mean L/M ratio at 2 hours was 0.77. These results clearly show that LRF facilitates the occurrence of lordosis in estrogen-primed females.

To determine if the response to LRF was specific, another releasing factor, TRF, was tested. This one seemed particularly appropriate since it is localized to the bed nucleus of the stria terminalis (*13*), a region near the LRF-containing and sex behavior centers. There was lordosis in only 1 of 16 tests with TRF, and in this instance the L/M ratio was low at 3/18.

The present results demonstrate that LRF exerts a facilitatory effect on the induction of mating behavior similar to progesterone. After an injection of LRF, ovariectomized female rats, pretreated with estrogen, displayed a lordosis pattern that differed little from that produced by progesterone, while only a few females exhibited the lordosis pattern in response to estrogen alone or estrogen in combination with LH, FSH, or TRF.

Although the estrogen-primed, LRF-treated animals showed mating behavior, it would be incorrect to characterize the behavior displayed as typical of "estrous behavior" as seen in the intact female rat. Female rats at a high level of sexual receptivity display a characteristic behavior including adoption of a stiff-legged, hopping gait, darting, and rapid vibratory movements of the ears (ear wiggling). In the present experiment, the majority of animals displayed hopping and darting behavior, but no ear wiggling was observed, so it is difficult to make any statement on the normality of the behavior patterns.

The dose level of LRF used in the present study was selected on the basis of other experiments by Zeballos (unpublished data) which indicated that this dose produced a large increase in LH release. A dose fivefold smaller produced only a very small effect on LH, so the dose used here is probably within the physiological range. If LRF is indeed released locally into the preoptic area when the LRF-secreting neurons are active, then very high concentrations might reach the cells concerned with the mating response. Thus, it is tempting to postulate that LRF released on the afternoon of proestrus may be involved after a delay in initiating mating behavior in female rats. It is still too early to say whether or not it is required for mating behavior. Lesions which eliminate LRF from this part of the nervous system would be required in order to test the possible requirement for the factor in inducing mating behavior.

The results are of extreme interest, since they indicate that another hormone in addition to estrogen and progesterone can induce mating behavior in the female rat. Particularly intriguing is the fact that this hormone is normally found in that area of the nervous system which is involved in mediating mating. It will be of extreme interest to determine if LRF can enhance mating behavior in males as well as females and to determine if these results obtained in a lower form have any application to humans. In this connection, one must be cautions, since ovarian steroids have little effect in inducing acute mating responses in the human subject. If indeed LRF can induce mating in humans, the implications would be far-reaching.

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18. This research was supported by PHS grant NS-10434. We are indebted to Dr. S. N. Preston of Parke, Davis and Company for their donation of Theelin and Lipolutin utilized in this experiment and to Dr. Romano Deghenghi, Ayerst, Ltd., Montreal, for the generous supply of LRF. LH (NIH, S-9) and FSH (NIH, P-1) were gifts of the Endocrinology Study Section, NIH. We also acknowledge the excellent technical assistance of Mrs. Betty Turicchi.

12 March 1973

Eye-Tracking Patterns in Schizophrenia

Abstract. *A significant number of schizophrenic patients show patterns of smooth pursuit eye-tracking patterns that differ strikingly from the generally smooth eye-tracking seen in normals and in nonschizophrenic patients. These deviations are probably referable not only to motivational or attentional factors, but also to oculomotor involvement that may have a critical relevance for perceptual dysfunction in schizophrenia.*

Eye-tracking difficulties in a simple test of smooth pursuit eye movements seem to be related to schizophrenic pathology. We report a study of 25 psychotic patients, 8 nonpsychotic patients, and 33 normal persons in the eye-tracking task.

The experimental task required the subject to watch an oscillating pendulum suspended at eye level 1 m from the seated subject. The pendulum excursions corresponded to 20° of visual angle. The period of oscillation was 2 seconds and thus the maximum eye velocity during nonerror tracking would be 31.4° per second. Silver–silver chloride skin electrodes were applied at the outer canthi of both eyes, and a ground electrode was applied to the middle of the forehead. Changes in field potential generated by the corneoretinal potential were recorded on a Beckman type R Dynograph as eye movements in the horizontal plane. Channel 1 of the Dynograph yielded readings of actual eye movements, and

channels 2 and 3 yielded the first derivative of actual eye movements as velocity in right and left directions. After the pendulum was tracked for ten cycles, the experimenter realerted each subject by reminding him firmly to watch the pendulum carefully. Eye-tracking was then monitored for five more oscillations of the pendulum.

