

- Iacono, W.G.; Tuason, V.B.; and Johnson, R.A. Dissociation of smooth-pursuit and saccadic eye tracking in remitted schizophrenics: An ocular reaction time task schizophrenics perform well. *Archives of General Psychiatry*, 38:991-996, 1981.
- Kuechenmeister, C.A.; Linton, P.H.; Mueller, T.V.; and White, H.B. Eye tracking in relation to age, sex, and illness. *Archives of General Psychiatry*, 34:578-579, 1977.
- Levin, S.; Lipton, R.B.; and Holzman, P.S. Pursuit eye movements in psychopathology: Effects of target characteristics. *Biological Psychiatry*, 16:255-267, 1981.
- Lindsey, D.T.; Holzman, P.S.; Haberman, S.; and Yassillo, N.J. Smooth-pursuit eye movements: A comparison of two measurement techniques for studying schizophrenia. *Journal of Abnormal Psychology*, 87:491-496, 1978.
- Lykken, D.T.; Iacono, W.G.; and Lykken, J.D. Measuring deviant eye tracking. *Schizophrenia Bulletin*, 7:204-205, 1981.
- Ong, J., and Harman, G.A. Eye movements simultaneously recorded by electro-oculographic and photoelectric methods. *Perceptual and Motor Skills*, 49:619-624, 1979.
- Oster, P.J., and Stern, J.A. Measurement of eye movement with electro-oculography. In: Martin, K., and Venables, P.H., eds. *Techniques in Psychophysiology*. New York: John Wiley & Sons, 1980. pp. 275-309.
- Shackel, B. Eye movement recording by electro-oculography. In: Venables, P.H., and Martin, I., eds. *A Manual of Psychophysiological Methods*. London: North-Holland, 1967. pp. 299-334.
- Smith, G.N., and Iacono, W.G. Evaluation of a sensitive and versatile method for measuring eye movements. *Psychophysiology*, 19:565, 1982.
- Tursky, B. Recording of human eye movements. In: Thompson, R.F., and Patterson, M.M., eds. *Bioelectric Recording Techniques*. New York: Academic Press, 1974. pp. 100-135.
- Young, L.R., and Sheena, D. Survey of eye movement recording methods. *Behavior Research Methods and Instrumentation*, 7:397-429, 1975.

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Is Eye Tracking Dysfunction Specific to Schizophrenia?

Abstract

Based on eye tracking studies in psychiatric patients, normal controls, and first-degree relatives of patients, Holzman, Proctor, and Levy et al. (1974) state that eye tracking dysfunction (ETD) is specific to schizophrenia and may be a genetic marker of that disorder. A review of numerous subsequent studies, however, suggests that ETD is not specific to schizophrenia, but is restricted to functional psychosis. Evidence that ETD is a genetic marker of functional psychosis is, as yet, inconclusive.

The specificity of eye tracking dysfunction (ETD) entails two interrelated issues: the prevalence/presence of ETD within and across diagnostic

categories and the stability of ETD over time in psychiatric patients in whom ETD has been identified. The specificity question was first raised by Holzman, Proctor, and Hughes (1973) and Holzman et al. (1974) who asserted, on the basis of smooth pursuit eye movement studies in psychiatric patients, normal controls, and first-degree relatives of schizophrenics, that ETD is specific to schizophrenia and may be a genetic marker of schizophrenic disorder.

Since the study of Holzman et al. (1974) appeared, a very substantial research literature bearing on the issue of diagnostic specificity has accumulated. Both Holzman and his collaborators and investigators in other laboratories (e.g., Iacono and Lykken 1979) have made important contribu-

tions to this literature, which will be critically reviewed here. Before this review is undertaken, however, certain methodological issues should be considered and certain concepts defined. There is considerable variation in diagnostic criteria and in method of diagnosis across pursuit eye movement studies in different laboratories. Such variation quite obviously has a critical bearing on the issue of specificity. Cross-study identification of similar or differing psychopathological groups is called into question when intrastudy criterion validity is in doubt. This problem is particularly troublesome in the diagnosis of schizoaffective illness because major diagnostic systems differ explicitly in the criteria used to define the condition. Although a critical comparative appraisal of criterion validity is beyond the scope of this review, the diagnostic criteria and/or method used in key studies will be noted.

