THE EFFECT OF LSD-25 AND ATROPINE UPON FIGURAL AFTER-EFFECTS. Richard P. Smith (Intr. by C. C. Pfeiffer). Departments of Psychology and Pharmacology, Emory University, Atlanta, Ga.

The effects of oral administration of LSD-25 (75 gamma), atropine (1.0 mgm.), atropine plus LSD-25, and a placebo upon the visual illusion termed the figural after-effect was investigated. Using a method suggested by Bevan (J. Gen. Psychol., 1951, 45:186) pairs of squares were projected in an area formerly occupied by a projected circular inspection figure. Ordinarily, a subjective shrinkage in the size of the square located within the area formerly occupied by the circle occurs. Eight healthy male volunteers, inmates of the U. S. Federal Penitentiary, Atlanta, Ga., served as Ss. All Ss were able to detect the presence of LSD-25 and were also able consistently to differentiate among LSD-25, placebo, and atropine but had less success in differentiating LSD-25 and LSD plus atropine. Several Ss were experiencing visual hallucinations when tested. Those Ss who had received LSD-25 frequently reported illusions of perspective and depth. Occasionally they reported illusions involving chromaticity, shape, and movement. Ss who had received LSD-25 or LSD-25 plus atropine stated that fixation was difficult and exhibited markedly increased motor activity and restlessness. While the expected figural after-effect illusion occurred in all Ss, no significant change in the magnitude of this induced illusion was produced by drug administration. No significant interaction between LSD-25 and atropine was observed. The implications of these findings will be discussed.

SYNAPTIC & BEHAVIORAL ACTIONS OF A WATER PERCOLATE OF KAVA (PIPER METHYSTICUM). E. Ross Hart, Oakley S. Ray,* Angelo R. Furgiele* & Amedeo S. Marrazzi. Vet. Admin. Res. Labs. in Neuropsychiatry and Dept. Pharmacology, University of Pittsburgh, Pgh. 6, Pa.

Mild but interesting euphoriant (and perhaps tranquilizing) properties have been reported for a Fiji Island ceremonial and social drink made from Kava root. A water percolate at ca 25°C (1 G/cc) has been found active in mice, rats and cats. 0.1-0.5 cc/kg. i.p. increased ease of handling mice and reduced activity cage counts by 1/2 without any visible depression. Intracarotid injection of 0.2 cc in the pentobarbitalized cat produced cortical synaptic inhibition in the transcallosal preparation, matching 40 mcg. of serotonin. 2-4 cc i.p. in thirsty rats, trained to obtain a water reward by pressing a lever on a tone signal, resulted in prolongation of stimulus - response latency to the 20 sec. point where trials are terminated without rewards. The cat and rat data are qualitatively similar to those we have obtained with LSD-25. The preliminary findings are consistent and point to a CNS inhibitory effect for the chemically as yet uncharacterized principle in the water percolate. These are the kinds of effects that have been demonstrated in these Laboratories for both psychotogens (including euphoriants) and tranquilizers.

EFFECTS OF PSYCHOTOGENS ON COMPLEX BEHAVIOR. Oakley S. Ray* & Amedeo S. Marrazzi. Vet. Admin. Res. Labs. in Neuropsychiatry, Pgh. 6, Pa.

Objective study of psychotogens in animals has been hampered by difficulty in eliciting and measuring drug induced confusion. A useful situation has been found in the thirsty rat trained to choose between 2 different tones, self-presented alternately by pressing the stimulus lever, and obtaining a reward by pairing operation of the water delivery lever with the correct tone. Reward terminates a trial. Within any trial the animal has complete control over the rate and number of times stimuli are presented prior to selection of a "correct" tone. LSD-25 (5-40 mcg/kg), mescaline (1-8 mg/kg) or amphetamine (0.25-1.75 mg/kg) were injected intraperitoneally. Low doses considerably increased the number of stimuli self-presented by the animal before making a final choice. This effect occurred without changing the speed or accuracy of response. Moderate doses of amphetamine decreased the number of stimulus presentations, while higher doses of any of the drugs blocked responding completely. A similar procedure in monkeys has produced comparable results thus far with LSD-25. The data is in accord with an interpretation that psychotogens are producing graded inhibition, operating to first increase selection frequency - presumably due to uncertainty - and then, with increasing intensity of effect, depressing responses in general.

CARDIOVASCULAR PHARMACOLOGY II
Room D-209

OBSERVATIONS ON THE REFLEXES INITIATED BY LOBELINE FROM THE HEART AND LUNGS. John A. Bevan and M. A. Verity (intr. by D. B. Taylor). Dept. of Pharmacology, UCLA Medical Center, Los Angeles, California.

The injection of small amounts of lobeline sulphate into the right atrium of cats anesthetized with α-chloralose produces hypotension, bradycardia and apnoea within one to two seconds. These effects are immediately followed by the well documented phase of hypertension and hyperphoea. After atropine, bradycardia is abolished, the hypotension diminished but the apnoea unaffected. After vagotomy the depressor phase is completely abolished. In 30 cats receiving the median effective dose for the depressor response, 15 μg./kg. in over 50% the hypotension was greater than the hypertension. On injection into the left ventricle hypotension, bradycardia but not apnoea were found. Injection into the thoracic aorta distal to the origin of the left common carotid produced little effect. The amplitude of the hypotensive effect is related to the mean arterial pressure. Under pentobarbital anesthesia, the response to the same dose of lobeline is considerably less than under α-chloralose.

DEPRESSOR EFFECTS ARISING FROM (-)-COTININE. Joseph F. Borzelleca,* Edward R. Bowman* and Herbert McKennis, Jr. Medical College of Virginia, Richmond, Virginia.

In a preliminary study, Bowman et al. (Abstr. of Comm., XXI Intern. Congr. of Physiol. Sci., Buenos Aires, p. 41, 1959) reported that the intravenous administration of (-)-cotinine, a mammalian metabolite of (-)-nicotine, produces a depressor response in the anesthetized dog. (-)-Cotinine failed to give the marked pressor response characteristic of nicotine. In an extension of these observations the depressor response from (-)-cotinine has been found to be markedly dependent upon the rate of injection. Doses of atropine or diphenhydramine sufficient to block the depressor responses from acetylcholine and histamine respectively failed to block the depressor response from (-)-cotinine. (-)-Cotinine elicited, in addition, a depressor response in the decerebrate and spinal dog. These observations led to the suggestion that the effect from (-)-cotinine is mediated through peripheral action of the compound or its metabolites. The quantities of (-)-cotinine necessary to produce the observed effects were in excess of those to be anticipated during the metabolism of lethal or nonlethal quantities of (-)-nicotine. (Aided by grants from The American Tobacco Company and the Tobacco Industry Research Committee.)