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Praxic and nonverbal cognitive deficits in a large family with a genetically transmitted speech and language disorder

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ABSTRACT A pronounced speech and language disorder affecting half of the 30 members of the four-generational KE family has been attributed by some researchers to a specific defect in the generation of morphosyntactic rules. The reported selectivity of the impairment has led to the view that the affected members suffer from a grammar-specific disorder. Our investigations of the same KE family indicate that the inherited disorder has a broad phenotype which transcends impaired generation of syntactical rules and includes a striking articulatory impairment as well as defects in intellectual, linguistic, and orofacial praxic functions generally. Although the evidence from this family thus provides no support for the existence of "grammar genes," their linguistic difficulties do constitute a prominent part of their phenotype. Investigations of the neural and genetic correlates of their disorder could therefore uncover important clues to some of the bases of the primary human faculties of speech and language.

A severe speech and language disorder has been described in about half of the male and female members of a large family (KE) of four generations. This implies that the disorder is transmitted by an autosomal dominant gene (1). Gopnik (2) and Gopnik and Crago (3) have reported findings suggesting that the affected members suffer from a specific impairment in grammar, namely, a selective inability to generate syntactic rules such as those for tense, number, and gender. The reported selectivity of the impairment has led these authors (2, 3) and others (4–6) to conclude that the KE family has an inherited grammar-specific disorder and thus provides evidence for the existence of "grammar genes" (5). Our initial (7, 8) and present investigations of the same (KE) family indicate that the affected members' disorder transcends the generation of morphosyntactic rules to include impaired processing and expression of other areas of grammar, grossly defective articulation of speech sounds, and, further, a severe extralinguistic orofacial dyspraxia. In addition, the affected family members have both verbal and performance intelligence quotient (IQ) scores that are on average 18–19 points below those of the unaffected members. This psychological profile indicates that the inherited disorder does not affect morphosyntax exclusively, or even primarily; rather, it affects intellectual, linguistic, and orofacial praxic functions generally. The evidence from the KE family thus provides no support for the proposed existence of grammar-specific genes.

Fig. 1 shows the family pedigree, with the affected and unaffected members provisionally classified on the basis of presence or absence of an articulatory impairment, best characterized as a speech dyspraxia. This impairment is so pronounced as to render the speech of many of the affected members unintelligible to the naive listener, and it is so disabling, particularly during childhood, that they have been taught a sign system to augment their speech. Despite intensive speech therapy, to the naive listener their discourse is still unintelligible over the telephone and on audio tapes, particularly when heard out of context.

Twenty-one members of the KE family (affected, $n = 13$; unaffected, $n = 8$) were evaluated on tests of language production and comprehension, including grammar, phonology, reading, and writing. (One additional unaffected member, III-18, was evaluated at age 3 only on clinical screening tests of speech and language function.) The 13 affected members had a mean age at testing of 24.4 years (range 6–75), whereas the 8 unaffected ones had a mean age of 14.1 years (range 8–21). With the exception of individual II-2, these family members are the same as those examined by Gopnik (2).

As indicated in Table 1, the affected members were significantly impaired relative to the unaffected ones on all but two of the language tests (object naming and picture vocabulary). When the second generation of the family was excluded from the comparison to better equate the affected and unaffected members for age at testing, the reliability of the group differences often increased and affected members were now impaired on all tests but one (object naming).

Against the background of such a diffuse speech and language disorder it is to be expected that the affected members would evidence grammatical deficits as well. Table 2 shows impaired performance on tests of grammatical structure, except for one subtest assessing grammaticality judgements of morphologically marked real words. Of the four tests of grammar, three specifically assess the ability to process inflections. The remaining test [TROG: Test for Reception of Grammar (16)] evaluates not only morphosyntactic knowledge but, on 3 of its 20 blocks, receptive knowledge of sentence embedding in the form of relative clauses. The affected and unaffected members differed significantly ($t = 2.98$, df = 15, $P < 0.01$) on these three blocks as well, indicating that the processing impairment of the affected members extends beyond inflections to include other aspects of grammatical structure.

