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Review

Reading in children with temporal lobe epilepsy: A systematic review

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ABSTRACT

Objective: Children with epilepsy have higher rates of reading difficulties compared to the general population. Reading difficulties are associated with lower academic attainments, higher school drop-out rates, greater risk of unemployment, lower income, and poorer adjustment. We examined the literature dealing with reading in children with the most common type of focal epilepsy, temporal lobe epilepsy (TLE), in relation to: presence of reading difficulties, contributing factors, and efficacy of treatments for reading difficulties.

Methods: We searched databases (MEDLINE, EMBASE, PsycINFO and PubMed) for studies published before September 2016. Included studies (i) reported on a group of children with TLE, (ii) used a standardized reading test or included a control group, (iii) involved original research published in peer reviewed journals in the English language.

Results: Of 2018 citations obtained through literature searches, six met inclusion criteria. Reading accuracy and/or reading comprehension were assessed using different tests. All but one study found statistical evidence of reading difficulties in children with TLE. Only two studies examined relations between cognitive deficits and reading. One found that memory contributed to reading accuracy and comprehension. Another found evidence of a small decline in reading accuracy, which was not associated with a decline in memory post-surgery. Several studies were underpowered, giving false negative findings and not allowing relations between epilepsy factors, underlying cognitive deficits, and reading to be adequately examined. No study examined efficacy of reading intervention in this patient population.

Significance: We showed that reading difficulties that are present in children with TLE are under researched, yet they have significant functional consequences through childhood and into adulthood. There is an urgent need to identify risk factors and investigate efficacy of treatments for reading difficulties in children with TLE, as this will enable early identification and evidence-based treatment to be delivered in clinical practice.

1. Introduction

Reading difficulties are more common in children with epilepsy (i.e., 12.8 to 32.2% [1]) compared to the general population (i.e., 6.0% to 9.0% [2]). Children with temporal lobe epilepsy (TLE) are likely to be particularly vulnerable to reading difficulties for two main reasons. First, pathology/seizure focus are often not restricted to the hippocampus, but also involve the temporal neocortex (e.g., Jambaqué and colleagues [3]), which is an integral part of the reading network that involves (but is not limited to) the left lateral superior, middle, and inferior temporal neocortex (see Richlan et al. [4] for meta-analysis). Second, seizures in TLE are often difficult to control with medication. As such, seizures can interfere with knowledge and skills acquisition, and reduce school attendance.

Surgical treatment for intractable TLE, which traditionally involves resection of the anterior temporal neocortex, may increase the risk of reading difficulties, as damage of this brain region is associated with deficits in reading of irregular words (surface dyslexia) and semantic memory deficits in adults with semantic dementia [5]. We note, however, that surgery for TLE, could also have a positive impact on reading, as the control of seizures, which is critical for development of reading skills, also increases school attendance post-surgery [6]. Moreover, this increased school attendance may be particularly beneficial for children (such as those in early primary school) whose regular school curriculum is focused on the acquisition of reading skills.

In addition to epilepsy-related factors, neurocognitive deficits could also contribute to reading difficulties. For example, difficulties with episodic memory, learning, and/or recall of newly-learned material in

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testing that are common in children with TLE (i.e., Nolan et al. [7]) could impact on acquisition of academic skills. The first study to examine the relationship between episodic memory and reading skills in children with TLE, however, found that episodic memory did not contribute significantly to reading comprehension and explained only 5% of variance in reading accuracy [8]. In contrast, semantic memory deficits remained unrecognized in children with TLE until recently [9,10]. Yet, semantic memory was found to explain 49% of the variance in reading comprehension and 39% of the variance in reading accuracy in children with TLE [8].

For children with TLE who are found to have reading difficulties, it is important to determine whether they will benefit from treatments that have been found to improve reading and normalize brain activation during reading tasks in children with reading difficulties who are free of epilepsy [11]. Children with TLE may be less responsive to reading treatments, as functional integrity of the very brain regions affected in TLE and/or surgical treatment is predictive of reading treatments' effectiveness. For instance, a recent magnetoencephalography study which involved children who had reading difficulties but were free of epilepsy showed that higher activation in the left middle and superior temporal lobes (alongside ventral occipitotemporal and the right mesial temporal cortex) pre-treatment predicted greater improvements in word reading post-remedial reading treatment at one-year follow-up [12].

Ideally, studies on reading in children with TLE would also consider cognitive theories and a body of knowledge arising from studies of reading in typically developing children and children with reading difficulties who are free of epilepsy. This body of work has shown that reading is a complex skill that requires accuracy and comprehension. Development of reading accuracy skills demands acquisition of (i) the ability to translate letters into sounds — phonological decoding skills [13,14] and (ii) word recognition — lexical skills [15]. Selective deficits in the acquisition of phonological decoding and lexical skills result in phonological and surface dyslexia, respectively [16]. Adequate reading accuracy is necessary, but not sufficient, for development of reading comprehension, which is closely related to semantic memory [17]. For example, children with specific reading comprehension difficulties, but adequate reading accuracy, were found to have significantly reduced semantic skills relative to control children matched for reading decoding skills [18]. Thus, assessment of reading should involve testing of reading accuracy and comprehension using age-appropriate instruments. Moreover, assessment of reading accuracy should test phonological decoding and lexical skills separately, which would increase diagnostic accuracy and inform specific interventions.

