Epilepsy & Behavior 99 (2019) 106487

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Are frontal and temporal lobe epilepsy dissociable in their memory functioning?

Michelle Y. Kibby [a,*], Morris J. Cohen [b], Lisa Stanford [c], Yong D. Park [d]

[a] Southern Illinois University, Department of Psychology, LSII, Room 281, Carbondale, IL 62901-6502, USA
[b] Pediatric Neuropsychology International, 2963 Foxhall Circle, Augusta, GA 30907, USA
[c] NeuroDevelopmental Science Center, Akron Children's Hospital, Considine Professional Building, 215 W. Bowery St., Suite 4400, Akron, OH 44308, United States of America
[d] Department of Neurology, Medical College of Georgia at Augusta University Children's Medical Center, 1446 Harper Street, Augusta, GA 30912, USA

ARTICLE INFO

Article history:
Received 15 April 2019
Revised 6 August 2019
Accepted 6 August 2019
Available online xxxx

Keywords:
Temporal lobe epilepsy
Frontal lobe epilepsy
Working memory
Learning and memory
Children
Children's Memory Scale

ABSTRACT

There is controversy in the literature as to how dissociable frontal lobe epilepsy (FLE) and temporal lobe epilepsy (TLE) are in terms of memory deficits. Some researchers have demonstrated that FLE is associated with greater executive dysfunction including working memory, whereas TLE is associated with greater memory impairment. Others have found the two groups to be comparable in memory functioning. Hence, we examined this question in children with FLE and TLE versus typically developing controls. We found most of the expected effects when the groups with focal onset epilepsy were compared to controls. Specifically, children with left TLE performed worse on verbal short-term memory/learning and long-term memory measures. In contrast, children with right TLE exhibited a more global pattern of difficulty on short-term memory/learning measures but performed worse than controls on long-term memory for faces. Children with FLE performed worse than controls on verbal working memory. Nevertheless, laterality effects were mild, as children with right and left TLE did not differ significantly from each other. Further, children with FLE did not differ from those with TLE on most measures except delayed facial recognition, where children with right TLE performed worse. In addition, attention problems and poor behavioral regulation were related to encoding problems in both the total epilepsy sample and in children with TLE specifically. Hence, our findings overall are consistent with prior studies indicating that children with TLE and FLE are commensurate in most aspects of memory impairment when compared to each other, likely related to rapid propagation between the frontal and temporal lobes, as would be expected with an excitatory lesion.
© 2019 Elsevier Inc. All rights reserved.

1. Introduction

Focal onset epilepsy has been associated with memory deficits in numerous studies across pediatric and adult populations [3,5,7–13,22–30]. The two most prevalent types of focal onset epilepsies have their onset in the temporal (TLE) and frontal lobes (FLE) [1,2]. While some studies find TLE and FLE to have dissociable deficits on memory testing, others do not as demonstrated in the following overview. Hence, we examined short-term, working, and long-term memory functioning in children/adolescents with focal onset seizures originating in the frontal or temporal lobes and typically developing controls to further address this controversy. For the purposes of this study, short-term memory (STM) refers to immediate memory and short-delay storage, including learning over trials. Working memory (WM) refers to STM that requires mental manipulation or updating of material. Long-term memory (LTM) refers to storage over intervals of 25 to 35 min.

In terms of frontal lobe epilepsy (FLE), some researchers have found the expected effects in memory. More specifically, attention control and WM problems have been documented in FLE [1,3–6]. Nevertheless, memory problems may extend beyond the deficits traditionally associated with frontal lobe functioning, as FLE also has been associated with poor STM and/or LTM [3,5,7–13]. As opposed to TLE, memory deficits in FLE may be due to executive dysfunction, including poor strategy usage during encoding and reduced interference control [1,3,8,14,15]. In addition, laterality effects may not be as common in FLE as they are in TLE. Although hemisphere-specific effects have been found in FLE [3,16,17], differences in laterality are not commonly present [7,8,12,18,19]. This may be due to the frontal lobes having strong interhemispheric connections and being prone to rapid propagation of epileptic discharges to the contralateral hemisphere [6,13,20]. Lastly, while many studies have found deficits in at least some form of memory in pediatric FLE, not all have [18,21].

Pediatric TLE is frequently associated with memory deficits, and laterality effects are commonly found. For example, memory for faces is commonly affected in right TLE [22–24]. Deficits in visual learning, STM, and/or LTM of geometric designs, patterns, and spatial arrangements

* Corresponding author.
E-mail addresses: mkibby@siu.edu (M.Y. Kibby), mcohen@augusta.edu (M.J. Cohen), lstanford@chmca.org (L. Stanford), ypark@augusta.edu (Y.D. Park).

https://doi.org/10.1016/j.yebeh.2019.106487
1525-5050/© 2019 Elsevier Inc. All rights reserved.

have been found as well [12,17,25–27]. Left TLE is associated with deficits in verbal LTM [12,25,28–30], likely due to more rapid forgetting than controls [17], along with poor encoding and consolidation of the material [12]. Relatedly, deficits in verbal STM/learning have been demonstrated in left TLE as well [12,25,27,29], and may be more pronounced with early seizure onset [31]. Although many studies have demonstrated laterality effects in pediatric TLE, some have not [27,31–33].

As shown through this review of the literature, STM and LTM may be affected in both FLE and TLE. Hence, it is debated how dissociable FLE and TLE are in terms of memory functioning. Some authors have found memory impairment for verbal and/or nonverbal material at commensurate levels in FLE and TLE [3,4,9,34,35]. The reason why memory impairment may be comparable between the two groups is rapid spread of propagation between the frontal and temporal lobes [36–39]. It also may be that although scores are similar, memory is impaired for different reasons, such as poor mnemonic/strategy usage, attention, and/or interference control in FLE [3,10,40] versus consolidation/binding problems in TLE [3,12,33].

Others have found TLE and FLE to differ in levels/types of memory impairment [6,12,18,41]. For example, Culhane-Shelburne and colleagues found pediatric TLE to have impaired verbal memory but spared executive functioning (EF), whereas FLE had the opposite profile. Nolan and colleagues found TLE to function worse than FLE in verbal memory; children with TLE also frequently had the lowest scores on visual memory and performed below average on most STM and LTM measures administered. Children with FLE only performed below the normative mean on a few STM measures and one delayed recall measure - story recall. Schraegle and colleagues found children with TLE performed worse than FLE in STM, but both groups were equivalent on long-delay recall. Further, TLE was associated with more retroactive interference than FLE, but FLE had worse learning efficiency (over trials) than TLE. In their review, Patrikelis and colleagues demonstrated that FLE may be more affected than TLE in sustained attention, resistance to distractors and EF, but TLE may be more affected than FLE in memory.