Subject groups consisted of eight nonparanoid schizophrenics, ten paranoid schizophrenics, three schizoaffective patients, four patients with manic-depressive illness, eight nonpsychotic patients (all of whom carried the diagnosis of personality disorder), and 33 nonpatient normal controls (*1*). All patients were hospitalized, but none for more than 6 months.

The pendulum-following task has been used as a clinical test of oculomotor function, and in our study was one of several procedures employed for investigating the oculomotor and vestibular system in schizophrenic patients. Clinicians have distinguished a variety of eye-tracking patterns, some of which are associated with various kinds of vestibular and central nervous system pathology (*2*, *3*), such as brainstem lesions, hemispheric lesions, Parkinson's syndrome, and intoxications from certain drugs, such as barbiturates. The polygraph tracing from an unimpaired eye-tracking performance is close to that of a smooth sine wave (Fig. 1a). Occasional discontinuities in pursuit movements, generally reflecting periodic inattention, also occur in normal people. These tracings resemble that of Fig. 1b. The abnormal patterns reported (*2*, *3*) resemble those in Fig. 1, c and d. However, these data were, for the most part, collected from persons referred for examination because of suspicion of vestibular disturbances, and the prevalence of such presumed pathological tracking patterns in the general population, without discernible organic lesions or intoxications, has not been determined.

In the disturbances of smooth eye-tracking seen in our subjects, either a number of fast, horizontal saccadic-like movements in both directions are superimposed on the pursuit, or there may be other significant deviations from the sinusoidal pattern, or both may occur in the same record. Ideally, the eye movement should mirror the constantly changing velocity of the pendulum. One way to quantify deviant eye-tracking patterns is to count the number of times that the eye comes to a complete stop, that is, the pursuit velocity temporarily falls to zero (here called "velocity arrests"). A second score is a count of the number of times eye velocity exceeds by 33⅓ percent the maximum speed of the pendulum (here called "positive saccades"). The relation between the two quantitative scores and eye-tracking patterns that are "normal" (the wave forms in Fig. 1, a and b) and "deviant" (the wave forms in Fig. 1, c and d) was assessed by biserial correlations. The correlations between tracking pattern and velocity arrests before and after realerting were .76 and .61, respectively. The correlations between tracking pattern and positive saccades before and after realerting were .77 and .59, respectively. It appears from these statistically significant and respectably high correlations that deviant tracking patterns can, to some extent, be reflected quantitatively in velocity arrests and in positive saccades. To test the reliability of eye-tracking patterns we tested 16 normal subjects in two sessions separated by an interval of approximately 2 months. The eye-tracking pattern remained the same in all subjects. Repeat reliabilities before and after realerting were .52 and .79, respectively, for velocity arrests, and .59 and .22, respectively, for positive saccades. Within the limits of our sample, we interpret these reliability statistics as indicating that tracking patterns tend to remain unchanged in these subjects and that, in particular, the number of velocity arrests after alerting is a satisfactorily stable score. The reliability coefficient of .22 for the positive saccades after realerting, however, is not significantly greater than zero. The meaning of the instability of this score is discussed later in this report.

