

XI. SOME QUALITATIVE PROPERTIES OF THE PSYCHOTOMIMETICS: A. T. Shulgin

Before embarking upon a discussion of the measurable qualities of psychotomimetic materials – their physical features, their distribution within the body, their metabolism, their behavioral nature, and their structure-activity relationships – Shulgin thought the group should talk about the qualitative comparisons between compounds within this broad family. These have already been mentioned briefly, and any value that might come from this approach can be appreciated only through presentation and comparison of properties that may be specifically assignable to individual drugs, rather than those that are common to all.

This entire area is usually regarded from one of two opposite viewpoints. Some investigators insist that all compounds produce identical psychological effects and that all lead to the same end point. There has also been much mention made of the term “toxic psychosis.” Implicit in such a designation is the assumption that all these materials differ only in their potencies and that the effective dose is merely a measure of toxicity. At the other extreme, many hold that each of these compounds is discrete and pharmacologically unique and that the specific aspects of the intoxication syndrome can be considered as valid individual properties. There is reason to believe that these two extremes are not irreconcilable; there is truth to be found in each. To this end, those properties that the psychotomimetics share in common should be considered, and those that may be discretely assignable to specific compounds should be examined separately.

Complete recall of details of the drug experience is one of the properties most frequently and consistently shared by all of these substances. There appears to be some question, worth examining, as to whether several of the parasympatholytics should properly be included under the general term “psychotomimetics.” The racemic compounds atropine and scopolamine, the optically active isomers hyoscyamine and hyoscyne, and the synthetic materials such as ditran, benactyzine, and a variety of glycolates and phenylacetates chemically related to the *Datura* alkaloids, can all be included in a single family. All have the properties of producing a delusional state, an amnesia, and a general pharmacological picture rather different from the psychotomimetics under discussion. The psychotomimetics not only allow subjects to remember the events that occurred during the period of intoxication but usually leave one with the desire to invest some time in the interpretation of those events.

An experience shared by most subjects under psychotomimetic intoxication is the amplification of imagery. There is interference with the visual system; unexpected things may be seen or may be thought to be seen. The details of such interference vary from compound to compound and will be discussed later, but the general concept of some visual change appears to be a consistent property of this class of compounds. Similarly, there is a change in the state of awareness. This is the basic topic of literally dozens of books currently popular, those which concern themselves with the religious and mystical interpretations of the drug experience; and, along with this heightened state of awareness, there is generally a development of a state of anxiety. (Discussion of the pharmacological details of this aspect is taken up under Chapter XIV.)

Another property that is shared by all of these compounds, is a capacity to precipitate some form of a psychotic episode. The so-called "bad trip" can be an immediate outgrowth of the experience, perhaps through the creation of, and the expansion upon, the anxiety state. The subject, rather than recovering normally after a proper time interval, appears to maintain a mental state that is difficult to ascribe directly to a drug effect. This has been explained as reflecting a predisposition to psychotic episodes. Such an event has occasionally been observed as a relapse that can appear weeks or even months after an apparent recovery. "Recovery" is here defined as an apparent return from a short-lived, and therefore reversible, psychotic state.

These are properties that all such compounds share in common; what properties can we list that can be used to distinguish among these several compounds? To wander in this area is to venture where angels fear to tread; the analysis is therefore presented with caution. Certainly, if one can argue differences from drug to drug, one must admit that there are, within the use of a given drug, differences to be expected between one person and another. It is hard to say what might be the property of the drug and what might be the property of the person; even within a single person from one day to another one can observe distinctly different responses.

These analyses become more complex when we consider certain pharmacological factors. The concept of habituation must be recognized as being closely related to the social aspects of drug use; tolerance will reflect frequency. Because there is the possibility of synergism between different drugs, one must consider not only the effects of an unknown or unevaluated drug but also the potential for a concurrent unsuspected drug history, which may contribute to some peculiar response. These constitute

hazards in the casual incorporation of data from uncontrolled studies into a compilation such as this. Yet more subtle are personal moods, the set and setting of the experiment, and especially the past history of the drug user. These would certainly have a gross influence upon the specific syndrome observed with a given drug.

Many aspects of the intoxication syndrome, both objective and subjective, can be assigned to specific drugs without argument. The appearance of the well-known symptoms of physical distress — nausea, mydriasis, tachycardia, and ataxia — to a large measure depends upon the amount of the drug used. Those drugs that are relatively insensitive and require employment of doses of hundreds of milligrams, for example, mescaline, trimethoxyphenylisopropylamine (TMA), ibogaine, and harmaline, almost always produce signs of physical toxicity ahead of the mental changes. Some nausea or malaise is always found, whereas with compounds that are more potent, requiring a smaller total amount of material, there is less tendency to physical distress. LSD, which is the most potent, rarely displays these effects.

