tone, evaporating a suitable aliquot, and chromatographing in the same manner. However, since the free cholesterol in the adrenal gland is relatively very low, one must use a large aliquot and dilute the ester fraction after chromatography if the free cholesterol level is desired.

Although the ester fraction can be determined by using the method of Brown *et al.* (*3*), the free adrenal cholesterol is accompanied by turbidity, which interferes slightly with this method. Turbidity is not observed with a modified Lieberman-Burchard procedure. Because of its sensitivity, the modified Tschugaeff reaction of Hanel and Dam (*4*) may be better suited to the determination of free cholesterol in adrenal tissue after chromatography on silicic acid.

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References and Notes

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21 December 1956

Actions of d-Lysergic Acid Diethylamide and Its 2-Bromo Derivative on Heart of Venus mercenaria

Physiological evidence indicates that the inhibitor nerves of the heart of the mollusk, *Venus mercenaria,* are cholinergic in nature (*1*), and that the activity of the excitor nerves is mediated by 5-hydroxytryptamine (5-HT, serotonin) (*2*). *d*-Lysergic acid diethylamide (LSD) was found to be an antagonist of serotonin on certain mollusk hearts under the conditions of the experiments (*3*). An early report that LSD was an effective antagonist on the *Venus* heart was later modified (*4*) when it became clear that LSD had a marked excitor action on this heart. This action persisted for long periods of washing during which a maximum amplitude of beat obscured the action of large doses of serotonin. It was stated that on the *Venus* heart, LSD acts as an essentially irreversible analog of serotonin (*4*). Recently, Shaw and Woolley (*5*) confirmed this observation.

The importance of a proper understanding of the fundamental mode of action of LSD prompts us to report further our earlier studies with LSD and our more recent observations of the action of 2-bromo-lysergic acid diethylamide (Bol-148, bromo-LSD) on the *Venus* heart (*6*). At a concentration of $10^{-6}M$, both serotonin and LSD produce a nearly maximal increase in amplitude in less than 10 minutes. After a heart has been washed for a few minutes, it recovers from serotonin; but after many hours of washing a heart that has been treated with LSD may still be greatly excited. No way has yet been found, including washing at a high *p*H, to restore quickly an LSD-excited heart. At concentrations below $10^{-9}M$, serotonin seldom excites the isolated *Venus* heart. If hearts are allowed to remain in a 10-ml bath of $10^{-10}M$ LSD, they are maximally excited in 1.5 to 2 hours. At a $10^{-16}M$ concentration of LSD, up to 3 hours may be required for the heart to adsorb an amount of LSD that produces near maximal excitation. Axelrod *et al* (*7*), from studies of tissue distribution, calculate that LSD exerts its characteristic effect in man at a level of 0.0003 μg/g of brain tissue. The *Venus* heart responds maximally at a tissue concentration that must be below this, for 10 ml of $10^{-16}M$ LSD contains only 602,000 molecules.

An important problem not yet resolved is whether the "LSD psychosis" results from central blocking of serotonin, or from a serotoninlike action of LSD, or for other reasons. 2-Bromo-lysergic acid diethylamide may prove useful in helping to solve this problem. Cerletti and Rothlin (*8*) found bromo-LSD to be a more effective antagonist of serotonin than LSD at a number of sites in mammals. This blocking action was highly specific, and they saw no signs of antihistamine, antiadrenaline or antiacetylcholine action. Certain of these observations have been amply confirmed and extended (*9*). Cerletti and Rothlin, however, failed to find any indication of an abnormal psychic disturbance produced by doses of bromo-LSD even 20 times as great as effective doses of LSD. They concluded that their results with bromo-LSD make it difficult to correlate the psychic effects of LSD with its antiserotonin property. The interesting observation has now been made by Ginzel and Mayer-Gross (*10*) that bromo-LSD, when it is administered 1 or 2 days before LSD, abolishes or greatly reduces the LSD psychosis without, by itself, having significant central action even in 2- to 3-mg amounts.

On the *Venus* heart, bromo-LSD is an effective antagonist of serotonin. On some hearts, high concentrations (10^{-4} to $10^{-5}M$) have a weak stimulating action resembling that produced by LSD, while on others there is no apparent effect. However, after treatment of hearts with bromo-LSD in concentrations in the range of 10^{-4} to $10^{-6}M$ for 1 hour or longer, the excitor action of a molar concentration of serotonin one-tenth as great is completely blocked. It is of further interest that previous exposure of a *Venus* heart to bromo-LSD abolishes or greatly reduces the excitor action of LSD that is subsequently applied. For example, on some hearts, pretreatment with $10^{-4}M$ bromo-LSD may completely prevent the otherwise marked excitor action of $10^{-6}M$ LSD.

Serotonin appears to be a normal regulatory neurohumor of the *Venus* heart. This heart is extremely sensitive to LSD, which has an excitor action resembling that of serotonin. Unlike serotonin, however, the action of LSD is very slowly reversed by washing. Bromo-LSD antagonizes the actions of both serotonin and LSD on the *Venus* heart. These several actions and interactions appear to parallel rather closely those seen in the mammalian central nervous system.

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13 September 1956

Technique for Behavioral Analysis of Human Observing

The monitoring of a display (for example, a search radar) by human beings raises problems of considerable practical and theoretical interest. In general, the probability of detection of a signal varies directly with the signal rate; is a function of the temporal arrangement of the signals; and, in the case of low signal rates, varies inversely with the duration of the monitoring task. Such monitoring situations are badly in need of a descriptive behavioral analysis that would permit isolation of the variables which control the behavior underlying the probability of signal detection.