Two prior studies on focal onset epilepsy and localization of function have been published using the current dataset. The first directed its analysis of memory functions by hemisphere of onset and found the typical laterality effects [42]. More specifically, Kibby and colleagues found children with left foci performed worse than controls on measures of paired associate delayed recall and semantic memory, whereas children with right foci performed worse than controls on delayed facial recognition. Both groups with epilepsy performed poorly on measures of focused attention and long-term passage retention. The second study used a subset of the present study's sample (N = 28; 10 FLE & 18 TLE) to investigate EF and found frequency of impairment on the Attention/Concentration Index of the Children's Memory Scale (CMS) to be greater in FLE than TLE, among other EF findings [43]. Finally, a separate study compared children with comorbid attention-deficit/hyperactivity disorder (ADHD)/partial epilepsy to those with either disorder in memory functioning [44]. Both children with ADHD and children with focal onset epilepsy had deficits in focused attention/simple span; children with epilepsy also had additional STM/encoding problems. Those with comorbid epilepsy/ADHD performed similarly to children with either disorder, with slight additive effects. Localization effects were not investigated in this paper.

The purpose of this study was to determine whether children/adolescents with TLE or FLE are dissociable in their short-term, working, and LTM deficits from each other and controls. Frontal lobe epilepsy was studied as one group due to the rapid propagation between the frontal lobes and limited number of studies finding laterality effects within the frontal lobes. Based upon the bulk of the literature reviewed, it was hypothesized that children with left TLE would perform worse than controls on all verbal memory measures (STM/learning and LTM), and children with right TLE would perform worse than controls on all visual memory measures (STM/learning and LTM). Finally, children with FLE were hypothesized to perform worse than controls in WM. Although the literature is quite disparate when comparing FLE to TLE directly, it was hypothesized that children with right TLE would perform worse than children with FLE on memory for faces, both STM and LTM, due to the large volume of literature demonstrating deficits in this ability in children with right TLE. Children with left TLE were expected to perform worse than children with FLE in verbal LTM recall for stories, as this deficit is commonly found in left TLE. Further analyses were performed to determine whether LTM deficits were due to encoding, long-term storage, or retrieval problems.

2. Material and methods

2.1. Participants

Participants included 91 children, ages 6–15 years, with focal onset epilepsy (27 FLE, 34 left TLE, 30 right TLE) who were consecutive referrals to one of two pediatric neuropsychology clinics affiliated with tertiary care pediatric epilepsy centers (one in the Southeast and one in the Midwest). See Kibby and colleagues [42] for more in-depth information on the total sample.

For all sites, Institutional Review Board (IRB) approval was obtained prior to, and during, data collection. The epilepsy sample was diagnosed by pediatric neurologists. Seizure location and epilepsy diagnosis were based on video electroencephalogram (EEG) monitoring, neuroimaging, and seizure semiology, blind to neuropsychological testing. Exclusion criteria included intellectual disability (IQ below 70), bilateral foci, and prior epilepsy surgery. Children with frontal-temporal foci (spread of propagation was too quick to determine whether onset was frontal or temporal) also were excluded. Groups with epilepsy were comparable in age, socioeconomic status (SES), race/ethnicity, full-scale intelligence quotient (IQ), handedness, age at seizure onset, duration, seizure type, and number of antiepileptic drugs (AEDs); etiology was comparable also once mesial temporal sclerosis (MTS) was removed from the

Table 1
Participant demographic data.

Characteristic	Controls	FLE	Left TLE	Right TLE
Gender (% male)	53.1	48.1	52.9	46.7
Race/ethnicity (% Caucasian)	68.8	63.2	63.0	56.5
Handedness (% right-handed)	87.5	92.3	93.8	96.4
Seizure type (%)				
Simple partial		3.7	2.9	0.0
Complex partial		59.3	70.6	66.7
Unknown[a]		37.0	26.5	33.3
# of AEDs (%)				
0		11.1	2.9	3.3
1		33.3	41.2	56.7
2		51.9	47.1	33.3
3 or more		8.8	6.7	
Etiology (%)[b]				
Idiopathic		15.4	14.7	20.0
Tumor		15.4	11.8	16.7
Developmental lesion		26.9	23.5	26.7
MTS		0.0	38.2	26.7
TBI/acquired		42.3	11.8	10.0
	M(SD)	M(SD)	M(SD)	M(SD)
Age (years)	9.97(2.65)	10.98(2.79)	11.17(2.40)	10.16(2.10)
WISC-III/IV Full-Scale IQ	91.22 (13.46)	84.74 (13.74)	81.82 (16.59)	85.37 (18.46)
Seizure onset (years at onset)		5.60(3.57)	5.10(3.62)	4.91(3.51)
Epilepsy duration (years)		5.42(3.89)	6.00(4.41)	6.04(5.17)

[a] The Midwest epilepsy center did not provide information on seizure type beyond that they were focal onset epilepsy cases.
[b] Groups did not differ when MTS was excluded from the equation. Groups did not differ on the rest of the variables ($ps > 0.10$).

equation ($ps > 0.10$) (see Table 1). Many children in the epilepsy sample had intractable epilepsy, being evaluated as candidates for epilepsy surgery, and the vast majority were on one or more AEDs (95%).

Thirty-two controls were obtained from the CMS normative sample with permission from the Psychological Corporation, Pearson. They were selected from the linking sample to match the epilepsy sample in age, gender, race/ethnicity, handedness, and full-scale IQ as closely as possible, blind to CMS data. We were unable to equate on SES, as our measure of SES was not collected on the children in the CMS standardization sample, but it is believed that the two groups are equivalent (see [42] for further information). Exclusion criteria for the normative sample were significant learning problems (repeating a grade, reading below grade level, and being referred for, or already in, Chapter/Title I services or special education) and being diagnosed with a neurological disorder. For all groups, participants were not included in this study if IQ was below 70.

2.2. Measures

The CMS [45] assesses verbal and nonverbal memory in the areas of focused attention/WM, STM, and LTM. As noted in the CMS manual, its psychometric properties are good to excellent, with reliability quotients of 0.71–0.91 across ages at the subtest level. Further, its criterion validity was demonstrated via moderate to high correlations with the Wechsler Memory Scale-III. The CMS is described in more detail in Kibby et al.'s article [42], but a brief description is provided below.

