–24.

RANDALL, W. and TRULSON, M. (1974). A serotonergic system involved in the grooming behaviour of cats with pontile lesions. *Pharmac. Biochem. Behav.* **2:** 355–360.

RANDALL, W., TRULSON, M. and PARSONS, V. (1975). The role of thyroid hormones in the development of an abnormal grooming behaviour in thyroidectomized cats and cats with pontile lesions. *J. comp. physiol. Psychol.* (In press).

SCHEIBEL, M. E. and SCHEIBEL, A. B. (1958). Structural substrates for integrative patterns in the brain stem reticular core. In: *Reticular Formation of the Brain* (JASPER, H. H., PROCTOR, L. D., KNIGHTON, R. S., NOSHAY, W. C. and COSTELLO, R. T., Eds.) pp. 31–55, Little Brown and Co., Boston.

SHERRINGTON, C. (1906). *The Integrative Action of the Nervous System* pp. 325, Yale University Press, New Haven.

SILBER, R., BUSCH, R. and OSLAPAS, R. (1958). A practical procedure for the estimation of corticosterone or hydrocortisone. *Clin. Chem.* **4:** 279–285.

SPRAGUE, J. (1963). Cortical-fungal projections to the superior colliculus in the cat. *Anat. Rec.* **145:** 288.

TRULSON, M. (1974). Relationship of a serotonergic system in the superior colliculus and glucocorticoids to elicitable consummatory grooming fragments in cats with pontile lesions, frontal neocortical lesions and in thyroidectomized cats. Doctoral Dissertation, The University of Iowa.

TRULSON, M., NICOLAY, J. and RANDALL, W. (1975). Abnormalities in grooming behaviour and tryptophan hydroxylase activity in the superior colliculi in cats with pontile and frontal neocortical lesions. *Pharmac. Biochem. Behav.* **3:** 87–94.

TRULSON, M., and RANDALL, W. (1973). 5-Hydroxytryptamine metabolism, superior colliculus and grooming behaviour in cats with pontile lesions. *J. comp. physiol. Psychol.* **85:** 1–10.