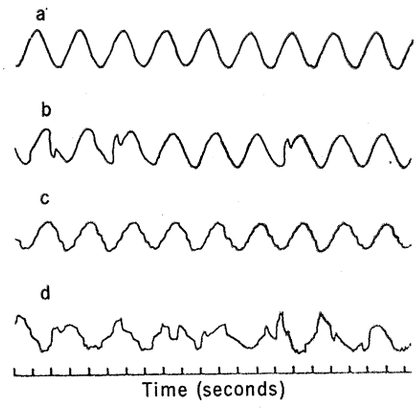

Fig. 1. Four eye-tracking patterns in response to a moving pendulum: (a) smooth pursuit; (b) smooth pursuit with occasional brief interruptions and resumption of accurate tracking; (c) deviant tracking pattern in which rapid saccadic movements are superimposed on the slow pursuit; and (d) deviant tracking with alterations in amplitude, frequency, and symmetry. [From Benitez (*3*)]

Without knowledge of the diagnosis of the patients, two independent judges classified the eye-tracking patterns for all subjects into two broad categories, "normal" and "deviant," using the patterns in Fig. 1 as guides. They agreed on 97 percent of the tracings and could easily reconcile the remaining differences (*4*). Using the eye velocity tracings of channels 2 and 3, they also computed (i) the number of velocity arrests and (ii) the instances of positive saccades for all subjects, both before and after realerting.

All eight nonparanoid schizophrenic patients, six of ten paranoid schizophrenics, and two of three schizoaffective patients showed an abnormal sinusoidal tracking pattern. In contrast, one of four manic-depressive patients, no nonpsychotic patients, and only four of 33 normal controls showed an abnormal tracking pattern. The differences among these subject groups with respect to the number of deviant patterns of eye-tracking were statistically significant, as determined by a chi-square test ($\chi^2 = 38.874$; $P < .01$). On further investigation two of four normal subjects with abnormal tracking manifested a right-beating spontaneous nystagmus, evidence of possible organic vestibular or oculomotor disturbance (*5*).

The numbers of velocity arrests in the subject groups were also compared. All of the schizophrenic groups produced more velocity arrests than did the nonschizophrenic patients and controls (Fig. 2a). The nonparanoid schizophrenics had an average of 72 velocity arrests before alerting, the paranoid schizophrenics had 65, and patients with schizoaffective disorders had 73. Manic-depressive and nonpsychotic patients displayed significantly fewer velocity arrests (56 and 48, respectively) than did the patients with schizophrenic pathology, but had somewhat more velocity arrests than did normal controls (40 arrests) prior to realerting. A repeated-measures analysis of variance showed that these differences between groups were highly significant ($F = 4.01$; $P = .0008$). The interaction between groups and the number of velocity arrests before and after realerting was not significant, a result indicating that in none of the groups were subjects able to reduce the number of velocity arrests in response to the realerting instructions. Thus, when subjects were realerted to the

task, there was not significant change in the distribution of velocity arrests among the groups.

In any task involving schizophrenic subjects, one must consider whether schizophrenic patients respond poorly because of inattention or motivational factors (*6*). The positive saccade score is relevant to that issue. The measure of positive saccades shows that prior to realerting, all psychotic patients, whether schizophrenic or manic-depressive, are statistically different from nonpsychotic patients and from normals, although the groups of psychotic patients do not differ from each other. However, after the realerting instruction, all groups improved to the point that differences among them disappeared (Fig. 2b). A repeated-measures analysis of variance showed a borderline-significant difference between groups ($F = 1.96$, $P = .07$); a significant interaction between groups and positive saccades ($F = 2.78$, $P < .01$) indicates that the groups did not differ from each other after alerting. As discussed earlier, the reliability of the positive saccade score after alerting was no greater than zero, and the score distribution shows that, when realerted, almost all subjects were able to eliminate the positive saccades. Thus, our two quantitative scores behaved differently in response to the realerting instruction: The number of velocity arrests continued to differentiate the groups, with the schizophrenic subjects showing the highest number of velocity arrests, but the positive saccade score tended to diminish significantly for all subjects. These data indicate that the number of velocity arrests is less subject to voluntary control; this score is an indication of the nonvoluntary, automatic nature of smooth pursuit movement. The positive saccade score, on the other hand, is a measure of effort, attention, or involvement in the task. All subjects, including the schizophrenics, reduced their positive saccades to a minimum, a result reflecting attention to and involvement in the task, but none could reduce their velocity arrests. Thus, we assert that the eye pattern differences between the schizophrenics and other subjects in our sample do not reflect differences in motivation or attention deployment, but are differences referable to difficulties in eye-tracking. While no differences in any measures were found between patients treated with phenothiazines and those who were not, the numbers are too small to permit definitive analysis (*7*).