Of particular interest are the results we obtained on a test of tense production designed by K. E. Patterson (personal communication). This test assesses the ability to change common regular and irregular verb forms from the present to the past tense and vice versa ($n = 20$ trials each). It was previously suggested (2, 3) that the affected family members suffer from a selective morphosyntactic defect, reflected in the generation of the inflected forms of regular verbs, since they were relatively unimpaired in the production of the appropriate forms of irregular verbs. The difference was attributed to the fact that the irregular verbs are not governed by rules but rather are learned as lexical items (4). In the present study, although the affected members were clearly impaired on the test of tense production, their impairment was equally evident

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Abbreviation: IQ, intelligence quotient.

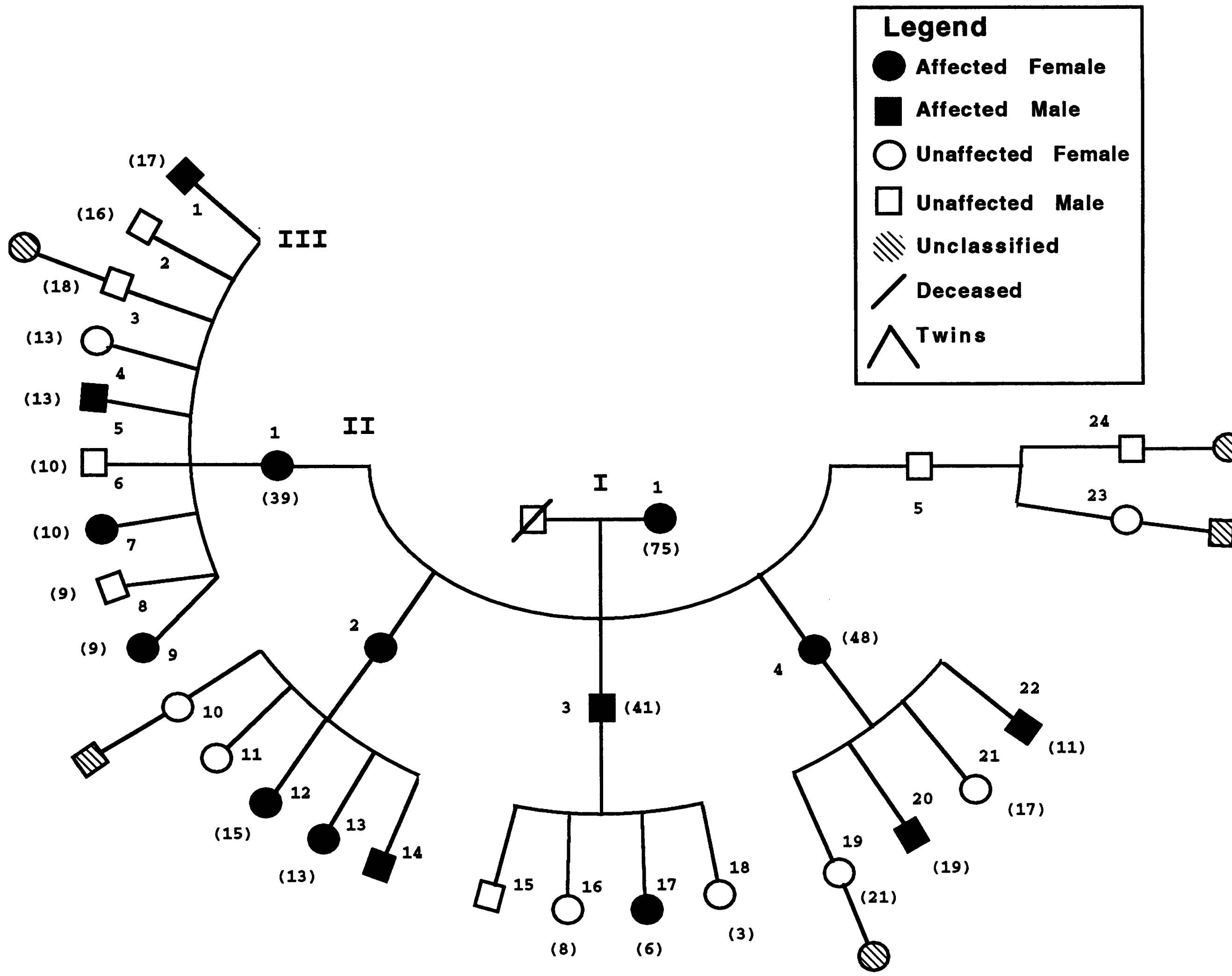

FIG. 1. Family pedigree showing the provisional classification of affected and unaffected members. Roman numerals indicate the generation, and arabic numerals outside parentheses indicate the member's pedigree number within a generation. (Numbers within parentheses indicate age at testing for those members who participated in this study.) Fourth generation members are infants and so have not yet been classified.

on irregular forms (t = 5.79, df = 16, $P < 0.001$) and regular forms (t = 8.08, df = 16, $P < 0.001$) (Fig. 2).

The finding of an impairment on irregular verb forms cannot have arisen because such forms occur infrequently. On the contrary, irregular verbs occur with a higher frequency than do regular ones; yet the affected members were impaired to about the same degree on these as on the regular forms.

An unexpected feature of the affected members' responses on this test was the incidence of overregularizations, which constituted 41% of all errors. The occurrence and frequency of such errors demonstrate that the affected members possess at least some knowledge of the inflectional rule for marking tense. Table 3 presents the incidence of overregularized forms in the affected members.

