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List-learning and verbal memory profiles in childhood epilepsy syndromes

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ABSTRACT

Findings of material-specific influences on memory performance in pediatric epilepsy are inconsistent and merit further investigation. This study compared 90 children (aged 6 years to 16 years) with childhood absence epilepsy (CAE), frontal lobe epilepsy (FLE), and temporal lobe epilepsy (TLE) to determine whether they displayed distinct list-learning and verbal memory profiles on the California Verbal Learning Test — Children's Version (CVLT-C). Group comparison identified greater risk of memory impairment in children with TLE and FLE syndromes but not for those with CAE. While children with TLE performed worst overall on Short Delay Free Recall, groups with TLE and FLE performed similarly on Long Delay Free Recall. Contrast indices were then employed to explore these differences. Children with TLE demonstrated a significantly greater retroactive interference (RI) effect compared with groups with FLE and CAE. Conversely, children with FLE demonstrated a significantly worse learning efficiency index (LEI), which compares verbal memory following repetition with initial recall of the same list, than both children with TLE and CAE. These findings indicated shallow encoding related to attentional control for children with FLE and retrieval deficits in children with TLE. Finally, our combined sample showed significantly higher rates of extreme contrast indices (i.e., 1.5 *SD* difference) compared with the CVLT-C standardization sample. These results underscore the high prevalence of memory dysfunction in pediatric epilepsy and offer support for distinct patterns of verbal memory performance based on childhood epilepsy syndrome.

1. Introduction

Epilepsy is one of the most common neurological disorders in childhood and one that affects not only physical functioning but also cognitive, social, emotional, and behavioral functioning. While the majority of patients show an intellectual level within the average range [1], children and adolescents with epilepsy as a group are more at risk for poor academic achievement [2–4], diminished health-related quality of life [5], and worse psychosocial outcomes [6,7]. This calls attention to the importance of the neuropsychological evaluation to detect potential deficits, which may underlie suboptimal functioning [8–12], and to provide useful information for presurgical planning [13].

Past research has indicated that children with epilepsy display specific cognitive weaknesses, with a number of studies demonstrating deficits in the domain of memory [2,8,9,14–19]. It has been hypothesized that children with focal seizures involving the temporal lobe and hippocampus may be particularly vulnerable to verbal memory difficulties and that these deficits may be related to interhemispheric specialization [8]. As prefrontal and medial temporal lobe systems likely interact during verbal learning and memory [20,21], different patterns of memory deficits may be expected in specific epilepsy syndromes.

In the adult literature, reliable patterns of verbal memory functioning have been demonstrated based on specific epilepsy syndromes, with temporal lobe epilepsy (TLE) being the most studied. Typically, patients with TLE show deficits in delayed recall for verbal information and verbal retention [22–25] and increased retroactive interference (RI), which have been identified as reliable markers of perirhinal and hippocampal impairment [26–28]. Specifically, RI occurs when new learning disrupts memory for previously learned information. The degree of susceptibility to RI effects has been shown to be an indicator of dominant hippocampal functioning [26,27,29–31]. This may occur as the hippocampus establishes distinct memory traces through a process known as pattern separation, which allows the system to effectively differentiate between memory traces [32,33]. Therefore, it stands to reason that measuring one's susceptibility to RI effects would offer clinical utility in evaluating the integrity of dominant hippocampal functioning for presurgical evaluation [34,35]; however, this metric has yet to be fully explored in children and adolescents with epilepsy.

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There is also substantial evidence for the contribution of frontal lobe systems in memory processes, with attention and executive functions playing a critical role in both the acquisition and retrieval of new memory traces [17,20,21,36]. Interestingly, adults with FLE often show greater susceptibility to proactive interference [17], which is associated with shallow encoding due to poor executive control [21,37–40]. Proactive interference (PI) occurs when previously learned material disrupts memory for newly learned information. Similarly to RI, PI has yet to be fully investigated in pediatric epilepsy.

While the nexus between epilepsy syndrome and memory deficits is more established in adults, findings are still equivocal within the pediatric epilepsy literature. For example, comparisons made between children with focal epilepsies and children with generalized epilepsies found that children with focal epilepsies perform worse on tasks of verbal memory [8,11,16]. Conversely, other studies comparing children with localization-related epilepsies with children with generalized seizures have not found significant differences in memory functioning [2,14,15]. These discrepant findings may be related to several contributing factors, including sample heterogeneity due to less rigorous classification methods, different grouping criteria among studies, inconsistent use of neuropsychological measures, and different age ranges across studies. Additionally, seizure-specific variables may contribute to inconsistent outcomes across studies, as past research has shown that earlier age of seizure onset [8,9,11,16,19], longer duration of disease [8,19], seizure frequency [3,9,11,19], and polytherapy [3,8,19] can all contribute to poorer cognitive outcomes in children and adolescents with epilepsy.

Taking the existing body of research into account, it is clear that additional studies are necessary to explore the relationship between seizure syndrome and verbal memory at this time. The goal of the present study was to compare verbal learning and memory profiles of children and adolescents with three common epilepsy diagnoses, including childhood absence epilepsy (CAE), frontal lobe epilepsy (FLE), and temporal lobe epilepsy (TLE). The current study utilized the California Verbal Learning Test — Children's Version (CVLT-C) [41], which not only allows for the examination of verbal learning and memory profiles over time but also allows for contrasting performance at different time points (e.g., PI, RI, and others). The impact of epilepsy-specific variables on verbal learning and memory was also assessed.

