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The Association of MRI Findings and Neuropsychological Functioning after the First Recognized Seizure

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Summary

Purpose—To explore relationships between MRI abnormalities of the brain and neuropsychological functioning in children who were evaluated following their first recognized seizure.

Methods—Subjects were children aged 6 to 14 years with a first recognized seizure within the past 3 months who participated in a larger prospective study of child adaptation. The 249 children with neuropsychological testing and neuroimaging were studied. Children underwent neuropsychological examination an average of 2.8 months and MRI examination an average of 1.3 months after the first recognized seizure. On factor analysis four factors were found for neuropsychological function: LANG = Language, PS = Processing Speed, EC = Executive/Construction, VMEM = Verbal Memory and Learning. For analysis, structural abnormalities found on MRI were classified as significant (yes/no) based on whether they were presumed to be related to the seizure condition.

Results—On MRI, 34 (14%) had structural abnormalities that were judged to be significant in that they were possibly related to their seizures. Children with significant abnormalities had significantly lower estimated IQ scores and significantly lower language, processing speed, executive/constructional ability, and verbal memory and learning factor scores than did children without significant abnormalities.

Conclusions—Children who have structural brain abnormalities at onset have slightly lower cognitive functioning overall, and all neuropsychological domains seemed to be affected relatively

equally. This pattern was apparent even when we restricted the analysis to children with intellectual functioning in the broadly normal range.

Keywords

Seizures; Epilepsy; Child; Neuropsychological tests; Cognition; Neuroimaging

Structural brain abnormalities of various types can lead to epilepsy, and many are associated with delays in cognitive development or specific cognitive deficits. Genetic cortical malformations (e.g., lissencephaly, schizencephaly, heterotopias, and polymicrogyria) are often characterized by seizure disorders, typically with significant delays in broad cognitive development (Guerrini, 2005). Similarly, tuberous sclerosis is characteristically associated with seizures and developmental delays. More importantly, the degree of intellectual deficit appears to be related to the degree of structural abnormality (i.e., the number of tubers) (Jambaque et al., 1991).

Hippocampal sclerosis, a common finding in temporal lobe epilepsy in adults, has been associated with specific deficits in verbal memory and language or spatial memory in a manner consistent with the hemisphere affected (e.g., Baxendale et al., 1998); intelligence and other functions are relatively spared (e.g., Bourgeois et al., 1983; Ellenberg et al., 1986; Martin et al., 1999; Rodin et al., 1986). The degree of neuropsychological deficit is related to hippocampal volumes in adulthood (Baxendale et al., 1998; Hermann et al., 2002). The nature and extent of these neuropsychological deficits appear to be related to age of seizure onset, with lower memory scores and smaller hippocampal volumes observed among individuals with childhood onset (Baxendale et al., 1998). Furthermore, these effects might even be moderated by age of onset, with earlier age of onset being associated with not only hippocampal volume loss but an additional reduction in total brain volume, together with broader neuropsychological deficits that extend outside of the memory domain (Hermann et al., 2002).

These findings support an association between the presence of structural brain abnormalities and cognitive deficits in children with epilepsy. For some conditions (e.g. tuberous sclerosis complex), the extent of the structural abnormalities is related to the severity of neuropsychological dysfunction (Jambaque et al., 1991; O'Callaghan et al., 2003; Weber et al., 2000). Moreover, the type and location of the structural abnormalities can be related to the nature of neuropsychological deficits affecting specific cognitive domains (e.g., Hermann et al., 2002).

Shinnar and colleagues followed 411 children in New York City after their first unprovoked afebrile seizure (Shinnar et al., 2001). That study helped to characterize a new onset sample with regard to structural brain abnormalities; however, there are potential limitations that could affect the conclusions and generalizability of those findings. First, although the sample was large, only 27% (n = 59) of the children had MRIs; the majority (73%) had CT scans. As would be expected, abnormalities were detected in higher proportions of children using MRI (34%) compared to CT (22%). Therefore, that study likely underestimated the extent of structural brain abnormalities in this population. Second, there was no differentiation between abnormalities that seemed to be related to the seizure disorder versus those that were not related. In addition, imaging data were collected over the course of the children's disorder in order to use the most sensitive imaging study for each participant that was available at the time of the 2001 publication (Shinnar, 2006). Consequently, many of the children in that sample completed their imaging studies many years after onset.