There is also some variation in scoring systems employed in studies of pursuit eye movement in psychiatric patients. Holzman and collaborators, as well as some investigators in other laboratories, have used both qualitative ratings (deviant/normal) and quantitative scores (velocity arrests, log signal/noise ratio or root-mean-square error deviation). A number of other investigators, however, have applied quantitative scoring exclusively. In studies in which qualitative ratings have been made, it is possible to estimate ETD prevalence percentages within diagnostic categories. Wherever possible such percentages will be reported here and compared across diagnostic categories and investigations. In studies employing quantitative scoring exclusively, the presence or absence of ETD (but not prevalence) within a given diagnostic category can be inferred from comparisons of psychiat-

ric patients with neurologically intact, age-equated normal controls. Whenever such comparisons have been made in studies under review here, their results will be reported in terms of presence or absence of eye movement dysfunction.

Prevalence/Presence of Eye Movement Dysfunction in Psychiatric Patients

In their 1974 study Holzman et al. examined pursuit eye movement in a large sample of psychiatric inpatients, their first-degree relatives, and normal control subjects. When subgroups within that sample were constituted by hospital diagnosis, deviant eye tracking was manifest in 86 percent of chronic schizophrenics, 52 percent of recent schizophrenics, 50 percent of schizoaffectives, 44 percent of first-degree relatives of schizophrenics, 22 percent of manic-depressives, 10 percent of relatives of non-schizophrenics, 21 percent of nonpsychotic patients, and 8.3 percent of normal controls. A chi-square test of this distribution was found to be highly significant. When these subgroups were reconstituted by diagnosis based on psychological test data and compared in terms of both pre-alert and post-alert velocity arrest scores, it was found that schizophrenics, schizoaffectives, and the relatives of schizophrenics, combined as a single group, showed significantly more velocity arrests than "other groups which included the other psychotic patients and their relatives."¹

¹ It is of interest to note here, in relation to the role that variation in diagnostic criteria and methods may play in influencing judgments concerning the specificity hypothesis, that when subgroups within the sample of psychiatric patients studied by Holzman et al. (1974) were consti-

There were, however, no significant differences in mean velocity arrest scores between recent and chronic schizophrenics, paranoids and non-paranoids, and good and poor pre-morbid patients.

Shagass, Amadeo, and Overton (1974) also examined pursuit eye movement in a large sample of psychiatric inpatients. They used both velocity arrest scores and qualitative ratings to compare hospitalized schizophrenics and affective disorder patients with age-matched normal controls. Psychiatric diagnoses in this investigation "represented the consensus of two or more senior psychiatrists." Their findings indicated that eye tracking impairment in chronic schizophrenics is significantly greater than in age-matched normal controls and that paranoid and nonparanoid subjects do not differ from each other in this regard. Schizoaffective patients, whose mean velocity arrest scores were greater than those of the control subjects, did not, however, differ significantly from the controls. In the affective disorders group, both "depressed" and "manic" psychotic patients manifested significantly greater eye tracking dysfunction than age-matched controls. Moreover, when five schizoaffective-depressed patients were combined with the depressed psychotic patients, this subsample was found to show significantly poorer eye tracking than the normal controls.

