

FAMILIAL AND SPORADIC SCHIZOPHRENIAS : A STUDY OF PURSUIT EYE MOVEMENTS

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15 familial schizophrenics, 15 sporadic schizophrenics, 15 normal sibs of familial schizophrenic probands, 15 normal sibs of sporadic schizophrenic probands and 15 normal subjects were examined by electro-oculogram (EOG) for the quality of their smooth pursuit eye movements. Results confirm the previous findings of SPEM dysfunction among schizophrenics as a group, but the trait-marker status of SPEM impairment of schizophrenia has been questioned and discussed. It has been suggested that the increased prevalence of impaired pursuit eye movement among sporadic schizophrenics may be due to the environmental factors of specific or non-specific nature. SPEM dysfunction could also be of pathoplastic significance in the manifestation of psychosis.

In an earlier study (Sharan *et al.*, 1990) we have reported that schizophrenics as a group have higher prevalence of impaired smooth pursuit eye movement (SPEM).

The work in recent years has been directed towards identifying whether SPEM dysfunction could be a genetic trait marker which indicates a vulnerability for schizophrenic disorders (Erlenmeyer-Kimling and Cornblatt, 1987; Holzman *et al.*, 1985; Holzman, 1988).

Such a genetic association is more likely in familial schizophrenics than among sporadic schizophrenics.

It has been suggested that the familial schizophrenics may form a separate group and may be distinct from the sporadic schizophrenics (Kendler and Hays, 1982; Kinney and Jacobsen, 1978; McNeil, 1988 and Shur, 1982). Sporadic schizophrenics are more often winter born (Kinney and Jacobsen, 1978; McNeil, 1988 and Shur, 1982), are more likely to have obstetric complications (Lewis and Murray, 1978) and C.T. Scan abnormalities (Murray *et al.*, 1985; Lewis *et al.*, 1987) than familial schizophrenics. Thus, the sporadic schizophrenics may be predominantly determined by environmental factors in contrast to

familial schizophrenia which may have predominant genetic determinants.

If the SPEM dysfunction is a genetic trait marker of schizophrenia, then the SPEM dysfunction would be expected to be more prevalent among the familial schizophrenics and the first degree relatives of the familial schizophrenics compared to the sporadic schizophrenics and their first degree relatives respectively. The familial schizophrenics would also be expected to show higher prevalence of SPEM impairment compared to normals. The present study was designed to investigate these issues.

MATERIAL AND METHOD

SUBJECTS

There were 5 groups of subjects which consisted of 15 familial schizophrenics, 15 sporadic schizophrenics, 15 normal sibs of familial schizophrenics, 15 normal sibs of sporadic schizophrenics and 15 normals.

The schizophrenics (both the familial and the sporadic groups) were selected from the psychiatry out-patient department of Na-

tional Institute of Mental Health and Neurosciences, Bangalore. 15 consecutive cases of familial schizophrenia and 15 consecutive cases of sporadic schizophrenia who fulfilled the study criteria and consented to participate in the study were taken. A total of 75 subjects from whom an informed consent was obtained were examined.

(A) FAMILIAL SCHIZOPHRENICS

Schizophrenic patients with first degree relatives with schizophrenia is defined as familial schizophrenics. The diagnosis of schizophrenia was made according to the DSM-III criteria (American Psychiatric Association, 1980).

The diagnosis of schizophrenia in the first degree relatives was based on the "Family History Research Diagnostic Criteria (FH-RDC) (Andreasen *et al.*, 1977; Endicott *et al.*, 1975). A minimum of two informants, sibs and/or parents, apart from the patients were interviewed to reach a diagnosis of schizophrenia in the first degree relatives who were ill, were also examined in person. Many of the first degree relatives who were ill had also sought a consultation at this institute. The diseased first degree relatives of only 7 probands could be interviewed in person, while FH-RDC diagnosis of the diseased first degree relatives of two other probands was confirmed after reviewing their hospital records. All the diseased relatives who were interviewed in person also were given a DSM-III diagnosis.

(B) SPORADIC SCHIZOPHRENIA

The patients who did not have a family history of psychosis, alcoholism, suicide or any kind of psychiatric intervention and who fulfilled the DSM-III criteria for schizophrenia is defined as sporadic schizophrenics. Even if there was a history of any relative having had a

long standing personality problem as evidenced by an inability to hold a constant occupation, the presence of severe interpersonal conflicts or having undergone psychotherapeutic interventions these probands were not included in the study.