In a subsequent and parallel study, Berg and colleagues followed 613 children in Connecticut following a second unprovoked seizure (Berg et al., 2000). The Connecticut study improved

on many of the limitations in the New York City study. The majority of children in the Connecticut study completed MRI studies (vs. CT), and the imaging was obtained in conjunction with the initial evaluation at onset. Consequently, the lower proportion of children showing abnormalities in the Connecticut sample (12.7%, using more sensitive imaging but closer to onset) versus the New York City sample (21%, using less sensitive imaging but more chronic seizures) raises the possibility that some of these abnormalities might develop or become more detectable over the course of the disorder. However, it is possible that differences in exclusion criteria and/or definitions of onset also contributed to the differences in rates of abnormalities. In an effort to start addressing these differences, it would be beneficial to replicate these findings in a new sample with many of the strengths of the Connecticut study. All of these imaging studies have documented the potential for structural abnormalities at the onset of seizures in children. However, it is unclear if these abnormalities are related to cognitive function. Neuropsychological data were not reported for any of these studies.

Neuropsychological deficits have been well documented in children with epilepsy (see Fastenau et al., 2003, for brief review), but there have been mixed findings in children at the onset of the disorder. Williams and colleagues (Williams et al., 1998) examined a small cohort ($n = 37$) of children newly diagnosed with epilepsy prior to initiation of antiepileptic drug therapy and found no differences in neuropsychological performance compared to children newly diagnosed with diabetes. However, others have documented subtle deficits at onset in children. Ostrom and colleagues (Ostrom et al., 2003) compared 51 children with new onset of epilepsy (i.e., at least two seizures) to a group of 48 healthy same age classmates with nearly identical IQ. At baseline they found that children with epilepsy showed deficits in attention and learning compared to the control group. None of these studies examined the relationship between structural abnormalities and neuropsychological deficits at the onset of the disorder.

In this study, we explored the relationships between MRI abnormalities of the brain and neuropsychological functioning in children who were evaluated following their first recognized seizure. In the analyses we separated the MRI abnormalities into those that seemed to be related to the seizure disorder and into those that were not related.

METHOD

Participants

Children were prospectively recruited from July 2000 through June 2004 as part of a larger ongoing longitudinal study to identify factors that predict children's adaptation to epilepsy. Families were requested to participate at two large academic medical centers located in Cincinnati, Ohio, and Indianapolis, Indiana. At the Indianapolis site fliers were also sent to physicians in private practice and to school nurses requesting them to forward the fliers to appropriate families. Children aged 6 to 14 years who had experienced a first recognized seizure within the past 3 months were recruited. Children were excluded if their seizure resulted from an acute situational etiology such as toxin, infection, or trauma or if the seizure was associated with a mass lesion. Thus, all of the first recognized seizures in this sample of children were unprovoked. Children were also excluded if they had a chronic illness limiting their activities of daily living or if they had a functional impairment such as a hemiparesis or cerebral palsy that limited their activities of daily living. Children were not excluded if it was determined that they had had a prior seizure that had not been previously recognized as such. This study was approved by the institutional review boards at both participating institutions. Parents signed consent forms, and children signed assent forms before participation.

Of the 350 children enrolled in the larger study, 281 (80%) had an MRI examination within 6 months of their first seizure. Thirty-eight children without an MRI had either had CT ($n = 19$) or had MRI more than 6 months after the first seizure ($n = 19$). Thirty-one children had no