Klein et al. (1976) studied eye tracking performance in women "previously hospitalized for schizophrenia or depression disorder," their

tuted in terms of hospital diagnosis, schizophrenics, their relatives, and other psychotics did not differ significantly from each other in mean post-alert velocity arrest scores.

spouses, their adolescent offspring, and normal controls. Diagnosis was by consensus among three senior psychiatrists employing relatively conservative criteria. Comparison of eye tracking in schizophrenic and in nonschizophrenic women showed no significant differences, although both groups of patients manifested significantly greater impairment than normal controls. Similar findings are reported for the offspring of these patients. This study appears to invite the same interpretation due the study of Shagass, Amadeo, and Overton (1974)—namely, that eye tracking dysfunction occurs in *both* schizophrenic and affective disorder patients. However, this interpretation in the case of the Klein et al. study is rendered equivocal because most of the “schizophrenic” patients in that study were, in fact, specifically diagnosed as schizoaffectives, whose velocity arrest scores were comparable to those of schizoaffectives in the study of Shagass, Amadeo, and Overton.

Lipton, Levin, and Holzman (1980) examined eye tracking performance in “first break” hospitalized manic-depressive and schizophrenic patients. Both groups showed significantly more impaired eye tracking than normal controls and did *not* differ in this regard from each other. Both manic-depressives and schizophrenics in this study were identified by an “experienced diagnostician,” applying the criteria of Feighner et al. (1972), and both revealed similar prevalence rates: “around 50%.”

Finally, in most studies of smooth pursuit eye movement in which nonpsychotic psychiatric patients were included (Holzman et al. 1974; Shagass, Amadeo, and Overton 1974; Pass et al. 1978; Miallet and Pichot 1981), no evidence was reported to suggest that such patients

differed significantly from normal controls in eye tracking performance. There are, however, two rather ambiguous exceptions in this regard. Pivik (1979) reported that “psychiatric inpatients,” comprising *both* schizophrenic and other psychotic patients (63 percent) and nonpsychotic patients (37 percent), exhibited significantly more velocity arrests than schizophrenic outpatients and normal controls.

Bala et al. (1981) found more frequent “irregular eye pursuit movement” in hyperactive boys (mean age = 7.4 years) than in normal boys (mean age = 8 years). These irregularities were stable over a 3-year period in unmedicated subjects but were normalized by “stimulant medication.” While the eye tracking records of hyperactive boys in this study bear striking resemblance to deviant records of adult schizophrenics, the possibility of differing underlying pathological mechanisms, particularly in light of the normalizing effects of medication, cannot be readily ruled out.

It will be evident, of course, from the above review that the hypothesis that ETD is specific to schizophrenia is no longer tenable. An empirically more appropriate reformulation would be that ETD is evident primarily in functional psychosis.

Eye Tracking Dysfunction as a Trait in Functional Psychosis

The question of whether ETD is a trait in functional psychosis bears on the theoretical significance of the phenomenon. Holzman’s genetic marker hypothesis requires that ETD be a trait in functional psychosis. Similarly, the hypothesis that ETD is closely linked to primary pathology or vulnerability in functional psycho-

sis and plays a role in the etiology of these disorders entails the assumption that ETD has trait characteristics. The most compelling evidence on behalf of the trait hypothesis would be derived from longitudinal studies in which the persistence of ETD in individuals at risk for the trait throughout all phases of the illness and before, during, and after drug treatment was determined. Although there are test-retest reliability studies which have fulfilled, in part, the above longitudinal study requirements, most of the studies, regarded by their investigators as bearing on the trait hypothesis, have been cross-sectional in nature. Positive findings in such studies—e.g., concordance of ETD in monozygotic twins discordant for schizophrenia or the presence of ETD in asymptomatic, remitted schizophrenics—are logically compelling, but nonetheless engender a residue of doubt about the persistence of ETD in individuals tested on only one or two occasions.

Some support for the trait hypothesis is derived from three test-retest reliability studies. Both Holzman et al. (1974) and Shagass, Amadeo, and Overton (1974) found moderately high test-retest reliability coefficients for eye tracking performance (velocity arrest scores and ratings) in psychiatric patients over periods ranging from 9 to 60 days. Iacono and Lykken (1979) reported high test-retest reliability of eye tracking performance over a 2-year period in normal monozygotic twins.