In terms of focused attention/WM, the CMS includes measures of forward digit span (Numbers Forward), backward digit span (Numbers Backward), forward spatial span (Picture Locations) and verbal WM via sequence manipulation (Sequences). Sequences starts out simple and then becomes more complex, such as counting forward or backward, saying the days of the week or months of the year forward or backward, to alternating between numbers and letters while counting.

Short-term memory/learning and LTM are measured via Stories, Word Pairs, Dot Locations, and Faces. During Stories Immediate, children are asked to listen to a story and immediately repeat it. Two stories are presented, with the ones being presented varying in length/complexity with age. Stories Delayed (free recall) is presented after a 25 to 35-min delay, and Stories Delayed Recognition (forced choice, yes/no format) is presented immediately thereafter. During Word Pairs Learning children are presented with a list of 10 or 14 word pairs over three learning trials, with the length of the list being dependent upon age. Most word pairs are not semantically related. After each presentation of the list, the first word of the pair is presented, and the child is asked to say the second word of the pair. After the third trial, immediate recall is presented, where the child is asked to recall the pairs on their own, in any order. Word Pairs Delayed is presented after a 25 to 35-min delay and uses the same format as immediate recall. Word Pairs Delayed Recognition is presented immediately thereafter and uses a forced choice (yes/no) format. Dot Locations also measures learning over three trials. During Dot Locations Learning, children see an array for 5 s of 6 or 8 dots depending upon age. Immediately after each trial, they are asked to place chips on a grid where they saw the dots. They are then presented with a distractor trial with a new array of different colored dots, after which they are asked to recall the array presented during the learning trials (short-delay recall). After a 25 to 35-min delay they are presented with Dot Locations Delayed (free recall format). Faces uses a recognition format. During Faces Immediate, the child is presented with a series of 12 or 16 faces for 2 s each, with the number of faces being dependent upon age. Immediately following initial presentation, the child views another series of faces that includes foils along with the target faces and is asked whether each face was in the target group via a yes/no format. Faces Delayed works in a similar fashion, but the foils are different to reduce interference.

Handedness was determined via observation of handwriting and verified with parent report. Socioeconomic status was measured by level of parent income (group with focal onset epilepsy) or parental education (control group). Intelligence was measured with the Wechsler Intelligence Scale for Children, Third or Fourth Edition (WISC-III or -IV) for the group with epilepsy, and WISC-III for controls. As the group with epilepsy was tested during a neuropsychological evaluation, the latest edition of the test had to be used ethically. Attention control and behavioral regulation were measured in the groups with epilepsy with the Behavior Assessment for Children (BASC/BASC-2) Attention Problems and Hyperactivity/impulsivity scales, respectively, using whatever the current edition was at the time of testing. This measure was not available for the control group.

2.3. Procedures

For all groups, children were tested individually in accordance with the administration procedures described in the CMS manual. Permission to test was obtained from the parent and child, and parental consent was obtained to use their child's de-identified data in research. For the group with epilepsy, it was verified with the child's parent (s) that a seizure had not occurred within 24 h prior to the evaluation.

2.4. Data analysis

Initially, equivalency of groups was examined using Analysis of Variance (ANOVA) test or chi-square, as indicated in Section 3.1. Four Multivariate Analysis of Variance (MANOVA) tests were used to test for group differences (FLE, right TLE, left TLE, controls) in focused attention/WM, STM/learning, LTM, and long-term verbal recognition, with Tukey Honestly Significant Difference (HSD) test for post hoc analyses. To determine source of the LTM impairment (i.e., encoding, storage, retrieval), repeated measures ANOVA was used on the measures where memory impairment was found. The relationships between attention control, behavioral regulation, and initial encoding were examined across the four STM/learning measures in an exploratory fashion using Pearson correlations in the epilepsy sample to determine whether attention control and/or behavioral regulation deficits may be related to the findings. This analysis was performed because prior research has shown that attention control and/or behavioral regulation may affect initial encoding in individuals with epilepsy [3,10,40]. More sophisticated analyses were unable to be performed here due to insufficient power. Exploratory analyses with the group with FLE also were performed to minimize Type II error.

3. Results

3.1. Preliminary analyses

The success of the match between the control group and groups with focal onset epilepsy was evaluated using ANOVA or chi-square, as indicated by the nature of the variable. Groups were comparable in age, gender, race/ethnicity, handedness, and WISC-III/WISC-IV Full Scale IQ ($ps > 0.10$) (see Table 1). In terms of Wechsler IQ, when using MANOVA groups were comparable ($ps > 0.05$) in verbal and nonverbal reasoning (Verbal Comprehension Index (VCI) and Perceptual Reasoning Index (PRI)/Perceptual Organization Index (POI), but they differed in verbal working memory (WMI/Working Memory Index (WMI)/Freedom from Distractibility Index (FDI), $F(3, 114) = 5.26$, $p = .002$, and processing speed (PSI), $F(3, 114) = 6.11$, $p = .001$. Post hoc analysis with Tukey HSD revealed FLE ($p = .004$), and left TLE ($p = .005$) performed worse than controls in verbal WM, and FLE ($p = .001$) and left TLE ($p = .01$) performed worse than controls in PSI (see Table 2). Intelligence quotient was not used as a covariate because WM and PSI are commonly affected in focal onset epilepsy, PSI is correlated with WM functioning, WM is a focus of this investigation, and the groups are comparable in reasoning and Full-Scale IQ.

Table 2
WISC III/IV differences between groups.

Variable	Controls	FLE	Left TLE	Right TLE	$F(3,114)$	Partial η^2	p
	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)			
VCI	91.97(13.06) [86.43–97.50]	91.37(14.10) [85.63–97.11]	82.94(15.77) [77.75–88.13]	87.76(16.84) [82.22–93.30]	2.35	0.06	0.08
PRI/POI	92.14(14.39) [86.24–98.03]	89.41(15.55) [83.30–95.52]	89.88 (15.32) [84.35–95.40]	90.10(18.57) [84.21–96.00]	0.16	0.004	0.92
WMI/FDI[a]	98.97(14.30) [93.07–104.87]	83.96(15.04) [77.85–90.08]	85.09(15.42) [79.56–90.62]	89.27(19.00) [83.38–95.18]	5.26	0.12	0.002
PSI[b]	100.59(14.42) [94.52–106.65]	82.93(12.68) [76.64–89.21]	87.27(18.82) [81.60–92.96]	92.79(18.56) [86.73–98.86]	6.11	0.14	0.001

Note. a = FLE and left TLE differed from controls at $p < .01$; b = FLE differed from controls at $p = .001$, and left TLE differed from controls at $p = .01$. 95% confidence intervals for the means are presented in brackets.

