Chapter 13

Quantified LSD Effects on Ego Strength

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The ego has been characterized by Smith [1] as "a coherent organization of mental forces which arranges the processes of the mind in relation to time and reality," and ego strength according to Mora [2] is "an empirical measure of the level of integration." It is from such emphasis on the organizational and integrative aspects of mental health and the disorganizing effects of hallucinogens such as LSD that our proposal to measure ego strength stems.

The background thinking and data that led us, independently, to arrive at our own similar [3] view of the cerebral homeostatic situation and the possibilities that its failure might account for cerebral dysfunction, as in mental disturbance, are suggested and summarized in Fig. 1. In this figure we have outlined the various levels, along with the means we have used to examine them, of the interrelated adaptive systems making up the cerebral homeostatic equilibrium.

This originates at the synaptic level, where we have found [4], utilizing evoked potentials, a continuous equilibrium existing between neurohumoral excitatory and inhibitory forces, with a transient, readily reversible distortion of equilibrium in one or the other direction constituting a physiological transaction. The dynamic relation between various areas of the brain, interconnected by functioning of the synapses, carries the equilibrium to the organizational level, and the total interrelation of equilibria brings it to the integrative level, which is expressed as behavior.

As we have said elsewhere [5], "normal behavior is the homeostatic response of the organism. It operates to preserve life and generally by preserving equilibrium in relation to its environments, internal and external, to achieve satisfaction through the reduction of the signal overload that would otherwise result. Regulatory control ultimately requires central representation of all events and the responses to them—proposed or actual—as input and output signals. Such monitoring, internal display, and command signaling goes on in the central nervous system where total homeostasis can be achieved through the integrative interaction of its signals, the nerve impulses. The recording of such signals affords a means of identifying some of the elements of integrative interactions, and drugs offer an extremely useful tool for analysis of these interactions."

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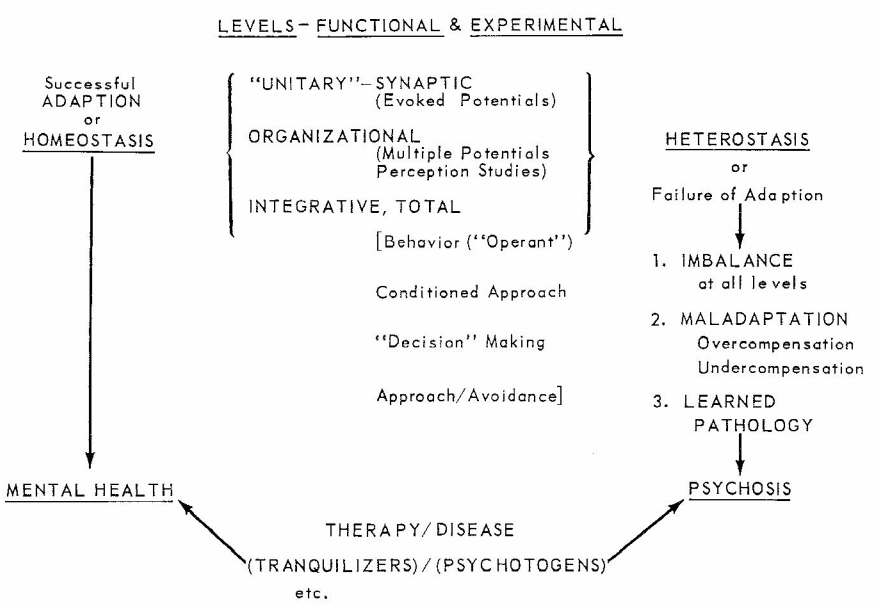

Fig. 1. Cerebral adaptive systems.

Coming back to our diagram, we see that successful preservation of equilibria at the various levels is the homeostasis essential to mental health indicated on the left, while failure results in the consequences indicated on the right as leading to psychosis. The interconversion between these two eventualities is represented at the bottom, as taking place through the operation of disease and LSD on the hand and tranquilizers and other therapy on the other.

Since much of the data has been obtained from experimental animals, we present in Table I a comparative approach to illustrate that we are dealing, not with individual peculiarities, but with synaptic and behavioral effects that follow an orderly and parallel relation in a series progressing through a subhuman primate to man.