The great majority of schizophrenic patients in whom ETD has been identified were receiving antipsychotic medication at the time of testing. This fact suggests the possibility that ETD is produced by antipsychotic medication and cannot therefore be regarded as a trait. On the basis of fairly substantial data, this possi-

bility can be discounted. Holzman et al. (1974) and Shagass, Amadeo, and Overton (1974) have reported indirect evidence indicating that ETD is not dependent on drug state. Moreover, Spohn et al. (1982) found, in a placebo-controlled study, that antipsychotic medication neither elicits nor normalizes ETD in chronic schizophrenics.

Evidence obtained in two twin studies (Holzman et al. 1978, 1980) is also indirectly supportive of the trait hypothesis and directly supportive of the genetic marker hypothesis. In both studies a substantial number of monozygotic twin pairs discordant for schizophrenia were concordant for ETD. Moreover, in the second study, at least one monozygotic twin pair discordant for manic-depressive illness proved to be concordant for ETD.

Iacono, Tuason, and Johnson (1981) have shown that schizophrenic outpatients in remission manifested significantly greater ETD than normal controls. This finding suggests that ETD is *not* a function of florid psychopathology during an acute episode and thus also indirectly supports the trait hypothesis.

A study by Salzman, Klein, and Strauss (1978) bears on the trait hypothesis in affective psychosis. These investigators obtained data from a sample employed by Klein et al. (1976) "augmented" somewhat by additional subjects. They found that predominantly schizoaffective outpatients in remission did not differ significantly in eye tracking performance from nonschizophrenic depressive patients also in remission and that degree of ETD in both groups was positively correlated with severity of illness during a prior acute episode, but *not* with current, residual symptomatology. In its relation to the trait hypothesis, this study is cu-

riously ambiguous. The linkage of severity of illness with degree of ETD in affective psychosis patients tends to negate the trait hypothesis. On the other hand, that this linkage is not found in remission and that both remitted schizoaffective and nonschizophrenic depressives manifest greater ETD than normal controls (Klein et al. 1976) does tend to support the trait hypothesis.

Finally, a more recent study (Iacono et al. 1982) bears less ambiguously on the trait hypothesis in affective disorders. These investigators found that both unipolar and bipolar depressives—by Research Diagnostic Criteria (RDC; Spitzer, Endicott, and Robins 1978) consensus diagnosis—in remission did not differ significantly in eye tracking performance from normal controls. However, patients receiving the antimanic medication lithium tended to perform more poorly than patients not receiving lithium. Schizophrenic patients in remission when compared with the two depressive groups manifested greater tracking dysfunction than both groups, but significantly so only with respect to the unipolar and not the bipolar patients. A larger proportion in the latter group were receiving lithium than in the former group. The investigators indicated that these findings are consistent with the interpretation that "tracking dysfunction is not a trait characteristic of affective disorders," but quite appropriately call for further study of this issue.

Summary and Conclusions

When the research literature reviewed here, ranging as it does from 1908 to 1982, is considered in terms of its bearing on specificity, Holzman and Levy's (1977) conclusion that eye

tracking dysfunction in neurologically intact psychiatric populations is confined to and characteristic of functional psychosis still seems entirely valid. Thus, while eye tracking deviance has been shown to be widely prevalent within an otherwise heterogeneous schizophrenic population and is found in all phases of schizophrenic illness, the presence of eye tracking dysfunction, to some degree, in affective psychoses has also been demonstrated.

Similarly confident conclusions concerning the status of ETD as a trait variable are more difficult to come by. However, although additional longitudinal studies need to be done, the evidence that ETD is a trait in schizophrenia is already quite strong and thus supportive of the genetic marker hypothesis. Moreover, that the prevalence of ETD is substantially higher in chronic schizophrenics than in recent onset schizophrenics suggests the possibility that ETD may be a trait variable only in chronic schizophrenics and in recent onset patients destined for chronicity. It may be useful therefore to design longitudinal studies with this hypothesis in mind and to direct research efforts to the identification of recent onset schizophrenics *not* destined for a chronic course, on the hypothesis that genetic loading in such patients may differ from genetic loading in chronic patients.