While it was anticipated that left and right FLEs would be comparable in memory functioning based upon the literature reviewed, this was verified using independent samples *t*-tests to minimize Type II error. Right and left FLEs were comparable on all CMS measures ($ps > 0.10$). Hence, FLE was studied as a single group in subsequent analyses.

3.2. Main results

In the focused attention/WM analysis, the dependent variables included Numbers Forward, Numbers Backward, Picture Locations, and Sequences. The omnibus equation was significant, $\lambda = 0.73$, $F(12, 222.54) = 2.36$, partial $\eta^2 = 0.10$, $p = .007$. At the univariate level, groups differed in Numbers Forward, with all three groups with epilepsy performing worse than controls ($ps < 0.01$) but comparably to each other. See Table 3 for descriptive CMS data.

For the STM/learning analysis, the dependent variables included Stories Immediate, Word Pairs Learning, Dot Locations Learning, and Faces Immediate. The omnibus equation was significant, $\lambda = 0.76$, $F(12, 301.91) = 2.79$, partial $\eta^2 = 0.09$, $p = .001$. Groups differed on Word Pairs Learning and Faces Immediate, and there was a trend on Dot Locations Learning. On Word Pairs Learning the group with left TLE performed worse than controls ($p = .01$). On Faces Immediate, right TLE performed worse than controls ($p = .003$) and FLE ($p = .04$). On Dot Locations learning right TLE displayed a trend versus controls ($p = .06$).

For the LTM analysis, the dependent variables were Stories Delayed, Word Pairs Delayed, Dot Locations Delayed, and Faces Delayed. The omnibus equation with four dependent variables was significant, $\lambda = 0.74$, $F(12, 301.91) = 3.06$, partial $\eta^2 = 0.10$, $p < .001$. Groups differed on all but Dot Locations Delayed. On Stories

Table 3
CMS differences between groups.

Variable	Controls	FLE	Left TLE	Right TLE	F	Partial η^2	p
	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)			
Focused attention/WM analysis					*df*(3,87)		
Numbers F.	100.00(14.76) [94.35–105.65]	82.67(17.82)[a] [74.41–90.92]	86.00(16.07)[a] [79.61–92.39]	82.11(16.86)[a] [74.77–89.44]	7.18	0.20	<0.001
Numbers B.	98.28(11.54) [93.19–103.37]	88.33(16.76) [80.90–95.77]	91.80(14.92) [86.04–97.56]	96.84(16.43) [90.24–103.45]	2.09	0.07	0.11
Sequences	98.44(11.67) [92.37–104.51]	90.00(21.12) [81.14–98.86]	93.40(20.35) [86.54–100.27]	91.32(17.55) [83.44–99.19]	1.13	0.04	0.34
Picture Loc.	94.53(15.10) [88.37–100.69]	86.33(17.16) [77.34–95.33]	93.40(16.75) [86.43–100.37]	86.58(22.11) [78.59–94.57]	1.34	0.04	0.27
STM/learning analysis					*df*(3117)		
Stories	91.72(14.29) [85.62–97.82]	93.70(18.48) [87.06–100.34]	85.63(18.00) [79.52–91.73]	86.33(18.84) [80.03–92.64]	1.54	0.04	0.21
Word Pairs	95.94(16.48) [89.62–102.25]	86.67(18.71) [79.79–93.54]	81.72(16.97)[a] [75.40–88.04]	87.83(20.03) [81.31–94.36]	3.41	0.08	0.02
Dot Locations	99.06(15.78) [93.17–104.95]	91.48(15.80) [85.07–97.90]	95.31(15.81) [89.42–101.20]	88.17(19.63)[b] [82.08–94.25]	2.42	0.06	0.07
Faces	93.91(10.45) [88.87–98.94]	91.48(16.92) [86.00–97.00]	88.28(16.20) [83.24–93.32]	81.00(13.48)[a,c] [75.80–86.20]	4.61	0.11	0.004
Delayed recall analysis					*df*(3117)		
Stories	93.91(15.23) [88.13–99.68]	89.26(16.91) [82.97–95.55]	80.47(15.57)[a] [74.70–86.24]	84.33(18.28) [78.37–90.30]	3.97	0.09	0.01
Word Pairs	100.62(14.69) [94.74–106.51]	89.63(15.00)[b] [83.22–96.04]	85.00(19.34)[a] [79.11–90.89]	89.33(17.16)[b] [83.25–95.41]	5.00	0.11	0.003
Dot Locations	99.22(13.45) [94.03–104.41]	96.30(16.15) [90.64–101.95]	92.34(14.86) [87.15–97.54]	94.17(15.00) [88.80–99.53]	1.26	0.03	0.29
Faces*	95.94(14.39) [90.53–101.35]	89.07(14.48) [83.18–94.96]	82.81(16.60)[a] [77.40–88.22]	80.17(16.11)[a] [74.58–85.76]	6.47	0.14	<0.001
Verbal delayed recognition analysis							
Stories	95.63(16.55) [89.00–102.25]	92.59(20.54) [85.38–99.81]	86.52(21.23) [79.99–93.04]	82.50(17.01)[d] [75.66–89.34]	2.99	0.07	0.03
Word Pairs	95.78(14.32) [88.72–102.84]	89.07(21.88) [81.39–96.76]	86.06(23.38) [79.11–93.01]	89.50(20.06) [82.21–96.79]	1.32	0.03	0.27

Note. Numbers F. = Numbers Forward, Numbers B. = Numbers Backward, and Picture Loc. = Picture Locations. a = differed from controls at $p \leq .01$; b = differed from controls at $p < .10$; c = differed from FLE at $p < .05$. d = differed from controls at $p < .05$. 95% confidence intervals for the means are presented in brackets. *Faces uses a recognition format.

Delayed recall left TLE performed worse than controls ($p = .01$). On Word Pairs Delayed recall both left TLE ($p = .002$) and right TLE ($p = .046$) performed worse than controls, and FLE displayed a trend versus controls ($p = .07$). On Faces Delayed both right TLE ($p = .001$) and left TLE ($p = .01$) performed worse than controls. Finally, the omnibus equation focused on verbal delayed recognition, with Story Delayed Recognition and Word Pairs Delayed Recognition as dependent variables, was not significant but displayed a trend, $\lambda = 0.91$, $F(6, 234.00) = 1.89$, partial $\eta^2 = 0.05$, $p = .08$. Right TLE differed from controls on Stories ($p = .04$).

