Apparent Eye Level Test

Its Background and Use in Psychopharmacology

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THE INTRODUCTION of drugs as part of the therapeutic armamentarium in psychiatry has fostered, in recent years, ever burgeoning research activity concerned with elucidating the central mechanism of action of psychoactive drugs. A significant part of this activity involves attempts to correlate the behavioral action of psychoactive drugs with biochemical changes in man. Since no practical way exists for directly assessing the action of such drugs on brain chemistry in man, biochemical changes, by necessity, have been followed peripherally in the blood and urine. The lack of direct methods has led researchers to rely heavily on animal data to form the basis for postulating the mechanisms of action of psychoactive drugs in man. When one studies these data, however, it becomes apparent that psychoactive drugs have different chemical, pharmacologic, and behavioral effects in different species or classes of animals (see for example, Resnick [1]). Thus, although the animal data have been the source of many fruitful hypotheses, they have left largely unanswered the question of mechanisms of action in man.

Some six years ago we began to approach this problem by bringing to bear the relevant aspects of theory and methods which each of the disciplines we represented (psychology, biology, and psychiatry, respectively) could contribute. Our research strategy evolved from the considerations discussed above: the lack of translatability of animal results to man has led us to the direct study of man himself; further, the lack of direct means for chemical analysis of the human brain in an intact organism has led us to the use of a variety of indirect methods. These are of two types: on the one hand, three general classes of agents (enzyme inhibitors, precursors of biogenic amines, and amine releasers) are employed singly and in various combinations as a means of altering man's brain chemistry; and on the other hand, a broad spectrum of assessment criteria are utilized to measure the effects of these inferred alterations. Included in these latter criteria are peripheral biochemical determinations, autonomic assessments, neurological and clinical psychiatric assessments, as well as objective and subjective psychological measurements.

The present paper is concerned with one of the psychological assessment techniques —the Apparent Eye Level Test—which has proved particularly valuable in our work. It has provided a behavioral measure which has effectively distinguished between effects of different classes of drugs (eg, tranquilizers as compared to antidepressants); it has been sensitive in differentiating the effect of a given drug given singly in contrast to the same drug given in combination with other agents; and it has differentiated the effects of given drugs administered to different groups (eg, prisoners as compared to nonprisoners, schizophrenics as com-

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pared to normals). The test features objectivity and reliability, simplicity and rapidity of administration and scoring, as well as a minimum financial investment. The effectiveness of the instrument has attracted the interest of investigators representing may disciplines pursuing psychopharmacological research; accordingly, it appeared useful to bring together in summary fashion, a description of the origins of the test in psychological theory, and the considerable body of findings from psychopharmacological research (both published and unpublished) which has accumulated over the past half dozen years.

Test Description

Briefly described, the test consists in locating, while seated in a darkened room, that position in physical space experienced as being at eye level. More specifically Ss, seated in a dark room, are presented with a luminous square which appears suspended in space; the square measures 8 × 8 inches, and is horizontally bisected by a black line ⅝ inches wide. S is instructed to fixate this line and instruct E how to move the entire stimulus figure so that the black line appears to be at eye level. S is seated approximately 10 to 12 feet from the stimulus figure, with his head fixed by means of an adjustable headrest to eliminate head movement.

The stimulus figure is mounted on a rack and gear device so that it may be moved slowly up and down a plumb line directly in front of S. Objective eye level is ascertained separately for each S by measuring the height of S's pupils above the floor.

Early studies utilized two trials with a starting position such that the black line of the stimulus figure was at objective eye level. More recent studies utilize six trials (two trials at each of three starting positions, viz, at objective eye level, 30 cm above and 30 cm below objective eye level) arranged in a double-fatigue order.

The measure most commonly utilized is the mean of the six trials in relation to objective eye level, although measures reflecting the influence of starting position (high starting trials minus low starting trials) have been utilized, as have variability scores reflecting differences among trials.

Testing time per subject requires approximately five minutes.

Background of Test

The Apparent Eye Level Test, as specifically described in this paper, grew out of attempts at Clark University over the past 15 years to evolve an organismic-developmental theory of cognition including perception (see for example, Werner and Wapner[2-5]). A considerable portion of these efforts were devoted to the study of the development of space perception. The review here will be restricted to one aspect of space localization, namely, the up-down dimension of space as measured by the Apparent Eye Level Test. Three avenues of research are of particular relevance to the psychopharmacological research applications described later: (1) The study of changes in space perception during the course of normal development including aging. (2) The study of space perception as manifested in psychopathology as compared to normality. (3) The study of the effects of changes introduced into other organismic processes on space perception.