Although the table has gaps (which we are in the process of filling in), it shows that LSD has a synaptic inhibitory action qualitatively identical to that of the cerebral neurohumor, serotonin, and that this inhibition is reflected in an impairment of behavior manifested as an increase in conditioned approach latency, an increase in conditioned avoidance latency, a decrease in ability to differentiate between correct and incorrect stimuli, and also as an inhibition of inhibition or disinhibition that releases the animal from optimum control and allows intersignal responses, i.e., responses without "stimulus signal," to appear.

In man, as we shall discuss in detail, behavioral inhibition was measured as a decrease in perceptual association.

The synaptic inhibitory action of LSD is exercised throughout the brain, but the resulting pattern manifested is a function of the different

thresholds characteristic of particular synapses, so that a variety of patterns may be elicited as increasing doses involve more synapses. It is of particular interest that doses involving chiefly low-threshold synapses are bound to dissociate parts of the brain that would otherwise work in unison. Figure 2 is a diagram of the type of experimental setup that enabled us to evoke (in this case, in the cat) potentials alternately in the primary visual receiving area, through electrodes B, and in an association area, through electrodes A. Both sets of stimulating and recording electrodes are shown in the inset surface map and in the coronal section. In this way it became clear [14] that the visual association area has one of the lowest thresholds to the synaptic inhibitory action of LSD, one which would effectively dissociate this reference area from its primary receiving area.

It seemed to us likely that the disintegrative effect of the difference in thresholds, making experience stored in the association areas less available, would result in aberrant perception. This difficulty in comparing new with past information in forming a percept and in "reality checking" might, indeed, be a mechanism of hallucination. Therefore, we have examined this concept and the corollary that, in fact, the psychoses so characterized are the evidence and result of failure of integration. In

Table I. Comparative Neuropharmacology*

Species	Mode	Serotonin	LSD-25	CPZ protection versus
Rat	Synaptic†	Inhibition [6]		
	Behavioral		C.Ap.L.↑[4, 7] C.Av.L.↑[4, 7] Diff. ↓ [4, 6, 7] Intersignal responses↑[6]	LSD-25 on C.Ap. [4, 7]
Cat	Synaptic	Inhibition [7]	Inhibition [7]	Serot. [7]: LSD-25 [7, 8]
	Behavioral		Intersignal responses↑[18] (No. of responses)	
Dog	Synaptic	Inhibition [9]	Inhibition [9]	
Monkey	Synaptic	Inhibition [19]	Inhibition [19]	Serot.: LSD-25 [19]
	Behavioral		C.Ap.L.↑[10] Diff. ↓ [10] Intersignal responses↑[10]	LSD-25 on C.Ap. [10]
Man	Synaptic		Inhibition [11]	
	Behavioral		Hallucination [12, 13] Perceptual assoc. ↓[5]	LSD hallucination [12, 13]

*Notation: ↑, increased; ↓, decreased; C.Ap.L., conditioned approach latency; C.Av.L., conditioned avoidance latency; Diff., differentiation (tone or time).

†In this table, synaptic refers to transcallosally (except [11]) activated cortical synapses. However, as indicated in the table "Generality of Cerebral Synaptic Drug Response" published elsewhere [5], synaptic inhibition by serotonin and LSD-25 is obtained at a variety of cerebral synapses, including cortical, subcortical, and brainstem synapses.