To determine whether deficits in LTM on Stories, Word Pairs, and Faces was due to poor initial encoding into STM, poor consolidation into LTM/potential loss over time, or poor retrieval, repeated measures ANOVA was used, including STM, LTM free recall, and LTM recognition for Stories and Word Pairs. It was used to compare Faces Immediate and Delayed recognition as well. The omnibus equations analyzing Stories and Stories * Group were significant [Stories: $\lambda = 0.91$, $F(2, 118) = 5.94$, $p = .003$; Stories * Group: $\lambda = 0.85$, $F(6, 236) = 3.37$, $p = .003$]. The Quadratic within-subjects contrasts were significant for Stories and Stories * Group as well [Stories: $F(1, 119) = 7.45$, $p = .01$; Stories * Group: $F(3, 119) = 32.87$, $p = .04$]. Further, the between-subjects contrast was significant, $F(3, 119) = 3.27$, $p = .02$, with left TLE differing from controls ($p = .05$) (see Fig. 1).

The omnibus Word Pairs * Group equation was not significant, $\lambda = 0.98$, $F(6, 236) = 0.40$, $p = .88$; the omnibus Word Pairs equation displayed a trend, $\lambda = 0.95$, $F(2, 117) = 2.82$, $p = .06$. None of the within-subjects contrasts were significant, quadratic, or linear ($ps \geq 0.10$), but the between-subjects contrast was significant, $F(3, 118) = 4.05$, $p = .01$. It was driven by the group with left TLE performing worse than controls ($p = .005$). See Table 3 for means and standard deviations. As Faces only has Immediate and Delayed recognition, analysis did not include quadric contrasts. The omnibus equations for Faces [$\lambda = 0.98$, $F(1, 118) = 1.99$, $p = .16$.] and Faces * Group were not significant [$\lambda = 0.96$, $F(3, 118) = 1.87$, $p = .13$]; the same was true of the within-subjects linear contrasts ($ps \geq 0.10$). Similar to the previous findings, the between-subjects contrast was significant [$F(1, 118) = 6.55$, $p < .001$], with both right TLE ($p < .001$) and left TLE ($p = .02$) differing from controls and right TLE differing from FLE ($p = .04$). See Table 3 for means and standard deviations. Based upon these findings, it appears that LTM problems on Faces and Word Pairs are due to poor initial encoding of the material.

3.3. Exploratory analyses

Teacher-report BASC/BASC-2 Attention Problems and Hyperactivity/impulsivity were examined in relation to the STM/learning measures using Pearson correlations. Hyperactivity/impulsivity was related to Stories ($r = -0.33$, $p = .02$), Word Pairs ($r = -0.38$, $p = .01$), and Faces ($r = -0.44$, $p = .001$); Dot Locations was not significant ($p > .10$). Attention Problems were related to Word Pairs ($r = -0.43$, $p = .002$) and Faces ($r = -0.33$, $p = .02$) and displayed a trend with Stories ($r = -0.25$, $p = .08$); Dot Locations was not significant ($p > .10$). To ensure the findings were not being driven by the group with FLE solely, the analyses were repeated with patients with TLE only. Hyperactivity/impulsivity was related to Stories ($r = -0.37$, $p = .03$), and Faces ($r = -0.45$, $p = .01$); but Word Pairs was no longer significant ($p > .10$). Attention Problems were related to Faces ($r = -0.41$, $p = .03$) and displayed trends with Stories ($r = -0.32$, $p = .06$) and Word Pairs ($r = -0.31$, $p = .07$).

Because of small sample size, FLE effects may have been obscured, especially on the WM measures where they had the lowest means versus the other groups. To protect against Type II error, FLE was compared versus controls on the two WM measures using independent samples *t*-tests: Numbers Backward and Sequences. Frontal lobe epilepsy performed worse than controls on Numbers Backward, $t(57) = 2.02$, $p = .047$, and displayed a trend on Sequences, $t(44) = 1.90$, $p = .06$. Next, presence of impairment was assessed to determine whether FLE had the greatest number of children with impairment on the two WM measures. Impairment was defined as performing greater than a standard deviation below the mean on that measure. Groups differed on Numbers Backward ($X^2 = 7.86$, $p = .049$), with FLE having the greatest percentage of children impaired (30% of FLE versus 24% of left TLE, 23% of right TLE and 0.03% of controls). There was a trend on Sequences ($X^2 = 7.08$, $p = .07$).

4. Discussion

The purpose of this study was to investigate memory functioning in children with FLE and TLE and to determine how dissociable their memory deficits are. Some researchers have found children with TLE and FLE to be comparable in memory functioning [3,9,34,35]. Others demonstrated that children with TLE and FLE have dissociable memory functioning, with TLE having more pervasive memory deficits [12,18]. We

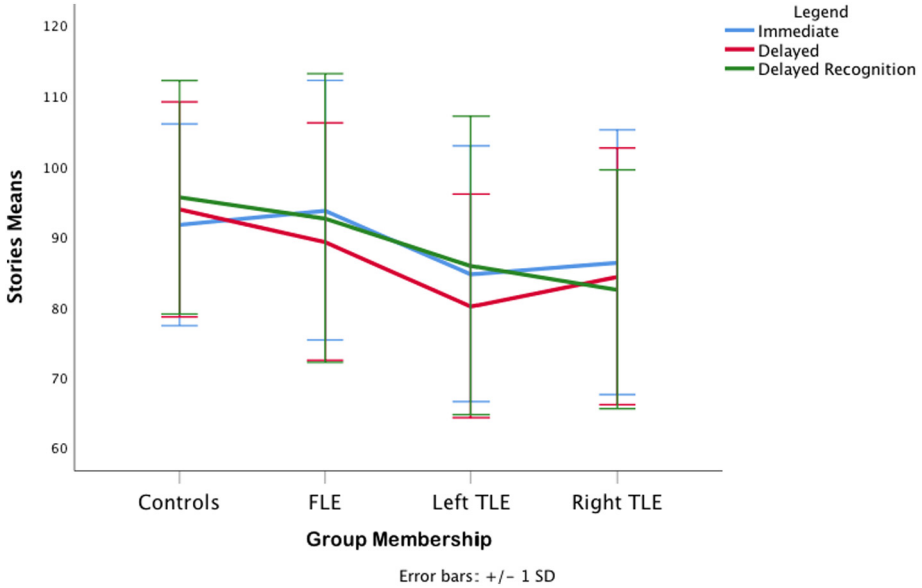

Fig. 1. Stories interaction.

found a middle ground where some differences in functioning were demonstrated when comparing children with TLE and FLE to controls, but only one difference was found between children with TLE and FLE when compared to each other.