The duration of the effects of these chemicals reveals another objective parameter. N,N-dimethyltryptamine (DMT) is unusually rapid regardless of the mode of administration. By inhalation it is effective in a matter of seconds (although orally it is not active at all), and the effects are to a large extent over within an hour. The homolog of DMT, N,N-diethyltryptamine (DET), is longer lasting, reaching a peak in about 1 hour. This is still a more rapid onset of intoxication than that observed with most of the materials being discussed here. The usual time structure for the psychotomimetics is yet longer, with an onset of intoxicative symptoms from between 30 min to 1 hour, an intensity plateau achieved perhaps between 2 and 3 hours, and a total duration of 8 to 12 hours. At the other extreme, 2,5-dimethoxy-4-methylphenylisopropylamine (DOM, STP) has been well documented as maintaining disruptive effects into the second day. As Snyder has shown, this drug clears quite readily from the body, although its residual effects may be apparent for days. It may be a good candidate, therefore, for those materials which sustain biological activity even after they have left the body.

The subjective distinctions between these drugs are somewhat more difficult to classify, but this aspect has three facets: drug effects upon the senses, upon the soma, and upon the psyche.

The Senses

The most conspicuous effects are upon the visual processes. The effects of drugs such as mescaline or TMA on color perception provide the most incontrovertible evidence of distortion of the visual sense. There are virtually no instances of subjects under the effects of these drugs who have failed to volunteer, without external suggestion, that color changes, color distortions, and color syntheses are the most dramatic effects noted. However, we must freely acknowledge that many accurate and candid observers of drug experiences will say, "Well, I have heard someone mention this on another drug," or "I didn't see this happen." Almost every one of these properties has been seen at one time or another with almost every drug. Yet there are particular observations that have been reported time and time again, unsolicited, with certain drugs and rarely with others, which lead one to believe that these properties can be ascribed to specific drugs. Many of the other perceptual changes, such as distortions of the size, the shape, the motion of viewed objects, all of which have been observed with mescaline, TMA, and 2,4,5-trimethoxyphenylisopropylamine (TMA-2), have frequently been experienced with most of the other related compounds. We might expect, then, that this aspect of the drug intoxication may appear quite independently of the identity of the drug.

Examples of sensory hallucination affecting the sense of touch are rare. There is, certainly, a change in the acuity of the sense of touch, but this is usually a matter of a subject's efforts to confirm or challenge what is seen. A subject, upon viewing an object and deciding that its surface is odd, may extend his hand and rally his entire motor system in an effort to verify or to bring into perspective the reality of what he sees. There are extremes, as has been observed with some of the polymethoxylated phenylisopropylamines, in which the process of confirmation of texture will lead to damage or even destruction of the object in view. On the other hand, the intense empathy associated with the mescaline state makes it almost impossible even to touch an object to determine if it is hard or soft, for fear of hurting it.

There is rarely any invention in the auditory area. This sensory field is frequently affected by compounds of the atropine group, but with the psychotomimetics there are almost never hallucinations in auditory input. It is not uncommon, however, to observe a distortion in what is actually heard, or, especially, an unexpected interpretation of sounds.

Again, although all psychotomimetics have been assigned these properties at one time or another, there are several compounds that seem to be characteristically associated with unusual auditory experience. Both psilocybin and marijuana have been mentioned repeatedly in the literature as materials that evoke unusual responses to music. With both of these drugs, the subject often undergoes a three-dimensional incorporation into what he is hearing. This experience is generally accompanied by some degree of time distortion, resulting in a change in tempo and style of the music, which often leads to an extraordinary interpretation.

The Soma

Certain compounds, notably psilocybin and DOM, have been reported to produce synaesthesia, wherein there is an interchange of senses. Touch, for example, may evoke the sense of sound, or sound itself brings forth the appearance of colors (chromaesthesia).

Depersonalization is the principal somatic change that is subjectively observed. This phenomenon has been noted often with DOM and is observed very consistently with LSD. As for phenomena that concern subjective time, we are still uncertain into which category — sense, soma, or psyche — to place them. They are introduced here only because the autonomic biological rhythms are somatic. As mentioned above, psilocybin and marijuana change the interpretive quality of the musical experience by slowing subjective time. All of the materials to be discussed below, those that lead to some form of visual synthesis, as a rule create the tendency to compress many events into a small amount of real time. These observations are usually spontaneously volunteered by the test subject, and should not be considered consequences of suggestion.