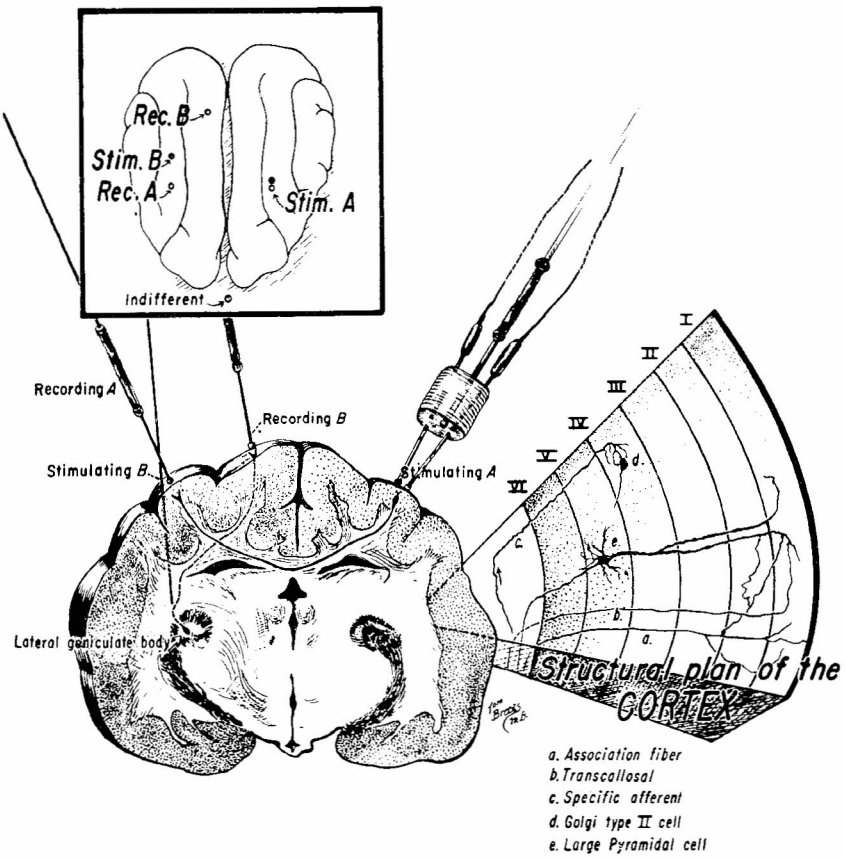

Fig. 2. Structural plan of the cortex.

keeping with our opening quotes on the nature of the ego, the ease with which aberrant perception can be induced could be utilized as a measure of ego strength, or—emphasizing the adaptive, homeostatic aspects—we might consider this to be an indication of psychic reserve, i.e., of integrative capacity [15].

To test the hypothesis, we have set up an experimental visual perceptual conflict between the mental image of a room distorted by aniseikonic lenses and the recollection of the cubical nature of rooms. Figure 3 shows a picture of such a five-sided room, as it looks to the subject, who views it from the open sixth side. He sees walls, floor, and ceiling which have been textured with leaves to minimize rectangularity (hence the name "leaf room"). The bar in the center is remotely controlled by the subject, who is instructed to keep it parallel to the floor line, when tracking the horizontal distortion produced by one set of lenses, as seen in Fig. 4, and to the side-wall line when tracking the vertical distortion produced by the other set.

The binocular fusion of the disparate images formed in the two eyes, in the case of one set of lenses, and in different optical fields, in the case of the other set, results in new information which competes with past experience of rooms. Consequently, the subject initially rejects the distortion. Gradually past experience is supplanted by new information, which becomes dominant in inverse proportion to ego strength. The extent of this is instrumentally determined by having the subject track the development of distortion by matching the guide bar to the apparent slope appearing in the floor line or side-wall line. The adjustments are automatically recorded and the resulting curve rises slowly, over approximately a minute, to reach a plateau. Figure 5, a graph of such an experiment, shows readings taken every 15 min for an hour previous to and several hours after a test dose with a subclinical amount of LSD, which ordinarily produces—in our laboratory atmosphere—no overt symptoms. Under these circumstances, the dose is 65 μg by mouth.

We are thus challenging the subject's reality-checking by the disintegrative effect of LSD on function. This graph presents all the data typically obtained in such a run. The lower two curves represent the distortion expressed as bar settings (rotation), plotted in arbitrary units on the ordinate against time on the abscissa. The curve obtained with the lenses producing "horizontal" distortion is dashed, while that with "vertical" distortion is solid. The corresponding upper two curves plot