Research into reading in children with TLE is critical, as children with reading difficulties have lower academic attainments [19] and higher drop-out rates in high school [20] relative to their peers. In adulthood, people with reading difficulties have a significantly greater risk of unemployment [21], lower income [22] and poorer social and psychological adjustment (see Maughan [23]) compared to people without reading difficulties. Given the functional significance of reading for academic and vocational outcomes, it is important to establish which children with TLE are at risk of reading difficulties, inform parents and children about possible risks or benefits of surgery for development of reading, and provide evidence-based treatments for reading difficulties to children with TLE. Thus the aims of the current study were to systematically examine the literature dealing with reading in children with TLE and provide evidence of relevance for clinical work in relation to epilepsy and cognitive factors that are associated with reading difficulties in children with TLE and effective treatments of reading difficulties in this patient population.

2. Methods

2.1. Literature searches and study selection

Four databases were initially searched in November 2014: MEDLINE, EMBASE, PsycINFO, and PubMed. The searches were limited to English language. The searches were updated using the same strategies in August 2016. Search details were as follows:

Database: Medline

Search 1 (18.11.2014): Ovid Medline (R) 1946 to October Week 4 2014
Search 2 (05.08.2016): Medline via OvidSP limit yr = "2014–current" (July Week 4 2016)
Search terms 'exp epilepsy/' AND ('exp reading/' OR 'exp dyslexia/') AND Limited to English language

Database: Embase

Search 1 (18.11.2014): Elsevier B.V.
Search 2 (05.08.2016): Embase via Ovid SP limit yr = "2014–current" (2016 August 04)
Search terms 'epilepsy'/exp AND ('reading'/exp OR 'dyslexia'/exp) AND [English]/lim

Database: PsycINFO

Search 1 (18.11.2014): OvidSP — 1806 to November Week 3 2014
Search 2 (05.08.2016): PsycINFO via OvidSP limit yr = "2014–current" (July Week 4 2016)
Search terms 'exp Epilepsy/' AND ('exp Reading' OR 'exp dyslexia') AND Limited to English language

Database: PubMed

Search 1 (18.11.2014)
Search 2 (05.08.2016): filter activated: publication date from 2014/10/30 to 2016/12/31
Search terms ([MeSH Terms] OR [All Fields]): ((Reading) OR Dyslexia) AND Epilepsy AND English[lang].

Studies included in the current review (i) reported original empirical research (i.e., not reviews, meta-analyses, editorials or letters), (ii) were conducted with a group of patients (i.e., not case studies), (iii) were published in peer-reviewed journals, (iv) included patients with TLE, (v) reported data (*M*, *SD*) of patients with TLE separately, if other patient groups were included, (vi) involved children and adolescents with TLE and reported data for children and adolescents separately, if adults with TLE were also included, and (vii) assessed reading using at least one reading task that was standardized or compared scores of participants with TLE to a control group, if non-standardized reading tests were used (i.e., not based on parental interview, school reports or clinical impression alone). The reference lists of articles that met the inclusion criteria were examined for studies not identified in the main search.

Two independent raters marked (i) all titles and abstracts obtained in the search against the inclusion criteria and (ii) selected full texts in both searches. Disagreements were resolved by discussion and consensus.

We used the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement and guidelines to summarize evidence and report results [24].

2.2. Quality appraisal

We appraised methodological quality of studies included in this review with the adapted version of the Downs and Black [25] checklist, which can be used to assess quality of intervention studies as well as observational studies. The checklist assesses studies on the quality of reporting, internal validity, external validity, and power. The checklist was found to have good test–retest reliability ($r = .88$), inter-rater reliability ($r = .75$), and internal consistency (Kruder–Richardson formula 20 = .89). The appraisals of studies included in our review were completed by two reviewers independently. Any discrepancies in rating were resolved via discussion.

3. Results

3.1. Study selection

The study selection process is displayed in Fig. 1. In November 2014, 1706 studies were identified. After removal of duplicates, 1038 studies remained. Titles and abstracts of these 1038 studies were reviewed against pre-determined inclusion criteria and 71 were selected. On review of full texts of these remaining 71 studies, three met the inclusion criteria. Scrolling through the reference lists of the full-text articles identified three additional relevant articles. In August 2016, the search was updated. An additional 312 studies were found, of which 97 were duplicates. On review of titles and abstracts of 215 remaining papers against criteria, 15 were selected for the full-text review. One of these 15 full-text articles met the inclusion criteria. Overall, 6 manuscripts met the inclusion criteria and were reviewed in this manuscript (see Tables 1 and 2 for details of the studies).

3.2. Study characteristics

Six studies included 237 participants in total; 30 typically developing children and 207 children with epilepsy (154 with TLE; 19 with frontal lobe epilepsy (FLE); 12 with benign child epilepsy with centrotemporal spikes (BCECTS); 12 with idiopathic generalized epilepsy (IGE); and 10 with generalized absence seizures (ABS)). The number of TLE participants were: 10 in three studies [26–28], 27 [29], 40 [30] and 57 [8] in one study each. Only one study included healthy control participants [28].