The Psyche

It is in the area of the psyche that one finds the most dramatic effects, although they are, unfortunately, the most difficult to put into a neat classification. The term "hallucination" was bandied about earlier with much vigor. Perhaps that discussion should not be reintroduced, but one must define a hallucination if one uses the term "hallucinogen." This term, which has been applied rightfully or wrongfully to this group of compounds, deserves a few words.

Certainly, no objection can be taken to a broad definition of the term "hallucination" — that it is a change of some sensory input which is

not objectively confirmable. Because, in the area of psychotomimetic intoxication, the sense most commonly affected is that of sight, hallucinations are usually conceived of as visual changes. The classification of events that may be considered as "hallucinations" may range from the volatile images, those seen with the eyes closed but lost upon looking about, to the more compelling and persistent illusions, those that can be watched with open eyes.

At the "eyes-closed" side of this spectrum, specific mention should be made of a group of drugs, the methylenedioxy compounds, that share this property. Their structures and quantitative properties will be discussed later. Qualitatively, however, methylenedioxyphenylisopropylamine (MDA), the monomethoxy analog, 3-methoxy-4,5-methylenedioxyphenylisopropylamine (MMDA), and its somewhat more potent dimethoxy analogs, 2,5-dimethoxy-3,4-methylenedioxyphenylisopropylamine and 2,3-dimethoxy-4,5-methylenedioxyphenylisopropylamine (DMMDA and DMMDA-2), all produce eyes-closed hallucinations of a commanding sort. There is quite consistently a recollection of past events, of childhood memories, a reliving of earlier times that appear to be, as far as can be documented, quite accurate. These compounds have found some value in experimental psychotherapy through the release of subconscious material. Harmaline evokes an unusual eyes-closed hallucination in which there are synthetic structures of imagery that are certainly entertaining, although they appear to have no particular bearing on reality at all. The most general type of eyes-closed effect, that of moving lines, billows of light, arabesque patterns, and a multitude of entertaining maneuverings of the visual field, can apparently be induced by virtually all of these compounds. One would be very reluctant to assign any of them as a specific property to any specific compound.

The "eyes-open" hallucination can arise from one of two stimuli. The one can create a distortion of something that is really viewed, a confirmably real thing, and find that it is modified into something absurd and yet quite believable. The other style of illusion is represented by a completely synthetic image that is projected upon the actual visual field. The subject may look at the wall, but there is a world interposed between him and the wall, and it is this illusory world that commands his attention. The distortion of the field is quite common with LSD and with mescaline and can be considered a hallmark of these compounds. The latter phenomenon, the superimposition of a hallucination upon the background rather than the development of the hallucination as an outgrowth of the background is quite rare, and to my knowledge has been

reported only with DMT, mescaline, and psilocybin. I know of no well-established instances in which any other materials actually produced a totally synthetic hallucinatory structure. High levels of most psychotomimetics will lead to some of these symptoms. Within the concept of the toxic psychosis, when one considers the dose employed as opposed to the intensity of the response evoked, there seems to be a reconvergence of many of these symptoms; although all different from one another, these compounds may all still share many properties in common.

We must now concern ourselves with the aspects of insight in these states. Any drug experiment, when observed within the structure of the "psychedelic" experience, has the potential of reviewing the former world with some unexpected interpretation. This latter view is automatically accepted as being real, certainly more usable than the image of one's life and environment that had been accepted earlier. Because this is a recallable phenomenon, it can strongly influence the subject's subsequent behavior. This is a dramatic property of LSD, which may be potentially a virtue of, and is certainly a hazard in, the use of the compound. The reinterpretations and re-evaluations can also be extended to include the internal world as well. It is within this province that one encounters the transcendental, mystical, or religious experiences wherein the internal world is reassembled, incorporating that which was first understood during the drug intoxication. Again, it is LSD that is most frequently associated with this internal revolution.

Shulgin believes that all of these compounds have the potential for achieving this, and that these chemically diverse materials may, after all, lead to the same end result. Their differences might be considered as different scenic tours along the general route to the same destination. With all of this variation, perhaps only the simplest generalizations should be attempted. One can say that those materials which are catecholamine-like, the methoxyamphetamines and the methylenedioxyamphetamines, are to a large extent entertaining, oriented primarily towards the visual processes. There is not the profoundness that is found within the indole group where there is more proclivity to extensive psychological interpretation.

These ideas are advanced merely as colorings and hints in the formulation of an explanation to account for the action of these materials. To ignore the fact that there may be differences between the psychotomimetic drugs, would be to ignore a potentially useful tool.