*VI LSD No. 348 (§ 102a)
Frenquel (§ 111w)

M 500 effect on salamander
M 341 behaviour
M 405 EEG

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Behavior of the salamander under the influence of LSD-25 and Frenquel, and accompanying electrical activity of brain and spinal cord.

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PROBLEM: see Title.

MATERIAL, METHOD & DOSAGE: About 60 male salamanders (aquatic phase of Triturus viridescens). LSD (0.7-0.8 mg/g), or Frenquel (0.3 mg/g) dissolved in 0.05-0.1 ml distilled water and injected into abdominal cavity. The following behavioural tests were applied: 1). the withdrawal response, evoked by touching the tail and involving a spinal arc. 2). the righting response, involving the 8th nerve and the vestibulospinal system. 3). the corneal reflex, involving the 3rd, 5th, 7th cranial nerves and associated structures. 4). the swimming response. 5). the walking response (these two are a patterned automatic sequence of movements involving the striatum). 6). the visual response, in which the head and eyes undergo optokinetic nystagmus in following black and white stripes on a moving drum (this is a measure of attention and involves the 2nd cranial nerve, the optic tectum, the tecto-spinal and tecto-bulbar paths). These tests were applied every 15 minutes for 2 hours following the drugs and then every half-hour for ten hours. Electrical activity was recorded from electrodes inserted into the skull over the olfactory and tectal areas and from electrodes in the skin over the upper thoracic and lumbar segments of the spinal cord.

RESULTS:

1). LSD: Within 5 minutes of injection, the salamander, when placed in water, showed disturbances of equilibrium during which the animal slowly writhed, came to rest on its side, back or belly, and assumed statue-like postures representing some stage in standing or walking. These floating postures were interrupted by slow movements of trunk or limbs as if the salamander were trying to keep its balance. The trunk and limbs were not limp but had the firmness of soft wax, so that the animal allowed itself to be moved passively, especially in water. At this stage, tactile stimuli applied to the tip of the tail caused a prompt escaping reaction, a slow response delayed for 5-10 seconds or

no response at all. The visual test was negative but electrodes applied to the optic area of the brain indicated that flashes of light on the eyes resulted in corresponding changes in the visual mechanism. A touch of the cornea was followed by withdrawal of the eyeball. The lumen of peripheral blood vessels and blood flow were normal. These effects on behaviour became apparent 5-15 minutes after LSD, reached their peak in 15-30 minutes and gradually disappeared in 2-3 hours. The intensity and duration of effects varied from animal to animal, even with the same dosage. Generally the effects disappeared by the following day; however, in some animals there was stiffness in walking and a slower response to stimulation for 1-2 days after LSD.

A few minutes after the injection of LSD the electrical activity of brain and spinal cord showed a brief drop in potential, but this was soon followed by the appearance of a strong and sustained increase in potential, especially in the spinal cord, even though the salamander appeared quiet and motionless. These high potential waves consisted predominantly of 18-22/sec waves, on which were superimposed some 30-40/sec waves of lower amplitude. The sustained electrical discharge lasted 5-15 minutes and was occasionally interrupted by movement artefacts. After approx. 30 minutes electrical activity of brain and spinal cord dropped to a potential slightly below normal.

2). Frenquel: Within 30-60 minutes of injection, the salamanders showed abnormalities in walking and swimming. Walking was marked by unsteadiness of gait and a limp in the forelegs. At times the weakness became so extreme that locomotion was accomplished mainly by use of the hind limbs. After Frenquel, swimming movements were wobbly and the forelimbs were extended somewhat laterally instead of pointing caudally and kept close to the trunk.

Some animals showed a slight, temporary swelling and pinkness of the abdominal region but peripheral blood flow appeared normal. The remaining neurological responses were unaffected. The peak effect on behaviour was reached after about 3 hours and maintained for 3 hours. Behaviour returned to normal in 12-24 hours.

When Frenquel was exerting its maximum effect on behaviour, the electrical activity of brain and spinal cord showed an extremely low amplitude, with dominant frequencies of 10-12 and 18-22/sec waves. Doses over 0.4 mg/g intensified the effects described above and resulted in an extreme swelling of the abdominal region, circulatory disturbances and death in a few days.

3). Frenquel followed by LSD: When LSD was injected at the peak

of action of Frenquel, the salamanders still exhibited disturbances of equilibrium, statue-like postures, and slow writhing movements when in water. The trunk lacked the firmness found in animals given LSD alone.

The electrical activity of the brain and cord indicated that LSD may raise the low electrical potential found in salamanders given Frenquel alone. However, after Frenquel LSD did not evoke from the spinal cord the prolonged electrical discharge of high potential seen after LSD alone. Frenquel and LSD mutually modified the effects of one another. When used together, they exerted depressant effect on behavioural responses and produced a weakened condition lasting 12 hours or more.

COMMENT: No previous studies of LSD have been made in the salamander.

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(Einfluss von LSD und Frenquel auf Verhalten und elektrische Gehirn- und Rückenmarksaktivität des Salamanders)

LSD und Frenquel verursachten beim Salamander Triturus viridescens Veränderungen des Verhaltens. Ausserdem bewirkte LSD im Rückenmark und gelegentlich auch im Gehirn elektrische Aktivität von hoher Frequenz und Amplitude, während Frenquel in Rückenmark und Gehirn Aktivität von niedriger Amplitude auslöste. LSD und Frenquel zusammen verabfolgt verminderten die Lebhaftigkeit des Verhaltens, wobei die Wirkung beider Mittel sich gegenseitig modifizierte.

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(Influence de LSD et Frenquel sur le comportement et l'activité électrique cérébrale et spinale du salamandre)

Chez le salamandre Triturus viridescens, LSD et Frenquel provoquent des modifications du comportement. Le LSD provoque en outre dans la moelle épinière et parfois aussi dans le cerveau und activité électrique à haute fréquence et haute amplitude, tandis que Frenquel déclenche dans la moelle épinière et dans le cerveau une activité à amplitude basse. LSD et Frenquel, administrés ensemble, diminuent la vivacité du comportement, les effets de chaque agent se modifiant mutuellement.

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