With respect to the ontogenesis of space perception, Wapner and Werner,[4] found that the young child (6 years of age) locates apparent eye level at a position physically above objective eye level. With increase in age there is a systematic shift in the position of the apparent eye level downward so that by age 20 the young adult locates apparent eye level at a position physically below objective eye level and approximately as much in error as the child of 6 years of age. This position is characteristic of adults from 20 to 50 years of age, following which there is a shift to a position above objective eye level from 65 to 90 years of age. (Krus, unpublished data, which indicates that mean apparent eye level is located 3 cm above objective eye level in a group of 84 community active aged 65-89 years of age.) The total life course with respect to apparent eye level, then, is characterized by a positioning of the apparent eye level above objective eye level in children, a systematic shift downward with an increase in age to a maximum low point from 20 to 50 years of age and then a rise to a position above objective eye level, analogous to that of the child, during the course of aging.

These data were utilized as an empirical standard against which the study of psychopathology was undertaken. Assuming a regression hypothesis, it was expected that schizophrenics (viewed as developmentally regressed), would locate apparent eye level at a position above objective eye level analogous to children (viewed as developmentally immature) and older normals (viewed as developmentally regressed). Numerous studies have supported this expectation as well as contributed to even further differentiation among groups of schizophrenics. For example, it has been found that although chronic schizophrenics as a group indicate regressed perceptual behavior, ie, higher location of apparent eye level, in comparison to normal adults of the same age, they may be further differentiated into subgroups which in themselves represent a developmental ordering. Carini,[6] for example, found that paranoids do not exhibit as much regression as do a combined group of catatonics and hebephrenics insofar as a catatonic-hebephrenic group locates eye level significantly higher than does a paranoid group. It might be noted that the interpretation of this finding is in consonance with psychodynamic theories of psychopathology, which view paranoids

as less regressed than catatonics and hebephrenics with respect to ego structures mediating reality contact.

In summary, the first two avenues of research, viz, space perception in normal development and in psychopathology, provide evidence consistent with the view that developmental immaturity (young child, aged, and psychotic) is behaviorally manifested by a higher location of apparent eye level in comparison to developmental maturity (normal adult). It should be noted that the definition of developmental maturity (immaturity) within the theory utilized, is in formal structural terms, ie, in terms of the theoretical notions of differentiation and hierarchic integration, so that formal similarity of behavioral performances in no way implies identity of process. It should be further noted that the precise nature of the factors or processes designated as "maturity" are as yet unspecified, but are almost certainly different in children as compared to aged as compared to psychotics despite similarity or even identity of behavioral performance.

The third avenue of research which provided both theoretical and empirical background of relevance for psychopharmacological research concerns studies which attempted to demonstrate that other ongoing processes in the organism (eg, attitudes, motivational and affective states, etc) would influence space localization. One study had as a guiding rationale the general notion that certain changes in affect could be viewed theoretically as changing vectorially the general status of the organism. If perception is viewed as a process reflecting both the nature of the stimulus and the ongoing state of the organism (Werner and Wapner[5]), then one might expect these vectorial changes to be reflected in relevant perceptual changes. The underlying assumption here is that the way in which the external world is cognized reflects the subjective state of the organism (Werner and Wapner[7]). A more concrete example of this notion derives from a consideration of everyday language usage in which mood states such as elation, euphoria, etc, are characteristically described in spatial terms such as "I feel high"; mood states such as depression are characteristically described in spatial terms such as "I feel low." Thus, in general, "positive" mood states imply upward vectorial components while "negative" mood states imply downward vectorial components.

Studies were undertaken in the Clark laboratories to determine whether changes in mood states were related to actual changes in spatial organization as implied in these everyday usages of spatial referents to characterize affect. In one pertinent study, Wapner et al,[8] demonstrated that laboratory induced experiences of success and failure were systematically related to upward and downward shifts, respectively, in the position of apparent eye level, ie, the experience of success was accompanied by upward shifts in the position of apparent eye level, while experiences of failure were related to downward shifts of apparent eye level. Rosenblatt[9] carried these studies a step further. On the assumption that the affective psychoses defined individuals characterized by relatively enduring, intense affect states, he studied the organization of perceptual space in manic-depressives and found that an elated group located apparent eye level at a significantly higher position than did a depressed group, with a normal control group falling between these two extremes. Thus, these studies indicated that variations in affective state, whether transiently induced in the laboratory or representing rather permanent characteristics of individuals, are behaviorally manifested by changes in perceptual space.