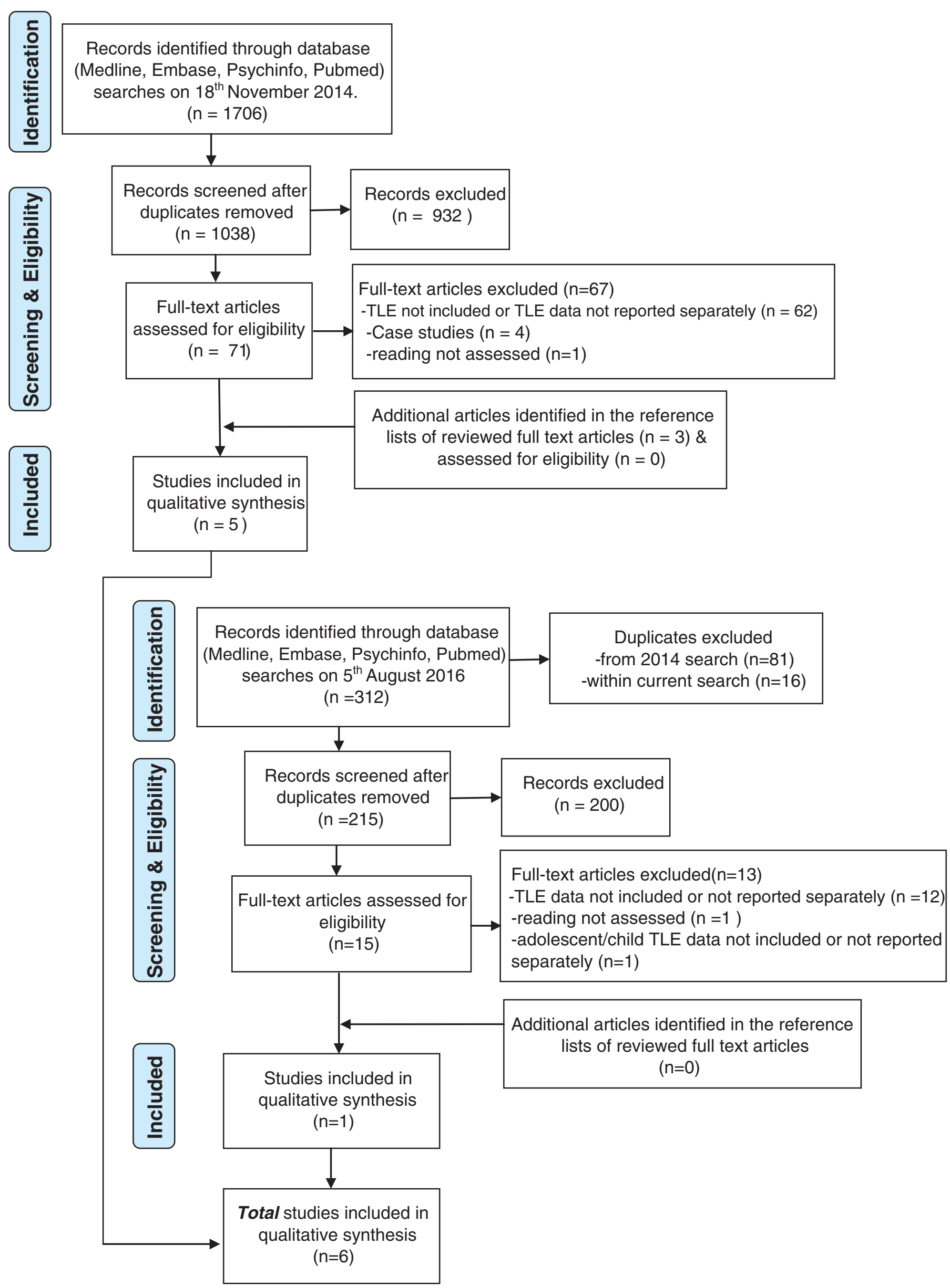

Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram.

Table 1
Study design and clinical characteristics.

