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FULL-LENGTH ORIGINAL RESEARCH

Language in pediatric epilepsy

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SUMMARY

Purpose: This study examined the severity and range of linguistic impairments in young, intermediate, and adolescent youth with epilepsy and how these deficits were associated with illness effects, nonverbal intelligence, psychopathology, and reading.

Methods: Tests of language, intelligence, achievement, and structured psychiatric interviews were administered to 182 epilepsy youth, aged 6.3–8.1, 9.1–11.7, and 13.0–15.2 years, as well as to 102 age- and gender-matched normal children. Parents provided demographic, seizure-related, and behavioral information on their children.

Results: Significantly more epilepsy subjects had language scores 1 standard deviation (SD) below average than the age-matched control groups did. The intermediate and adolescent epilepsy groups also had significantly lower mean language scores compared to their matched controls. The older compared to the younger epilepsy groups had more language impairment and a wider range of linguistic deficits. Longer duration of illness, childhood absence epilepsy, psychiatric diagnosis, and socioeconomic status were associated with linguistic deficits in the young group. Prolonged seizures, lower Performance IQ, and minority status predicted low language scores in the intermediate epilepsy group. In the adolescent group, language impairment was associated with poor seizure control, decreased Performance IQ, and lower socioeconomic status. Linguistic and reading deficits were significantly related in each epilepsy group.

Conclusions: The age-related increase in linguistic impairment, different profiles of predictors in each age group, and the relationship of linguistic deficits with poor reading skills have important clinical, developmental, theoretical, and academic implications.

KEY WORDS: Language, Childhood absence epilepsy, Complex partial seizures, Cognition, Psychopathology, Development.

Despite the importance of language in children's academic performance [See review in (Schuele, 2004)] and social functioning (Beitchman et al., 1996; Conti-Ramsden & Botting, 2004; van Daal et al., 2007), this topic is understudied in children with epilepsy with normal intelligence. Although language measures, such as naming, verbal fluency, vocabulary, reading, and writing have been included in studies of the neuropsychological functioning and academic achievement of children with epilepsy (Fastenau et al., 2004; Aldenkamp et al., 2005; Hermann et al., 2006, 2007; Guimarães et al., 2007; Hermann et al., 2008), few have examined a wider range of basic linguistic skills. Moreover, most of the extant studies have been conducted on children with benign rolandic epilepsy (Staden et al., 1998; Gunduz et al., 1999; Lindgren et al., 2004; Monjauze et al., 2005; Northcott et al., 2005; Papavasiliou et al., 2005; Wolff et al., 2005; Northcott et al., 2006; Riva et al., 2007; Volkl-Kernstock et al., 2009), with only few studies on children with absence epilepsy (Henkin et al., 2003; Caplan et al., 2008), generalized epilepsy (Henkin et al., 2003), temporal lobe epilepsy (Schoenfeld et al., 1999; Caplan et al., 2004; Guimarães et al., 2007), and recent-onset epilepsy (Hermann et al., 2007). These studies demonstrate linguistic difficulties including impaired phonologic processing, verbal memory, auditory processing, verbal learning, and discourse skills.

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Filling in the gap in our knowledge about language in pediatric epilepsy and its correlates is important for clinical, academic, and theoretical reasons. From the clinical perspective, this topic deserves attention because children with poor academic achievement and cognitive problems frequently have undiagnosed language difficulties (Im-Bolter & Cohen, 2007) as well as behavioral and emotional problems (Cohen et al., 1993; Handwerk & Marshall, 1998; Vallance et al., 1999; Fujiki et al., 2002; Gilmour et al., 2004; Corapci et al., 2006). In fact, children presenting to psychiatric clinics for both internalizing and externalizing behavior problems (Cohen et al., 1993; Vallance et al., 1999) and conduct disorders (Gilmour et al., 2004) often have undiagnosed language and social pragmatic problems. In addition, there is a high rate of behavioral and emotional problems (Cantwell & Baker, 1987; Beitchman et al., 1996; van Daal et al., 2007; Conti-Ramsden & Botting, 2008), as well as poor literacy (Conti-Ramsden & Durkin, 2007) in children with language disorders. Given frequent learning, behavior, and social problems in children with epilepsy [See reviews in (Austin & Caplan, 2007; Drewel & Caplan, 2007; Plioplys et al., 2007)], the diagnosis and treatment of associated language problems is essential for the clinical care of these children.

The lack of studies on language in pediatric epilepsy is also striking from the theoretical perspective in view of interest in how epilepsy is related to the lateralization of linguistic functions. Therefore, recent functional (Berl et al., 2005; Yuan et al., 2006) and structural imaging studies (Gaillard et al., 2007) indicate asymmetry of cortical activity during linguistic tasks and atypical lateralization of language in individuals with epilepsy, including children.

In addition, little information is available on the developmental impact of ongoing seizures, particularly age of onset, chronological age, and duration of illness, on the development of children's language. Whereas some studies found a relationship of linguistic deficits with seizure variables (Schoenfeld et al., 1999; Caplan et al., 2004; Lindgren et al., 2004; Monjauze et al., 2005; Wolff et al., 2005), others have not confirmed these relationships (Northcott et al., 2005).