In sum, then, three avenues of research indicated that the organization of perceptual space, as measured in the Apparent Eye Level Test, undergoes systematic changes during normal development including aging, in psychopathology, and under variations in affective states. These findings are interpreted as indicating that spatial organization is affected by at least two general classes of factors: maturity (developmental) factors and affective factors. The importance of these data and their interpretations for research in psychopharmacology is discussed in the following section.

Applications to Psychopharmacological Research

Research directed toward the study of drug-induced changes in cognitive behavior has been proceeding in the Clark laboratories since 1955. Initially, as now, the researches relied on the rationale that certain classes of drugs could be conceived as primarily a pharmacologic means of inducing developmental (maturity) changes, while others could be conceived as primarily a pharmacologic means of inducing changes in affect. To exemplify, the psychotomimetics may be viewed as a pharmacological means of inducing developmental regres-

TABLE 1.—*Effect of LSD-25 at Different Dosage Levels on Position of Apparent Eye Level in Normal and Schizophrenic Adults*

	Means, Cm		
Normals (N=12)		Schizophrenics (N=9)	
Placebo	−9.4	Placebo	+9.8
40μg LSD	−0.6	75μg LSD	+12.0
75μg LSD	+6.6	150μg LSD	+16.9
F (conditions) significant at	<0.01	F (conditions) significant	<0.05

* A plus score indicates position above, a minus score indicates position below objective eye level. Measurements taken approximately two hours following oral ingestion of drug (placebo).

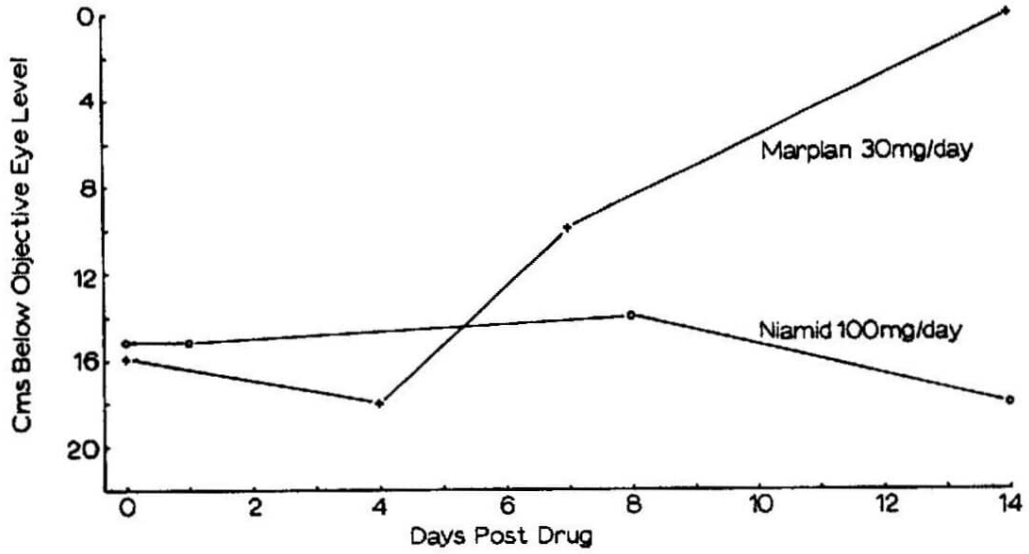

Fig 1.—Isocarboxazid (Marplan) and nialamide (Niamid) effects on apparent eye level. Normal noninstitutionalized volunteers.

sion, while the tranquilizers and antidepressants may be conceived as a means of inducing changes in affect. These notions are utilized as working hypotheses and are not meant to imply a "real" dichotomy since it is obvious that a psychotomimetic such as LSD-25 can dramatically alter mood states, while a tranquilizer employed therapeutically in a schizophrenic group is more readily conceived as directed toward inducing developmental progression. Since these issues are not the central concern of this paper, the working hypothesis guiding the studies presented below will be briefly stated while the focus will be on the results obtained using a variety of drugs. Similarly, specific research designs will not be described. Each study involved appropriate counterbalancing of conditions as well as single or double-blind controls, etc. For convenience, studies will be grouped according to whether a single agent or a combination of agents was involved.