imaging study. Of the 281 children, 249 (89%) completed at least some neuropsychological testing. Neuropsychological testing was not completed for 32 children for a number of reasons, including difficulty scheduling the testing visit or time constraints limiting its duration. Demographic and clinical characteristics of the sample of 249 children are presented in Table 1. Age of onset is distributed across the specified age range (ages 6 to 14 years). There were roughly equal numbers of boys and girls. IQ was estimated from the Kaufman Brief Intelligence Test (K-BIT) (Kaufman and Kaufman, 1990), a brief screening instrument that correlates highly ($r = 0.80$) with a Full Scale IQ obtained on the Wechsler Intelligence Scale for Children-Revised in children spanning the age range of this study. IQ estimates in this sample covered a broad range spanning from mild deficiency to the superior range; the mean and median IQs fall in the middle of the average range, which has been observed in other studies (e.g., Oostrom et al., 2005). The sample represents a relatively broad sampling of onset ages and seizure types; the majority of children (91%) had only one seizure type. Children with partial seizures slightly outnumbered those with generalized seizures, which is characteristic of this population (Hauser, 2001). The etiology was equally distributed between idiopathic/familial and symptomatic, which is somewhat different from population estimates that favor idiopathic/familial by approximately 2:1 (Cowan et al., 1989). Among children with symptomatic epilepsy syndromes, there were roughly equal proportions of common causes (malformation, neonatal, trauma, infection), which is consistent with population estimates (Cowan et al., 1989).

MRI examinations

The children underwent MRI examination an average of 1.3 months after their first recognized seizure. Over the course of the study one of three neuroradiologists coded MRI data. The ratings for a randomly selected group of 30 children were compared among the three raters. For each of the 30 children, the percent of ratings that were the same among pairwise comparisons of the raters was calculated. The mean percent agreement was 99%. The minimum percent agreement for any individual child's scan was 96%. Neuroradiologists were blind to EEG and neuropsychological findings when they coded the data from the MRIs. Most (78%) MRIs were completed at one of the two study sites. MRI examinations at both sites were performed on 1.5 Tesla GE Signa Horizon (GE Healthcare), platform LX scanners, running current system software (presently 9.x) using a standardized pediatric seizure protocol. The standardized protocol consisted of the following scanning sequences: sagittal T₁-weighted spin echo (SE), axial T₂-weighted fast spin echo (FSE), coronal oblique fast T₂-weighted FLAIR, coronal oblique FMPIR, axial diffusion (single-shot, SE-EPI, $b = 1000$, all directions), and axial 3D-SPGR. The total imaging time for all sequences was about 26 min.

Some of the MRIs (22%) were performed on MRI units at referring facilities. These were performed on magnet systems varying from 0.5 to 1.5 Tesla and consisted of standard sagittal, axial and/or coronal images, using typical clinical sequences. All of these studies were rated as adequate or better in scan quality and were read and coded by the neuroradiologists involved in this study.

Abnormalities on MRI were classified as either significant or nonsignificant based on an a priori system of classification developed by the three study neuroradiologists (Doescher et al., 2006) to indicate whether an MRI abnormality was judged as being possibly related to seizures. Under this classification system, abnormalities that fall under the classification of "significant" include leukomalacia/gliosis, encephalomalacia, any gray matter lesion, mass lesion, hemorrhage, vascular lesion, hippocampal abnormality, ventricular enlargement >1.5 cm, or prominence of extra-axial fluid spaces >1 cm. Other abnormalities are reviewed on a case-by-case basis.

Neuropsychological examinations

Children underwent neuropsychological examination an average of 2.8 months after the first recognized seizure. Testing was administered in a neurology or neuropsychology clinic by psychometrists who were trained, observed, and certified on the test battery by a pediatric neuropsychologist.

Instruments

Participants completed a 3 hours battery of neuropsychological tests and measures of academic achievement. All instruments are well-established in the field and were administered according to the standardized procedures for each test; scores were converted to age-corrected standardized scores using the best available national norms for all tests except WRAML Design Copy, which was designed by our research group and for which no norms are available. The battery included the following tests: *Clinical Evaluation of Language Fundamentals, 3rd Edition* (CELF-3) (Semel et al., 1995); *Comprehensive Test of Phonological Processing* (CTOPP) (Wagner et al., 1999); *Conners' Continuous Performance Test, 2nd Edition* (CPT-II) (Conners, 2000); *Kaufman Brief Intelligence Test* (K-BIT) (Kaufman and Kaufman, 1990); *Coding and Symbol Search Subtests of the Wechsler Intelligence Scale for Children, 3rd Edition* (WISC-III) (Wechsler, 1991); *Wide Range Assessment of Memory and Learning* (WRAML) (Adams and Sheslow, 1990); *WRAML Design Copy*; and the *Wisconsin Card Sorting Test* (WCST) (Heaton et al., 1993).