However, the interrelationship among seizure variables, cognition, and behavior [See review in (Austin & Caplan, 2007)] and relatively small sample sizes in prior studies preclude conclusions on how epilepsy might affect language development in children with epilepsy. Moreover, the protracted development of children's linguistic skills from the toddler period through adolescence [See review in (Caplan, 1996)] and parallel ongoing maturation of language-related brain regions (Sowell et al., 2003; Gogtay et al., 2004) further underscore the importance of this developmental question.

To determine if linguistic deficits in children with epilepsy who have normal intelligence are associated with age or developmental stage, the study presented in this report compared language measures in a large sample of young, intermediate, and adolescent epilepsy subjects to those of age- and gender-matched children without epilepsy. In addition to age, it examined the role played by cognitive, psychopathology, seizure, and demographic variables in the linguistic skills of the epilepsy subjects in each age group. It also investigated the relationship between linguistic and reading deficits in the epilepsy subjects.

We hypothesized that children with epilepsy would have significantly impaired linguistic skills compared to children without epilepsy in the young, intermediate, and older age groups, controlling for Performance IQ differences. On the basis of the assumption that the brains of younger children with active developmental processes (Ben-Ari & Holmes, 2006), such as language, are more vulnerable to the effects of ongoing seizures than are those of older children, we predicted that the young epilepsy subjects would have significantly more linguistic impairments than the intermediate group, who in turn, would have more deficits than the older group. Because chronologic age, age of onset, and duration of illness are related developmental variables, we also examined which of these three variables were related to linguistic deficits within each age group.

In each epilepsy age group, we hypothesized that children with more severe illness would have significantly more linguistic deficits than those with less severe illness. Given the previously reviewed inconsistent relationship among illness severity, cognition, behavior, and language, we explored if, above and beyond effects of seizure variables, Performance IQ, psychopathology, and demographic variables (i.e., ethnicity, socioeconomic status) would be associated with language impairment. Finally, we posited an association of poor reading with impaired linguistic skills in each epilepsy age group.

Methods

Subjects

The study included 284 children, 104 with cryptogenic epilepsy who had complex partial seizures (CPS) and 78 children with childhood absence epilepsy (CAE), aged 6.3–15.2 years, as well as 102 children without epilepsy, aged 6.6–15.5 years. Table 1 presents demographic, perinatal, and family history features of the sample divided into young, intermediate, and adolescent epilepsy and control groups. A detailed description of the diagnosis, inclusionary criteria, exclusionary criteria, and recruitment of the children with epilepsy and the children without epilepsy can be found in Caplan et al., (2004) and Caplan et al., (2008).

There was a significantly higher rate of lower socioeconomic status (SES) subjects in the adolescent epilepsy

Table 1. Demographic, perinatal, family history, IQ, and psychopathology features by age group

	Epilepsy (n = 182)			Normal (n = 102)		
	Young	Intermediate	Adolescent	Young	Intermediate	Adolescent
n	59	87	36	29	55	18
Mean age (SD) yrs	7.18 (0.90)	10.42 (1.27)	14.14 (1.11)	7.45 (0.82)	10.14 (1.130)	14.20 (1.32)
Age range (yrs)	6.3–8.1	9.1–11.7	13.0–15.2	6.6–8.3	9.0–11.3	12.9–15.5
Male	44%	49%	50%	38%	51%	44%
SES (Low)[a]	41%	40%	42%	35%	31%	11.8%
Minority	44%	49%	40%	55%	42%	22%
Delivery problems	13%	10.3%	20.7%	17.4%	13.5%	6.2%
Pregnancy problems	28%	28%	17.2%	26.1%	37.8%	18.7%
Family History						
Epilepsy[b]	20.7%	23.1%	8.3%	6.2%	4.3%	0%
Psychopathology	20%	30%	50%	18.7%	26.1%	37.5%
Full scale IQ[c]	94.4 (15.13)	94.4 (14.44)	91.4 (14.00)	112.3 (14.25)	114.0 (11.36)	116.3 (10.60)
Verbal IQ[d]	93.7 (16.34)	94.2 (16.00)	91.5 (13.06)	112.0 (14.30)	116.8 (12.43)	119.1 (9.80)
Performance IQ[e]	95.0 (15.97)	95.0 (12.99)	91.7 (16.22)	110.6 (15.23)	109.8 (10.94)	110.4 (12.41)
Psych. diagnosis[f]	46.5%	57.6%	55.6%	7.4%	18.4%	17.7%
Disruptive	17.2%	16.5%	22.2%	0%	6.1%	5.9%
Affective/anxiety	20.7%	15.3%	8.4%	3.7%	8.2%	0%
Disrupt/affect/anx.	6.9%	22.3%	25%	3.7%	2.0%	5.9%
Other	1.2%	3.5%	0%	0%	2.1%	5.9%