Evidence supporting the hypothesis that ETD is a trait in schizoaffective patients is only cross-sectional and really quite fragmentary. Indeed, both in light of lingering doubts concerning prevalence in schizoaffective patients *per se*, and because of recent findings that a small proportion of schizoaffective patients share genetic loadings with schizophrenics while a larger proportion of schizoaffectives share genetic loadings with affective

disorder patients (Mendlewicz, Linkowski, and Wilmote 1980), schizoaffective patients in future longitudinal studies should be treated as a sample independent of schizophrenic and affective disorder patients. Also, some efforts should be made to discriminate schizoaffectives sharing genetic loadings with schizophrenics from schizoaffectives sharing genetic loadings with affective psychotics. Such information would afford an opportunity, among others, to determine whether ETD is a trait and a genetic marker in functional psychosis.

Cross-sectional studies in acute and remitted manic-depressive/bipolar patients suggest the possibility that ETD is *not* a trait in manic-depressive illness and that it may be a function of severity of psychopathology and/or antimanic drug treatment. Because of the importance of the bearing of this interpretation on the hypothesis that ETD is a genetic marker of functional psychosis, longitudinal studies of the kind called for above are urgently needed. At the same time, larger scale studies than those of Holzman et al. (1974) of pursuit eye movement in first-degree relatives of manic-depressive patients would be useful in resolving doubts concerning the diagnostic scope of the genetic marker hypothesis.

References

- Bala, S.P.; Cohen, B.; Morris, A.G.; Atkin, D.; Gittelman, R.; and Kates, W. Saccades of hyperactive and normal boys during ocular pursuit. *Developmental Medicine and Child Neurology*, 23:323-336, 1981.
- Feighner, J.P.; Robins, E.; Guze, S.B.; Woodruff, R.; Winokur, G.; and Munoz, R. Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, 26:57-62, 1972.
- Holzman, P.S.; Kringlen, E.; Levy, D.L.; and Haberman, S.J. Deviant eye tracking in twins discordant for psychosis: A replication. *Archives of General Psychiatry*, 37:627-631, 1980.
- Holzman, P.S.; Kringlen, E.; Levy, D.L.; Proctor, L.R.; and Haberman, S. Smooth pursuit eye movement in twins discordant for schizophrenia. *Journal of Psychiatric Research*, 14:111-120, 1978.
- Holzman, P.S., and Levy, D.L. Smooth pursuit eye movements in functional psychoses: A review. *Schizophrenia Bulletin*, 3:15-27, 1977.
- Holzman, P.S.; Proctor, L.R.; and Hughes, D.W. Eye tracking patterns in schizophrenia. *Science*, 181:179-181, 1973.
- Holzman, P.S.; Proctor, L.R.; Yasillo, N.J.; Meltzer, H.Y.; and Hurt, S.W. Eye tracking dysfunctions in schizophrenic patients and their first degree relatives. *Archives of General Psychiatry*, 31:143-151, 1974.
- Iacono, W.G., and Lykken, D.T. Eye tracking and psychopathology. *Archives of General Psychiatry*, 36:1361-1369, 1979.
- Iacono, W.G.; Pelloquin, L.J.; Lumry, A.E.; Valentine, R.H.; and Tuason, V.B. Eye tracking in patients with unipolar and bipolar affective disorders in remission. *Journal of Abnormal Psychology*, 91:34-44, 1982.
- Iacono, W.G.; Tuason, V.B.; and Johnson, R.A. Dissociation of smooth pursuit and saccadic eye tracking in remitted schizophrenics: An ocular reaction time task that schizophrenics perform well. *Archives of General Psychiatry*, 38:991-996, 1981.
- Klein, R.H.; Salzman, L.F.; Jones, F.; and Ritzler, B. Eye tracking in psychiatric patients and their offspring. (Abstract) *Psychophysiology*, 13:186, 1976.
- Lipton, R.B.; Levin, S.; and Holzman, P.S. Horizontal and vertical pursuit eye movements, the oculocephalic reflex, and the functional psychoses. *Psychiatry Research*, 3:193-203, 1980.
- Mendlewicz, J.; Linkowski, P.; and Wilmote, J. Relationship between schizoaffective illness and affective disorders of schizophrenia. *Journal of Affective Disorders*, 2:289-302, 1980.
- Mialet, J.P., and Pichot, P. Eye tracking patterns in schizophrenia: An analysis based on the incidence of saccades. *Archives of General Psychiatry*, 38:183-186, 1981.
- Pass, H.L.; Salzman, L.F.; Klorman, R.; Kaskey, G.B.; and Klein, R.H. The effect of distraction on acute schizophrenics' visual tracking. *Biological Psychiatry*, 13:587-593, 1978.
- Pivik, R.T. Smooth pursuit eye movements and attention in psychiatric patients. *Biological Psychiatry*, 14:859-879, 1979.
- Salzman, L.F.; Klein, R.H.; and Strauss, J.S. Pendulum tracking in remitted psychiatric patients. *Psychiatry Research*, 14:121-126, 1978.
- Shagass, C.; Amadeo, M.; and Overton, D.A. Eye tracking performance in psychiatric patients. *Biological Psychiatry*, 9:245-260, 1974.
- Spitzer, R.L.; Endicott, J.; and Robins, E. *Research Diagnostic Criteria (RDC) for a Selected Group of Functional Disorders*. 3rd ed. New York: New York State Psychiatric Institute, 1978.
- Spohn, H.E.; Larson, J.; Mittleman, F.; and Coyne, L. "Eye Tracking in