STATISTICAL ANALYSIS

Factor analysis of neuropsychological test variables

As part of the larger study, neuropsychological test scores for each child were computed and, for children with complete data, subjected to exploratory factor analysis to reduce the number of neuropsychological variables. The rotation method used was promax and the factor extraction method used was principal axis factoring. Two subtests from the CELF-3, Word Classes and Recalling Sentences, were excluded from the factor analysis because the other two subtests, Concepts and Directions and Formulated Sentences, have been observed to be the most robust measures of receptive and expressive language, respectively (Fastenau et al., 1999). In addition, the Design Memory subtest from the WRAML was excluded because of its high correlation with the Story Memory subtest from the WRAML in this sample.

Imputing neuropsychological data

For 16 children, the CPT-II was discontinued prematurely after the children required more than two prompts. For these children, we substituted the median scores for all children who completed the task and who required two or more prompts, as described in Fastenau and colleagues (Fastenau et al., 2006). For all other missing neuropsychological data, missing values were imputed by identifying which factor the missing value was associated with and, as long as at least half of the data within that factor were not missing, substituting the missing value with the mean of the standardized scores from each nonmissing variable within that factor.

Comparison of neuropsychological factors by MRI abnormalities

Children were first classified into three groups based on the results of their MRI: (1) no MRI abnormalities present ($n = 174$); (2) at least one MRI abnormality present but none classified as significant ($n = 41$); and (3) at least one significant MRI abnormality present ($n = 34$). Differences in the findings on the neurological exam and neuropsychological test scores between children with no MRI abnormality and children with MRI abnormalities judged to be nonsignificant were examined using chi-square and two-sample t -tests. The proportion of

children with abnormal neurological exams was not significantly different between these two groups. Similarly, none of the neuropsychological test scores was significantly different between these two groups on average (based on two-sample *t*-tests). Therefore, these two groups were combined into one group labeled “without significant abnormality.” Chi-square tests and two-sample *t*-tests were used to compare the demographic and clinical characteristics of the children with and without significant MRI abnormalities. *T*-tests were used to compare these two groups on the factor scores for each of the neuropsychological factors that were identified based on the item factor loadings that resulted from the factor analysis. The dependent variables were the K-BIT and the four neuropsychological factor scores and the independent variable was significant MRI abnormality (with/without). Site differences were examined as a possible covariate using two-way analysis of variance, but there were no differences between the two sites on any of the dependent variables. Therefore, site was not included in the final models.

RESULTS

Description of neuroimaging findings

Of the 249 children with both MRI and neuropsychological data, 34 (14%) had MRI abnormalities that were judged to be significant in that they were possibly related to their seizures. The demographic and clinical characteristics of the two subsamples are reported in Table 1. Frequencies of significant abnormalities are detailed in Table 2. There were no mass lesions, vascular lesions, areas of hemorrhage, abnormal prominence of extra-axial fluid spaces, or relevant structural lesions. An additional 41 children (16%) had MRI abnormalities that were judged to be nonsignificant or unlikely to be related to their seizures. These included prominent or dilated perivascular spaces (*n* = 13), Chiari I malformation (*n* = 6), nonspecific foci of signal change (*n* = 4), hemosiderin or calcium deposit (*n* = 1), retrocerebellar cyst (*n* = 1), volume loss (*n* = 1), and cerebellar tonsillar ectopia (*n* = 1).

Neuropsychological test results

All neuropsychological and academic test scores were converted to standardized scores using the best available demographic corrections for each test. The standardized scores for the sample are presented in Table 3; normative values for each test are also provided for reference.