Comparing epilepsy and normal groups:
[a]Adolescent X^2 (1) = 4.73, $p < 0.03$.
[b]Intermediate X^2 (1) = 3.75, $p < 0.05$.
[c]Young t (86) = 4.05, $p < 0.0001$, Intermediate t (140) = 7.60, $p < 0.0001$, Adolescent t (52) = 5. 38, $p < 0.0001$.
[d]Young t (86) = 3.86, $p < 0.0002$, Intermediate t (134) = 8.06, $p < 0.0001$, Adolescent t (52) = 6.45, $p < 0.0001$.
[e]Young t (86) = 2.72, $p < 0.008$, Intermediate t (134) = 5.65, $p < 0.0001$, Adolescent t (52) = 3.03, $p < 0.004$.
[f]Young X^2 (1)12.60, $p < 0.0004$, Intermediate X^2 (1)19.35, $p < 0.0001$, Adolescent X^2 (1)6.9275, $p < 0.009$.
SD, standard deviation.

group and of a family history of epilepsy in the intermediate epilepsy group compared to their respective normal control groups (Table 1). However, there were no significant differences in the demographic variables of the epilepsy and normal age groups. Fifty-four percent of the subjects (n = 153) were recruited during 1994–1998 and 46% (n = 131) during 1999–2003, with similar proportions of old and new cohorts in the young (55%/45%), intermediate (44%/56%), and adolescent age groups (44%/56%).

The parents' and children's medical records provided information on seizure frequency during the preceding year, current antiepileptic drugs (AEDs), age of onset, illness duration, the number of febrile convulsions, and prolonged seizures (i.e., >5 min) needed to examine hypotheses related to illness severity (Table 2). Of the 104 CPS patients, 29 had no focal epileptic activity according to electroencephalography (EEG) done at the time of the initial epilepsy diagnosis; 22 had left, 23 right, 19 bilateral epileptic activity, and about one-third had epileptic activity in the frontotemporal region. EEG findings were unavailable for 11 subjects. Eight CPS patients had secondary generalization, 12 CAE had generalized tonic–clonic convulsions, and 34 (28 CPS, 6 CAE) had background slowing. In the current study, 56% of the CPS and 36% of the CAE subjects were recruited from tertiary centers and 44% CPS and 64% CAE subjects from community sites. Significantly more subjects were recruited from the community in the CAE versus the CPS

Table 2. Epilepsy features of study subjects by age group

	Young	Intermediate	Adolescent
CPS	26	50	28
CAE	33	37	8
Age of onset (years)[a]	4.28 (1.83)	6.06 (3.02)	8.03 (3.95)
Duration (years)[b]	2.95 (1.81)	4.36 (3.10)	6.08 (4.08)
Uncontrolled seizures[c]	48%	53%	69%
Antiepileptic drugs			
None	6.8%	4.6%	5.6%
Monotherapy	72.9%	75.9%	58.3%
Polytherapy	20.3%	19.5%	36.1%
Febrile convulsions	15.2%	17.1%	20%
Prolonged seizures	23.7%	29.1%	40%

[a]$F(2,179) = 18.94$, $p < 0.0001$.
[b]$F(2,179) = 12.52$, $p < 0.0001$.
[c]Uncontrolled seizures = >5 seizures in year prior to participation in study.
CAE, childhood absence seizure; CPS, complex partial seizures.

subjects [$X^2(1) = 7.06, p < 0.008$] and in the new (64%) versus the old (36%) cohort [$X^2(1) = 4.88, p < 0.03$].

Procedures

This study was conducted in accordance with the policies of the Human Subjects Protection Committees of the University of California, Los Angeles. Written informed assents and consents were obtained from all subjects and their parents, respectively.

Language

All subjects underwent testing with the Test of Language Development (TOLD)-2 (Newcomer & Hammil, 1988). We administered the TOLD-2 Primary (TOLD-P), normed for children aged 4–8 years, to 59 epilepsy and 29 normal subjects; the TOLD-2 Intermediate (TOLD-I), normed for children aged 8–12 years, to 87 epilepsy and 55 children without epilepsy; and the Test of Adolescent Language (TOAL), normed for adolescents aged 12–18 years, to 36 epilepsy and 18 normal subjects. The TOLD manual provides normative data and findings of studies indicating reliability and validity of the instruments (Newcomer & Hammil, 1988). Tables 3, 4, and 5 present the TOLD-P, TOLD-I, and TOAL quotients and subtests used to generate these quotients**.** The quotients were the dependent variables in the study's data analysis**.**

Unlike the TOAL, the TOLD-P and TOLD-I do not have a reading subscale. We, therefore, included reading scores from the Wechsler Individual Achievement Test (WIAT) (Wechsler, 1992) for the young and intermediate age groups to determine if the predicted impaired linguistic skills of these children were associated with poor reading.

Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS)

The Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiologic Version (K-SADS-E) (Orvaschel & Puig-Antich, 1987) during 1994–1998 and the Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997) during 1998–2005, were administered separately to each child and parent by R.C. or a research assistant trained in the administration of the interview, as detailed in (Caplan et al., 2004).

Cognition

The Wechsler Intelligence Scale for Children-Revised (WISC-R), (Wechsler, 1974) given to children tested from 1994–1998, and the Wechsler Intelligence Scale for Children-3rd edition (WISC-III) (Wechsler, 1991), administered to children tested from 1999–2005, generated Full Scale, Verbal, and Performance IQ scores (See detailed description in (Caplan et al., 2004). All study subjects had IQ scores of 70 or higher.