The dysfunction noted here strongly implicates smooth pursuit eye movements in schizophrenic pathology. It suggests that schizophrenic dysfunction involves the fine regulation of neuromuscular activity which is required for smooth pursuit. Whether the dysfunction involves solely the musculature, the neuromuscular junction, or a disruption in the central nervous system pathways necessary for accurate tracking requires special experimental study. Nor can we, on the basis of these data, decide whether the dysfunction reflects specific impairment in the eye-tracking or more general neuromuscular involvement as suggested in the work of Meltzer (*8*), or in studies by Fish (*9*) and Bender and Freedman (*10*) of postural-motor disorders in infants vulnerable to schizophrenia. However, although superficial attention does not account for these results, a core attentional deficit may nevertheless be involved (*11*).

These smooth pursuit eye movements, reflecting as they do the coordination of eye velocity with object velocity, represent a critical factor in visual perception. Their impairment in schizophrenic patients may be associated with the impaired and idiosyncratic reality appraisal typical of these patients, inasmuch as visual perception, a central factor in reality contact, involves the organization of the entire perceptual system and requires effective motor response and feedback for its adaptive task.

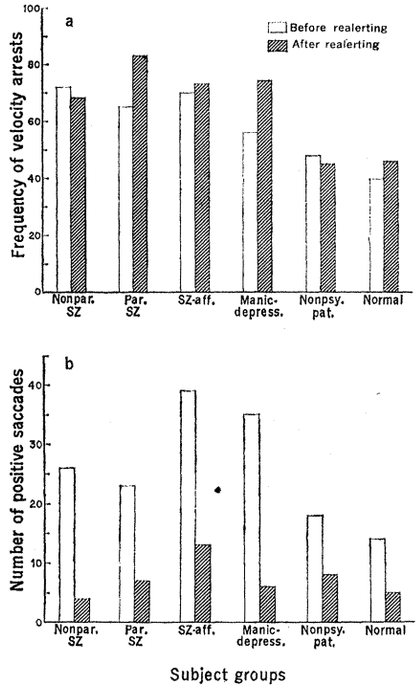

Fig. 2. Comparison of six subject groups tracking a pendulum for ten cycles before a realerting instruction and five cycles after realerting. The data for the realerting condition are prorated for ten cycles. The two measures are (a) frequency of velocity arrests and (b) number of positive saccades. The latter measure appears to reflect attention to the task. Abbreviations: *Nonpar. SZ*, nonparanoid schizophrenic; *Par. SZ*, paranoid schizophrenic; *SZ-aff.*, schizoaffective; *Manic-depress.*, manic-depressive; and *Nonpsy. pat.*, nonpsychotic patients (diagnosis of personality disorder).

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1. Diagnoses were official hospital diagnoses as agreed upon by two psychiatrists working independently of this project. Normal controls as a group were matched with the psychiatric patients for age (mean age, 26.3 years) and sex. The patients and controls were distributed among the five Hollingshead-Redlich social class categories, with the median for all patients falling in class 4 and that for controls in class 3. No relation was found between eye-tracking patterns and age, sex, or educational level.
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4. Definitive scoring criteria for classifying eye-tracking patterns will be presented (P. S. Holzman, L. R. Proctor, D. W. Hughes, in preparation).
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11. Subsequent testing showed that a statistically significant number of first-degree relatives (parents and siblings) of the schizophrenic patients also showed similar eye-tracking impairments, while relatives of nonschizophrenic patients did not (P. S. Holzman, L. R. Proctor, D. W. Hughes, in preparation). These results suggest that this eye-tracking anomaly may provide a genetic marker for schizophrenia.

12. Supported in part by a grant from the Benevolent Foundation of the Scottish Rite, Northern Masonic Jurisdiction, and by PHS grant MH-19477. We thank D. Levy and A. Welsh for help in data collection, the Illinois State Psychiatric Institute and the Institute for Psychosomatic and Psychiatric Research of Michael Reese Hospital, Chicago, for providing the patient population and many facilitating courtesies, and N. Yasillo for technical consultation.

13 November 1972; revised 19 March 1973