Factor analysis of neuropsychological variables

For the factor analysis, we used the data from the 246 children out of the entire sample of 350 children with complete neuropsychological data (70% of 350). Four latent factors underlying the neuropsychological variables were identified (see Table 4). About 67% of the total variance was explained by the four factors, and the scree plot appeared to reach an asymptote at four factors. Factor 1, “Language,” consisted of measures of verbal concept formation, phonological awareness, and phonological memory. Factor 2, “Processing Speed,” consisted of measures of psychomotor speed and rapid naming. Factor 3, “Executive/Constructional,” consisted of measures of sustained attention, problem solving, and visual-construction. Factor 4, “Verbal Memory and Learning,” consisted of measures of story recall and rote verbal learning.

Group comparisons

For the group comparison, we included both 201 children with fully observed data plus 40 children who had complete neuropsychological data after scores were imputed for missing data. Thirty-seven of the 40 children only had one value imputed, two had two values imputed, and one had three values imputed. Thus, the total sample size for the group comparisons was 241 (97% of 249). Factor score comparisons for children with and without significant MRI abnormality are shown in Table 5 and also graphically in Fig. 1. If a child scored at the mean

on each component of the factor, his or her factor score would be zero. Thus, a positive factor score mean indicates that the average score was above the sample mean, and a negative factor score mean indicates that the average score was below the sample mean. Children with significant abnormalities scored significantly lower on the K-BIT [$F(1,247) = 6.58, p = 0.011$] and had significantly lower language [$F(1,239) = 4.57, p = 0.034$], processing speed [$F(1,239) = 6.02, p = 0.015$], executive/constructional ability [$F(1,239) = 7.70, p = 0.006$], and verbal memory and learning [$F(1,239) = 6.83, p = 0.010$] factor scores than did children without significant abnormalities.

Given the possibility that these group differences may have been driven by a few children in the group with MRI abnormalities who also had generalized cognitive problems (i.e., low IQ), 15 children were excluded and the same analyses were repeated. These 15 children had estimated IQs below 70 on K-BIT and/or data from parents, teachers, or school records indicating intellectual disability. The group differences following this procedure were enhanced, however, rather than attenuated. Children with significant abnormalities scored significantly lower on the K-BIT [$F(1,232) = 10.67, p = 0.001$] and had significantly lower language [$F(1,226) = 7.33, p = 0.007$], processing speed [$F(1,226) = 6.48, p = 0.012$], executive/constructional ability [$F(1,226) = 9.66, p = 0.002$], and verbal memory and learning [$F(1,226) = 8.97, p = 0.003$] factor scores than did children without significant abnormalities.

Post hoc examination of the neuropsychological profiles (Fig. 2) of individual children with hippocampal abnormalities on MRI ($n = 7$) failed to show a convincing pattern of memory and language deficits formerly reported in studies of patients with longer seizure histories, typically adults (Baxendale et al., 1998; Hermann et al., 2002). Notably, four children scored more than 1 SD below the mean for verbal memory and two children scored more than 1 SD below the mean on all factors.

DISCUSSION

The purpose of this study was to explore relationships between MRI abnormalities of the brain and neuropsychological functioning in children with first recognized seizures. Our finding that 14% of the sample of 249 children had significant MRI abnormalities that were judged to be related to their seizures is generally consistent with the few previous studies examining such patients (Salmenpera et al., 2005; Shinnar et al., 2001).

Our findings indicate that, among children with newly recognized seizures, those children with a significant brain abnormality performed more poorly than children without a significant MRI abnormality on measures of intelligence, language, processing speed, verbal memory and learning, and executive functions. Furthermore, this pattern remained unchanged when the 15 children with generalized cognitive problems were excluded from the analyses. These findings suggest that some of the variability in neuropsychological functioning in children with newly recognized seizures might be caused by underlying brain abnormalities. That is, the presence of structural brain abnormality at the onset of seizures is a risk factor for concurrent neuropsychological deficits. It may be that these children will comprise that subset of children with epilepsy who demonstrate a cognitive decline over time (Bourgeois et al., 1983; Rodin et al., 1986). Although the Bourgeois and Rodin studies did not include MRI results, they document the pattern of gradual decline for some children with epilepsy which we speculate may be related to structural brain abnormalities.