Data analysis

Prior to statistical analyses, all data were inspected for outliers, skewness, kurtosis, and homogeneity of variance to ensure their appropriateness for parametric statistical tests. Multivariate analyses of variance (MANCOVAs), controlling for demographic variables (namely, gender, socioeconomic status, and ethnicity) and Performance IQ, were used to compare the three epilepsy and normal age groups on mean language quotient scores. Separate analyses were conducted for measures in each age level (young, intermediate, and adolescent). Given the relationship of

Table 3. TOLD-P quotients and predictors in young epilepsy group

Quotients	Subtests Generating Sum of Standard Scores	Predictors: Seizure-related	Predictors: Other
Spoken	Picture Vocabulary, Oral Vocabulary, Grammatical Understanding, Sentence Imitation, Grammar Completion, Word Discrimination, Word Articulation	Duration: $X^2(1) = 4.45, p < 0.04$	
Listening	Picture Vocabulary, Grammatical Understanding, and Word Discrimination	Duration: $X^2(1) = 5.65, p < 0.02$ CPS/CAE: $X^2(1) = 5.32, p < 0.03$	
Speaking	Oral Vocabulary, Sentence Imitation, Grammar Completion	Duration: $X^2(1) = 9.97, p < 0.002$	SES: $X^2(1) = 6.31, p < 0.02$
Semantics	Picture Vocabulary, Oral Vocabulary	Duration: $X^2(1) = 8.48, p < 0.004$	Ethnicity: $X^2(1) = 3.97, p < 0.05$
Syntax	Grammatical Understanding, Sentence Imitation, Grammar Completion	Duration: $X^2(1) = 8.20, p < 0.005$	
Phonology	Word Discrimination, Word Articulation	Duration: $X^2(1) = 5.43, p < 0.02$	Affective/Anxiety: $X^2(4) = 8.55, p < 0.004$

CPS/CAE, complex partial seizures or childhood absence epilepsy; CAE, childhood absence epilepsy; SES, socioeconomic status; Affective/anxiety, depression and/or anxiety disorder diagnosis.

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Table 4. TOLD-I quotients and predictors in intermediate epilepsy group

		Predictors	
Quotients	Subtests Generating Sum of Standard Scores	Seizure-related	Other
Spoken	Sentence Combining, Vocabulary, Word Ordering, Generals, Grammar Comprehension, Malapropisms	Prolonged: $X^2(1) = 8.40, p < 0.004$	PIQ: $X^2(1) = 7\ 0.51, p < 0.006$
Listening	Vocabulary, Grammar Comprehension, Malapropisms	Prolonged: $X^2(1) = 7.90, p < 0.005$	PIQ: $X^2(1) = 9.48, p < 0.002$
Speaking	Sentence Combining, Word Ordering, Generals	Prolonged: $X^2(1) = 6.52, p < 0.02$	PIQ: $X^2(1) = 5\ 0.75, p < 0.02$ Ethnicity: $X^2(1) = 11.48, p < 0.0007$
Semantics	Vocabulary, Generals, Malapropisms	Prolonged: $X^2(1) = 5.07, p < 0.03$	PIQ: $X^2(1) = 9\ 0.83, p < 0.002$ Ethnicity: $X^2(1) = 6.35, p < 0.02$
Syntax	Sentence Combining, Word Ordering, Grammar Comprehension	Prolonged: $X^2(1) = 10.50, p < 0.002$	PIQ: $X^2(1) = 6.15, p < 0.01$ Ethnicity: $X^2(1) = 5.01, p < 0.03$

Prolonged = seizures lasting 5 or more minutes; PIQ = Performance IQ.

language with gender, SES, and ethnicity (Noble et al., 2007), we controlled for these demographic measures in the between-group comparisons. We also controlled for Performance IQ in these comparisons, since there are significant differences in IQ between the epilepsy patients and normal controls in this study (Table 1), and without controlling for Performance IQ, group differences in language scores may be simply due to generally lower cognitive ability levels in these subjects. Age was not used as a covariate in these analyses, since the language quotients are themselves age-corrected. We used Fisher's exact tests to compare the proportion of epilepsy and normal subjects within each age group who had average language scores to those with language scores 1 standard deviation (SD) below average using the population mean of 100 and standard deviation of 15. All tests were two-tailed, and a significance level of 0.05 was adopted.

Using logistic regression, we then determined which of the Performance IQ, psychopathology, seizure, and demographic variables (age, gender, SES, ethnicity) were predictive of impaired language scores in each of the epilepsy age groups. All the epilepsy subjects were classified as either impaired (performing 1 SD below average) or not impaired. The seizure variables that were used as predictors included type of epilepsy, age of seizure onset, duration of illness (time from age of onset to participation in study), poor seizure control (i.e., >5 seizures in year prior to participation in the study), history of prolonged seizures, history of febrile convulsions, and number of AEDs (subdivided into no AEDs, monotherapy, and polytherapy). To reduce the number of predictors, we first examined pair-wise relationships between all the predictors of interest and the language measures, and considered only those variables that showed at least a trend ($p < 0.1$). We included all these variables as predictors in a stepwise logistic regression model, and determined a subset of predictors that contributed ($p < 0.1$). We then computed a logistic regression using this subset of predictors and carefully pruned the resulting model by verifying the importance of each predictor included in the model and checking for variables whose coefficients changed markedly in magnitude when other variables were excluded. This process of deleting, refitting, and verifying was performed until a final model was obtained that explained the data. Such models were estimated for each of the quotients in the three age groups. The findings from these final models, which included no more than four predictors, are presented in the Results section.

