CASE REPORTS

LSD-LIKE DELIRIUM FOLLOWING INGESTION OF A SMALL AMOUNT OF ITS BROM ANALOG (BOL-148) * †

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In 1943 Hoffmann 1 detected in himself strange mental effects from a compound that he and Stoll 2 had prepared in 1938 and reported in 1943 as an oxytocic agent similar to ergonovine. This observation of the effect of lysergic acid diethylamide (LSD) led to the investigation of other derivatives of this compound in research on experimentally induced mental disorders. 3 LSD and most of its related compounds have been found to produce an anti-5-hydroxytryptamine (serotonin) effect both peripherally and, it has been assumed, centrally by blocking the action of serotonin. 3a

Cerletti and Rothlin 4 have reported on a compound, 2-bromo-d-lysergic acid diethylamide, coded BOL-148. When 0.65 mg. of this agent was given to their laboratory workers, they observed no changes in mentation similar to those produced by LSD. From this observation in 1955 they concluded that the theory of the production of mental changes being secondary to the antiserotonin action of LSD must be challenged, since BOL-148 produced no psychic symptoms.

Ginzel and Mayer-Gross 5 gave BOL-148 to volunteers for two days and observed that when LSD was given on the third day psychologic symptoms did not appear. They further observed that in three other cases, when BOL-148 was given for only one day previous to the LSD, the changes were “reduced to abortive and short lasting.” When the experiment was reversed and the BOL-148 was given at the height of the LSD symptoms there were no noticeable or persistent changes in the symptoms of LSD intoxication. They concluded that BOL-148, which was closely related to LSD chemically, was effective in blocking the effects of the latter agent on mentation.

Abramson 6 has alleged that the best antidote to LSD is LSD itself. Others 7, 8 have shown that individuals given the agent on successive days developed a rapid tolerance to the compound.

Snow 9 has administered as much as 7.5 mg. of BOL to patients with metastasizing carcinoid tumors, a condition associated with the accumulation of large amounts of serotonin, without reporting mental disturbances.

The disturbances of mental function induced by LSD and some of its derivatives 3b, 10 include disturbances of affect and thought, distortions of perception

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and body image, and manifestations of depersonalization. Visual illusions and hallucinations are common, though auditory hallucinations (akin to those of schizophrenic psychosis) are not. Distortions of color perception and the conversion of straight lines into undulating ones are common. When given in small amounts euphoria may occur, and in high amounts a condition resembling complete withdrawal, or "catatonia," develops. It is interesting to note how similar the experiences of these subjects are to those of toxic deliria from severe systemic diseases, i.e., fever, sepsis, bacteremia, uremia, hypoxia, etc. When the effects of a single administration of LSD are compared to the delirium associated with an acute systemic disease that has been given prompt etiologic treatment, the courses of the effects of the two toxins closely resemble each other, especially in their response to attempts to help the subject orient himself, to make him feel secure and to identify his surroundings.

The effects of LSD include a decrease in blood pressure and pulse rate, and an increase in body temperature, urinary output and rate, and intestinal motility. These effects may be modified if during the mental changes the individuals are very anxious. Hoch suggested that these symptoms occurred without the psychic manifestations, although the reverse was not observed. He suggested that this variability in response may be related to the amount of the drug given, and that the effect on the blood pressure, pulse, body temperature, etc., could "spill over into some psychic manifestations."

Since there is a variability in the production of psychic symptoms which is greater than the variability in the production of symptoms referable to blood pressure, pulse and body temperature, it is postulated that the two chemically related compounds, LSD and BOL-148, are related in pharmacologic and psychologic effects, and differ only as to the amounts necessary to produce such effects. The following is a summary of events that support this thesis.

**Case Report**

A moderately anxious 28 year old worker in this laboratory, who usually controlled and repressed his affective expressions, took BOL-148 during a vascular headache for the purpose of observing the effect of this agent on his headache. This man was mildly hypertensive and subject to vascular headaches. He ingested 0.5 mg. of BOL-148 approximately two hours after the onset of a moderately severe, bitemporal, "pounding" vascular headache. About 15 minutes later his mood became elevated, he sought aid for his state, and he became more and more talkative in louder and louder tones. He complained of lightheadedness and expressed the fear that he might lose consciousness. Twenty-five minutes after ingesting BOL-148 his headache was reduced in intensity. However, his head remained tender, and deep pain thresholds, which had been low at the onset of headache, were not elevated. Some 40 minutes after the agent was taken he first noted distortions of body image, i.e., he felt as though one arm were growing longer and out of proportion to the other arm, and as though his abdomen were increasing in girth. His elevated mood gave way to one of intense anxiety merging into panic, which was "controlled only by great effort of will." Tachycardia and palpitations occurred, along with nausea and finally vomiting and urgency of defecation about one hour after ingesting the agent. Most frightening for the subject, according to his utterances, was the inability to concentrate and the sensation of seeing things as smaller or out of proportion. He became clumsy, bumping into things and people in a very familiar surrounding. His speech became slurred and thick.
He reported altered color perception, in that things would change hue and thereby become very annoying. This could be abolished by closing the eyelids. The lines of bricks on the wall of the building across the court became wavy. He was restless and had a fine tremor. Tinnitus was present and persistent.