TABLE 2.—*Effects of Four Months Chlorpromazine Treatment on Position of Apparent Eye Level in Chronic Schizophrenics*

	Means, Cm *	
	Placebo Group (N=9)	Chlorpromazine Group (N=9)
Premedication	−1.3	+3.2
Medication termination	+0.9	−2.4

* A plus score indicates position above, a minus score indicates position below objective eye level.

Single Agent Studies

The following presentation of results will utilize general drug classes. Included will be psychotomimetics (LSD-25); antidepressants (isocarboxazid [Marplan] and nialamide [Niamid]); tranquilizers (reserpine, tetrabenazine, chlorpromazine, meprobamate); and a general category describing preliminary evidence concerning a barbiturate, an amphetamine, and several steroids.

1. *Psychotomimetics.*—The only drug of this class we have studied extensively in normal and schizophrenic (chronic) samples is Lysergic acid diethylamide (LSD-25). Utilizing the notion that LSD-25 induced developmental regression, Wapner and Krus,[10] showed that, in keeping with expectation, the mean position of apparent eye level in 24 normal adults (12 men and 12 women) was located significantly higher (4.5 cm above objective eye level) two hours following oral ingestion of 75μg LSD-25 as compared to the mean position assessed by measurements taken two hours following placebo ingestion (5.7 cm below objective eye level). These results, indicating upward shifts under LSD-25, have been replicated many times, and are analogous to results obtained in studies of chronic schizophrenic samples. Further, increasing dosage level of LSD-25 was found by Krus to be linearly related to rise in position of apparent eye level, insofar as a higher dosage level was accompanied by a higher location of apparent eye level. These previously unpublished results are summarized in Table 1.

A note of caution should be introduced here. Current studies of time-dose relationships in normals

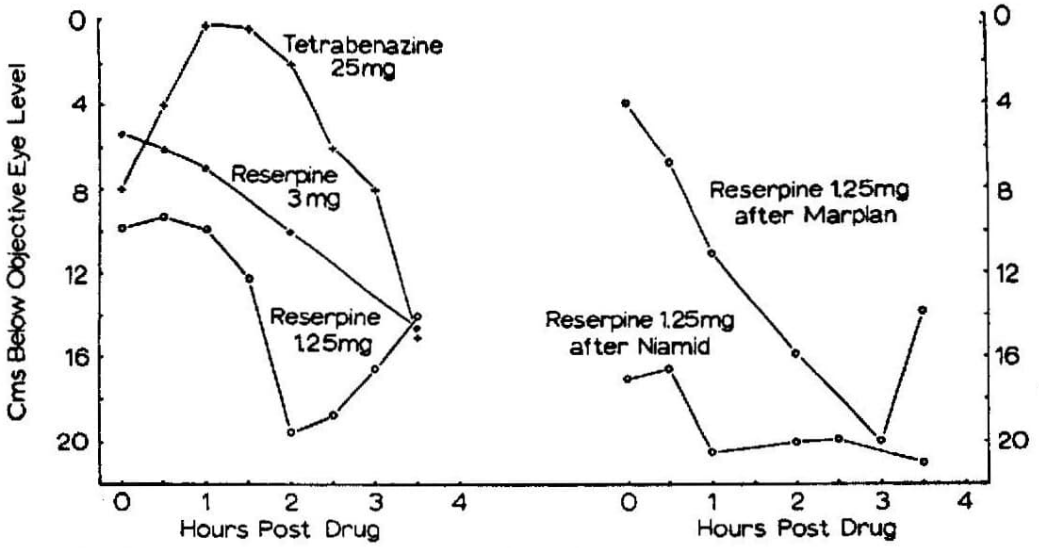

Fig 2.—Reserpine action on apparent eye level with and without isocarboxazid (Marplan) and nialamide (Niamid) pretreatment. Normal noninstitutionalized volunteers.

and schizophrenics indicate there may be more complex interactions which are not apparent in the data presented here. These more recent data, under preparation for separate publication, indicate dose-dependent as well as dose-group dependent "biphasic" actions on position of apparent eye level when time-course data are examined.