The discrepancy between the present results on the test of tense production and those reported by Gopnik (2) and Gopnik and Crago (3) may be due to the use of a larger sample of verbs and test sentences in the present study than in the earlier ones. For example, Gopnik and Crago (3) presented the family members with only 10 test sentences (4 requiring past tense, 2 future tense, 2 present tense, and 2 progressive aspect forms). Only two regular forms ("kissed" and "walked") and two irregular forms ("went" and "was") were contrasted. It is clear from the use of a much larger sample of verbs that while the affected group are significantly impaired on both regular and irregular verbs, their use of overregularization indicates that they know more about the rule for English past tense than was previously claimed (2, 3).

The pronounced impairment in articulation raises the possibility that there may be an underlying praxic disorder that affects oral and facial movements of all kinds. To examine this possibility, we designed two tests of orofacial praxis. The first test assessed the production of animal and machine noises (6 items) and meaningless noises (e.g., "click your tongue"; 5 items), singing (e.g., "hum a tune"; 4 items), the execution of nonvocal movements (e.g., "bite your lip"; 10 items), eyelid movements (e.g., "close your left eye"; 4 items), and movement sequences (e.g., "stick out your tongue, lick your upper lip, and smack your lips"; 3 sequences). The movements were performed to command. Nonparametric analyses revealed significant differences between the affected (n = 12) and unaffected (n = 7) groups (Z = −3.55, P = 0.0004).

The foregoing impairment could have been due to a difficulty in understanding the commands, even though, from their general behavior during the session, this did not appear to be a major factor. Nevertheless, to examine this possibility we carried out a second test on the affected members (n = 11). They were asked to imitate 8 simple movements (e.g., opening the mouth), 9 complex movements (e.g., protruding the lower lip and jaw), 11 sets of 3 parallel movements (e.g., opening the mouth, protruding the tongue, and vocalizing), and 11 sets of 3 sequential movements (e.g., closing the lips, then opening the