We hypothesized that children with left TLE would perform worse than controls on all verbal STM and LTM measures. This aspect of Hypothesis 1 was partially supported: children with left TLE performed about a standard deviation below the normative mean on all verbal STM and LTM measures, and they significantly differed from controls on most of them. Nevertheless, laterality effects were mixed as children with left TLE performed worse than controls on delayed facial recognition, at a level comparable to children with right TLE, and they performed in the low average range overall on immediate facial recognition. This may be due to rapid propagation between the hemispheres affecting the contralateral hemisphere's functioning [25,46] and/or to left TLE being unable to verbally mediate the task well resulting in poor encoding [25,42].

Children with right TLE were hypothesized to perform worse than controls on all visual STM and LTM measures. This prediction was partially supported as well. At the STM level, children with right TLE significantly differed from controls or showed a trend on both nonverbal STM measures, consistent with work demonstrating more broad nonverbal memory deficits in right TLE [12,27]. Nevertheless, at the LTM level, only delayed facial recognition differed. Further, although there was a trend on spatial location learning versus controls, children with right TLE had their best mean performance on spatial locations of the four STM/LTM measures, whereas facial recognition was their worst score for both STM and LTM. These findings are consistent with the work of Gonzalez and colleagues [23] who showed that facial recognition had the greatest sensitivity to laterality effects. Despite facial recognition having the lowest mean in children with right TLE within and across groups, it should be noted that all scores were in the low average range at the STM level, suggesting at least mild, global difficulties with initial encoding. This could be related to the right hemisphere helping with semantic language functioning [47], which is consistent with right TLE's mean Wechsler VCI performance. It also could be related to chronic spreading of epileptic discharges to the left hemisphere, affecting its functioning [25,46].

Of note, when analyzing LTM both groups with TLE had their lowest mean performance on story recall and facial recognition. Prior research has suggested that of the two verbal measures used in this study, story recall may be more sensitive to hippocampal/mesial temporal functioning as material is only presented once during initial encoding, providing less opportunity for the hippocampus to perform its binding functions compared to multitrial learning [27,32,42]. Similarly, other research has demonstrated that facial recognition may be more sensitive to mesial temporal functioning than spatial locations [23]. As our TLE sample only had a subset with MTS, and it is unknown whether the other etiologies were in the mesial or lateral temporal lobes, future research is indicated to determine whether childhood mesial temporal epilepsy has greater impairment on memory for stories and faces than on word pairs and spatial locations.

It was hypothesized that FLE would perform worse than controls in WM. This hypothesis was partially supported. In the initial analysis on focused attention/WM, WM did not differ significantly from controls, but this could be related to power as FLE performed the worst of the four groups on backward digit span and sequential WM. When only FLE was compared to controls, group differences were found; further, FLE had the greatest number of individuals impaired on backward digit span of the four groups. Moreover, FLE performed worse than controls on the Wechsler Working Memory Index. Hence, verbal WM problems appear to be present in the group with FLE when compared to controls. A difference between FLE and controls also was found on forward span. This was true for all three groups with epilepsy, however, who were comparable to each other. Hence, focused auditory attention may be more globally affected in focal onset epilepsy, consistent with what was found in the larger study [42]. This finding may be related to long-term AED use (see [42]).

A related purpose of our study was to determine whether memory performance was dissociable between FLE and TLE. When comparing children with FLE or TLE to controls, the expected deficits were found: memory problems in TLE and WM problems in FLE. This is consistent with prior research demonstrating that TLE and FLE have dissociable memory deficits [12,18]. Nevertheless, our hypothesis regarding TLE and FLE differences was only partially supported. Children with right TLE did perform worse than children with FLE on delayed facial recognition, but differences between children with FLE and TLE were not found on the other measures. Hence, our findings also are consistent with prior work suggesting that FLE and TLE have comparable levels of memory impairment [3,9,34,35], representing a middle ground.

There are at least two potential reasons for comparable impairment as noted in the literature review: rapid propagation of impulses between the frontal and temporal lobes [36–39] and differing sources of the memory deficits despite the scores being equivalent [3,10,12,33,40]. Our data are more in-line with the first proposition. For all groups on most measures, LTM problems, when they occurred, appeared to be due to poor initial encoding based upon the repeated measures analyses. These results are consistent with what was found when analyzing the total sample [42]. As noted by Hersey and colleagues [31], STM deficits are common in TLE when seizure onset is early. Based upon our exploratory analyses investigating attention control's and behavioral regulation's relationships to the STM/learning measures, it appears that both attention control and behavioral regulation are related to initial encoding when deficits in encoding occur. This is true for the total epilepsy sample as well as the TLE sample specifically. As both of these functions are presumed to be performed by the frontal lobes, it suggests that rapid propagation between the frontal and temporal lobes may be affecting performance. On story recall, an interaction occurred on the repeated measures analysis. As observed in Fig. 1, most groups performed similarly on immediate recall and delayed recognition within group, suggesting initial encoding affected retrieval performance on delayed recall. In contrast, children with right TLE had their worst mean Stories performance on delayed recognition, suggesting problems with susceptibility to interference. This is consistent with literature suggesting that the right prefrontal region plays a role in interference control [48]. Both of these problems, poor initial encoding/retrieval and susceptibility to interference, could be frontally-based [47].

A strength of our sample is its size for the groups with TLE and the careful diagnostic process used to determine focal onset epilepsy. Another strength of the sample is that the groups with epilepsy were comparable across key variables: age, SES, race/ethnicity, IQ, handedness, seizure onset, duration, seizure type, and number of AEDs; etiology was comparable as well once MTS was removed from the equation. Nevertheless, there are limitations that need to be addressed in future research. One limitation is that the control and epilepsy samples had different measures of SES. A second limitation is that the most recent version of the WISC, and BASC had to be used in the epilepsy sample for ethical reasons as it was a clinic sample. This resulted in two somewhat different WISC and BASC versions being used in the epilepsy sample, but at least the correlations between the two versions are high according to the respective manuals. A third limitation is that the BASC/BASC-2 was not administered to the control group.