Author	Design	Aims: To investigate	Group: no. of Pts	Laterality of speech representation	Diagnostic criteria	Age M (SD) years: At onset, duration of disorder, at surgery	Medication	Seizure frequency	Surgery and outcome
Blanchette and Smith [26]	Longitudinal Retrospective	Language functions pre- & post-surgery	TLE: 10 (5 L, 5 R) FLE: 9 (5 L, 4 R) Control: NA	Left, all participants	Video EEG, structural neuroimaging and neuropsychology	Onset TLE: 4.4 (2.1) FLE: 3.6 (2.9) Duration (at pre-surgery assessment) TLE: 7.1 FLE: 7.2 Surgery Not reported	Not reported	Not reported	NA
Camfield et al. [29]	Cross-sectional Prospective	Whether children with left TLE differ from children with right TLE in behavior, school performance and cognitive abilities	TLE: 27 (13 L, 14 R)	Not reported	EEG, neurological examination and interview	Onset: 8.5 Duration 4.2 (3.4)	Number (0/1/>1) 5/15/7 Type Carbamazepine (17), phenytoin (7), phenobarbital (4), valproic acid (2)	≤1/yr: 17 2–10/yr: 4 11–49/yr: 3 >50/yr: 3	NA
Chaix et al. [27]	Cross-sectional Prospective	Reading and establish the impact of (i) specific cerebral dysfunction and (ii) side of epilepsy focus on reading	TLE: 10 (5 L, 5 R) BCECTS: 12 IGE: 12	Not reported	Not reported	Onset TLE: 6.3 (3.5) BCECTS: 7.2 (2.87) IGE: 6.12 (2.1) Duration[a] TLE: 2.3 (0.4–7.7) BCECTS: 1.5 (0.4–2.8) IGE: 1.3 (0.5–4.1) Surgery NA	Number (0/1/2/3) TLE: 0/3/4/1 BCECTS: 6/6/0/0/ IGE: 0/8/3/1	Subgroups: Rare spikes (<5 per min) vs. Frequent spikes (>10 per min.	NA
Vanasse et al. [28]	Cross-sectional Prospective	Reading deficits in children with epilepsy and impact of epilepsy type on reading and metaphonological abilities	Epilepsy, non-lesional TLE: 10 (8 L, 2 R) FLE: 10 (8 L, 2 R) ABS: 10 (NA) Control: 30	Not reported	Seizure type, fMRI	Onset TLE: 3.7 (3.2) FLE: 3.9 (2.6) ABS: 5. 8 (2.5) Duration TLE: 6.0 (2.9) FLE: 6.4 (3.6) ABS: 3.5 (2.6) Surgery: NA	TLE Mono: 4 Poly: 6 FLE Mono: 7 Poly: 3 ABS Mono: 5 Poly: 5	Past year TLE: 11.4 (15.46) FLE: 57 (156.0) ABS: 65 (157.3)	NA
Lah and Smith [8]	Cross-sectional Retrospective	Relationship between memory (episodic and semantic) and literacy skills	TLE: 57 (33 L, 24 R)	Left: 43 Right: 3 Bilateral: 4 Not tested: 7 (all R handed)	Telemetry, MRI	Onset LTLE: 8.5 (4.6) RTLE: 7.1 (4.4) Duration LTLE: 5.00 RTLE: 6.3 Surgery NA	LTLE None: 0 Mono: 18 Poly: 15 RTLE None: 1 Mono: 12 Poly: 11	LTLE 1 or > per day: 10 1 or > per week: 10 1 or > per month: 6 >1 per month: 5 Clusters: 2 RTLE 1 or > per day: 10 1 or > per week: 10 1 or > per month: 6 >1 per month: 5 Clusters: 2	NA

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Table 1 (*continued*)

Author	Design	Aims: To investigate	Group: no. of Pts	Laterality of speech representation	Diagnostic criteria	Age M (SD) years: At onset, duration of disorder, at surgery	Medication	Seizure frequency	Surgery and outcome
Lah and Smith [30]	Longitudinal Retrospective	i) Pre-surgical to post-surgical changes in verbal memory and literacy and (ii) relationship between changes in memory and literacy.	TLE: 40 (22 L, 18 R)	Left: 30 Right: 1 Bilateral: 3 Not tested 7 (all R handed)	Video-EEG & MRI. Some cases, MEG and PET.	Onset LTLE: 9.00 (4.65) RTLE: 7.15 (3.76) Duration (at surgery) LTLE: 5.79 (4.25) RTLE: 6.50 (4.72) Surgery LTLE: 14.79 (2.99) RTLE: 13.66 (3.77)	Presurgery LTLE None: 0 Mono: 10 Poly: 12 RTLE None: 1 Mono: 9 Poly: 8 Postsurgery LTLE None: 1 Mono: 10 Poly: 11 RTLE None: 1 Mono:12 Poly: 5	Presurgery LTLE 1 or > per day: 9 1 or > per week: 6 1 or > per month: 4 >1 per month: 1 Clusters: 2 RTLE 1 or > per day: 9 1 or > per week: 2 1 or > per month: 5 >1 per month: 1 Clusters: 1 Post surgery LTLE Sz free: 14 Not sz free: 8 RTLE Sz free: 10 Not sz free: 8	Hippocampus spared/resected: 10/30 Hippocampus completely/incompletely/unable to determine resected: 25/4/1

ABS: generalized absence seizures; BCECTS: benign child epilepsy with centro-temporal spikes; EEG: electroencephalography; FLE: frontal lobe epilepsy; IGE: idiopathic generalized epilepsy; L: left; LTLE: left temporal lobe epilepsy; MEG: magnetoencephalography; MRI: magnetic resonance imaging; NA: not applicable; PET: positron emission tomography; R: right; RTLE: right temporal lobe epilepsy; TLE: temporal lobe epilepsy.

[a] Median and interquartile range.

While three studies were prospective [27–29], three were retrospective [8,26,30]. Four studies had a cross-sectional [8,27–29] and two studies had a longitudinal [26,30] design.

3.3. Reading skills

Reading accuracy was examined using materials that required reading of single words in all six studies. Only two studies examined and reported on phonological decoding and lexical skills separately employing materials that assessed reading of irregular words and regular/non-words, respectively [27,28]. Three of the six studies also assessed reading comprehension as well as accuracy [8,27,30]. No study examined reading comprehension alone.