To describe the reaction more vividly, a statement of the subject's recall of the experience follows:

"Anxiety was associated principally with uncertainty about how severe the mounting reaction would become and if it might even lead to death. The impairment in mentation and possible loss of consciousness also made me fearful. The effects of stimuli in all modalities, but particularly in regard to color, were amplified. Stimuli did not necessarily seem louder or brighter than usual, but their effects were poorly modulated, they seemed to mount in intensity and threatened to block other aspects of mentation. The phenomenon was most striking in regard to visual stimuli: I would become absorbed in the color of a sign on the door or in the whiteness of the sheets on the bed. The mounting intensity of the effects of these stimuli was frightening because I had difficulty controlling it. Reactions to the sound of a refrigerator motor or of a ringing in my ears became particularly frightening, since I could not exclude them, as I could the visual stimuli, by closing my eyes. Tactile sensations also led to effects that were amplified in this way. Stroking the skin lightly at times gave rise to sensations that were hard to distinguish from those of mild burning pain. The significance of other pain, such as mild muscle cramps, became exaggerated. Affect was modulated poorly; in one instance I imagined a recurrent rhythmic musical theme which became more and more insistently, causing feelings of excitement and exaltation accompanied by weeping. Early in the reaction I believed that part of myself was intact and I could remain detached and observe the phenomenon. Later, particularly after experiencing poorly modulated affective reactions, I began to doubt that I could trust my reactions at any level. Ideas of suicide or facetious comments that might be made entered consciousness and were rejected quickly, but with a recognition that the disturbances extended through all levels of awareness."

The subject was put to bed and an examination was begun about two hours after the ingestion of the agent, BOL-148. His movements were clumsy and awkward and he had difficulty in undressing.

Examination revealed: blood pressure, 180/120 mm. of Hg; pulse, 139; respirations, 30 per minute. The patient's face and body were flushed and felt warm to the touch. His heart was not enlarged to percussion, although the beat was forceful and bounding. His mentation was "cloudy," and tests showed poor calculation of simple problems and poor "serial sevens." Orientation to time, place and person was accurate. Pupils were 3 mm. in diameter and reacted readily to light and attempts at near vision. Speech was thick and the mouth was dry, although other functions of the mouth segment were unimpaired. There was a fine tremor of the outstretched extremity but no intention tremor. Fine movements were not graceful and smooth. Deep tendon reflexes were slightly hypoactive but symmetric. There was no loss of sensory perception. The patient complained of increased intestinal motility, although no borborygmi could be heard.

During the examination, which was purposely prolonged and done in especial detail to reassure the patient, he was less anxious and had fewer visual illusions. Blood pressure and pulse rate fell to 140/90 mm. of Hg and 96 to 100 beats per minute, respectively. On being left alone even for a few moments his anxiety and visual misinterpretations increased markedly. Because of continued restlessness and anxiety he was given chlorpromazine, 10 mg. by mouth, about four hours after ingesting the BOL-148. Approximately 15 minutes later he noted return of his visual illusions, "cloudy" mentation and color misinterpretation, exactly as he had noted them at the
height of the BOL-148 effect. The increased anxiety, panic, blood pressure, pulse, rumbling in the abdomen and urgency of defecation cleared in some degree about one and a half hours later, although he still reported difficulty in concentration and recall. Headache also returned in a mild degree. This being about midnight and about seven hours after first ingesting the BOL-148, he went to sleep. No dreams were recalled.

For the next three days he observed easy fatigue, both mental and physical, and little interest in work. A given task consumed excessive energy and work efficiency was diminished.

**DISCUSSION**

From these observations it is clear that BOL-148 in a relatively small amount produced a delirious reaction similar in almost all respects to that of LSD. Pupil, blood pressure and other cardiovascular changes were probably features of the subject's panic. This individual's experience calls for a reevaluation of the statement that BOL-148 does not produce mentation changes in low dosage.

Since LSD administered for several days can block its own effects, the suggestion of Ginzel and Mayer-Gross that BOL-148 blocks the effects of LSD does not necessarily indicate a different mode of action of the two drugs, but rather the development of a tolerance interchangeably between the two agents. It is interesting that when BOL-148 was given only one day prior to LSD, minor effects of LSD were noted, i.e., tolerance had not developed.