2. *Antidepressants.*—The general rationale guiding study of this class of agents was, as mentioned, that these drugs could be viewed as a means of inducing changes in affect in the direction of elation. An initial test of this hypothesis in chronic male schizophrenics (Krus et al [11]) indicated that iproniazid (Marsilid) shifted apparent eye level upward, but not significantly, as compared to placebo. Since measures were taken two to three hours following a single oral administration of 100 mg iproniazid, and since anywhere from seven to ten days of chronic administration is usually necessary for either biochemical or clinical changes to be manifest, it

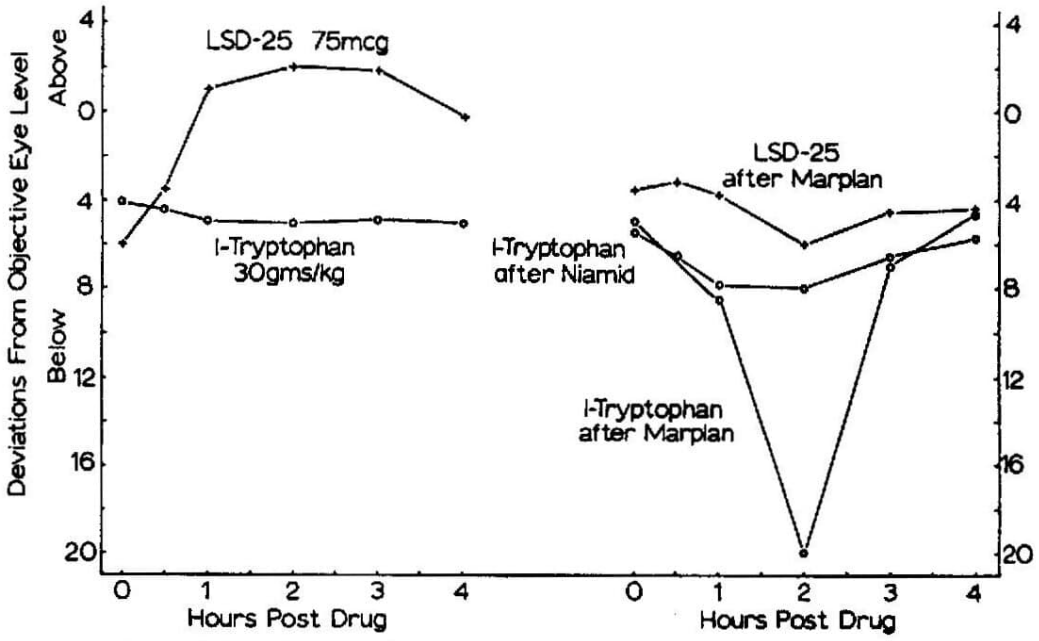

Fig 3.—LSD-25 and L-tryptophan action on apparent eye level with and without isocarboxazid (Marplan) and nialamide (Niamid) pretreatment. Normal noninstitutionalized volunteers.

was conjectured that chronic administration was required for changes on apparent eye level to be exhibited. The results presented below for isocarboxazid indicate this conjecture was probably accurate.

A. Isocarboxazid (Marplan): The results of several studies will be summarized here. Some have been published (Resnick et al[1,12-16]); others which replicate the published findings under identical procedures have not. In general, these studies indicate that chronic administration of isocarboxazid (30 mg a day) in normal noninstitutionalized volunteers is accompanied by a rise in apparent eye level beginning seven to ten days following the beginning of drug administration with a rise to maximum values by two weeks. These data are summarized in Fig 1 along with results obtained using the other antidepressant mentioned below. It is interesting to note that these behavioral changes follow much the same time course as reported in the literature for monoamine oxidase inhibition as inferred from peripheral biochemical assessments; it has also been found in the case of one normal volunteer, that, parallel to MAO levels, apparent eye level returns to base values approximately two weeks following termination of isocarboxazid administration.

Another set of studies, similar to the preceding but employing institutionalized but psychiatrically normal volunteers (jail prisoners), indicates that apparent eye level effects under isocarboxazid are opposite in this group, ie, chronic isocarboxazid administration (30 mg/day for 14 days) results in a systematic lowering of apparent eye level. This finding, since replicated in another study, is being investigated further in our current work.

B. Nialamide (Niamid): Results obtained using nialamide (Resnick et al[15] and unpublished data) do not parallel those obtained using isocarboxazid insofar as no change in apparent eye level is manifested at the dosage levels studied (100 and 200 mg a day). This lack of effect cannot be attributed to subject sample differences since many of the data presented in Fig 1 for isocarboxazid and nialamide involve the same normal noninstitutionalized volunteers.

