



Unique and shared areas of cognitive function in children with intractable frontal or temporal lobe epilepsy

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ABSTRACT

Objective: Previous findings have been mixed in terms of identifying a distinct pattern of neuropsychological deficits in children with frontal lobe epilepsy (FLE) and in those with temporal lobe epilepsy (TLE). The current study investigated the neuropsychological similarities and differences across these two pediatric medically intractable localization-related epilepsies.

Method: Thirty-eight children with FLE, 20 children with TLE, and 40 healthy children (HC) participated in this study. A comprehensive battery of standardized tests assessed five neuropsychological domains including intelligence, language, memory, executive function, and motor function. A principal component analysis (PCA) was used to distill our neuropsychological measures into latent components to compare between groups.

Results: Principal component analysis extracted 5 latent components: executive function (F1), verbal semantics (F2), motor (F3), nonverbal cognition/impulsivity (F4), and verbal cognition/attention (F5). The group with FLE differed from the HC group on F1, F2, F4, and F5, and had worse performance than the group with TLE on F1; the group with TLE had lower performance relative to the HC group on F2.

Conclusion: Our findings suggest that, in comparison with neurotypically developing children, children with medically intractable FLE have more widespread neuropsychological impairments than do children with TLE. The differences between the two patient groups were greatest for the factor score most clearly related to executive function. The results provide mixed support for the concept of specificity in neuropsychological dysfunction among different subtypes of localization-related medically intractable childhood epilepsies.

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1. Introduction

Neuropsychological impairment is a significant comorbidity in pediatric epilepsy [1–3]. A number of studies have evaluated neuropsychological profiles in childhood idiopathic and benign epilepsies [1]. However, few have investigated cognitive phenotypes in medically intractable pediatric localization-related epilepsies. The aim of the current study was to examine and contrast cognitive profiles in pediatric frontal and temporal lobe medically intractable epilepsies (FLE and TLE, respectively), as compared with healthy children.

Previous studies have examined neuropsychological profiles by broad syndrome type (i.e., generalized versus localization-related epilepsies) [4–6], in one type of localization-related epilepsy compared

with healthy controls (HC) [7,8], or have investigated only one or a narrow selection of neuropsychological domains [9,10]. Taken together, distinct syndrome-specific neuropsychological deficits are apparent across syndrome type, but patterns of shared deficits have also been documented [11].

In considering whether a distinct neuropsychological profile of children with FLE is evident, several areas of dysfunction are consistently documented, including executive function (i.e., attention, working memory, impulsivity, concept formation, planning; [4,12–15]), and motor coordination [12]. In contrast, the neuropsychological profile of children with TLE has most often been documented as impaired memory [9,16,17]. However, the deficits described above are decidedly not unique to each population [11]. Specifically, aspects of executive functioning (e.g., sustained attention, concept formation, mental flexibility/set shifting, perseveration, inhibitory control, and verbal fluency) have also been found to be impaired in children with TLE [4,8,18]. Analogously, the deficits in memory documented in children with TLE have been

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observed in children with FLE [19]. Also, language deficits have been documented in both left hemisphere FLE and left hemisphere TLE [17].

Recent studies have examined neurocognitive development in children with new-onset focal versus generalized idiopathic epilepsies [5,6,20]. Their results support the notion that, in pediatric epilepsy populations, the clinical epilepsy syndrome and neuropsychological status are not always closely linked [20,21]. For example, after identifying a number of cognitive domains (i.e., verbal ability, perceptual ability, executive function, cognitive/psychomotor speed, and attention) from a comprehensive neuropsychological testing battery, no significant associations were documented between those cognitive domains and epilepsy syndrome [20]. Patterns of shared deficits were evident across syndromes (e.g., psychomotor slowing [5]), and the identified cognitive phenotypes were independent of epilepsy syndrome [20].

Our research question addresses whether the more generalized pattern of impairment documented largely among children with relatively well controlled seizures (e.g., [20]) is also seen in the population of children with intractable epilepsy. Childhood epilepsy occurs during sensitive periods of brain development, which can interfere with the course of typical maturation of networks [17]. In addition, seizures themselves (regardless of the region of epileptogenic focus) may have a much broader impact on the developing brain, such as eliciting dysfunctional networks, which can in turn produce more generalized neuropsychological deficits. One might expect to see similar common impairments in medically intractable groups with FLE and TLE, as compared with HC. Conversely, because of the possibly more profound dysfunction in the underlying networks reflecting the intractability of the epilepsy, it is possible that more differentiating patterns of impairments may be observed, and hence, medically intractable children with FLE or TLE may show discrete neuropsychological profiles.