In summary, our results suggest that there is some dissociability between TLE and FLE memory functions when they are compared to controls. Children with TLE differed from controls in STM/learning and LTM functioning, whereas children with FLE differed from controls in WM functioning. Further, laterality effects were found in children with TLE when the two groups were compared to controls. Nevertheless, laterality effects were mild, as the two groups did not differ from each other, and right TLE was more globally affected at the STM level. Further,

children with FLE and TLE did not differ from each other on most measures except for LTM for faces, where children with right TLE performed worse. These findings in total are consistent with literature suggesting rapid propagation between contralateral homologous areas, as well as between ipsilateral frontal and temporal lobes, as would be expected with an excitatory lesion.

Acknowledgments

We would like to thank the families who participated in this study. We also would like to thank the students and staff who assisted with testing. Without them this work would not have been possible.

Declaration of competing interest

Morris Cohen is the author of the CMS. Nevertheless, the epilepsy data presented here were gathered at outpatient clinics, separate from the normative process. No grant funding or test development funding was received for this manuscript or its epilepsy sample. The control sample was selected from the larger normative sample with permission from The Psychological Corporation, Pearson.

Michelle Kibby: None.

References

[1] MacAllister WS, Schaffer SG. Neuropsychological deficits in childhood epilepsy syndromes. Neuropsychol Rev 2007;17:427–44. https://doi.org/10.1007/s11065-007-9048-4.
[2] Manford M, Hart YM, Sander JWAS, Shorvon SD. National General Practice Study of Epilepsy (NGPSE): partial seizure patterns in a general population. Neurology 1992;42:1911–7.
[3] Hernandez MT, Sauerwein HC, Jambaqué I, Guise E, Lussier F, Lortie A, et al. Attention, memory, and behavioral adjustment in children with frontal lobe epilepsy. Epilepsy Behav 2003;4:522–36. https://doi.org/10.1016/j.yebeh.2003.07.014.
[4] Longo CA, Kerr EN, Smith ML. Executive functioning in children with intractable frontal lobe or temporal lobe epilepsy. Epilepsy Behav 2013;26:102–8. https://doi.org/10.1016/j.yebeh.2012.11.003.
[5] Matricardi S, Deleo F, Ragona F, Rinaldi VE, Pelliccia S, Coppola G, et al. Neuropsychological profiles and outcomes in children with new onset frontal lobe epilepsy. Epilepsy Behav 2016;55:79–83. https://doi.org/10.1016/j.yebeh.2015.12.006.
[6] Patrikelis P, Angelakis E, Gatzonis S. Neurocognitive and behavioral functioning in frontal lobe epilepsy: a review. Epilepsy Behav 2009;14:19–26. https://doi.org/10.1016/j.yebeh.2008.09.013.
[7] Braakman HM, Vaessen MJ, Hofman PA, Debeij-van Hall MH, Backes WH, Vles JS, et al. Cognitive and behavioral complications of frontal lobe epilepsy in children: a review of the literature. Epilepsia 2011;52:849–56. https://doi.org/10.1111/j.1528-1167.2011.03057.x.
[8] Braakman HM, Ijff DM, Vaessen MJ, Debeij-van Hall MH, Hofman PA, Backes WH, et al. Cognitive and behavioural findings in children with frontal lobe epilepsy. Eur J Paediatr Neurol 2012;16:707–15. https://doi.org/10.1016/j.ejpn.2012.05.003.
[9] Fuentes A, Smith ML. Patterns of verbal learning and memory in children with intractable temporal lobe or frontal lobe epilepsy. Epilepsy Behav 2015;53:58–65. https://doi.org/10.1016/j.yebeh.2015.09.038.
[10] Lopes AF, Monteiro JP, Fonseca MJ, Robalo C, Simões MR. Memory functioning in children with epilepsy: frontal lobe epilepsy, childhood absence epilepsy, and benign epilepsy with centrotemporal spikes. Behav Neurol 2014:e218637. https://doi.org/10.1155/2014/218637 [8 pages].
[11] Luton LM, Burns TG, DeFilippis N. Frontal lobe epilepsy in children and adolescents: a preliminary neuropsychological assessment of executive function. Arch Clin Neuropsychol 2010;25:762–70. https://doi.org/10.1093/arclin/acq066.
[12] Nolan MA, Redoblado MA, Lah SS, Sabaz MM, Lawson JA, Cunningham AM, et al. Memory function in childhood epilepsy syndromes. J Paediatr Child Health 2004;40:20–7. https://doi.org/10.1111/j.1440-1754.2004.00284.x.
[13] Riva D, Avanzini G, Franceschetti S, Nichelli F, Saletti V, Vago C, et al. Unilateral frontal lobe epilepsy affects executive functions in children. Neurol Sci 2005;26:263–70.
[14] Centeno M, Thompson PJ, Koepp MJ, Helmstaedter C, Duncan JS. Memory in frontal lobe epilepsy. Epilepsy Res 2010;91:123–32. https://doi.org/10.1016/j.eplepsyres.2010.07.017.
[15] Johnson-Markve BL, Lee GP, Loring DW, Viner KM. Usefulness of verbal selective reminding in distinguishing frontal lobe memory disorders in epilepsy. Epilepsy Behav 2011;22:313–7. https://doi.org/10.1016/j.yebeh.2011.06.039.
[16] Riva D, Saletti V, Nichelli F, Bulgheroni S. Neuropsychological effects of frontal lobe epilepsy in children. J Child Neurol 2002;17:661–7.
[17] Svoboda WB. Memory. Childhood epilepsy: language, learning, and behavioral complications. United Kingdom: Cambridge University Press; 2004. p. 289–309.
[18] Culhane-Shelburne K, Chapieski L, Hiscock M, Glaze D. Executive functions in children with frontal and temporal lobe epilepsy. J Int Neuropsychol Soc 2002;8:623–32 [10.1017.S1355617702801308].
[19] Hernandez MT, Sauerwein HC, Jambaqué I, De Guise E, Lussier F, Lortie A, et al. Deficits in executive functions and motor coordination in children with frontal lobe epilepsy. Neuropsychologia 2002;40:384–400.