Such exclusion criteria was decided because of two main reasons :

1. There is mounting evidence that certain personality disorders e.g. schizotypal personality disorder may be genetically linked to schizophrenia (Kety *et al.*, 1975; Rosenthal *et al.*, 1971 and Spitzer *et al.*, 1979) and may have SPEM dysfunction similar to that reported among schizophrenics (Siever *et al.*, 1984).

2. Employing the family history method to arrive at the diagnosis of schizotypal personality disorder and differentiating this from the other personality disorders is both arduous and unreliable. Hence, in order to prevent the sample of sporadic schizophrenics from being contaminated by the 'genetic factors' related to familial schizophrenia, all the cases of schizophrenia with family history suggestive of any kind of abnormal personality were excluded.

As was the case with familial schizophrenics, in the group of sporadic schizophrenics also a minimum of two informants besides the patients were interviewed. The informants invariably comprised of atleast one parent.

Pertinent information concerning every member of the family of the probands upto 3 generations was obtained. Thereafter, an attempt was also made to find out whether any other member of the family had a history of mental illness.

Only such families with a large number of members (a minimum of 8 first degree relatives including the parents) were selected.

Despite the rigorous criteria employed, as a considerable number of sibs were still within the 'risk-period', the possibility of inclusion of false negatives in the sample of the sporadic schizophrenics can not be overruled.

All the patients (familial schizophrenics and sporadic schizophrenics) were receiving varying doses of antipsychotic drugs and trihexphenidyl. Severity of psychopathology of the patients was rated on the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962).

(C) SIBS OF FAMILIAL AND SPORADIC SCHIZOPHRENICS

The normal sib who was closest in age to the proband was selected for the study.

A sib of a proband was considered normal if he had no past and present history suggestive of psychosis, drug addiction, alcohol dependence, attempted suicide, epilepsy or significant head injury. Special care was taken to see that none of the sibs included in the study fulfilled the criteria for any of personality disorders specially borderline personality disorder

and schizotypal personality disorder (DSM-III, A.P.A.-1980).

(D) NORMAL CONTROLS

Fifteen controls who had never participated in similar studies of ocular movements in the past were selected mainly from the postgraduate and doctoral student population of the institute.

Other inclusion and exclusion criteria for the subjects have been described in detail previously (Sharan *et al.*, 1990). Similarly details regarding target, EOG procedure, rating of EOG have been discussed in detail in our previous paper (Sharan *et al.*, 1990).

The data were analysed using chi square test, t test, analysis of variance (ANOVA) and Phi coefficient (Welkowitz *et al.*, 1971).

RESULTS

SEX AND AGE DISTRIBUTION (Table 1)

Table 1 : Sex and age distribution of subjects

	Sex			Age	
	Male	Female	Total	Mean (Years)	Range (years)
Familial schizophrenics	9	6	15	30.87±5.49	20-38
Sibs of familial schizophrenics	11	4	15	27.73±7.99	16-42
Sporadic schizophrenics	12	3	15	29.73±4.97	22-38
Sibs of sporadic schizophrenics	9	6	15	30.13±6.53	18-40
Normal controls	8	7	15	31.33±8.46	23-57
Statistical significance	$X^2 = 3.18$, d.f. = 4, N.S.; $F = 0.84$, d.f. = 4, 70, N.S.				

The groups were comparable with respect to age and sex distribution.

ILLNESS VARIABLE (Table 2)

Familial schizophrenics and sporadic schizophrenics did not differ significantly on the total score on the BPRS, score on the withdrawal retardation higher order factor of the BPRS (i.e. sum of scores on three items, emotional withdrawal, motor retardation and blunted affect) and the duration of illness.

PREVALENCE OF SMOOTH PURSUIT DYSFUNCTION (Table 3)

Comparison of the five groups together revealed significant overall differences among them (Two tailed $\chi^2 = 10.714$, d.f. = 4, $p < 0.05$). Pairwise comparison among the normals, familial schizophrenics, sibs of familial schizophrenics and sibs of sporadic schizophrenics, using chi-square test of significance did not demonstrate significant differences in the prevalence rates. However, 86.67% of sporadic schizophrenics had impaired SPEM which differed significantly from normals ($\chi^2 = 7.033$, d.f. = 1, $p < 0.01$) and sibs of sporadic schizophrenics ($\chi^2 = 8.888$, d.f. = 1, $p < 0.01$). When all the schizophrenics were grouped together and compared with nor-

Table 2 : Duration of illness and severity of illness according to BPRS.