Table 1. Scores of KE family members on tests of language

Test (ref.) [Instructions]	Maximum score	Score: Affected	Score: Unaffected	t value	P	P (third generation only)
Digit span (9, 10) [Repeat this list of numbers (forwards and backwards)]	10 ± 3	6.3 ± 2.40	10.00 ± 2.83	3.14	0.005	0.001
Alphabet words [Repeat this word (each begins with a different letter)]	39	29.58 ± 4.66	38.75 ± 0.71	6.70	<0.001	<0.001
Repetition of words (11) [Repeat this word]	40	18.00 ± 5.92	37.33 ± 2.81	7.50	<0.001	<0.001
Repetition of nonwords (11) [Repeat this nonword exactly as I say it]	40	16.38 ± 5.44	34.88 ± 5.38	7.59	<0.001	<0.001
Lexical decision (11) [Is this a real English word?]	60	46.91 ± 6.95	54.57 ± 4.89	2.53	0.022	0.004
Sentence repetition (12) [Repeat this sentence exactly as I say it]	20	3.64 ± 5.01	12.25 ± 5.75	3.48	0.003	0.001
Object naming* (13) [Tell me the name of the object in this picture]	36	26.33 ± 4.38	30.13 ± 2.80	0.02	0.903	0.307
Picture vocabulary* (14) [Show me the picture for this word]	100 ± 15	65.38 ± 11.37	85.13 ± 10.84	4.26	0.054	0.038
Phoneme deletion (15) [Say this nonword without its first sound—e.g., varg → arg]	24	12.50 ± 5.62	22.14 ± 1.57	5.58	<0.001	0.001
Phoneme addition (15) [Say this nonword adding this first sound—e.g., arg → varg]	24	14.08 ± 5.98	21.00 ± 3.65	2.76	0.013	0.029
Nonword reading (15) [Read this nonword (pronounceable but meaningless)]	30	9.08 ± 5.11	23.00 ± 9.76	4.12	0.001	0.005
Nonword spelling (15) [Write this nonword as if it were a real English word]	30	7.83 ± 7.30	19.86 ± 7.95	3.36	0.004	<0.001
Rhyme production [Tell me a word that rhymes with this word]	24	13.00 ± 5.73	20.86 ± 7.47	2.52	0.023	0.011

Scores are presented as mean ± SD.
*Scores on this test correlated significantly with performance IQ ($P < 0.05$); the values reported are therefore based on an analysis of covariance.

mouth, then protruding the tongue). The performance of these subjects was compared with the performance of 55 age-matched normal control subjects. All the movements were videotaped and scored by inspection of the tapes. Fig. 3 shows that the affected members were impaired overall ($t = 5.07$, df $= 11$, $P < 0.001$). There was also a significant interaction of group × condition ($F = 2.92$, df $= 3$, $P < 0.05$), indicating that the affected members were significantly more impaired on the simultaneous and successive movements than on the single movements. Thus, the praxic deficits of the affected members are not confined to articulation but also involve nonlinguistic oral and facial movements.

A formal evaluation of intelligence (9, 10) was carried out to determine whether there was any indication of a selective impairment in the verbal domain, or whether nonverbal aspects of intelligence were impaired as well. The affected members obtained a mean verbal IQ of 75 (range, 59–91) [compare the unaffected members' mean score of 94 (range, 82–111)] and a mean performance IQ of 86 (range, 71–111) [compare the unaffected members' mean score of 104 (range, 84–119)]. [Six of the affected members and one of the unaffected obtained performance IQ scores below 85; this is commonly considered an exclusionary criterion for classification of a subject as having a specific language impairment (18, 19).] The difference between the IQ scores of the affected and unaffected members was statistically significant ($t = 4.25$, $P < 0.001$ for verbal IQ; $t = 3.28$, $P = 0.004$ for performance *IQ*). It is clear that the cognitive impairment of the affected family members is not confined to morphosyntax. Rather, it appears to extend to the verbal domain in general, and, indeed, is just as great in the nonverbal domain.

Our evidence that the affected members of the KE family suffer from severe extralinguistic difficulties does not imply that their speech and language impairments are uninformative with regard to the underlying genetic abnormality. In recent years evidence has accumulated in support of the genetic basis of speech and language disorders in many cases (18) and the heritability of associated problems of learning (19) and reading (20). Nevertheless, inherited difficulties in speech and language of such severity as that documented here, and in such a

Table 2. Scores of KE family members on tests of grammar

Test (ref.)	Maximum score	Score: Affected	Score: Unaffected	t value	P	P (third generation only)
Reception of grammar (16)	80	71.10 ± 4.82	76.57 ± 3.74	2.51	0.024	0.007
Tense production*	40	19.91 ± 5.24	37.43 ± 3.55	7.74	<0.001	<0.001
Production of morphological markers [includes derivations and inflections]† (17)						
Words	20	14.17 ± 2.86	19.29 ± 0.76	5.87	<0.001	<0.001
Nonwords	20	6.83 ± 2.76	16.00 ± 1.63	7.96	<0.001	<0.001
Judgements of morphological markers‡ (17)						
Words§	24	14.20 ± 5.15	20.86 ± 2.19	0.47	0.502	0.440
Nonwords	24	9.22 ± 3.67	14.14 ± 5.01	2.27	0.039	0.029

