tency of pituitary glands; neither normal rabbit serum nor sheep heart antiserum had any effect. A pattern of vaginal cycling was observed after antihormone treatment which was not apparent in cycles of controls. No important differences were found in thymus weight or in adrenal or thyroid histology.

1. Ely, C. A., *Cancer Research,* 1959, v19, 37.
2.———, *Endocrinol.,* 1957, v60, 718.
3. Henry, S. S., van Dyke, H. B., *J. Endocrinol.,* 1957, v16, 310.
4. Marvin, H. N., Meyer, R. K., *Anat. Rec.,* 1943, v85, 177.
5. Noble, R. L., Rowlands, I. W., *J. Endocrinol.,* 1939, v1, 22.
6. Rowlands, I. W., *Proc. Roy. Soc. London* (Series B), 1937, v121, 517.
7. Zondek, B., PROC. SOC. EXP. BIOL. AND MED., 1939, v42, 338.
8. Ely, C. A., *ibid.,* 1953, v84, 501.
9. Kupperman, H. S., Meyer, R. K., Hertz, R., *Endocrinol.,* 1939, v24, 115.
10. Kupperman, H. S., Mellish, C. H., McShan, W. H., PROC. SOC. EXP. BIOL. AND MED., 1941, v48, 79.
11. McShan, W. H., Meyer, R. K., *J. Biol. Chem.,* 1943, v151, 259.
12. Selye, H., Collip, J. B., Thomson, D. L., *Endocrinol.,* 1933, v17, 494.
13. Hooker, C. S., Forbes, T. R., *ibid.,* 1947, v41, 158.
14. Mandl, A. M., Zuckerman, S., *J. Endocrinol.,* 1956, v13, 243.
15. Levine, W. T., Witschi, E., PROC. SOC. EXP. BIOL. AND MED., 1933, v30, 1152.
16. Vermande-Van Eck, G. J., Chang, C. H., *Cancer Research,* 1955, v15, 280.
17. Maddock, W. O., Jungck, E. C., Rigas, D. A., Heller, C. G., *Fed. Proc.,* 1949, v8, 103.
18. Meyer, R. K., Kupperman, H. S., Finerty, J. C., *Endocrinol.,* 1942, 662.
19. Maddock, W. O., Heller, C. G., PROC. SOC. EXP. BIOL. AND MED., 1947, v66, 595.
20. Rinaldini, L. M., *J. Endocrinol.,* 1949, v6, 54.
21. Leathem, J. H., Fisher, C. J., *Anat. Rec.,* 1959, v133, 302.
22. Screbnik, H. H., Nelson, M. M., *ibid.,* 1957, v127, 372.
23. Mason, K. E., Wolfe, J. M., *ibid.,* 1930, v45, 232.
24. P'an, S. Y., Van Dyke, H. B., Kaunitz, H., Slanetz, C. A., PROC. SOC. EXP. BIOL. AND MED., 1949, v72, 523.
25. Herlant, M., *Arch. de Biol.,* 1943, v54, 225.
26. Selye, H., *Brit. J. Exp. Path.,* 1936, v17, 234.
27. Cranston, E. M., PROC. SOC. EXP. BIOL. AND MED., 1958, v98, 320.

Received June 21, 1960. P.S.E.B.M., 1960, v105.

Effects of Psychotropic Drugs on Limbic System of Cat.* (26028)

WILLIAM SCHALLEK AND ALFRED KUEHN
Dept. of Pharmacology, Hoffmann-La Roche, Nutley, N. J.

There has been increasing evidence that the limbic system (rhinencephalon) is involved in emotional responses(1). This suggests that drugs which alter mood might produce changes in this part of the brain. The present paper describes effects on the septum, amygdala and hippocampus of the cat of 2 psychodepressant drugs (chlordiazepoxide† and meprobamate) and 2 psychostimulant agents (iproniazid and imipramine).

Methods. Thirty cats were prepared under ether anesthesia. The trachea was cannulated for artificial respiration and the left femoral vein for drug injection. Bipolar concentric electrodes were inserted with the aid of a Baltimore stereotaxic instrument in anterior and posterior portions of septum, amygdala and hippocampus. Recording electrodes were placed on frontal and occipital areas of cortex. All wound edges were infiltrated with procaine. The ether was withdrawn and the animals immobilized with decamethonium (C_{10}). Stimulation was carried out with a Grass S-4 stimulator, using the following parameters: frequency, 40 per sec.; pulse

* A brief report was presented to Am. Soc. Pharmacol. and Exp. Therap., Seattle, Wash., Aug. 21, 1960.

