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COMMUNICATIONS

In communications with more than one author, an asterisk (*) denotes the one who presented the work.

Some properties of a behaviour-depressing material obtained from mammalian brain

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At a previous meeting of the British Pharmacological Society (January, 1967) it was reported that a high molecular weight material was present in mammalian brain which caused a loss of righting reflex. When injected intravenously or intracerebrally into mice, rats or rabbits recovery of the righting reflex was followed by prolonged behavioural depression. The activity is found in the brain and spinal cord of eight mammalian species, including man, but is absent from non-nervous tissue. The ED50 ranges from 150 mg/kg for the whole rat brain to 6 mg/kg for the frontal cortex of the human brain. During the loss of righting reflex the cortical e.e.g. is markedly depressed, and this period is associated with a reduction in brain ATP, creatine phosphate, glucose and glycogen and an increase in brain lactate levels.

The method of preparation and the partial purification of this material has already been described (Riddell & Leonard, 1968). Subcellular fractionation studies have shown the material to be associated with the microsomal fraction of nerve cells. Further purification with Sephadex columns suggests that the activity is associated with a non-dialysable compound (molecular weight 100–150,000). Behavioural depression is produced within 30 sec of intravenous injection into mice, so either the material readily penetrates into the brain unchanged or the activity is associated with a smaller molecule combined with brain proteins. The latter explanation is probably correct, for after pretreating the partially purified material with trypsin, the activity is associated with dialysable material (molecular weight 10,000). Further details of the composition and properties of the active material will be presented.

REFERENCE

RIDDELL, D. & LEONARD, B. E. (1968). Some properties of a pharmacologically active compound isolated from nervous tissue. *Biochem. J.*, **106**, 14*P*.

Evidence for the humoral control of the hypothalamic-pituitary-adrenal axis

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The activity of the pituitary gland is regulated by the hypothalamus through the release of specific neurohumoral agents into the pituitary portal vessels. The hypo-

thalamus itself is under the control of higher nervous centres; structures inhibiting the hypothalamic–pituitary–adrenal axis have been described particularly in the cerebral cortex, in the midbrain and in the limbic system.

Evidence for chemical transmission of impulses within the central nervous system suggests that the inhibitory effect on the secretion of ACTH exerted by the cerebral cortex might also be humorally mediated. This hypothesis has been substantiated by the data which will be presented. Intravenous injections of crude acetic acid extracts of acetone-dried powder obtained from bovine cerebral cortex significantly reduced plasma corticosterone levels in female Sprague–Dawley rats. Following gel filtration on a column of Sephadex G–25 and elution with 0.1 N ammonium acetate buffer, three different fractions inhibiting the pituitary–adrenal axis have been obtained. Their molecular weight is less than 1000; their inhibitory activity is reduced following acid or enzyme hydrolysis. The most active fraction blocks the pituitary–adrenal axis at a dose level of <50 μg.

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Effect of midbrain transections on the content of gamma-aminobutyric acid (GABA) in the cerebral cortex of the cat

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We have measured the content of GABA and glutamic acid in the cerebral cortex in cats transected (*a*) at midpontine pretrigeminal level, showing a predominantly activated e.e.g. (Batini, Moruzzi, Palestini, Rossi & Zanchetti, 1958) and (*b*) at collicular level showing a permanently synchronized e.e.g.

The transections were made with a stereotaxically oriented spatula in adult cats under halothane anaesthesia. The anaesthesia was discontinued and the cats resumed spontaneous respiration. Blood pressure was normal. The cats were killed by exsanguination 3 hr after the end of the anaesthesia and cortical samples of about 1 g were excised from both hemispheres. GABA was extracted and determined by the method of Maynert, Klingman & Kaji (1962) using one-dimensional paper chromatography. The same method of extraction was used for glutamic acid but separation was obtained by triple run chromatography. The recovery of GABA and glutamic acid added to brain homogenates was in the range of 80–90%.

TABLE 1

Level of transection:	Midpontine pretrigeminal		Collicular		
Hemisphere	Right	Left	Right	Left	
GABA (μmoles/g$\pm$S.E.)	2·06$\pm$0·1 (6)	2·09$\pm$0·1 (6)	1·41$\pm$0·04 (6)	1·33$\pm$0·09 (6)	$P<0·01$
Glutamic acid (μmoles/g$\pm$S.E.)	8·37$\pm$0·5 (4)	8·22$\pm$0·2 (4)	8·35$\pm$1·3 (3)	9·17$\pm$1·6 (3)	N.S.

Number of determinations in brackets.