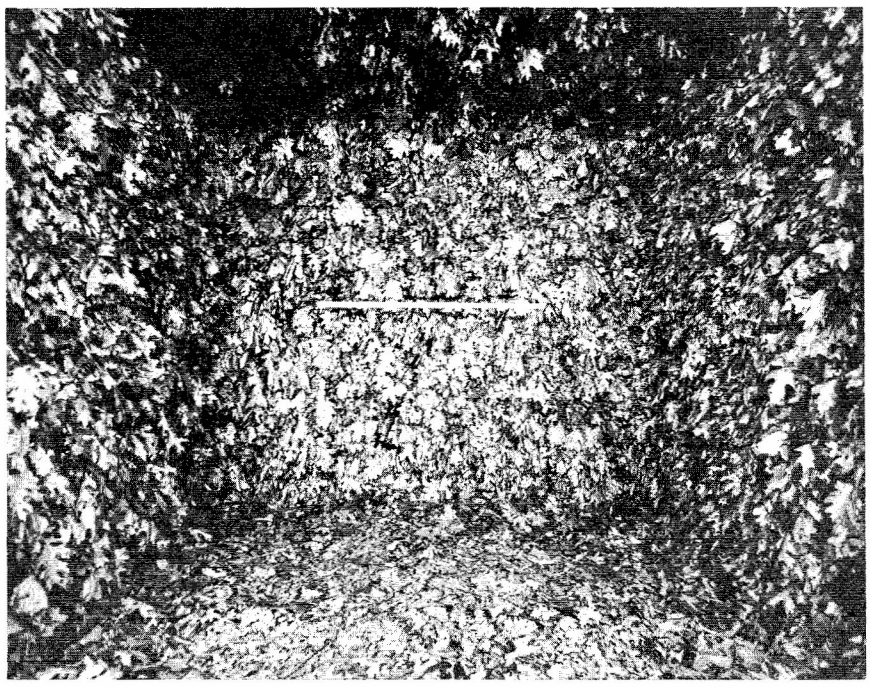

Fig. 3. The "leaf room" as viewed from the open sixth side.

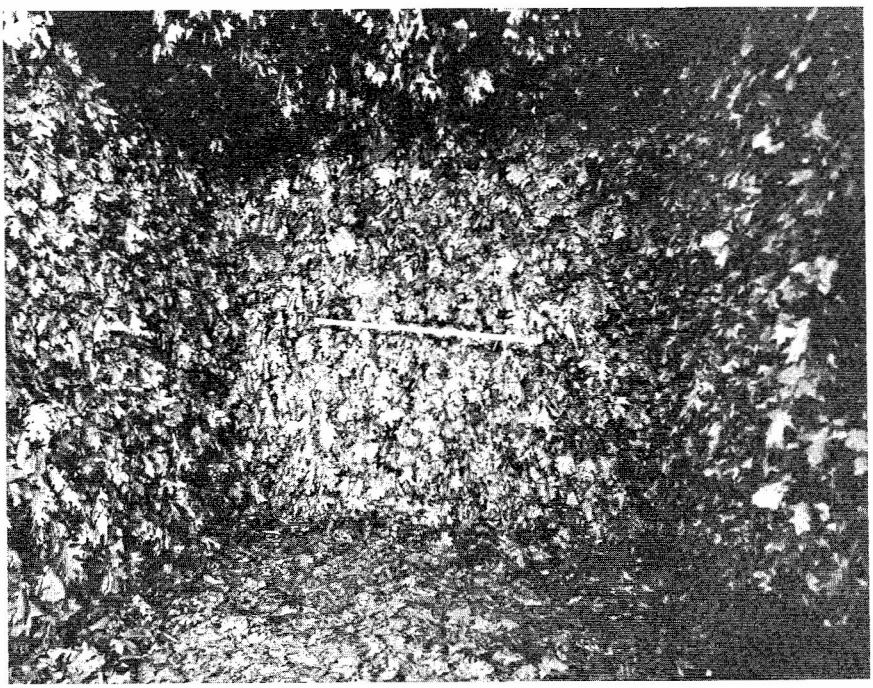

Fig. 4. Horizontal distortion of the "leaf room" produced by one set of lenses.