† Librium® formerly referred to as methaminodiazepoxide.

TABLE I. Statistically Significant Drug Effects. Figures show mean ± stand. error of mean.

Site of stimulation	Drug	Dose, mg/kg i.v.	No. of exp.	Duration of after-discharge, sec. Pre-drug	Post-drug*	Difference	Statistical significance‡
Septum	Saline		4	31 ± 8.7	66 ± 17	+ 35 ± 11	
	Chlordiazepoxide	10	3	39 ± 11	27 ± 7.9	− 12 ± 12	<.02
	"	20	4	42 ± 8.3	19 ± 3.5	− 23 ± 10	<.01
	Imipramine	10	3	33 ± 14	1.7 ± .88	− 31 ± 14	"
	Meprobamate	20	4	39 ± 27	11 ± 6.1	− 28 ± 31	<.05
Amygdala	Saline		3	20 ± 12	21 ± 6.0	+ 1.3 ± 8.5	
	Iproniazid	5†	3	8 ± 2.9	64 ± 17	+ 56 ± 17	"
Hippocampus	Saline		4	23 ± 7.9	46 ± 11	+ 23 ± 9.2	
	Chlordiazepoxide	10	3	38 ± 7.5	23 ± 13	− 15 ± 8.5	"
				Amplitude of after-discharge, μV			
Amygdala	Saline		4	1300 ±436	1297 ±435	− 2.5 ± 2.5	
	Chlordiazepoxide	10	4	1060 ±410	310 ±110	−750 ±240	<.02
	"	20	4	" "	210 ± 60	−850 ±370	"

* Maximum effect.
† Pre-treated for 5 days with 5 mg/kg i.p. "Pre-drug" value immediately before inj. of 5 mg/kg i.v.
‡ "p" values for drug *vs* saline figures in "Difference" column.

duration, 2 msec; intensity, 8 volts; duration of stimulation, 5 sec.; interval between stimulations, 5 min. Subcortical centers were stimulated in the following sequence: anterior septum, amygdala, hippocampus; posterior septum, amygdala, hippocampus. Recordings were made on a Grass III-C electroencephalograph. Only one drug was administered to each animal. Iproniazid was tested at 5 mg kg i.v. in cats pre-treated for 5 days with 5 mg/kg i.p. The other drugs were tested in animals without pre-treatment; a dose of 10 mg/kg i.v. was followed 1 hr later by 20 mg kg. To minimize cardiovascular effects, drugs were injected over a 10 min period at the rate of 1 ml/min. Significance of results was determined by "t" test. Electrode locations were confirmed histologically.

Results. (Table I): *Saline controls*: Stimulation of limbic centers produced after-discharges of high amplitude (1000 μV or more) with frequency of 3-21 per sec. These after-discharges spread throughout the limbic leads; they were usually marked by abrupt termination. Duration of discharge following successive stimulations remained relatively constant in the amygdala, but progressively increased in septum and hippocampus.

Chlordiazepoxide showed the following statistically significant effects at 10 mg/kg i.v.: decreased duration of after-discharge in septum and hippocampus; decreased amplitude of discharge in amygdala. *Meprobamate,* 20 mg/kg, shortened duration of discharge in septum. *Imipramine* showed the same effect at 10 mg/kg. *Iproniazid* had no effect in cats without pre-treatment; following administration of 5 mg/kg i.p. for 5 days, 5 mg/kg i.v. significantly increased the duration of discharge of the amygdala.

Discussion. Delgado(2) observed that stimulation of the amygdala in unanesthetized monkeys "increased aggressiveness and fighting." The increased activity of the amygdala which we observed with iproniazid might be involved in the psychostimulant effect of this drug. Delgado also observed that stimulation of the septum produced "loss of leadership." If the septum has a restraining influence on behavior, the depression of this area which we observed with imipramine might produce psychostimulant effects. However, depression of the septum could hardly produce both psychostimulant effects with imipramine and psychodepressant effects with meprobamate.