3. *Tranquilizers.*—As implied earlier, two working hypotheses guided investigations in which tranquilizing agents were employed. One of these is based on the conception that these drugs are a pharmacologic means of inducing an affect change in the direction of depression; this conception is utilized in studies of subjects (usually normal volunteers) given a single administration of a given drug. The other working hypothesis stems from the view that these agents are a therapeutic technique designed to influence change in behavior (in psychopathological groups) toward a valued end, namely, improvement. These changes can in turn be conceived as constituting developmental progression. Though different, each conception leads to the same expectation that apparent eye level should change in a downward direction under the influence of these drugs, consonant with the downward changes found under conditions of laboratory-induced failure experiences (Wapner et al[8]), and the downward changes found during the course of ontogenesis by Wapner and Werner,[4] respectively.

A. Reserpine (Serpasil): Krus et al[11] found that a single administration of 2 mg reserpine to chronic male schizophrenics significantly lowered apparent eye level when measurements were taken approximately two hours following oral drug (placebo) ingestion. Resnick et al[12] extended these findings by delineating the time course of action of reserpine in normal volunteers. These data, together with additional data gathered more recently (all summarized in Fig 2), indicate an initial rise in apparent eye level one half hour following intramuscular administration of 1.25 mg reserpine followed by a drop to a maximum low point at two hours with a return toward baseline values (predrug administration) by 3½ hours postdrug administration. This "biphasic" aspect of response (initial rise followed by drop) disappears if dosage is increased to 3 mg reserpine (I.M.) insofar as this procedure results in a drop in position of apparent eye level within the first one half to one hour following administration, with no evidence of the initial rise apparent at the lower dosage level.

B. Tetrabenazine: Preliminary studies utilizing central- and peripheral-acting anologs or reserpine were undertaken by Resnick et al. Normal noninstitutionalized volunteers were administered 25 mg tetrabenazine intramuscularly following which apparent eye level measures were taken each one half hour for a period of 3½ hours. The results, previously unpublished, are summarized in Fig 2, and indicate apparent eye level changes similar to those obtained with 1.25 mg reserpine insofar as there is an initial rise followed by a drop. It should be pointed out that the comparative effects of drugs on apparent eye level described in Fig 1, 2, and 3 will be discussed primarily in terms of *pattern* of effect rather than in terms of points of maximum effect, duration of effect, etc. This is because the curves are based, in many cases, on different samples (N's ranging from 6 to 15 Ss) varying in many ways. In our experience, it has been *pattern* of response which is most stable (and hence generalizable) across individuals differing in terms of initial (placebo) apparent eye level positions, etc. That the contribution of subject differences to differential drug action on apparent eye level constitutes an important problem is, of course, readily acknowledged.

C. Chlorpromazine: The effects of chlorpromazine on apparent eye level were evaluated as part of a clinical trial of this drug conducted with chronic schizophrenics at Worcester State Hospital by Freeman et al (unpublished study). Measures were taken prior to commencement of drug (placebo) administration and on the termination date of medication four months later. Dosage level of chlorpromazine was increased to individual tolerance levels as determined by the attending physician, with the

average daily dosage per individual reaching 1,400 mg per day by the end of the fourth month treatment period. With respect to apparent eye level changes, Krus found results as summarized in Table 2.

These results, when analyzed by analysis of variance techniques, do not reach statistical significance (F ratio, $0.10>P>0.05$), but are suggestive both in terms of the mean drop in position of apparent eye level in the chlorpromazine group, as well as in the finding that eight of the nine patients in this group evidenced such a downward shift in comparison to random shifts in the placebo group (five shifts upward and four downward). It is also interesting to note that there was correlative psychiatric improvement noted in the chlorpromazine group although the degree of this relationship was not statistically evaluated.

D. Meprobamate: A study of the effects of a single oral administration of 400 mg meprobamate in nine geriatric cases (65 years and older) at Medfield State Hospital was conducted by Krus (unpublished data) who found a significant downward shift in apparent eye level (mean position under placebo is 13.3 cm above objective eye level as compared with a mean position under meprobamate of 3.7 cm above eye level, mean difference: $P<0.05$). A replication of this study with another nine geriatric cases yielded analogous results which did not, however, reach the required level of statistical significance. (Placebo mean value of 3.1 cm above objective eye level, meprobamate mean value of 0.2 cm below, mean difference: $P>0.05$.)