Neuropsychologically, our total sample was very similar to the Dutch study sample at baseline (Ostrom et al., 2005), showing normal IQ and neuropsychological functioning overall at onset. However, it is clear from the present study that children with new onset of seizures are not a homogeneous group. Children who have structural brain abnormalities at onset have slightly

lower cognitive functioning overall, and all neuropsychological domains seemed to be affected relatively equally. This pattern is apparent even in children with intellectual functioning in the broadly normal range. It remains to be seen whether or not this group of children will continue to show adverse change over the course of the disorder.

The subgroup of patients with hippocampal abnormality is interesting for two reasons. First, only 7 of 249 (3%) showed hippocampal abnormality at onset. This rate is less than half that of the 8% of newly diagnosed adults showing hippocampal volume loss (Salmenpera et al., 2005). Second, these few children who showed hippocampal abnormality at onset exhibited considerable variability in their neuropsychological profiles, as opposed to showing selective deficits in memory and language that are more characteristic of adult patients with much longer duration of the disorder (Baxendale et al., 1998). This finding is consistent with the supposition that chronic epilepsy causes specific hippocampal damage resulting in a specific epilepsy-related cognitive phenotype. Our seven patients probably had hippocampal abnormalities caused by different insults at different points in brain development resulting in a variety of cognitive symptoms as well as seizures.

The findings by Salmenpera and colleagues (Salmenpera et al., 2005) with newly diagnosed adults and by Farina and colleagues (Farina et al., 2004) with newly diagnosed children suggest that greater abnormality could be expected by 18 to 36 months from onset. Longitudinal follow-up with this sample will help to map the course of neuropsychological changes relative to structural changes.

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FIG. 1.

Average factor scores for children with and without significant MRI abnormalities. LANG, language; PS, processing speed; EC, executive/construction; VMEM, verbal memory and learning.

FIG. 2.
z-Scores for children with hippocampal abnormalities. LANG, language; PS, processing speed; EC, executive/construction; VMEM, verbal memory and learning.

TABLE 1

Demographic and clinical characteristics of the sample

	Total sample (n = 249)	Without significant MRI abnormality (n = 215)	With significant MRI abnormality (n = 34)
	Mean (SD)	Mean (SD)	Mean (SD)
Age	9.6 (2.5)	9.6 (2.5)	9.2 (2.3)
IQ (estimated from K-BIT) *	101.8 (15.1)	102.7 (15.3)	94.9 (12.1)
	%	%	%
Gender (% female)	51	51	53
Handedness (% left-handed)	11	9	21
Race			
White/non-Hispanic	82	83	76
African-American	12	12	15
Multiracial	2	2	3
Hispanic	1	0	3
Asian	1	1	0
Other/unknown	2	2	3
Primary seizure type			
Generalized tonic-clonic	29	30	26
Atonic, akinetic, myoclonic	1	1	0
Complex partial seizures	23	22	29
Simple partial	6	7	3
Partial with secondary generalization	27	26	30
Absence	13	13	12
Unknown/unclassified	1	1	0
Etiology of seizures *			
Idiopathic/familial	48	50	32
Symptomatic/cryptogenic	47	42	68
Unknown	5	7	0
Neurological exam *			
Normal	96	97	88
Abnormal	4	3	12

* p < 0.05

TABLE 2

Percentages of children with specific types of significant MRI abnormalities

Significant MRI abnormality ^a	n	%
Leukomalacia/gliosis	18	52.9
Encephalomalacia	4	11.8
Hippocampal atrophy	4	11.8
Hippocampal signal abnormalities	3	8.8
Gray matter cortical dysplasias	3	8.8
Gray matter heterotopias	3	8.8
Other gray matter lesions	2	5.9
Ventricular enlargement > 1.5 cm	5	14.7

^aNote: N = 34 children. Some children had more than one abnormality.