Scores are presented as mean ± SD.
*Past: "Every day I *wash* my clothes; yesterday I [*washed*] my clothes." Present: "Yesterday I *washed* my clothes; every day I [*wash*] my clothes." This test was designed by K. E. Patterson (personal communication).
†Words: "This creature is *smaller* than this one, but this creature must be the [*smallest*]." Nonwords: "This creature is *ponner* than this one, but this one must be the [*ponnest*]."
‡Which sentence is correct? Words: "Planes are *faster* than trains, or planes are *fastest* than trains." Nonwords: "Planes are *donker* than trains, or planes are *donkest* than trains."
§Scores on this test correlated significantly with performance IQ; the values reported are therefore based on an analysis of covariance.

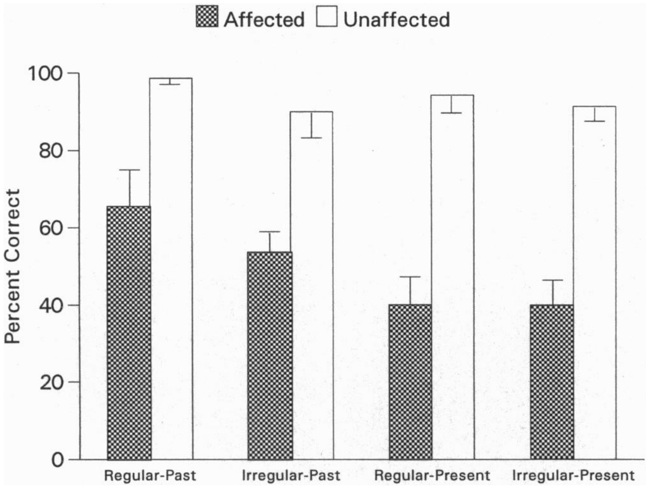

FIG. 2. Production of tenses. Scores are means ± standard errors. See Table 2 for examples of test items.

Table 3. Overregularizations made on the production of the past tense form of irregular verbs

Affected subject	No. of over-regularizations	Total no. of errors (per 10 verbs)
I-1	2	5
II-1	3	3
II-3	0	0
II-4	0	3
III-1	3	8
III-5	4	5
III-7	2	6
III-9	0	4
III-12	0	4
III-20	3	4
III-22	4	9

large cross-generational family, are extremely rare. While they constitute only a part of the affected members' total syndrome, these speech and language difficulties are an important aspect of their phenotype. Knowledge of the neural and genetic correlates of this phenotype could thus provide important clues to some of the underpinnings of the primary human faculties of speech and language as well as of the many other functions in which the affected members are also impaired.

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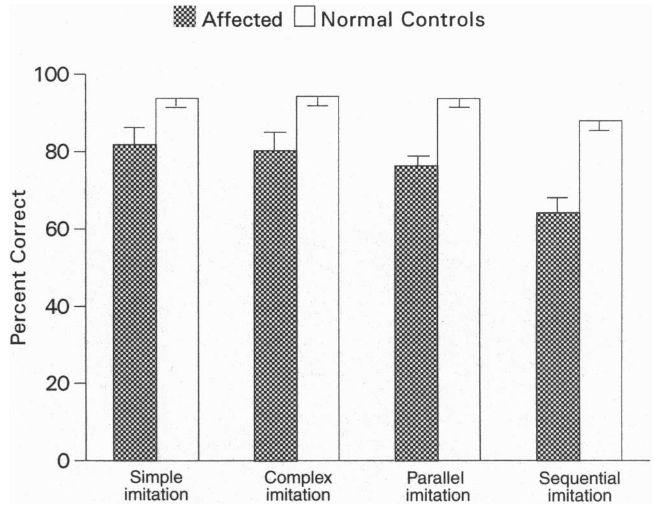

FIG. 3. Imitation of oral and facial movements. Scores are means ± standard errors.

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