The similarity of the effects of "psychotomimetic" drugs such as LSD, BOL-148, bufotenin, mescaline, bulbocapnine, etc., and the states produced by fever, sepsis, uremia, bromides, carcinomatosis and cerebral arteriosclerosis in some individuals, is to be emphasized. The similarity is in fact that an abnormal mental state can be produced by all, and that a chemical agent in small amounts can produce effects of short duration. All produce delirium.

In regard to the potentiation of the effect of the BOL-148 by chlorpromazine, Abramson stated in the case of LSD that the variable effect of 50 mg. of chlorpromazine by mouth on the LSD reaction was related to the time of administration of the two drugs. In at least two out of five subjects in his studies, when both agents were given at the same time there was a potentiation of the LSD reaction. Hoch, however, found that the same amount (50 mg.) of chlorpromazine intravenously abolished the effects of LSD.

**CONCLUSIONS**

1. BOL-148 in a relatively small amount produced LSD-like effects in a male laboratory worker.
2. The effects of both of these agents are similar to those of a toxic delirium or acute exogenous reaction.
3. The hypothesis that BOL-148 and LSD are dissimilar in regard to psychic effects but similar in regard to all other antiserotonin reactions must be revised. It is likely that they are different only in degree.

**SUMMARIO IN INTERLINGUA**

Le similitude inter certes del symptomas de psychose schizophrenic e le effectos de intoxication per diethylamido de acido lysergic (in le texto = LSD)—i.e. distortiones perceptual, illusiones, "hallucinationes," alterationes de imagines corporee,
alteraciones de postura, e disturbaciones emotional del typo de anxietate, depression, euphoria, e sensation de dispersonalisation—ha stimulate un grande numero de studios con LSD e simile agentes in le spero de obtener un plus complete comprehension del natura de psychose schizophrenic.

Un varietate de iste agentes "psychotomimetic" es antimetabolitos de serotonina, un substantia que ha recentemente essite recognoscite como occurrente in le systema nervose e specialmente in le cerebro. Es suggerite que tal agentes psychotomimetic affice le systema nervose principalmente per disturbar le activitate de serotonina in le cerebro. Multes del agentes psychotomimetic es analogos structural de serotonina, e lor action antagonistic al action de serotonina pote esser demonstrate in musculo lisie in vitro.

Le rolo de serotonina in iste alterationes mental esseva questionate per le ob­
servation de Cerletti e Rothlin que diethylamido de acido 2-bromo-d-lysergic (in le texto = BOL-148) esseva un forte antagonista del effectos in vitro de serotonina sed que illo non produceva le disturbance mental que es caracteristic de LSD.

In le observationes hie reportate, un juvene adulto (un technico de laboratorio) prendeva 0,5 mg de BOL-148 per via oral. Circa un hora post le ingestion, ille experientiava un euphoria transiente, sequite per distortiones perceptual e illusiones (primarimente visual sed etiam auditori e tactile), distortiones de imagine corporee, hyper-reaction a color, sensation de dispersonalisation, seveur grados de anxietate, tremor, disquietude, e defectos de mentation—i.e. concentration, memoria, calculation, subtraction serial de 7 ab 100, discrimination a duo punctos, e recognition de numeros traciate al superficie del bracio. Iste reactiones persisteva durante circa 24 horas e esseva sequite per un secunde periodo de 24 horas de leve grados de depression e de un sensation de exhaustion.

Iste disturbance esseva identic con illos observate in casos moderamente sever de intoxication per LSD, describite per multe altere autores e observate a iste laboratorio.

Con le exception de lor breve duration, le effectos del intoxication per BOL-148 e per LSD es typic pro le delirio classic observate in stato de febrilitate, in morbo cardiac o renal, in hypoxia o vulneration del capite, e in statos post le prolongate administration de bromuros, etc. Le mesme aspectos general del delirio es notate sin reguardo al identitate del agente causative, sed intra le limites de iste aspectos commun il occurre marcate variationes que es determinate in grande parte per le reactiones characteristic del personalitate del individuo in question, per su etate, su debilitate general, su experientias premorbide, le ambiente cultural e social, e le duration del abreaction.

Iste observationes indica que BOL-148—ben que plus grande quantitates de illo es requirite que de LSD pro producer disturbance mental—es etiam capace, in relativamente basse quantitates, a producir disturbance de comportamento e de mentation.

BIBLIOGRAPHY

   (a) ibid. pages 47-82.
   (b) ibid. pages 236-258. Chapter on experimentally induced psychosis in man.
   (c) ibid. pages 9-84. Chapter on LSD and related compounds.
   (d) ibid. pages 29-30.