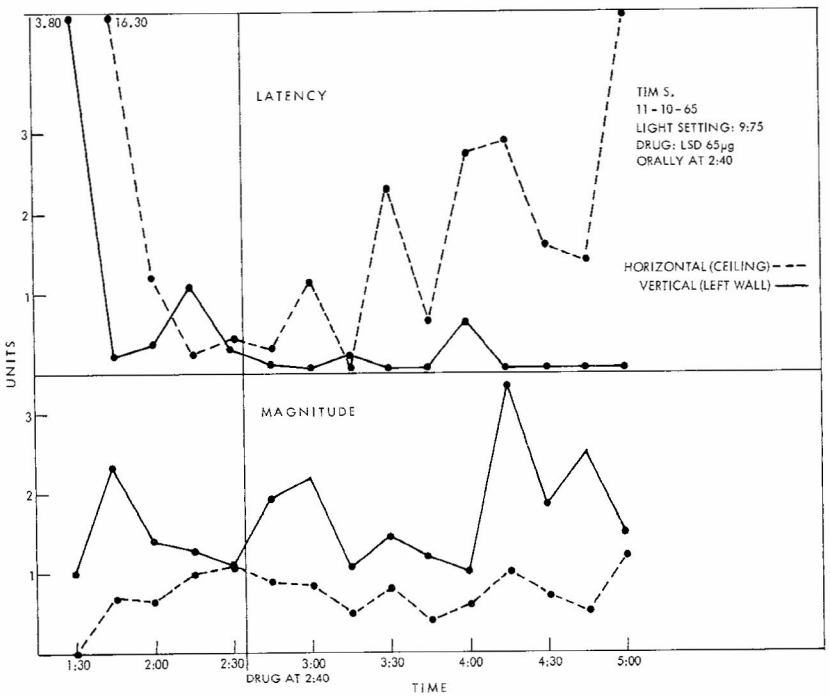

Fig. 5

the latencies for arrival at the final bar-adjustment (plateau) points plotted below. It is apparent that extent of distortion and latency tend to bear an inverse relation to each other, so that, as in this special case, there may be little change in "horizontal" distortion after LSD but a distinct increase in latency, as opposed to less increase in latency of setting but more change in the bar settings after LSD indicating "vertical" distortion. Figure 6 is a simplified presentation of representative data from a series, which up to now includes 12 patients and 30 carefully screened "normal" student volunteers. For this comparison only, the horizontal-distortion bar settings are shown.

The students were selected to represent the norm on the basis of MMPI ratings, an interview by the clinical psychologist, an interview by Dr. Marrazzi, and, in case of doubt, an interview by a psychiatrist. The students were tested and gave similar curves for the same subject on two preliminary 2-hr no-drug runs and one 6-hr placebo run, before being run on LSD. The psychotics and neurotics were from the psychiatry service of the University of Minnesota Hospital. Tranquilizers and antidepressants were withheld for one week and sedatives for 12 hr before testing.

Although the results are still preliminary, they definitely suggest that, as indicated by the measured increased distortion produced by LSD, psychotics are distinguishable from volunteers and neurotics, neither of which groups showed any increased distortion due to LSD compared to their predrug control.

The neurotic group does have a higher control level than the normals, but the significance of this is not yet clear. The stability of performance of the neurotics on this test is evidenced by the lack of change with even higher doses of LSD, 100 μg in patient B. T. and 200 μg in J. B. All repeat

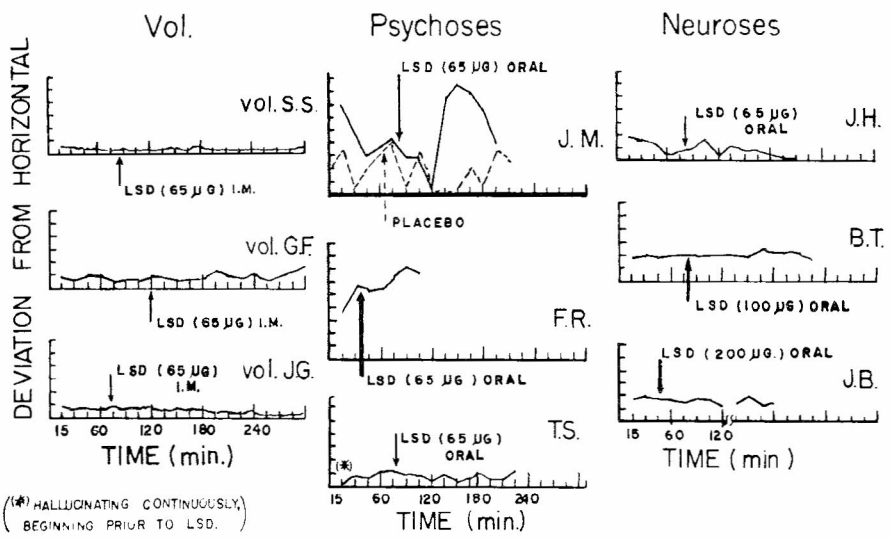

Fig. 6. LSD effects on visual perception (with aniseikonic lenses).

