

Subjective Effects of Anti-Cholinergic Hallucinogens

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Lysergic acid, tryptamine and phenylethylamine derivatives have received most attention in studies of hallucinogens because of their extraordinary range of effects and their relationship to plants used in certain "primitive" religions. Other chemicals synthesized in laboratories merit attention because of similarly dramatic effects on consciousness and psychological processes.

The series of piperidyl benzilate esters have "psychotomimetic" properties first described by Abood and others (Abood, Ostfeld & Biel 1958). This series, including JB-318, JB-328, and JB-329 (Ditran), lacks the characteristic indole ring or phenylethylamine structure of better-known hallucinogens.

The pharmacological activity of the piperidyl benzilate esters appears to be a blocking of acetylcholine, the neural transmitter for the parasympathetic autonomic system. Acetylcholine is also involved at the myoneural junctions (between motor nerves and muscles) and plays an unknown role in the central nervous system. Therefore, these substances produce physiologic effects similar to atropine and scopolamine, prototypical anti-cholinergic compounds.

Since the parasympathetic and sympathetic branches of the autonomic nervous system have opposite effects, these anti-cholinergic chemicals produce reactions, via parasympathetic blocking, identical to those produced by LSD and tryptamine derivatives by

sympathetic stimulation. In both classes of compounds one finds pupil dilation and increased heart rate, but through different mechanisms.

Although some of the physiologic effects of the piperidyl benzilates can be attributed to their acetylcholine-blocking action, it is doubtful whether the central (psychologic) effects are also brought about this way. The precise role of acetylcholine in the CNS is unclear. At any rate, these new compounds share most of the central effects of atropine and scopolamine, what has been called the "central anti-cholinergic syndrome," consisting of "impairment of thoughts, disturbances of recent memory, drowsiness, a sort of non-aggressive excitement, ataxia and asynergia, and hallucinations" (Longo 1966).

SUBJECTIVE EFFECTS OF JB-328

Three normal subjects, all with previous experience of LSD and other psychedelic agents over periods of years, were given 10mg of JB-328 (N-ethyl, 3-piperidyl, cyclohexylphenylglycolate) orally. The following observations are based on a total of four ingestions (one subject had two trials).

Somatic effects typically reported include dizziness, muscle weakness and heaviness of the legs. Since acetylcholine is the neural transmitter for myoneural junctions, it is probable that this kind of muscular flaccidity is a direct peripheral anti-cholinergic effect. Drowsiness is also reported in the later stages of the reaction, which lasts approximately 8-10 hours.

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Perceptual changes were most marked in the visual modality. JB-328 seemed to produce a breakdown of perceptual constancies, not unlike that produced in the early stages of LSD reactions: stationary objects moved, walls undulated and swirled with wave-like motions, moiré-like gratings and lattices seemed superimposed on blank surfaces. Unlike LSD, JB-328 apparently produced no enhancement of color, brightness, significance or beauty.

Strikingly, one subject reported the appearance of some fibrous material, organized into lattice-structures, which lay on the floor. The subject reported picking it up and handling it for a short time until it disintegrated. The non-drug observer could not see the material. Whether JB-328 reveals moiré-like mechanisms in the tactile modality remains open to further investigation.

Hallucinations are definitely produced by these substances. Objects are seen that are not objectively there, and other objects that are present, are not perceived. For example, one subject saw a man sitting on a chair in the middle of the room and talked with him. When the subject walked close, man and chair disappeared. All of the subjects reported, and were observed, walking into doors or furniture, which they had not seen. Sometimes the basis of the hallucinations was clear: e.g., a coat on a bed would be seen as a small dog. In other instances, no such transformation seemed to underlie the hallucination. For example, one subject saw a friend of his, the size of a three story building, crawling around the garden on his hands and knees, eating the tops of trees.

In comparison with the effects of LSD, the nature of these hallucinations is commonplace — ordinary objects or people are formed or transformed. There is none of the mythic or other-worldly quality of LSD visions. Nor, unlike with LSD, is there awareness that these are hallucinations. None of the detached, multi-level observation of one's own vision, so characteristic of psychedelics is reported.

Thought and memory changes apparently dominate the experience. The subject finds that immediate memory mechanisms are rendered inoperative when trying to communicate or answer questions. Halfway through an answer, the subject forgets both question and answer, and other associations break into the thought sequence. Some qualities of James Joyce's writing in *Finnegan's Wake* reminiscent of this effect, have been attributed to his taking low doses of scopolamine for his glaucoma.

At the higher dosage studied here, speech become gibberish because of the inability to formulate a single thought or sentence. The inability to speak is not caused

by the overwhelming profusion and richness of thoughts and images flashing through the mind-brain after LSD ingestion, but by the disruption of even the simplest orderly sequences and the inability to hold attention on the thought. General awareness of the surroundings, mediated by long-term memory, and sense of identity seem to be intact; but immediate short-term memory is totally disrupted. There is no multi-level thinking or awareness as with LSD, no sense of insight or revelation.

Emotional aspects. Another striking differentiation from the typical LSD experience is the almost total absence of emotion. Subjects accept the sight of otherwise frightening occurrences, such as a giant crawling around in the garden eating trees, with slightly amused indifference or mild astonishment. There is tremendous frustration at the inability to think, or formulate thoughts clearly, and at the loss of motor coordination, but none of the outright terror which is possible in "bad" LSD reactions.

CONCLUSIONS

These observations are in essential agreement with the reports of other investigators. DeVito and Frank (1966) concluded that the primary effect of Ditrán (JB-329) in normals was "immediate amnesia" and "thought dissolution", while mood and emotional changes were secondary.

These anti-cholinergic drugs appear to be consciousness-altering, not consciousness-expanding. Their thought-disorganizing effect resembles natural psychosis more than LSD, but differs from psychosis in the marked absence of fear or other affect disturbances. Ditrán has met with reputed success in the treatment of depressions and some types of psychosis (English 1962). The disintegrative effect on thought combined with absence of fear may act here like a combination of the memory-disrupting action of ECT with the emotional calming of tranquilizers.

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