Reading of children with TLE was compared to the normative/control group using statistical analyses in three of these six studies [8,28,30]. In two of these three studies, reading accuracy of children with TLE was significantly below the norms [8,30], with the mean z scores of: -0.28, and -0.44, respectively. However, in one of these two studies, children with left TLE (LTLE) scored significantly below the norms only at post-surgical follow-up [30]. There was no significant deviation from the norms for the LTLE group pre-surgically and for the right TLE (RTLE) group at either time point. In another study, word reading accuracy of children with TLE (including reading of irregular words and regular/non-words) was not significantly lower relative to controls [28]. Both studies that compared reading comprehension of children with TLE to the norms found reading comprehension to be significantly reduced ($z = -0.41$; [8]) and ($z = -0.94$; [30]). In the second study, reading comprehension was significantly below the norms post- (but not pre-) surgery in children with LTLE only. The reading comprehension scores of children with RTLE were comparable to the norms pre- and post-surgery. The remaining three studies did not compare reading of children with TLE with the norms/control group, but examined how reading is impacted by epilepsy variables, with the primary interest being: surgery [26], side of TLE focus [29] and site of epilepsy focus/syndrome [27].

3.4. Epilepsy factors and reading

Impact of side of epilepsy focus on reading accuracy was examined in all but one study in which children presented with predominantly LTLE focus [28]. Only one of these five studies found that, compared to children with RTLE, children with LTLE had significantly lower reading accuracy as well as reading accuracy and speed [27], and the remaining four did not. Impact of side of seizure focus on reading comprehension was examined in three studies [8,27,30]. None found significant differences in reading comprehension between children with left compared to RTLE.

Impact of temporal relative to extra-temporal seizure focus/pathology on reading accuracy was investigated in two studies [26,27]. Reading accuracy of children with TLE was comparable to children with other types of focal and generalized epilepsy: FLE [26], BCECTS, and IGE [27]. In the only study that examined impact of the site of seizure focus on reading comprehension, children with TLE obtained significantly lower scores relative to children with BCECTS, but not IGE, on a test that considered comprehension and speed simultaneously [27].

Two studies examined pre- to post-surgery changes in reading in children with TLE [26,30]. In a study that included children with TLE only [30], a significant decline in reading accuracy (but not reading comprehension) was found following surgery. In a study that examined the impact of surgery and seizure site of onset (TLE and FLE) on reading outcomes, however, no impact of either surgery or group were found [26].

Relations between other epilepsy factors and reading were examined in three studies [8,27,30]. Frequency of

Table 2
Findings: Reading and cognitive skills.

Author	Age at assessment: M (SD) years	Reading skill assessed: instruments used	Reading skills: findings	Other cognitive skills (test): findings	Other findings
Blanchette and Smith [26]	TLE: 11.5 (2.6) FLE: 10.8 (2.7)	Accuracy: WRAT Comprehension: NA	Effects of side, site and time of testing *Accuracy* Site: NS Side: NS[1] Surgery: NS[2] *Comprehension* NA	Effects of side, site and time of testing Verbal IQ (WISC III): NS Receptive language Single word (PPVT) NS Sentences/grammar (TROG) Left < right on TROG Expressive language: Semantic aspect (vocabulary, WISC III & category fluency, word fluency) Left < right on category fluency Fluency Retrieval (phonemic fluency, word fluency) NS Spelling (WRAT III) NS	NA
Camfield et al. [29]	TLE: 12.7 (3.3)	Accuracy: WRAT Comprehension: NA	*Accuracy* Side: RTLE vs. LTLE: NS *Comprehension* NA	FSIQ, VIQ, PIQ (WISC-R or WAIS): NS Receptive vocabulary (PPVT): NS Helstead–Reitan: NS Sentence repetition (Rosner): NS Dexterity and speed (finger tapping, grooved pegboard): NS Spelling (WRAT): NS Arithmetic (WRAT): LTLE < RTLE	12 pairs of participants matched for age, sex, handedness, frequency of seizures, and age at onset of seizures: no differences between L and R TLE on any of the tests
Chaix et al. [27]	TLE: 10.6 (1.5) BCECTS: 9.4 (1.8) IGE: 9.2 (1.2)	Accuracy: 20 irregular words & 20 pseudowords Accuracy & speed: “l'Alouette” Comprehension & speed: “Le printemps”	*Accuracy* Site: NS [3]Side: LTLE < RTLE (Short & long irregular and pseudo-words) *Accuracy & speed* Site: TLE < BCECTS [3]Side: LTLE < RTLE *Comprehension & speed* Site: TLE < BCECTS [3]Side: NS	Verbal IQ (WISC III) Site: TLE < BCECTS Side: NS Expressive language Defining words (vocabulary, WISC III) Site: TLE < BCECTS Side: NS Word retrieval (Phonological & Sematic Fluency, Visual Confrontation Naming from the Chevrie-Muller language evaluation battery) Site: Sig. diff in phonology (fluency task, but groups not specified) Side: LTLE < RTLE in NS Receptive language A phoneme category perception test Ecosse test Site: NS Side: NS Spelling Chevrie-Muller language evaluation battery Site: NS Side: LTLE < RTLE (spelling and spelling of pseudo-words) Rapid naming (Stroop color naming; number naming) Site: NS Side: LTLE < RTLE (number naming) Phonemic awareness (deletion tasks) Site: NS Side: LTLE < RTLE (for syllable deletion & accuracy of phoneme deletion)	Epileptic discharges TLE: Subgroup of children with rare spikes (<5 per min) vs. frequent (>5 per min) spikes NS on any of the cognitive measures BCECTS: Subgroup of children with rare spikes vs. frequent spikes: NS on any of the cognitive measures IGE: subgroup of children in remission (5) compared to children not in remission (7) NS on any of the cognitive measures