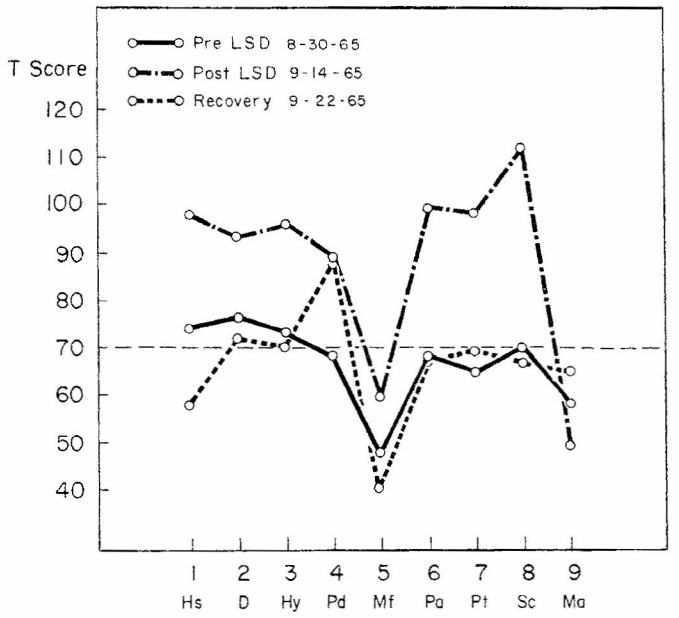

Fig. 7. MMPI profile of J.M., an 18-year-old female.

administrations were done at intervals of 10 days or more, i.e., intervals long enough to obviate tolerance phenomena.

The results were most interesting in the case of the psychotics, three types of which are shown in the middle column. The top curve for an acute schizophrenic and the middle curve for a manic-depressive show a marked increase in perceived distortion after LSD, though unfortunately the determination for the manic-depressive was interrupted by the necessity of returning the patient for supper. The bottom curve was obtained from T. S., an acute schizophrenic, who was actively hallucinating at the beginning to the test. Under these circumstances, the test dose of LSD was not adequate to produce gross changes. However, this is the same experiment presented in the more detailed Fig. 5 discussed above, where, although the settings tracking "horizontal" distortion showed, as here, no change, the latency was greatly enhanced and the "vertical" amplitude did rise. It thus seems possible by adding such refinements to our considerations to detect changes in this kind of patient also.

The top curves, for J. M., are especially interesting. These were from an 18-year-old girl, who was admitted with a very uncertain, stopgap diagnosis of personality disorder. Her mother had been hospitalized in the past with the same diagnosis. Her father is a chronic alcoholic who does not live with his wife and daughter. A placebo run (the dotted line) gave an erratic but otherwise unremarkable curve. The LSD curve (solid line) shows that an initial period of adaptation, which is not unusual, was interrupted by a sharp rise starting 35 min after the oral administra-

tion of LSD. The patient became uncooperative and 1 hr and 15 min later had to be returned to the ward, where she entered a period of mutism lasting 3 days. This was regarded as an abortive catatonia. The patient was given tranquilizers but required no further measures. Figure 7 shows this patient's MMPI before LSD (solid line), after LSD (dot-dash line), and after recovery from mutism (dash line). The pre-LSD curve is at the extreme of the normal range, the LSD curve is definitely abnormal, and the recovery curve shows return.

In this case, whether the acute symptoms were coincident with or precipitated by LSD, there was impressive agreement between our perception testing, the MMPI changes, and the clinical picture. The diagnosis was now revised to psychosis of the acute schizophrenic variety. We believe this is an example where the intensification of distortion by LSD paralleled a decline in ego strength as judged clinically and indicated by the course of the illness.