4. *Other Agents.*—The major portion of our research (both individually and collectively as a collaborative team) has involved the use of antidepressants isocarboxyazid and nialamide, the tranquilizer reserpine, and the psychotomimetic LSD-25. However, some limited evidence is available concerning a barbiturate, an amphetamine, and several steroids. In these studies Krus et al,[16] and (unpublished data) found that a single oral administration of phenobarbitol, dextroamphetamine (Dexedrine), progesterone, and several synthetic analogs of progesterone did not appreciably effect changes in position of apparent eye level.

Drug Combination Studies

The studies to be summarized in this section derive primarily from biochemical considerations. They employ the research strategy outlined at the outset of this paper, viz, various combinations of enzyme inhibitors, amine precursors, and amine releasers are used as an indirect means of altering man's brain chemistry, and the consequences of this alteration are assessed by the Apparent Eye Level Test and the other criteria mentioned at the outset of this paper. Other than to state that these studies are primarily concerned with the central role of the indoleamines (particularly serotonin) and catecholamines, specific rationales will not be presented for each study. Readers interested in more specific biochemical rationales are referred to Resnick et al.[1,12-18] It should also be noted that research designs are not delineated here. Just as in the previous studies, appropriate counterbalancing or randomizing of experimental conditions was employed as were single or double-blind controls, etc.

1. *Reserpine Action Following Pretreatment With Isocarboxazid and Nialamide.*—General results of this study have been published by Resnick et al[1,13]; quantitative data obtained concerning apparent eye level changes in normal volunteers have not, and are summarized in Fig 2. Comparing these data with those presented for reserpine effects without pretreatment with an MAO inhibitor (Fig 2 also), leads to several conclusions.

A. Biphasic changes in apparent eye level (initial rise, then drop) following 1.25 mg reserpine administered intramuscularly, are also found when reserpine administration is preceded by two weeks pretreatment with nialamide (100 mg per day).

B. Biphasic changes are *not* found where reserpine administration is preceded by two weeks pretreatment with isocarboxazid (30 mg per day). Instead, 1.25 mg reserpine now acts similar to higher dosages insofar as a rapid drop in apparent eye level takes place within the first hour following reserpine administration and continues for approximately three hours. Thus, pretreatment with isocarboxazid alters the effect on apparent eye level of reserpine, but nialamide does not.

2. L-*Tryptophan Action Following Pretreatment With Isocarboxazid and Nialamide.*—Again, general results of this study concerning tryptophan "intoxication," manifested following pretreatment with MAO inhibitors, are briefly described in Resnick et al;[13] the specific quantitative data concerning changes in apparent eye level presented in Fig 3 have not been previously published. Consideration of these data indicate the following.

A. Oral administration of L-tryptophan (50 mg/kg) in normal volunteers results in slight downward changes in apparent eye level.

B. Oral administration of L-tryptophan following pretreatment with isocarboxazid (30 mg/day for several weeks) indicates a rapid drop in position of apparent eye level to a maximum low point at approximately two hours following ingestion, with a return to initial values by four hours.

C. Similar but not so dramatic changes are evidenced when pretreatment consists of 100 mg/day of nialamide for a period of 14 days. Preliminary data on pretreatment with nialamide at 200 mg/day for two weeks indicate similar effects. It might be noted that a rise in apparent eye level during the course of pretreatment with isocarboxazid and the absence of such a rise under nialamide pretreatment was evidenced in this study analogous to the results obtained with these agents described earlier (Fig 1).

3. *LSD-25 Action Following Pretreatment With Isocarboxazid.*—General results obtained in this

study in which it was found that LSD-25 action was antagonized or reversed by pretreatment with isocarboxazid are summarized in Resnick et al;[13,14] quantitative data presented in Fig 3 have not been previously published. These data dramatically indicate the reversal of LSD-25 action inasmuch as the rise in apparent eye level which ordinarily occurs under LSD-25 is reversed to become a drop when LSD-25 administration (75μg orally) is preceded by pretreatment with isocarboxazid (30 mg/day for two weeks).

4. *LSD-25 Action Following Pretreatment With Progesterone.*—Krus et al,[16] found in normal male volunteers that LSD-25 action on a variety of cognitive processes was antagonized by oral administration of 600 mg progesterone one hour prior to 75μg LSD-25. The results with respect to apparent eye level indicated that the degree of starting position effect (influence of initial position of stimulus on adjustment to physical point in space experienced as being at eye level), which ordinarily occurs under LSD-25 was reduced in magnitude by progesterone pretreatment. It might be noted that starting position effects are greater in children as compared to adults (Wapner and Werner[4]) and hence these results are consistent with the working hypotheses mentioned earlier, ie, progesterone may be viewed as an agent which inhibits the developmental regression induced by LSD-25.

