Benign familial chorea: an association with intellectual impairment

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SUMMARY Twenty-four members of a family with benign familial chorea underwent testing for evidence of intellectual impairment. Lower verbal intelligence was found in affected individuals compared to unaffected family members, as were deficits in verbal abstract concept formation. These results challenge the notion that benign familial chorea uniformly spares the intellect in all kindreds.

Benign familial chorea is a hereditary disorder characterised by nonprogressive choreiform movements that appear in childhood and by the absence of dementia or mental retardation.¹⁻⁴ Genetic transmission of benign familial chorea follows the pattern of an autosomal dominant trait with incomplete penetrance⁵ though autosomal recessive transmission also has been reported.⁶

The preservation of mental faculties in individuals with benign familial chorea is a clinical hallmark distinguishing them from patients with Huntington's chorea. In cases of benign familial chorea where intellectual function has been formally assessed, scores often fall in the mildly retarded to low average range of intelligence, but typical indicators of organically based cognitive deterioration are not evident.¹⁻⁴ When borderline mental retardation has been noted, it has been uniformly attributed to socioeconomic factors or variables not related to CNS dysfunction.¹⁻⁴ In none of these cases, however, were attempts made to assess unaffected family members as a basis for comparison.

On the other hand, certain authors have described instances of educational difficulty and patterns of test results consistent with specific learning disabilities in patients with benign familial chorea.⁵ During clinical evaluation of a large kindred of

benign familial chorea in Alabama, we also found that many of the affected children were described by school officials as "slow learners", "learning disabled", "handicapped", and "needing special education". Intellectual assessments of a small sample of affected and unaffected individuals tended to support the impression that intellectual impairment was associated with benign familial chorea in this kindred. The present investigation has pursued these preliminary findings through a cross-sectional study of most of the family. The specific aims of this study were (1) to determine if intellectual impairment is associated with benign familial chorea, and (2) if so, to determine the nature of this impairment.

Methods

A four-generation Caucasian pedigree of benign familial chorea was identified in and about Jefferson County, Alabama. The disease appeared as a mutation in a woman (the *proposita*) who transmitted it to four of her five daughters (fig). Affected family members were diagnosed on the basis of historical information and physical findings by a board-certified neurologist (TWF) independently of the intellectual assessment.

Affected members in the kindred manifested choreiform movements of the hands and feet while awake early in the first year of life. The frequency and amplitude of the movements gradually increased into early childhood and occasionally as late as adolescence, after which they remained stable or improved somewhat. Chorea was subtle in some family members and obvious in others. Psychomotor development of those with benign familial chorea was commonly delayed. HLA typing in 20 individuals was normal. No other systematic laboratory studies were performed. In two individuals, haemogram, urine analysis, blood chemistries, ASO titre, ceruloplasmin,

Presented in part at the International Neuropsychological Society, Pittsburgh, Feb. 1982.

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Received 5 May 1983 and in final revised form 27 October 1983.
Accepted 18 November 1983

Table 1 Demographic and IQ Data in Benign Familial Chorea (BFC)

	BFC Affected Family Members				Unaffected Family Members			
	N	Mean	SD	Range	N	Mean	SD	Range
Age	18	21.28	11.43	6-45	6	17.83	12.35	5-40
Education	18	7.06	2.82	1-12	6	6.17	3.97	1-12
Verbal IQ	18	77.00	11.69	56-96	6	91.50	18.15	70-120
Performance IQ	18	83.11	14.80	57-103	6	86.67	9.11	76-100
Full scale IQ	18	78.33	13.07	56-98	6	88.50	14.57	71-112
Information	18	5.33	1.71	2-8	6	7.17	3.19	4-13
Comprehension	18	6.61	2.52	3-12	6	7.00	2.28	5-10
Arithmetic	18	6.06	2.13	3-10	6	7.50	2.26	6-12
Similarities	18	7.11	3.05	0-10	6	10.33	4.13	5-15
Digit Span*	17	7.65	1.54	6-11	5	8.80	3.63	4-12
Vocabulary	18	4.50	2.87	0-10	6	7.33	3.72	4-14
Coding*	17	6.00	1.80	2-9	5	7.40	2.07	4-9
Picture completion	18	8.06	2.36	3-12	6	6.83	1.94	3-8
Block design	18	6.78	3.00	2-12	6	7.17	1.72	5-9
Picture arrangement*	17	8.06	3.51	3-16	5	8.60	4.16	4-15
Object assembly*	17	7.82	3.03	2-12	5	8.40	2.19	6-10

*Scores from these subtests were unavailable for the two individuals who were administered the WPPSI.

unaffected family members.

For the dependent variables of age, educational level, and the 14 psychometric variables, the two samples were compared via a series of one-way analyses of variance using the least squares method for unequal sample sizes.* Chi-square analyses were used to determine if the samples differed in sexual composition of handedness.

Results

The two samples did not differ as a function of age ($F(1,22) = 0.537$, $p < 0.54$), education ($F(1,22) = 0.37$, $p < 0.55$), sex ($\chi^2(1) = 0.127$, $p < 0.28$), or handedness ($\chi^2(2) = 0.800$, $p < 0.33$). Inspection of the table indicates that the unaffected family members had higher mean intelligence test scores on 13 of the 14 variables with Picture Completion being the one exception. The two samples differed significantly on Verbal IQ ($F(1,22) = 5.24$, $p < 0.03$) and Similarities ($F(1,22) = 4.23$, $p < 0.05$) scores. Mean differences between the samples on Information ($F(1,22) = 3.30$, $p < 0.08$), and Vocabulary ($F(1,22) = 3.79$, $p < 0.06$) subtest scores also approached statistical significance.

Discussion

The IQ data depicted in the table and the results from the analyses of variance indicate that impaired verbal intellectual abilities are associated with the presence of benign familial chorea, independent of sex and education, in a kindred having a common socioeconomic background. The affected family members' verbal concept formation skills (Similarities subtest) were the most clearly affected abilities, with a tendency for their word knowledge

(Vocabulary subtest) and general fund of information (Information subtest) also to be affected. The nature of the global and specific intellectual deficits suggests that, relative to the nonaffected individuals, affected individuals from this kindred should perform more poorly on academic tasks requiring verbal mediation and abstract reasoning. These results are consistent with a case report in the literature⁵ and reports from the local school system concerning the presence of learning disabilities in several of the affected subjects in this kindred.

To assess the possibility that these group differences were due to drug related suppression of test performance, the Verbal IQ and Similarities scores from the four individuals taking medication were examined. Two of the three individuals taking oxazepam and the individual taking thorazine had Verbal IQ scores ranging from 84 to 93 and Similarities scores of 10, 10, and 9 respectively. These scores are well above the mean scores of the group with benign familial chorea for these variables (see table). The remaining individual taking oxazepam had a Verbal IQ of 72 and a Similarities score of 2 which are both very close to the group mean scores for the affected individuals depicted in the table. These data appear to rule out the suppression of test performance due to medication and if anything suggest that task performance may have been enhanced.

In conclusion, the results of this investigation suggest that intellectual impairment is associated with benign familial chorea in the present kindred. Further studies are obviously needed to demonstrate whether this relationship is universal or not. These results challenge the notion that benign familial chorea uniformly spares the intellect in all kindreds.

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