Because of the reduced availability of LSD and of other psychotogens, we are presently testing the utility of amphetamine [16] as a challenging agent. It would also be more acceptable for testing children. Figure 8 (right-hand side) shows that amphetamine reduces cerebral postsynaptic responses, here shown as a graph of the heights of the evoked potentials. This is an action qualitatively like that of LSD. Our animal-behavior data also resemble those obtained with LSD, and clinically amphetamine is known to be capable of producing psychosis. We are, therefore, trying amphetamine as a substitute in our perceptual testing.

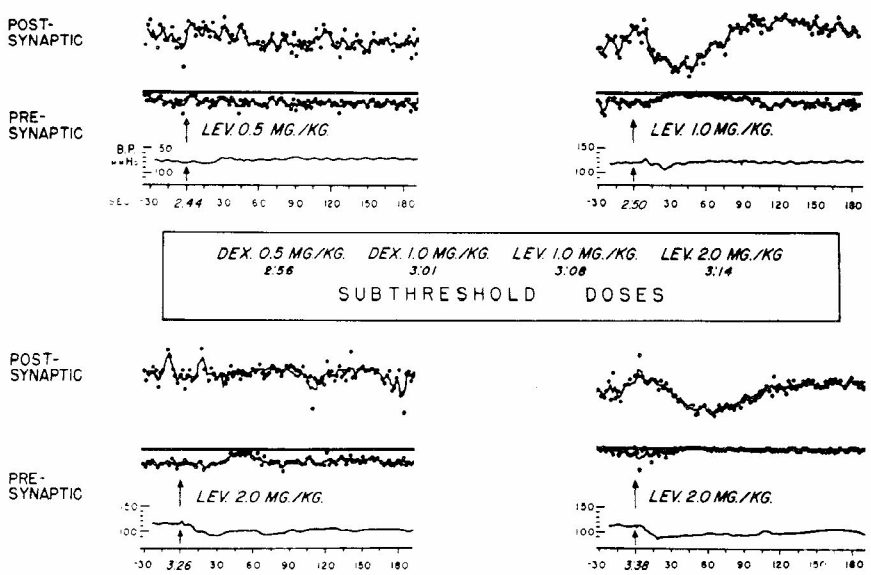

Fig. 8. Cerebral synaptic inhibition by L- and D-amphetamine. Neurone intercortical (transcallosal) system. Height of spike potentials evoked in optic cortex of the cat by electrical stimulation of contralateral cortex every 2 sec; injections into ipsilateral carotid artery.

In summary, we find, in support of the postulated nature of hallucination as an inadequate integration of new with stored information resulting in aberrant perception, that subclinical doses of LSD bring out a latent or accentuate an existing difficulty in resolving the perceptual conflict experimentally induced in psychotics as opposed to neurotics and normals, but add little if this conflict is so great that active hallucination already exists at the time of LSD administration. It is felt that this kind of drug evaluation of cerebral integration can help identify and measure abnormality characteristic of forms of mental disturbance in which a dissociative process is a fundamental feature. Contingent on further substantiation, the proposed LSD index holds promise of supplying the "clinical yardstick" to help in diagnosis and in following the course of mental illness and the efficacy of therapy.

The interpretation and utility of the proposed clinical yardstick in determining and monitoring an individual's cerebral integrative status will be examined in connection with the effort to make assessment of ego strength more than an empirical exercise. Some of our normal subjects have found it possible to cause a fully developed distortion to recede, i.e., to reverse the dominance resolving the perceptual conflict. We are exploring the possibility that the selection of cues to which to attend so as to revert to the dominance of past experience is a willed exhibition of ego strength that could be a further aid in its evaluation.

A further extention of the proposed testing might enable us to screen a population to identify individuals, who, though not sick, have used up much of their adaptive powers or "psychic reserve" and therefore would be unduly vulnerable to further stress and might be proper subjects for preventive psychiatry [17].

In conclusion, we wish to emphasize that the approach presented attempts to measure, in an objective fashion and by instrumental means, a process underlying cerebral dysfunction and critical to some forms of mental disturbance.

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