Medicated and Relapsed Chronic Schizophrenics." In preparation, 1982.

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Abnormal Patterns of Normal Eye Movements in Schizophrenia

Abstract

The multilevel control of eye movements for the researcher in the schizophrenic disease process includes the saccadic trajectory, the dual mode tracking system, and schematically directed eye movements in fixation, in scanpaths, and other looking strategies, and in reading. Coordination of eye movements with head movement in gaze and sensory consequences and concomitants of eye movements round out the picture. Recent studies with precise bioengineering instrumentation have defined two abnormal patterns of eye movements—saccadic intrusions and saccadic "smooth" pursuit. Although these signs are not pathognomonic, they raise interesting questions concerning the relationship of these eye movements to the schizophrenic disease process.

Multilevel Control of Eye Movements

Two different disciplines, neurology and bioengineering, have contributed to the concept of multilevel control of eye movements. The neurological contribution stems from the early work of Hughlings Jackson (Taylor 1958) who contrasted *lower level* control, which involved inputs to the final common pathway or motoneuronal pool, with *higher level* control at the brainstem and other subcortical integrative levels; he also used *highest level* control to mean the rather free cortical schematic in-

puts to motor control. For eye movement control he might have considered the motor program for the saccade trajectory as lower level control, the adaptive calibration of gain by the cerebellum as higher level control, and the schematic directing of the eye saccade to fixate an expected feature of interest in the periphery as highest level control.

Recent bioengineering contributions have added concepts of a feedback control path sharing with input the control of the feedforward path, and thus forming a closed loop feedback control system. The block of pulse-shaping algorithms for generating time-optimal saccadic trajectories would be lower level control. The block for the sample data control mechanism initiates eye movement, precedes this lower level block, but also lies in the forward loop path; it would be higher level control. Other blocks, out of the main feedback-feedforward loop, that calibrate gains and calculate spatial constancy and other features of associated sensory mechanisms would be highest level controllers. There remain similarities and differences between these two views of multilevel control. For each view, control of eye movement is a complex affair; some decomposition is necessary to study individual elements of control.

Saccadic Trajectory

The eye saccade is a rapid movement that occurs quite frequently, about 250,000 movements a day, in the