Kletzkin and Berger(3) studied the effects of meprobamate on the limbic system of the cat with a technic differing only slightly from ours (immobilization with succinylcholine, more frequent stimulation of 1 or 2 areas). They observed reduced duration of after-discharge in hippocampus and amygdala at 20 mg/kg i.v. If stimulation of the amygdala

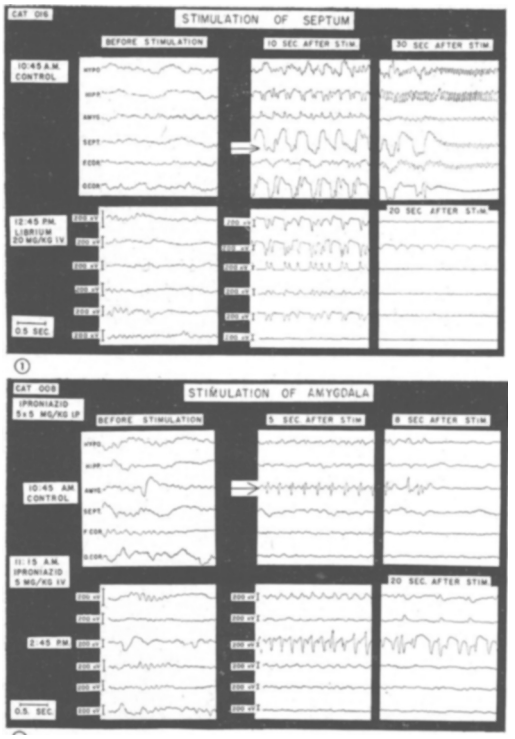

FIG. 1. Chlordiazepoxide, 20 mg/kg i.v., decreases duration of discharge in septum. Upper row is before, lower row 30 min. after, drug inj. First panel in each row is before, second and third panels after, electrical stimulation of area indicated by arrow. Note reduced amplification in second and third panels. EEG leads are hypothalamus, hippocampus, amygdala, septum, frontal and occipital cortex. Paper speed 6 cm/sec.

FIG. 2. Iproniazid, 5 mg/kg i.v. in cat pretreated for 5 days with 5 mg/kg i.p., increases duration of discharge in amygdala. Arrangement as in Fig. 1.

increases aggressiveness, reduced activity of this area might have a psychodepressant effect.

We found that chlordiazepoxide at 10 mg/kg i.v. had depressant effects on septum, amygdala and hippocampus. In other tests, this compound was found to be more potent than meprobamate in depressing the irritability of rats with septal lesions, and in reducing the aggressiveness of vicious monkeys (4). In the clinic, this agent "reduces anxiety and agitation but does not cloud consciousness or impair intellectual function"(5). Perhaps these psychodepressant effects are correlated with depression of the amygdala; much more experimentation is needed before any such relationship can be established.

Summary. Four psychotropic drugs had the following statistically significant effects on the limbic system of the cat: iproniazid increased duration of after-discharge of amygdala; imipramine and meprobamate decreased duration of discharge of septum; chlordiazepoxide decreased duration of discharge of septum and hippocampus, and decreased amplitude of discharge of amygdala.

We wish to thank Shirley Yerzy for the histology and Kay Eisenhuth for statistical analysis.

1. MacLean, P. D., *Am. J. Med.,* 1958, v25, 611.
2. Delgado, J. M. R., *Abstr., 21st Int. Physiol. Congr.,* 1959, 75.
3. Kletzkin, M., Berger, F. M., PROC. SOC. EXP. BIOL. AND MED., 1959, v100, 681.
4. Randall, L. O., Schallek, W., Heise, G. A., Keith, E. F., Bagdon, R. E., *J. Pharm. Exp. Ther.,* 1960, v129, 163.
5. Harris, T. H., *J. Am. Med. Assn.,* 1950, v172, 1162.

Received June 22, 1960. P.S.E.B.M., 1960, v105.

Effects of Selective Ultraviolet Irradiation of Cytoplasm of Living Cells.* (26029)

P. O'B. MONTGOMERY AND L. L. HUNDLEY
Dept. of Pathology, University of Texas Southwestern Medical School

The authors have reported some of the manifestations of ultraviolet irradiation damage in living cells(1,2). The effects reported concerned the nature of the response of the whole cell to ultraviolet irradiation, rather

* Supported by Atomic Energy Comm. Contract, Damon Runyon Memorial Fund for Cancer Research, and Southwestern Medical Fn.