Group	Duration of illness		Mean BPRS Scores	Scores on the withdrawal retardation higher order factor of BPRS
	Mean (months)	Range (months)		
Familial schizophrenics (N = 15)	87.13 ± 57.33	12-204	13.71 ± 7.06	4.71 ± 3.17
Sporadic schizophrenics (N = 15)	62.66 ± 38.05	8-108	15.92 ± 6.51	4.76 ± 3.63
Statistical significance t = 1.41, d.f. = 28, N.S. t = 0.85, d.f. = 25, N.S. t = 0.04, d.f. = 25, N.S.				

N.B.: One familial and two sporadic schizophrenics could not be rated on the BPRS.

Table 3 : SPEM dysfunctions : Prevalence rates and mean ratings.

	Familial schizophrenics			Sporadic schizophrenics			All Schizophrenics	All sibs	Normals
	Pro-bands	Sibs	Pro-bands + sibs	Pro-bands	Sibs	Pro-bands + sibs			
No. of subjects	15	15	30	15	15	30	30	30	15
No. of abnormal records	9	7	16	13	5	18	22	12	6
Prevalence of SPEM dysfunction	60%	46.60%	53.33%	86.66%	33.33%	60%	73.33%	40%	40%
Mean rating score (±SD)	2.73 ± 0.70	2.33 ± 1.04	2.53 ± 0.88	3.13 ± 0.63	2.00 ± 0.85	2.56 ± 0.92	2.93 ± 0.68	2.17 ± 0.93	2.26 ± 0.70

mals, a significant difference was found ($\text{Chi}^2 = 4.725$, $\text{d.f.} = 1$, $p < 0.05$). Total schizophrenics (familial schizophrenics + sporadic schizophrenics) differed significantly from the total number of sibs (sibs of familial schizophrenics + sibs of sporadic schizophrenics) ($\text{Chi}^2 = 7.147$, $\text{d.f.} = 1$, $p < 0.01$). There was no significant difference between the familial schizophrenics and sporadic schizophrenics, though the trends indicated that there was a greater degree of SPEM dysfunction among the sporadic schizophrenics in comparison with the familial schizophrenics. The sibs of familial schizophrenics did not differ significantly from the sibs of sporadic schizophrenics.

We found that 40% of our normals showed SPEM dysfunction. We have discussed

the possible reason for such a high prevalence rate in detail previously (Sharan *et al.*, 1990).

COMPARISON OF MEAN RATINGS (Table 4)

The mean rating of the two groups of schizophrenics, the two group of their sibs and normals were compared using ANOVA.

There was a significant difference among the groups ($F = 4.601$, $\text{d.f.} = 4, 70$, $p < 0.05$). Pair-wise comparison between the groups were made using "t" test of significance (two tailed) (Welkowitz *et al.*, 1971). The comparison between various groups resulted in a similar pattern of difference among the groups only, the sibs of the familial schizophrenics did not differ significantly from the sibs of sporadic schizophrenics. If the SPEM dysfunction is a

Table 4 : Comparison of mean ratings of the groups

Group	Familial schizophrenics	Sporadic schizophrenics	Sibs of familial schizophrenics	All schizophrenia schizophrenics	Sibs of sporadic
Normals	N.S.	$t = 3.58$, $\text{d.f.} = 28$ $p < 0.005$	N.S.	N.S.	$t = 3.08$, $\text{d.f.} = 43$, $p < 0.005$
Familial Schizophrenics	-	N.S.	N.S.	-	-
Sporadic schizophrenics	-	-	-	$t = 4.14$, $\text{d.f.} = 28$, $p < 0.001$	-
All the sibs of schizophrenics	-	-	-	-	$t = 3.61$, $\text{d.f.} = 58$, $p < 0.001$

DISCUSSION

The prevalence rates of deviant pursuit eye movements in the sibs of familial schizophrenics (46%) and that of sporadic

schizophrenics (33%) were comparable to the reported prevalence rates of 44% to 54% for the first degree relatives of the schizophrenics probands (Holzman *et al.*, 1974, 1977, 1978). But these results differ in two ways. Firstly,

genetic trait marker of schizophrenia it is to be as a comparison of their normal and abnormal ratings (Table 4).

were no significant differences in the prevalence rates of deviant pursuit eye movements between the sibs of sporadic and familial schizophrenics as compared to that of normals. Sec-expected that it would be more prevalent among the first degree relatives of schizophrenics, especially the first degree relatives of the familial schizophrenics. The present study questions the trait marker status of the SPEM dysfunction. However, it is conceded that the lack of statistically significant differences between the two group of sibs could be due to the small sample sizes and the possibility of false negative in the sporadic schizophrenic group. Thus, we regard this finding as a preliminary one requiring further investigation.