Results

Between-group differences

IQ and psychopathology

The epilepsy groups had significantly lower IQ scores and higher rates of a psychiatric diagnosis than their respective age-matched control groups (Table 1). Among the 64 epilepsy subjects with disruptive disorder diagnoses, 77% (n = 49) had attention deficit hyperactivity disorder (ADHD): 16.1% in the young group, 32.8% in the intermediate epilepsy group, and 46.3% in the adolescent groups. Sixty epilepsy subjects (young 23.7%, intermediate 29.8%, adolescent 25%) had affective/anxiety disorder diagnoses, with anxiety disorder diagnoses in 63%, depression in 20%, and both anxiety and depression in 17% (Table 1).

Language scores

MANCOVAs of the mean language scores (Fig. 1), with gender, ethnicity, SES and Performance IQ as covariates demonstrated significant differences in the intermediate ($F_{5,124} = 3.\ 80$, $p < 0.003$) and adolescent epilepsy ($F_{11,34} = 4.56$, $p < 0.0003$) versus normal groups but not in the young group ($F_{6,68} = 1.80$, $p < 0.11$). Post hoc ANCOVAs revealed that these findings were accounted

Table 5. TOAL Quotients and Predictors in Adolescent Epilepsy Group.

Quotients	Subtests Generating Sum of Standard Scores	Predictors	
		Seizure-related	Other
Adolescent Language	Listening Vocabulary, Listening Grammar, Speaking Vocabulary, Speaking Grammar, Reading Vocabulary, Reading Grammar, Writing Vocabulary, Writing Grammar	Seizure control: $X^2(1) = 3.73$, $p < 0.06$	
Listening	Listening Vocabulary, Listening Grammar		PIQ: $X^2(1) = 6\,0.39$, $p < 0.01$ SES: $X^2(1) = 6\,0.81$, $p < 0.01$
Speaking	Speaking Vocabulary, Speaking		
Reading	Reading Vocabulary, Reading Grammar		
Writing	Writing Vocabulary, Writing Grammar		PIQ: $X^2(1) = 9\,0.83$, $p < 0.002$ Ethnicity: $X^2(1) = 6.35$, $p < 0.02$
Spoken Language	Listening Vocabulary, Listening Grammar, Speaking Vocabulary, Speaking Grammar		PIQ: $X^2(1) = 4.58$, $p < 0.04$ SES: $X^2(1) = 4.41$, $p < 0.04$
Written Language	Reading Vocabulary, Reading Grammar, Writing Vocabulary, Writing Grammar	Seizure control: $X^2(1) = 5.66$, $p < 0.02$	
Vocabulary	Listening Vocabulary, Speaking Vocabulary, Reading Vocabulary, Writing Vocabulary.	Seizure control: $X^2(1) = 3.56$, $p < 0.06$	
Grammar	Listening Grammar, Speaking Grammar, Reading Grammar, Writing Grammar.	Seizure control: $X^2(1) = 3.56$, $p < 0.06$	
Receptive Language	Listening Vocabulary, Listening Grammar, Reading Vocabulary, Reading Grammar		PIQ: $X^2(1) = 7.31$, $p < 0.007$
Expressive Language	Speaking Vocabulary, Speaking Grammar, Writing Vocabulary, Writing Grammar	Duration: $X^2(1) = 4.07$, $p < 0.04$	

PIQ, Performance IQ; SES, socioeconomic status.

for by significantly lower mean Spoken Language, Listening, Speaking, Semantic, and Syntax Quotients in the intermediate epilepsy group compared to the normal group ($t_{134} = 3.22$–4.29, $p < 0.002$–0.0001); and mean TOAL adolescent Language, Listening, Speaking, Reading, Writing, Speech Language, Written Language, Vocabulary, Grammar, Receptive Language, and Expressive Language Quotients in the adolescent epilepsy compared to the adolescent normal group ($t_{45} = 2.76$–4.53, $p < 0.008$–0.0001).

As evident from Table 6, significantly more young, intermediate, and adolescent epilepsy subjects had language scores 1 SD below average than individuals in age-matched control groups. Across age groups, significantly more adolescent epilepsy subjects had language scores 1 SD below the mean than the young and intermediate patients [X^2 (1) = 11.56 – 20.89, $p < 0.001$–<0.0001].