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Table 2 (*continued*)

Author	Age at assessment: M (SD) years	Reading skill assessed: instruments used	Reading skills: findings	Other cognitive skills (test): findings	Other findings
				Phonological memory (Digit Span, WISC III; phonological span; visual span, Corsi blocks) Site: TLE < BCECTS on the Digit Span Side: NS Attention: d2test & Stroop (inhibition) Site: NS Side: NS Visual-spatial organization and planning ROCFT Site: NS Side: NS	
Vanasse et al. [28]	TLE: 10.4 (1.9) FLE: 10.1 (2.0) ABS: 10.1 (1.7)	Accuracy BELEC: Single word reading (regular and irregular words — 24 words each) Nonword reading task (40 items) Accuracy & speed: "l'Alouette" (reading age) Comprehension: NA	*Accuracy* Regular Epilepsy < NC Site ABS < NC Irregular Epilepsy < NC FLE < NC Nonword Epilepsy < NC FLE < NC *Accuracy & speed* (mean reading age deficit: years) TLE: 2.0 (1.4) FLE: 2.1 (1.7) ABS: 2.1 (2.1)	Cognitive functioning (PPVT): NS Expressive language (Denomination task) NS Attention/working memory (Digit Span from the WISC III) FLE < NC Metaphonological awareness (experimental tasks): Nonword repetition NS Rhyme production NS Phonemic synthesis FLE < NC Phonemic segmentation ABS < NC Phonemic inversion FLE < NC	In all groups of children with epilepsy (TLE, FLE, and ABS) the reading age was almost 2 years behind the expectations for their chronological age. The FLE, and to a lesser extent the ABS, also had deficits in metaphonological skills
Lah and Smith [8]	LTLE: 13.5 (2.9) RTLE: 13.4 (3.2)	Accuracy: WIAT[4] or WRAT Comprehension: WIAT[4]	*Accuracy* TLE < normative data Side: NS *Comprehension* TLE < normative data Side: NS	Intelligence (PIQ from WISC[5]) LTLE: 90.8 (13.6) RTLE: 93.8 (16.4) NS (LTLE vs. RTLE) Semantic memory (WISC[5]): vocabulary TLE < normative means Episodic memory (CAVLT or CVLT): delayed recall score. TLE < normative means	Reading accuracy correlated ($p < .05$) with semantic ($r = .57$), and episodic ($r = .27$) memory, respectively. In regression, each memory variable made a significant, unique contribution to the variance. Together, these memory skills explained 46% of variability in reading accuracy. Reading comprehension correlated ($p < .05$) with semantic ($r = .73$) memory only, which accounted for 54% of variability alone. Reading accuracy and comprehension were not related to any epilepsy variables: side of seizure focus, age of seizure onset, proportion of life with epilepsy, history of generalized seizures, monotherapy-polytherapy, atypical-typical language representation
Lah and Smith [30]	Baseline LTLE: 13.6 (2.9) RTLE: 13.0 (3.7)	Accuracy: WIAT[4], WRAT, WJ-III Comprehension: WIAT[4], WRAT, WJ-III	*Reading accuracy*: Time: Presurgery > Postsurgery LateralitySide: NS Time × LateralitySide: NS *Comprehension*: Time: NS Side: NS Time × side: NS	PIQ: LTLE < RTLE Semantic memory (Naming[6]) Time: NS LateralitySide: NS Time × LateralitySide: LTLE only, Presurgery > postsurgery Semantic memory (Vocabulary[7]) Time: NS LateralitySide: NS Time × LateralitySide: NS Episodic memory (CAVLT or CVLT): delayed recall score. Time: NS LateralitySide: NS Time × LateralitySide: NS	Decline in reading accuracy was not related to decline in naming. Epilepsy variables and postsurgical seizure outcome along with changes to episodic verbal memory and vocabulary were not related to decline in reading accuracy following surgery.

epileptiform discharges (rare vs. frequent) was not related to reading accuracy in one study [27]. Similarly, reading accuracy and comprehension were not related to any of the following epilepsy variables: history of generalized seizures, monotherapy-polytherapy, atypical–typical language representation, age of seizure onset, proportion of life with epilepsy [8] or postsurgical seizure outcome [30].

3.5. Cognition and reading

All studies involved assessment of several cognitive skills, but only two studies examined relations between cognitive skills and reading. Specifically, Lah and Smith [8] investigated whether semantic and episodic memory contributed to reading accuracy and comprehension in children with TLE. Semantic memory explained 39% of the variance in reading accuracy and 49% of the variance in reading comprehension. Episodic memory accounted for 5% of the variance in reading accuracy and 12% in reading comprehension. In the paper that followed up these children longitudinally, Lah and Smith [30] found that postsurgical decline in reading accuracy was not associated with a decline in semantic memory (naming) or changes in episodic verbal memory.

3.6. Treatments for reading difficulties

Our literature search did not reveal any studies that have examined the effectiveness of treatment for reading difficulties in children with TLE.