[20] Sumer MM, Atik L, Unal A, Emre U, Atasoy HT. Frontal lobe epilepsy presented as ictal aggression. Neurol Sci 2007;28:48–51.
[21] Jambaque I, Dulac O. Reversible frontal syndrome and epilepsy in an 8-year-old boy. Arch Fr Pediatr 1989;46:525–9.
[22] Beardsworth ED, Zaidel DW. Memory for faces in epileptic children before and after brain surgery. J Clin Exp Neuropsychol 1994;16:589–96. https://doi.org/10.1080/01688639408402670.
[23] Gonzalez LM, Anderson VA, Wood SJ, Mitchell LA, Harvey AS. The localization and lateralization of memory deficits in children with temporal lobe epilepsy. Epilepsia 2007;48:124–32. https://doi.org/10.1111/j.1528-1167.2006.00907.x.
[24] Mabbott DJ, Smith ML. Memory in children with temporal or extra-temporal excisions. Neuropsychologia 2003;41:995–1007. https://doi.org/10.1016/S0028-3932(02)00318-4.
[25] Cohen MJ. Auditory/verbal and visual/spatial memory in children with complex partial epilepsy of temporal lobe origin. Brain Cogn 1992;20:315–26. https://doi.org/10.1016/0278-2626(92)90024-G.
[26] Giovagnoli A, Casazza M, Avanzini G. Visual learning on a selective reminding procedure and delayed recall in patients with temporal lobe epilepsy. Epilepsia 1995;36:704–11. https://doi.org/10.1111/j.1528-1157.1995.tb01050.x.
[27] Jambaqué I, Dellatolas G, Fohlen M, Bulteau C, Watier L, Dorfmuller G, et al. Memory functions following surgery for temporal lobe epilepsy in children. Neuropsychologia 2007;45:2850–62. https://doi.org/10.1016/j.neuropsychologia.2007.05.008.
[28] Gadian DG, Isaacs EB, Cross JH, Connelly A, Jackson GD, King MD, et al. Lateralization of brain function in childhood revealed by magnetic resonance spectroscopy. Neurology 1996;46:974–7.
[29] Jambaqué I, Pinabiaux C, Dubouch C, Fohlen M, Bulteau C, Delalande O. Verbal emotional memory in children and adolescents with temporal lobe epilepsy: a first study. Epilepsy Behav 2009;16:69–75. https://doi.org/10.1016/j.yebeh.2009.07.006.
[30] Kurokawa T, Goya N, Fukuyama Y, Suzuki M, Seki T, Ohtahara S. West syndrome and Lennox Gastaut syndrome: survey of natural history. Pediatrics 1980;65:81–8.
[31] Hershey T, Craft S, Glauser TA, Hale S. Short-term and long-term memory in early temporal lobe dysfunction. Neuropsychology 1998;12:52–64. https://doi.org/10.1037/0894-4105.12.1.52.
[32] Cormack F, Vargha-Khadem F, Wood S, Cross J, Baldeweg T. Memory in paediatric temporal lobe epilepsy: effects of lesion type and side. Epilepsy Res 2012;98:255–9. https://doi.org/10.1016/j.eplepsyres.2011.09.004.
[33] Martins S, Guillery-Girard B, Clochon P, Bulteau C, Hertz-Pannier L, Chiron C, et al. Associative episodic memory and recollective processes in childhood temporal lobe epilepsy. Epilepsy Behav 2015;44:86–9. https://doi.org/10.1016/j.yebeh.2015.01.008.
[34] Jocic-Jakubi B, Jovic NJ. Verbal memory impairment in children with focal epilepsy. Epilepsy Behav 2006;9:432–9. https://doi.org/10.1016/j.yebeh.2006.07.010.
[35] Lendt M, Gleissner U, Helmstaedter C, Sassen R, Clusmann H, Elger CE. Neuropsychological outcome in children after frontal lobe epilepsy surgery. Epilepsy Behav 2002;3:51–9. https://doi.org/10.1006/ebeh.2001.029.
[36] Centeno M, Vollmar C, O'Muircheartaigh J, Stretton J, Bonelli SB, Symms MR, et al. Memory in frontal lobe epilepsy: an fMRI study. Epilepsia 2012;53:1756–64. https://doi.org/10.1111/j.1528-1167.2012.03570.x.
[37] Igarashi K, Oguni H, Osawa M, Awaya Y, Kato M, Mimura M, et al. Wisconsin Card Sorting Test in children with temporal lobe epilepsy. Brain and Development 2002;24:174–8.
[38] O'Muircheartaigh J, Richardson MP. Epilepsy and the frontal lobes. Cortex 2012;48:144–55. https://doi.org/10.1016/j.cortex.2011.11.012.
[39] Rzezak P, Fuentes D, Guimarães CA, Thome-Souza S, Kuczynski E, Li LM, et al. Frontal lobe dysfunction in children with temporal lobe epilepsy. Pediatr Neurol 2007;37:176–85.
[40] Auclair L, Jambaqué I, Dulac O, LaBerge D, Siéroff E. Deficit of preparatory attention in children with frontal lobe epilepsy. Neuropsychologia 2005;43:1701–12.
[41] Schraegle WA, Nussbaum NL, Stefanatos AK. List-learning and verbal memory profiles in childhood epilepsy syndromes. Epilepsy Behav 2016;62:159–65. https://doi.org/10.1016/j.yebeh.2016.07.021.
[42] Kibby MY, Cohen MJ, Lee SE, Stanford L, Park YD, Strickland SM. There are laterality effects in memory functioning in children/adolescents with focal epilepsy. Dev Neuropsychol 2014;39:569–84. https://doi.org/10.1080/87565641.2014.962695.
[43] Riccio CA, Pliego JA, Cohen MJ, Park Y. Executive function performance for children with epilepsy localized to the frontal or temporal lobes. Appl Neuropsychol Child 2015;4:277–84. https://doi.org/10.1080/21622965.2014.923774.
[44] Lee SE, Kibby MY, Cohen MJ, Stanford L, Park Y, Strickland S. Differences in memory functioning between children with attention-deficit/hyperactivity disorder and/or focal epilepsy. Child Neuropsychol 2016;22:979–1000.
[45] Cohen MJ. Children's Memory Scale. San Antonio, TX: Psychological Corporation; 1997.
[46] Holmes GL. Diagnosis and management of seizures in children. Philadelphia: Saunders; 1987.
[47] Kolb B, Wishaw IQ. Fundamentals of human neuropsychology. NY: Worth; 2009.
[48] Tang J, Critchley HD, Glaser DE, Dolan RJ, Butterworth B. Imaging informational conflict: a functional magnetic resonance imaging study of numerical stroop. J Cogn Neurosci 2006;18:2049–62.