The goal of the current study was to examine and contrast neuropsychological profiles in pediatric nonlesional focal medically intractable epilepsies, namely, in FLE and TLE. We also investigated factors (current age, age at seizure onset, duration of epilepsy, number of antiepileptic drugs [AEDs]) that may impact neuropsychological profiles in children with FLE and TLE [3,22]. Investigation of a nonlesional group of patients allows comparison with past studies of idiopathic focal and generalized epilepsies [5,6,20]. We utilized a comprehensive battery of neuropsychological tests that reflected a broad range of cognitive/motor domains. Given the mixed nature of previous findings with respect to neuropsychological profiles in childhood epilepsy syndromes, we hypothesized that both similarities (e.g., shared cognitive deficits in patient groups compared with controls) and differences (e.g., greater difficulties on

tasks of attention/executive function in the group with FLE compared with the group with TLE; greater difficulties on tasks of memory in the group with TLE compared with the group with FLE) in neuropsychological profiles would be evident in group with FLE and TLE, when compared with HC.

2. Methods

2.1. Participants

Participants included 38 children and adolescents with FLE, 20 with TLE, and 40 HC. All patients had medically intractable epilepsy (defined as failure to achieve sustained seizure freedom with adequate trials of two or more tolerated and appropriately chosen AEDs), were of nonlesional etiology, and had normal magnetic resonance imaging (MRI) (on a 3 T scanner); and the location of the epileptogenic zone was determined by ictal video electroencephalography (EEG). Inclusion criteria included Full Scale Intelligence Quotient (FSIQ) ≥ 70 , while exclusion criteria for patients included prior epilepsy surgery and extra-frontal or extra-temporal epileptogenic foci. All participants in the HC group had normal MRI and no history of neurological or psychiatric disorders. The HC group was recruited through notices posted in the hospital. This study was approved by the Research Ethics Board of The Hospital for Sick Children, and written informed consent was obtained from parents/guardians and assent from children.

2.2. Neuropsychological assessment

A comprehensive battery of standardized tests, assessing five neuropsychological domains including intelligence, language, memory, executive function, and motor function, was administered individually to all participants. A total of 19 scores, based on age-appropriate norms, were derived from these tests; and all were converted to z-scores prior to analyses (see Table 1 for test details). Testing was conducted at the hospital by trained psychometricians or research assistants; the majority of the patients and all of the control participants were tested during a separate research appointment; some of the patients had undergone clinical neuropsychological assessments, and scores were obtained from their clinical files. On average, testing required 3 h and was carried out during one appointment, with breaks provided as needed. Not all children completed all tasks because of time limitations, poor attention or cooperation, or special circumstances (one child was color blind and was thus unable to complete tasks where identification of color

Table 1
Neuropsychological tests, ability tested, and domain.

Domain	Ability	Test
Intelligence	Verbal	Wechsler Abbreviated Scale of Intelligence (WASI), vocabulary subtest
	Nonverbal	Wechsler Abbreviated Scale of Intelligence (WASI), matrix reasoning subtest
Language	Receptive	Peabody Picture Vocabulary Test, 4th Edition (PPVT-4)
	Expressive	Expressive Vocabulary Test, 2nd Edition (EVT-2)
Memory	Expressive, confrontation naming	Boston Naming Test (BNT)
	Verbal, long term	Children's Auditory Verbal Learning Test, 2nd Edition (CAVLT-2), delayed recall California Verbal Learning Test, 2nd Edition (CVLT-II)
Executive function	Nonverbal, long term	Children's Memory Scale (CMS) or Wechsler Memory Scale – III (WMS-III), face recognition, delayed test
	Generative naming	Delis–Kaplan Executive Function System (D-KEFS), Verbal Fluency (FAS)
	Cognitive switching/flexibility	Delis–Kaplan Executive Function System (D-KEFS), verbal fluency (Category Switching)
	Response inhibition	Delis–Kaplan Executive Function System (D-KEFS), color-word (inhibition)
	Response inhibition/switching	Delis–Kaplan Executive Function System (D-KEFS), color-word (inhibition/switching)
	Problem solving	Delis–Kaplan Executive Function System (D-KEFS), card sorting test
	Visual attention	Trail Making Test (TMT), A
	Visual attention, cognitive flexibility	Trail Making Test (TMT), B
Motor function	Sustained attention	Conners' Continuous Performance Test, 2nd Edition (CPTII), omission errors
	Attention, impulsivity	Conners' Continuous Performance Test, 2nd Edition (CPTII), commission errors
	Motor speed	Delis–Kaplan Executive Function System (D-KEFS), trail making test (condition 5)
	Fine motor dexterity and speed	Grooved pegboard (dominant hand)
	Psychomotor speed	Wechsler Intelligence Scale for Children-IV (WISC-IV), or Wechsler Adult Intelligence Scale – IV (WAIS-IV) coding

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