3.7. Quality ratings

On the Downs and Black Scale (see Table 3 in Appendix A) the ratings ranged from 12 to 16 out of 18 in cross-sectional studies ($n = 4$) and 16 to 21 out of 28 in longitudinal studies ($n = 2$). The chance of bias was categorized as high, average or low for each study. For cross-sectional studies, the studies that received 0 to 5 points, 6 to 11 points, and 12 to 18 points were classified as having high, average, and low bias, respectively. For longitudinal studies, the studies that received 0 to 9 points, 10 to 19 points, and 20 to 28 points were classified as having high, average, and low bias, respectively. All studies fell in the low ($n = 5$) or average ($n = 1$) chance of bias.

Focusing on shortcomings across studies, we noticed that no study reported power analyses. Neither of the two longitudinal studies that examined changes post-surgery was blinded or involved a randomized trial. In three out of six studies, it was unclear whether subjects were representative of the entire population; they seem to include convenience samples [26–28]. The remaining three studies included consecutive children seen at the same hospital over a defined time period [8,29,30], which are likely to be representative of the studied population. Turning our focus to strengths across studies, we noticed that all studies clearly described aims, main outcomes, and distribution of principal confounders. All studies used adequate statistical analyses, adjusted for confounds in the analyses (when needed), and employed valid and reliable measures for assessment of reading, but the tests used varied across studies. Furthermore, all studies recruited patients from the same populations: children's hospitals and adequately defined patient samples.

4. Discussion

The aim of this review was to examine reading in children with TLE, identify which epilepsy and cognitive factors impact reading, and examine evidence of treatment efficacy of reading difficulties in children with TLE, as this information assists management of children with TLE in clinical work. Our review revealed that reading is grossly under-researched in children with TLE, with just six studies identified, none of which examined treatments of reading difficulties in children with TLE.

4.1. Do children with TLE have reading difficulties?

Our review showed that children with TLE are at risk of reading difficulties involving accuracy and comprehension. However, this finding is somewhat equivocal as in one study children with TLE did not obtain significantly lower reading accuracy scores relative to healthy control children [28]. Inspection of the mean scores on the reading tasks provided in this review indicated that patients with TLE obtained lower scores across all three reading tasks that involved reading of regular words, irregular words, and non-words, thus showing a consistent trend of lower reading accuracy relative to controls across tasks. In addition, when scores obtained on reading of regular and irregular words were compared to expectations for the school grade, 40% of children with TLE, but less than 10% of control children, scored more than one academic year behind the school grade on regular and irregular word reading. There was no evidence of children with TLE having more difficulties reading regular than irregular words. As no power analyses were conducted and groups (TLE and control) included a small number of participants ($n = 10$ each), it is likely that the lack of significant difference in reading accuracy of regular, irregular, and non-words between TLE and control groups was due to the study being underpowered.

Notes to Table 2:
ABS: generalized absence seizures; BCECTS: benign childhood epilepsy with centro-temporal spikes; BELEC: Batterie d_évaluation du langage écrit et de ses troubles [32]; BILO: Bilan Informatise du Language Oral [33]; CAVLT: the California verbal learning test [34]; CVLT: children's auditory verbal learning test [35]; DEN 48: denomination test [36]; FLE: frontal lobe epilepsy; FSIQ: full scale intelligence quotient; IGE: idiopathic generalized epilepsy; LTLE: left temporal lobe epilepsy; [37]; ODEDYS: Outil de Depistage des Dyslexies [38]; NA: not applicable; NS: non-significant; PIQ; performance intelligence quotient; PRI: perceptual reasoning index; PPVT: Peabody picture vocabulary test–revised [39]; PSI: processing speed index; ROCFT: Rey–Osterrieth complex figure test [40]; RTLE: right temporal lobe epilepsy; TLE: temporal lobe epilepsy; TROG: test for reception of grammar [41]; VCI: verbal comprehension index; VIQ: verbal intelligence quotient; WAIS: Wechsler Adult Intelligence Scale [42]; WIAT: Wechsler Individual Achievement Test WISC: Wechsler Intelligence Scale for Children [44,45]; WISC R: Wechsler Intelligence Scales for Children — Revised [47]; WISC III: Wechsler Intelligence Scales for Children — Third Edition [48]; WJTCA: Woodcock–Johnson tests of cognitive abilities [49]; WJ-III: Woodcock–Johnson — 3rd Edition [49]; WMI: working memory index; WRAT: wide range achievement test [50]; WRAT III: the wide range achievement test — IIIc [51].

1 Impact of side of seizure focus/surgery examined in the entire group of children with epilepsy, not specifically in a group of children with TLE.
2 Impact of surgery examined in the entire group of children with epilepsy, not specifically in a group of children with TLE.
3 Side of seizure focus examined within the TLE group alone.
4 Wechsler Individual Achievement Test [45] or Wechsler Individual Achievement Test — 2nd Edition [44].
5 Wechsler Intelligence Scale for Children — Third Edition, Wechsler Intelligence Scale for Children — Fourth Edition [46] or Wechsler Adult Intelligence Scale — Third Edition [47].
6 Boston naming test [52], expressive one-word picture vocabulary test [53] or expressive vocabulary test [54].
7 Wechsler Adult Intelligence Scale — Third Edition [47], Wechsler Abbreviated Scale of Intelligence [55], Wechsler Intelligence Scale for Children — Third Edition [49], Wechsler Intelligence Scale for Children — Fourth Edition [46] or Wechsler Preschool and Primary Scale of Intelligence — Third Edition [56].

