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ACQUIRED AND CROSSED TOLERANCE TO MESCALINE, LSD-25 AND BOL-148

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Following our previous publication (1957), new experiments have been made in a total of 16 human subjects. Drug effects have been classified as follows: 1. autonomic, 2. motor, 3. emotional, 4. related to consciousness, 5. psychosensorial. It was possible to prove that tolerance to LSD-25 develops very rapidly in man, while tolerance to mescaline also occurs, but less rapidly and not so completely. Subjects tolerant to LSD-25 are very resistant to mescaline effects. Tolerance to mescaline is also related to a certain resistance to LSD-25 effects. Protracted BOL-148 administration does not cause the individual to develop marked resistance to LSD-25.

Repeated administration of LSD-25 (200 γ), at 8 hour intervals, does not produce any consistent tachyphylaxis.

The following points are stressed:

1. LSD-25 and mescaline act at greatly different molecular concentrations. If common receptors exist, very small amounts of mescaline should become pharmacologically active in the body.
2. Also with reference to tolerance, autonomic and psychical effects run parallel.
3. Tolerance to LSD-25 develops rapidly and completely, as does tolerance to morphine. Nevertheless an abstinence syndrome does not appear. This syndrome appears, therefore, related to the analgesic effect and not to the easily acquired tolerance to a drug.
4. The possible discovery of a pharmacologically inactive compound which, after prolonged administration, prevents the effect of LSD-25 and of other psychotoxic agents could be of the greatest therapeutic importance.