Cohort effects contributed to the between-group mean language quotient findings in the young but not in the intermediate and adolescent groups. Therefore, the old cohort had significantly lower scores then the new cohort for the Speaking Quotients in the young epilepsy [t (49) = 5.27, $p < 0.0001$] and young normal subjects [t (25.3) = 4.70, $p < 0.0001$] and for the Listening [t (49) = 2.58, $p < 0.02$] and Spoken Language Quotients [t (49) = 2.38, $p < 0.03$] in the young epilepsy subjects. Despite, lower Listening [t (53) = 3.99, $p < 0.0002$] and Semantics Quotients [t (53) = 2.80, $p < 0.007$] in the intermediate normal subjects and Writing Quotient in the adolescent normal subjects [t (16) = 2.15, $p < 0.05$] of the old versus the new cohort, these two epilepsy groups had significantly lower mean scores than the matched normal groups.

Variables Associated with Linguistic Deficits in the Epilepsy Groups

Young

Logistic regression demonstrated no significant association with Performance IQ (Table 3). The presence of a psychiatric diagnosis, particularly an affective/anxiety disorder diagnosis, was related to Phonetic Quotients 1 SD below average. Significantly more epilepsy subjects with Spoken Language, Listening, Speaking, Semantic, Syntax, and Phonology Quotients 1 SD below average had longer duration of illness than those with average language scores. There were also significantly more children with CAE whose Listening Quotients were 1 SD below average than those with CPS. Lower SES and minority status were associated with Speaking and Semantic Quotients 1SD below average, respectively.

Intermediate

Modeling (Table 4) demonstrated that the children with Spoken Language, Listening, Speaking, Semantics, and Syntax Quotients 1 SD below average had significantly lower performance IQ scores and a history of prolonged

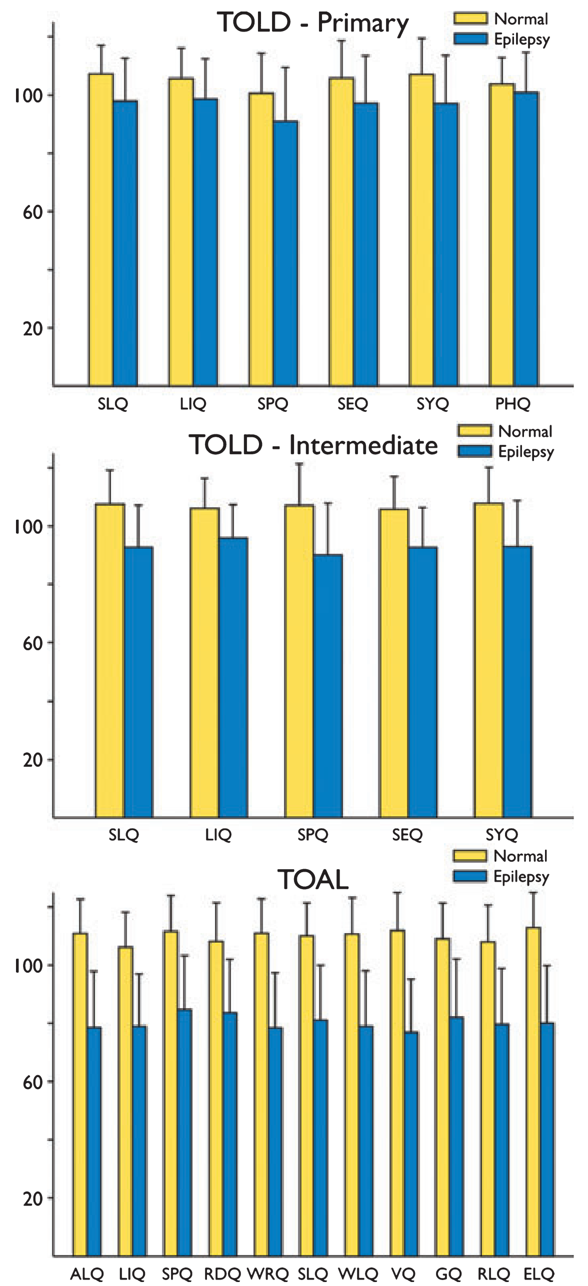

Figure 1.
Mean Language Scores of Epilepsy and Normal Groups by Age. TOLD, Test of Language Development; TOAL, Test of Adolescent Language; SLQ, Spoken Language Quotient, LIQ, Listening Quotient; SYQ, Syntax Quotient; SPQ, Speaking Quotient; PHQ, Phonology Quotient; ALQ, Adolescent Language Quotient; RDQ, Reading Quotient; WRQ, Writing Quotient; WLQ, Written Language Quotient; VQ, Vocabulary Quotient; GQ, Grammar Quotient; RLQ, Receptive Language Quotient; ELQ, Expressive Language Quotient.
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Table 6. Epilepsy and normal groups with language scores 1 SD < average

	Epilepsy	Normal	p-value (Fisher's exact test)
Young (%)			
Spoken Language	21.57	0	0.006
Listening	21.57	0	0.006
Speaking	42.86	13.79	0.008
Semantics	31.48	6.90	0.01
Syntax	21.82	0	0.007
Phonology	19.23	3. 45	0.09
Intermediate (%)			
Spoken Language	35.00	1.82	<0.0001
Listening	21.95	1.82	<0.0001
Speaking	45.68	7.27	<0.0001
Semantics	31.76	0	<0.0001
Syntax	39.24	5.45	<0.0001
Adolescent (%)			
Adolesc. Language	67.6	5.56	<0.0001
Listening	54.29	0	<0.0001
Speaking	47.22	5.56	0.002
Reading	55.88	5.56	<0.0001
Writing	71.43	0	<0.0001
Spoken Language	60.00	5.56	<0.0001
Written Language	61.76	0	<0.0001
Vocabulary	61.76	0	<0.0001
Grammar	61.76	5.56	<0.0001
Receptive Language	61.76	0	<0.0001
Expressive Language	65.71	5.56	<0.0001

seizures but no psychopathology compared to those with average scores. Other than Listening, significantly more children of minority status had TOLD-I Quotients 1 SD below the mean than Caucasian children.