Similar studies conducted by Krus et al (in preparation for publication) indicate certain synthetic progesterone-like steroids also operate in similar fashion with one operating to decrease the magnitude of rise upward of apparent eye level ordinarily found under LSD-25. Since the chemical breakdown of these compounds is not available at present, more detailed information cannot be offered here.

General Conclusions

Certain conclusions seem warranted from the data presented. The first concerns the use of the Apparent Eye Level Test as a means for differentiating the effects of a variety of psychotropic agents. It has been shown that LSD-25, isocarboxazid, and perhaps iproniazid raise apparent eye level, while reserpine, tetrabenazine, chlorpromazine and meprobamate lower apparent eye level. Nialamide, phenobarbitol, dextroamphetamine, and certain steroids have no demonstrated effects in and of themselves in the studies reported. From these data, we may entertain tentatively, at least, the notion that the test can be employed as a means of behaviorally differentiating the action of general classes of drugs, particularly as evidenced in the opposite actions of antidepressants (excepting nialamide—an exception Resnick et al,[1] speculate may be related to differences between Nialamide and isocarboxazid with respect to biochemical activity) and tranquilizers. Psychotomimetics, insofar as LSD-25 is representative, are behaviorally manifested like the antidepressants, although even here differentiations are probably possible if magnitude and pattern of response over time are considered. Within the general class of tranquilizers, there is as yet no evidence concerning means for further differentiations between, say, the rauwolfia alkaloids and phenothiazines. Perhaps systematic time-dose response studies with the more commonly employed phenothiazines could provide additional wherewithal toward this end. Similar studies with barbiturates and amphetamines would also be of value.

A second conclusion also seems warranted. This concerns the test's utility in differentiating the action of a given drug administered singly, as compared with the administration of that same drug in combination with other agents. Relevant here, for example, are the differential actions of reserpine, LSD-25, and tryptophan given singly as compared to their administration following pretreatment with isocarboxazid.

Two additional conclusions are warranted which must also be viewed in part as qualifications to the previous generalizations. One of these concerns the utility of the test in differentiating different dosage levels of the same drug; this utility is demonstrated, eg, in the biphasic action of reserpine at 1.25 mg versus the monotonic action at 3 mg, as well as in the biphasic action of LSD-25 at different dosages alluded to. To exploit this possibility of the test requires that the time course of effects of a drug be studied. The other conclusion concerns the use of the test to differentiate effects of a given agent in different subject samples; this is best exemplified in the differences in response to isocarboxazid of institutionalized (prisoners) and noninstitutionalized psychiatrically normal volunteers.

Finally, two additional observations are offered. First, it should be noted that indi-

vidual differences in response are found using this behavioral measure (apparent eye level) just as with virtually all other behavioral measures. For example, even though normal volunteers, on the average, respond to LSD-25 with a rise in position of apparent eye level; and even though this result has been replicated some seven different times in approximately 150 Ss; it is nonetheless true that some individuals evidence a lowering of apparent eye level under LSD-25, or an absence of any effect on this behavioral parameter at all. For this reason, our own research efforts are characterized by what might be called a clinical-experimental approach. This means that although our studies are conducted within the logic of experimental method, we attempt to make each S his own control for a variety of studies. Put in another way, we would rather study one individual in 100 experiments in preference to 100 individuals in one experiment.

The second observation is also a caution. It is trite to state that the behavior of man or any other animal, is enormously complex and defies encapsulation in any simple way. It is emphasized, however, that the Apparent Eye Level Test is not offered as a panacea for this problem and should not be so viewed. It is but one aspect of psychological behavior; its chief virtue is its sensitivity in reflecting changes attributable to a number of important variables of relevance to psychopharmacological research. Put in proper perspective, it is but one of a number of assessment criteria, psychological and otherwise, employed in our own work.

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Generic and Trade Names of Drugs

Isocarboxazid—*Marplan.*
Nialamide—*Niamid.*
Reserpine—*Rauloydin, Raurine, Rau-Sed, Reserpoid, Sandril, Serfin, Serpasil, Serpate, Vio-Serpine.*

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