Our a priori hypotheses were as follows: Compared with other epilepsy syndromes, (1) children with TLE would show significant deficits in immediate and delayed recall and a greater retroactive interference effect; (2) the group with FLE would perform significantly worse on initial verbal span (List A, Trial 1), flexibility (List B), and overall learning (A5) trials, with a significantly greater proactive interference effect; and (3) the group with CAE would outperform both groups in demonstrating average list learning and verbal recall. If verbal learning and memory patterns specific to epilepsy syndrome and clinical seizure variables can be identified, this could aid in the early identification of youths at risk of developing cognitive problems and in facilitating more reliable interpretation of data for children undergoing presurgical evaluation.

2. Methods

2.1. Participants

The current study included 30 children with CAE, 30 children with TLE, and 30 children with FLE, aged 6 to 16 years ($M = 11.60$, $SD = 3.10$). Study sample characteristics delineated by epilepsy syndrome are summarized in Table 1. Our sample included 57 males (63.3%) and 43 females (47.7%), with the majority of children identifying as Caucasian/White (83.3%). Most patients experienced seizure onset at an early age ($M = 5.65$, $SD = 3.96$), with syndrome-specific onset ranging between 4.83 years (CAE) and 6.55 years (FLE). Seizure frequency determined by parent report and medical records averaged one seizure per month, which was consistent across groups. Epilepsy duration (i.e., date of diagnosis to date of neuropsychological testing) averaged about 70 months for the entire sample and ranged from 60.2 months (FLE) to 79.6 months (TLE) across syndromes. The majority of children (54.4%) were prescribed multiple antiepileptic drugs (AEDs) [range: 1–9 AEDs].

Table 1
Demographics and seizure characteristics.

Variables	Syndrome		
	CAE (n = 30)	TLE (n = 30)	FLE (n = 30)
Chronological age (years) (SD)	11.1 (2.95)	12.18 (3.23)	11.48 (3.08)
Gender			
Male (%)[a]	14 (46.7%)	19 (63.3%)	24 (80.0%)
Female (%)	16 (53.3%)	11 (36.7%)	6 (20.0%)
Graphomotor			
Right (%)	24 (80.0%)	26 (86.7%)	25 (83.3%)
Left (%)	6 (20.0%)	4 (13.3%)	5 (16.7%)
Ethnicity			
Caucasian/White (%)	21 (70.0%)	22 (73.3%)	24 (80.0%)
Non-Caucasian (%)	9 (30.0%)	8 (26.7%)	6 (20.0%)
Age of onset (years) (SD)	4.83 (1.89)	5.57 (4.67)	6.55 (3.45)
Epilepsy duration (months) (SD)[b]	71.7 (52.7)	79.6 (59.7)	60.2 (46.3)
<60 months	14 (46.7%)	11 (36.7%)	12 (40.0%)
≥60 months	16 (53.3%)	19 (63.3%)	18 (60.0%)
Seizure frequency code			
Mean, SD	3.07 (1.6)	3.30 (1.6)	3.07 (1.4)
≥Weekly	13 (43.3%)	14 (46.7%)	11 (36.7%)
≤Monthly	17 (56.7%)	16 (53.3%)	19 (63.3%)
Number of AEDs (at time of testing)[c]			
Monotherapy	16 (53.3%)	13 (43.3%)	12 (40.0%)
Polytherapy	14 (46.7%)	17 (56.7%)	18 (60.0%)
Seizure lateralization			
Left (%)	N/A	15 (50.0%)	14 (47.7%)
Secondary generalization (%)	N/A	11 (36.7%)	10 (33.3%)
Verbal Comprehension Index (%)	89.5 (16.7)	84.9 (18.4)	85.0 (10.6)

[a] Significantly more males — FLE vs. CAE [$\chi^2_{2,87} = 7.18$, $p = 0.028$].
[b] Epilepsy duration ranged from 6 to 174 months.
[c] Number of current AEDs ranged from 1 to 9 medications.

The primary study inclusion criterion for each child was that he/she had a diagnosis of epilepsy (TLE, FLE, or CAE) and was currently seen through the Comprehensive Epilepsy Program at Dell Children's Medical Center of Central Texas. Diagnoses of TLE, FLE, or CAE were made by a pediatric epileptologist, based on clinical history and electroencephalography (EEG) findings, according to the guidelines of the International Classification of Epilepsy Commission [42]. All patients with CAE had EEG evidence of 3-Hz spike-and-wave in addition to absence seizures induced by hyperventilation. Children with focal epilepsies (FLE and TLE) were identified based on clearly defined unilateral EEG localization, semiology, and epileptologist consultation. Children with bilateral epileptiform activity were not included in the present study. Left hemispheric epileptic focus was identified in 50.0% of the group with TLE and 47.7% of the group with FLE. Additional exclusion criteria for patients included the following: multiple seizure types, previous epilepsy surgery, a neurological illness other than epilepsy, a chronic medical illness, the presence of or history of thought disorder or severe psychopathology, hearing impairment, and being non-English-speaking.

2.2. Measures

2.2.1. Verbal memory and list-learning measure

Verbal learning and memory were assessed with the California Verbal Learning Test — Children's Version (CVLT-C) [41]. Raw scores for CVLT-C were converted to age standard scores ($M = 100$, $SD = 15$) using normative data provided by the test developers. The following CVLT-C variables (in standard scores) were included in this investigation: total words correctly recalled on List A, Trial 1 (A1), total words correctly recalled on List A, Trial 5 (A5), total words correctly recalled on distracter List B (B), total words correctly recalled on Short