Adolescent

Significantly more adolescents with Spoken, Written, Receptive, and Expressive Language Quotients 1 SD below average had lower Performance IQ scores than those with language scores within 1 SD of the average (Table 5). There was no significant relationship between language scores and psychopathology. Regarding seizure variables, the epilepsy subjects with Adolescent Language and Writing Quotients 1 SD below average had significantly worse seizure control than those with scores within 1 SD of the average. There was also a trend for those with Verbal and Grammar Quotients 1 SD below average to have poor seizure control. In addition, duration of illness was longer in those with Expressive Language Quotients 1 SD below average. The adolescent epilepsy subjects with Listening and Spoken Language Quotients 1 SD below average were from significantly lower SES families than those with scores in the average range.

Secondary analyses

Despite a higher rate of psychiatric diagnoses in the young epilepsy subjects tested in 1994–1998 compared to those tested in 1999–2003 [X^2 (1) = 4.36, $p < 0.04$], there was no significant difference in the rate of anxiety disorder diagnoses in the old and new cohort of young epilepsy subjects. Although Performance IQ was not related to linguistic deficits in the young epilepsy group, it was associated with duration of epilepsy ($r = -0.26$, $p = 0.04$). However, the association of Performance IQ with the linguistic deficits of the intermediate and adolescent groups was not accounted for by seizure variables. There were also no significant differences in the Performance IQ of the old and new epilepsy cohorts in each age subgroup.

Association with Reading

Other than the Listening and Phonology Quotients, mean language scores 1 SD below average were significantly related to lower WIAT reading scores in the young epilepsy patients (t_{36} 3.35–3.72, $p < 0.002$). The intermediate epilepsy subjects with mean language scores 1 SD below average, except for the Semantic Quotient, had significantly lower WIAT reading scores than those with average language scores (t_{29} 3.19–4.04, $p < 0.004$). WIAT reading scores were available for only 12 of the 36 adolescent epilepsy subjects. However, as presented in Table 3, 52.9% of the epilepsy adolescent subjects had reading scores 1 SD below average and 47.2%–67.6% of the adolescent epilepsy subjects had language scores 1 SD below average.

Discussion

The study's findings highlight the clinical, theoretical, developmental, and academic importance of studying language in youth with epilepsy, aged 6–15 years, who have average IQ scores. The significantly higher rate of language scores 1 SD below average in the three epilepsy groups should alert clinicians to the need for language evaluations in epilepsy youth with normal intelligence. In contrast to our developmental predictions, we found an increase in the rate of language impairment from about one-fourth in the young group to one-third in the intermediate group, and then to more than one-half of the adolescent epilepsy subjects. In addition, there was a wider range of linguistic deficits in the older epilepsy subjects, and the predictors of language impairment differed in the three age groups.

These findings imply an age-related rise in vulnerabilities to linguistic deficits as well as differential effects of seizure variables during the long protracted course of language development. Two lines of evidence help clarify our unpredicted developmental findings. First, despite intact syntactic and semantic skills by age 5, these skills continue to develop and undergo acceleration during adolescence with an increase in syntactic complexity, advanced use of grammar and vocabulary, as well as abstraction (Nippold et al., 2005, Ravid, 2006; Berman & Nir-Sagiv, 2007). Maturation of these skills is attributed to the parallel complex growth in thought, cognitive flexibility, and integration of knowledge (Nippold et al., 2005; Ravid, 2006; Berman & Nir-Sagiv, 2007).

The association of Performance IQ with language deficits in the intermediate and adolescent epilepsy groups also implies that skills tapped by Performance IQ subtests might play a role in the accelerated integration of language and thought in the older children. Although Performance IQ and its associated functions did not independently contribute to impaired language in the young epilepsy group, TOLD-P and WISC Performance IQ subtests might not tap the same skills.

Second, corresponding development, first of the frontal and then the temporal lobe during adolescence and young adulthood, involves language-related regions (inferior frontal and superior temporal gyri) (Sowell et al., 2003; Gogtay et al., 2004). Given the role of the frontal lobe in executive function (Alvarez & Emory, 2006) and both the frontal and temporal lobes in basic and higher level linguistic functions (Poldrack et al., 1999; Bookheimer, 2002), these brain regions participate in the previously described integration of language and cognition (i.e., thought processes) (Hagoort et al., 2004).