TABLE 3

Descriptive statistics for neuropsychological test scores

	Total mean (SD) n = 249	Without significant MRI abnormality mean (SD) n = 215	With significant MRI abnormality mean (SD) n = 34	d ^a
CELF-3 Concepts and Directions ^b	9.41 (3.39)	9.52 (3.46)	8.76 (2.88)	0.22
CELF-3 Word Classes ^b	9.91 (3.42)	10.06 (3.44)	8.97 (3.20)	0.32
CELF-3 Formulated Sentences ^b	9.17 (2.91)	9.26 (2.98)	8.59 (2.36)	0.23
CELF-3 Recalling Sentences ^b	10.06 (3.46)	10.20 (3.47)	9.21 (3.29)	0.29
CTOPP Phonological Awareness ^c	94.63 (15.20)	95.01 (15.50)	92.23 (13.09)	0.18
CTOPP Phonological Memory ^c	94.03 (13.83)	94.61 (13.95)	90.38 (13.09)	0.31
CTOPP Rapid Naming ^c	98.31 (16.51)	98.84 (16.50)	94.97 (16.44)	0.23
CPT II hit RTSE ^d	43.57 (11.14)	43.58 (11.25)	43.55 (10.60)	0.00
WISC-III Coding ^b	9.63 (3.69)	9.77 (3.62)	8.71 (4.03)	0.29
WISC-III Symbol Search ^b	11.26 (4.02)	11.63 (4.00)	8.95 (3.31)	0.67
WRAML Story Memory ^b	9.69 (3.32)	9.77 (3.38)	9.18 (2.92)	0.18
WRAML Design Memory ^b	8.14 (2.94)	8.24 (3.00)	7.48 (2.44)	0.26
WRAML Verbal Memory and Learning ^b	10.77 (3.45)	11.00 (3.44)	9.29 (3.15)	0.50
WRAML Design Copy ^e	88.27 (16.45)	88.66 (16.16)	85.76 (18.34)	0.18
WCST percent total errors ^d	49.33 (11.94)	50.49 (11.72)	42.18 (10.90)	0.70

^a d is a measure of effect size, reflecting the difference in means relative to the pooled SD (comparing the two MRI groups). For example, d = 0.50 represents a one-half deviation difference between groups.

^b scaled score: mean = 10, SD = 3.

^c age-corrected standard score: mean = 100, SD = 15.

^d T-score: mean = 50, SD = 10 (reversed for CPT).

^e % correct.

TABLE 4

Neuropsychological tests: factor loading estimates for the exploratory factor analysis

	Language	Processing Speed	Executive Construction	Verbal Memory
CTOPP Phonological Memory	<i>0.65</i>	0.04	0.14	-0.15
CELF-3 Formulated Sentences	<i>0.62</i>	0.08	-0.04	0.16
CTOPP Phonological Awareness	<i>0.58</i>	0.16	-0.10	0.06
CELF-3 Concepts and Directions	<i>0.56</i>	0.01	0.09	0.15
WISC-III Coding	0.06	<i>0.81</i>	-0.07	-0.04
CTOPP Rapid Naming	0.06	<i>0.66</i>	0.08	-0.06
WISC-III Symbol Search	0.06	<i>0.59</i>	0.08	0.12
CPT II Hit RTSE-reversed	-0.09	0.16	<i>0.54</i>	-0.01
WCST percent Total errors	0.24	-0.15	<i>0.52</i>	-0.02
WRAML Design Copy	0.01	0.09	<i>0.49</i>	0.12
WRAML Story Memory	0.16	-0.04	0.03	<i>0.59</i>
WRAML Verbal Memory and Learning	0.00	0.28	0.13	<i>0.40</i>

Note: Bold, italicized loadings in each column identify subtests that have their primary loading on that factor.

TABLE 5

Descriptive statistics for neuropsychological factors

Neuropsychological factors	Total mean (SD) n = 241	Without significant MRI abnormality mean mean (SD) n = 208	With significant MRI abnormality mean (SD) n = 33	d ^a
Language	−0.03 (0.92)	0.02 (0.93)	−0.34 (0.78)	0.39
Processing speed	0.01 (0.94)	0.07 (0.94)	−0.36 (0.84)	0.46
Executive/construction	−0.05 (0.84)	0.01 (0.85)	−0.42 (0.73)	0.51
Verbal memory and learning	−0.03 (0.85)	0.03 (0.87)	−0.38 (0.67)	0.48

^a d is a measure of effect size, reflecting the difference in means relative to the pooled SD (comparing the two MRI groups). For example, d = 0.50 represents a one-half deviation difference between groups.