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Epilepsy and EEG findings in 18 males with fragile X syndrome

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Of the 24 males identified as having fragile X syndrome in the Northeast Essex screening programme, 25% had epilepsy. Epilepsy in individuals with fragile X syndrome is known to follow a benign course with seizures disappearing before the age of 20. However, half of our sample with a history of epilepsy continued to have seizures after the age of 20.

We reviewed the EEG reports of 18 of the 24 individuals (aged between 13 and 63 years) including all six individuals with epilepsy. We had 32 EEG recordings from 18 subjects, with nine people having more than one recording at different points. The EEG showed a definite improvement in only five individuals. Three individuals who had serial recordings (one with epilepsy) showed no significant changes over time and the EEG of one subject with epilepsy deteriorated.

The most common abnormal EEG findings were rhythmic theta activity (50%) and a slowing of background activity (28%). There were no characteristic features in the sleep EEGs performed on four subjects. The possible implications of these preliminary findings are discussed.

Key words: epilepsy; fragile X syndrome; EEG; longitudinal study.

INTRODUCTION

Fragile X syndrome is the most common cause of mental retardation after Down syndrome. It affects approximately 1 in 4000 (0.25/1000) males and 1 in 8000 (0.125/1000) females[1,2]. The prevalence of epileptic seizures in fragile X syndrome is lower than that in individuals with developmental disability due to other causes but considerably higher than that in the general population[3]. The actual prevalence of seizures as reported by studies vary from 14% to 50% with a mean around 22%[4,5].

The natural history of epilepsy in fragile X syndrome has been described as generalized seizures occurring in the first 15 years of life, responding well to anticonvulsants, particularly to carbamazepine, and disappearing after adolescence[5]. This typical benign course is questioned by the reports of epilepsy in older people with fragile X syndrome[23].

EEG findings in fragile X have been reported in a number of studies[10,16]. Although no characteristic EEG changes were noticed initially, a distinct pattern was later identified[20,22,23].

The present study examines the clinical features of epilepsy and the EEG abnormalities in a cohort of 24 males with fragile X syndrome. We further discuss the findings from this study in the context of the findings from the previous studies.

MATERIALS AND METHODS

This study was undertaken after obtaining the approval of the Local Research Ethical Committee. The sample of this study was identified in the Northeast Essex screening programme, which on the basis of cytogenetic screening identified a total of 24 males and one female in the North Essex region as having fragile

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Table 1: EEG findings in fragile X males in the literature.

Reference	Year	Epilepsy findings			EEG findings					
		Epileptic subjects/ Total subjects	Epilepsy rate	No. of patients studied by EEG	Normal pattern	Diffuse slowing background activity	Excess rhythmic theta activities	Epileptic discharges	Focal discharges	No. of epileptic patients
Wisnewski[5]	1991	14/62	23%	36	—	—	18	3	—	14
Lubs[6]	1968	1/4	25%	—	—	—	—	—	—	—
Escalante *et al.*[7]	1971	2/9	22%	—	—	—	—	—	—	—
Turner *et al.*[8]	1975	1/7	14%	—	—	—	—	—	—	—
Harvey *et al.*[9]	1977	4/20	20%	—	—	—	—	—	—	—
Brown *et al.*[10]	1978	2/6	33%	4	—	—	—	—	—	2
Labrisseau *et al.*[11]	1982	2/7	29%	4	—	3	—	2	—	2
Gardner *et al.*[12]	1983	1/8	13%	1	—	—	—	—	1	1
Brondum-Nielsen[13]	1983	4/25	16%	—	—	—	—	—	—	—
Jacobs *et al.*[14]	1983	1/5	20%	1	—	1	—	—	—	1
Fryns[15]	1985	4/44	9%	—	—	—	—	—	—	—
Wisnewski *et al.*[16]	1985	7/28	25%	10	6	1	—	3	3	3
Finelli *et al.*[17]	1985	7/16	44%	2	—	1	—	1	1	2
Sanfillipo *et al.*[18]	1986	3/4	75%	3	—	3	—	(3)	—	3
Veenema *et al.*[19]	1987	5/14	36%	—	—	—	—	—	—	—
Musumeci[20]	1988	6/12	50%	—	—	—	—	—	—	—
Vieregge[21]	1989	4/29	14%	12	4	6	—	3	1	1
Musumeci[22]	1991	8/18	44%	18	—	13	—	5	—	—

X syndrome[24]. The diagnosis was later confirmed in 1996 using Southern Blot techniques.

Using a 16-channel sleep model EEG machine and applying electrodes according to the international 10–20 system for positions as previously described[25], EEG recordings were taken from 18 of the 24 identified male patients. The present EEG reports were compared with the previous reports in nine individuals with multiple EEGs.

RESULTS

The 24 males included in this study varied from 13 to 63 years of age.

Epilepsy

Six out of 24 people had epileptic seizures, three with primary generalized epilepsy and the other three with focal epilepsy of temporal origin (associated with secondary generalization). While the onset of epilepsy was identified in three people under the age of 5, it was under the age of 20 in one person and 50 in another. The age of onset was unknown in one patient.

Three people in this sample stopped having seizures by the age of 20 and one at an unknown age after 20. One person, aged 27, continues to have seizures despite anticonvulsant medication, and the one with late onset seizures is controlled on anticonvulsant medication.

Table 2: EEG review results: features seen in 32 EEGs on 18 subjects.

Rhythmic theta	14/32	43.75%
Slow alpha/background	10/32	31.25%
Paroxysmal slow episodes	10/32	31.25%
Normal alpha	?18/32	56.25%
Sharp/spike discharges	8/32	25%
Sleep phenomena	4/32	12.5%

EEG findings

A total of 34 EEG recordings were available from the 18 subjects, with nine subjects having more than one EEG (Table 2). Five of the six individuals with epilepsy (83%) had more than one EEG. The ages when recordings were made ranged from 3 to 66 years, with a mean age of 29.15.

Only five out of 18 subjects had a normal EEG. A rhythmic theta activity was noted in half of the sample (9/18). It was bilateral, usually between 5–7 c/s, and often of highest amplitude over precentral/frontal or temporal regions. In individuals with this theta activity, it was seen consistently in all the reports when serial recordings were available.

In several EEGs alpha activity was scanty (7–21%), dominated by widespread background activity or more prominent (slower) rhythmic activity. Slowing of the alpha rhythm and background activity was evident in five individuals (27.7%). Episodes of high amplitude slow activity were seen in four individuals (22%), but three of these were children.