Therefore, our findings suggesting increased rather than decreased vulnerability of linguistic functions to the ongoing effects of seizures with age, might reflect the continued, active development of these brain regions. However, prospective language and imaging studies that replicate our cross-sectional findings are warranted to confirm this explanation. Furthermore, different subtests in the TOLD-P, TOLD-I, and TOAL probably contributed to the wider and different range of linguistic deficits and predictors in the three epilepsy age groups.

Yet, the different profile of the correlates of impaired language in the three epilepsy age groups, as found for the higher level linguistic deficits of children with CPS and CAE (Caplan et al., 2006), suggest changing vulnerability during the prolonged parallel development of language and language-related brain-related structures (Gogtay et al., 2004). In the current study, the association of increased duration of epilepsy with five of the six linguistic measures (e.g., Spoken Language, Listening, Semantics, Syntax, and Phonology) in the young group implies that continued illness impacts all aspects of ongoing language development in young children. In addition, significantly more young children with CAE than CPS with listening deficits might represent the attentional impairment (Levav et al., 2002) and predominant dorsolateral prefrontal involvement (Holmes et al., 2004) found in CAE.

Although the intermediate epilepsy group did not have a higher rate of prolonged seizures than the other epilepsy groups (Table 2), this seizure variable was significantly related to lower Spoken Language, Listening, Speaking, Semantics, and Syntax quotients in this age group. The association of linguistic deficits with a history of prolonged seizures might be similar to the evolving, long-term effect of prolonged seizures on cognitive and learning deficits in animals [See reviews in (Ben-Ari & Holmes, 2006) and (Sankar & Rho, 2007)].

In the adolescent epilepsy group, the relationship of lower language scores with poor seizure control is analogous to increased higher-level linguistic deficits in older children with CPS who had worse seizure control (Caplan et al., 2006). Poor expressive language in adolescents with longer duration of illness and increased deficits in overall language, writing, vocabulary, and grammar in those with poor seizure control further highlight the linguistic vulnerability of adolescents with epilepsy.

Independent of the reported relationship between illness severity and IQ in children with epilepsy (Caplan et al., 2004, 2008; Pulsipher et al., 2009), the association of both Performance IQ and demographic variables (i.e., ethnicity, SES) with language deficits is reported in children without epilepsy who have language impairment (Im-Bolter & Cohen, 2007; Beitchman et al., 2008). Clinically, these findings underscore the importance of language testing in youth with epilepsy with lower IQ scores and who come from minority and economically disadvantaged families.

Unlike our psychopathology predictions, the presence of a psychiatric diagnosis was significantly related to linguistic deficits only in the young group. The relationship between poor phonology skills and the presence of an affective/anxiety disorder in the young group is interesting for several reasons. First, phonologic processing is an important first-stage process in language learning in young children (Bishop, 1997). Second, phonologic difficulties are associated with reading deficits in children without epilepsy [See review in (Schuele, 2004)] and in children with epilepsy (Chaix et al., 2006; Northcott et al., 2007). Third, young children without epilepsy with phonologic difficulties are rated by their parents on the Child Behavior Checklist (Achenbach, 1991) as anxious and withdrawn (van Daal et al., 2007). These findings further emphasize the clinical importance of testing language and reading in young children with epilepsy, particularly if they have affective/anxiety disorders.

From the academic perspective, the association of impaired language with poor literacy is described in cross-sectional (Conti-Ramsden & Durkin, 2007) and prospective data [See review in (Schuele, 2004)] of children without epilepsy who have language impairment and in a large sample of 173 children with epilepsy who had both low reading and writing achievement scores (Fastenau et al., 2004). As children go from elementary to middle and then to high school, there is greater demand on their language-based learning skills (i.e., reading, writing). Undiagnosed and untreated linguistic deficits might, therefore, play an important role in the poor long-term educational outcome of pediatric epilepsy (Sillanpaa et al., 1998; Wirrell, 2003).

Study limitations include language test construction, sample size, illness variables, cohort effects, and cross-sectional study design. Different subscales and subscale definitions in the TOLD-P, TOLD-I, and TOAL, together with the small sample size of the adolescent epilepsy group, limit generalization of the study's developmental findings. Few adolescent CAE subjects (Table 2) also preclude reaching conclusions on the lack of an association of language impairment with type of epilepsy in adolescence.

In addition, parents' report on seizure variables, including prolonged seizures could be subject to memory loss, particularly in the parents of the older children. No evidence for a relationship of language scores with lateralization and localization of epileptic activity in the EEG of the CPS subjects should be confirmed with concurrent EEG data. Significantly higher language scores in the new versus old normal intermediate and adolescent cohorts might have contributed to the between-group language score differences (i.e., epilepsy < normal). Finally, although our findings suggest age-related differences in the severity, range, and predictors of linguistic deficits in children with epilepsy, they need to be replicated using the same language instrument across ages by a prospective rather than a cross-sectional study.

Notwithstanding these limitations, the age-related higher rate of language impairment, wider range of linguistic deficits, and different association with seizure and Performance IQ variables together with the relationship with poor reading have important clinical, developmental, theoretical, and academic implications. Most importantly, these findings underscore the need for language assessment and intervention for a wide age range of children with epilepsy with average intelligence.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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