The prevalence rates of impaired SPEM of the familial schizophrenics and the sporadic schizophrenics were 60% and 86.67% respectively. These prevalence rates are comparable to the prevalence rates reported in the previous studies, which varies from 50% to 86% [Recent schizophrenics 52%, chronic schizophrenics 86% (Holzman *et al.*, 1974); Schizophrenics 50% (Lipton *et al.*, 1980); schizophrenics from a twin sample 69% (Holzman *et al.*, 1977, 1978)]. In comparison with the normals, familial schizophrenics did not differ significantly while the sporadic schizophrenics differed significantly. Once again these results are unexpected and challenge the genetic trait-marker status of the smooth pursuit eye movements. Given the postulation that the SPEM dysfunction is a genetic trait-marker of schizophrenia, the familial schizophrenics in contrast to the sporadic schizophrenics are expected to show a higher prevalence of the SPEM dysfunction. It can be argued that the sporadic schizophrenics were not truly sporadic due to the presence of false negatives. But, this alone can not explain the higher prevalence of SPEM dysfunction in a group definitely containing lesser number of

familial schizophrenics i.e. sporadic group compared to the group of familial schizophrenics.

It can be assumed that sporadic schizophrenia is predominantly caused by environmental factors, while, the genetic factors play a more important role in familial forms of schizophrenias. Indeed, there are evidences to suggest that sporadic schizophrenia has important environmental determinants (Kendler and Hays, 1982; Kinney and Jacobsen, 1978; Lewis and Murray, 1987; Lewis *et al.*, 1987; McNeil, 1988; Murray *et al.*, 1985; Shur, 1982).

Impaired SPEM, remarkably similar to that found in schizophrenics has been described in various neurological disorders and drug-induced states (Baloh and Honrubia, 1979; Benitez, 1970; Corvera *et al.*, 1973; Holzman *et al.*, 1975; Levy *et al.*, 1981, 1985). But, the evidences are strongly in support of the genetic control of smooth pursuit eye movements too (Holzman, 1982; Holzman *et al.*, 1977). The quality of pursuit movements may be genetically determined in certain individuals while in the others it may be a manifestation of CNS insult due to various non-specific environmental factors. Thus, one way of explaining the higher prevalence of deviant pursuit among sporadic schizophrenics is to attribute it to environmental factors causing CNS dysfunction.

Alternatively, it is postulated that the deviant eye pursuit movements as a trait may be one of the many vulnerability factors rather than a specific genetic trait-marker for the development of schizophrenia. Individuals with deviant pursuit eye movements as a trait may be more prone to develop schizophrenia when this trait interacts with certain other environmentally or other genetically determined factors which may be specific to schizophrenia, while the familial schizophrenia could be unrelated to the quality of pursuit eye movements.

It is likely that the deviant pursuit eye movements may be associated with certain

psychological traits (Iacono and Lykken, 1979; Siever *et al.*, 1982a, 1982b, 1984) which may have a pathoplastic effect on psychosis of any origin. Thus, a person with deviant eye movements, if he were to decompensate into psychosis, would demonstrate schizophrenic symptomatology. Such a conclusion seems reasonable because the association between sporadic schizophrenia and SPEM dysfunction was found to be weak (prevalence of SPEM dysfunction among sporadic schizophrenics vs. normals, Chi-square = 7.033, $N = 30$, Phi coefficient = 0.4841).

In this study, though 86.67% of the sporadic schizophrenics and 60% of the familial schizophrenics had impaired SPEM, the statistical analysis did not show any significant difference. This could be due to a smaller sample size which indeed is the major limitation of this study. A replication study using a larger number of subjects and first degree relatives will be more informative (Eaves *et al.*, 1986).

Future studies should be directed towards exploring possible interactions between various environmental and genetic factors and the type of pursuit eye movements in causation of schizophrenia.

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