4.2. Which epilepsy and treatment factors impact reading in TLE?

Contrary to the expectation that surgery, when it resulted in reduction of seizures, could improve reading, neither of the two studies that examined changes in reading pre- to post-surgery found evidence of a significant improvement in reading at 1 year post-surgery [26,30]. This lack of improvement in reading is unlikely to be explained by poor seizure control, as 60% of the children reportedly became seizure-free post-surgery in one study and seizure status post-surgery (seizure-free vs. not seizure-free) was not related to a change in reading skills [30]. Moreover, we expected that improvements in reading were more likely to be found in children who underwent surgery at a younger age as more regular school attendance was likely to be particularly beneficial for this age group because reading instruction takes place in the early school years. Nevertheless, age at surgery was not associated with a change in reading at 1-year follow-up. This lack of improvement in reading post-surgery when seizures subside suggest that underlying neural abnormality may be a more important contributor to cognitive deficits than the seizures themselves as there is evidence that academic and cognitive deficits are apparent at or before the time of seizure onset [31]. Instead of an improvement, a small, but significant decline in reading accuracy and no change in reading comprehension were evident on follow-up [30]. The reason for this decline, however, remains unclear. We proposed that surgical treatment for TLE could also be associated with a risk of decline in reading, as damage to the anterior temporal neocortex (which is often resected) is related to acquired reading difficulties (affecting irregular words in particular) in adults with semantic dementia [5], but the relations between a decline and extent of anterior temporal lobe resection were not investigated. Moreover, it is unclear whether a reduction in reading accuracy involved reading of irregular words but spared reading of regular words/non-words, as reading tests used in this study do not provide separate scores for regular/non-words and irregular words. This finding of a significant decline in reading accuracy post-surgery [30] is at odds with an earlier published study [26] that found no significant change in reading post-surgery. Nevertheless, inspection of scores provided in this earlier study shows that the mean reading scores of children with TLE were lower post- relative to pre-surgery. The study included only a small number of patients ($n = 10$) and the authors themselves recognized that the decline in the reading scores pre- to post-surgery possibly failed to reach significance due to the lack of statistical power.

Evidence for side of seizure focus having a significant impact on reading in children with TLE is very tenuous. Although five studies examined the impact of side of seizure focus on reading, only one study found that side of seizure focus relates to reading. Children with LTLE scored significantly below children with RTLE on tests of reading accuracy [27] which is surprising as meta-analysis of neuroimaging studies showed that the left (lateral superior, middle, and inferior) temporal neocortex is particularly important for reading [4]. We noticed that unlike other studies, Chaix et al. [27] assessed word reading accuracy using tests that included separate materials for assessment of lexical (irregular words) and phonological (pseudowords) skills, as well as a test of reading speed. Children with LTLE were less accurate in reading both types of words and were significantly slower in reading relative to children with RTLE.

While research into the relation between other epilepsy factors and reading has been very limited, studies conducted thus far provide little evidence of reading being associated with other seizure factors, such as site of epilepsy focus (i.e., temporal vs. extratemporal), seizure frequency, antiepileptic medication (mono vs. polytherapy), age of seizure onset or proportion of life with epilepsy.

4.3. Which cognitive skills impact reading in TLE?

Research into relations between cognitive skills and reading is restricted to two studies. Both studies examined relations between memory (semantic and episodic) and reading. A deficit in semantic and to a much lesser extent episodic memory were found to be related to poor reading in children with TLE pre-surgery [8]. A decline in semantic memory that was found post-surgery, however, was not associated with a decline in reading post-surgery [30]. Perhaps this lack of relation between decline in semantic memory and reading was due to the decline in semantic memory being limited to naming. No change in the ability to describe the meaning of different words was noticed pre-to post-surgery, suggesting that while the access to semantic system was somewhat limited, the system itself was preserved. It is possible that printed words could have facilitated access to the semantic system, and hence no relations between changes in naming and reading were found.

Cognitive skills that have been found to be important for development of reading skills in typically developing children, such as phonemic awareness and rapid naming skills, were assessed in one study only [27]. Nevertheless, whether these skills related to reading was not examined.

4.4. Limitations of this review

Although this review was conducted in accordance with PRISMA guidelines, some limitations are present. It is possible that including only English language articles may have resulted in publication bias. Furthermore, limiting literature searches to peer reviewed publications may have reduced the number of studies included in this review. However, such an approach enhances the likelihood that studies included in this review were of good quality as they have undergone peer review process before publication. Due to the limited number of studies and the heterogeneity of tests used to assess reading, it was not possible to undertake meta-analyses, which would provide more precise information about the magnitude of reading difficulties in children with TLE, let alone meta-regression that would examine impact of epilepsy and cognitive factors across studies. Furthermore, in all studies children were recruited through neurology departments, and in several instances through comprehensive epilepsy programs of major children's hospitals. While this approach to recruitment could potentially bias the samples to include children with epilepsy who are more impaired, it is important to note that TLE is often difficult to control with medication, hence children with TLE are likely to be referred to specialized epilepsy centers at tertiary children's hospitals.

Quality of studies included in this review, as per ratings on the Downs and Black [25] checklist, was good. However, close review of the items included in the scale identified areas of particular weakness that were apparent across the studies. No study reported power analyses. Conversely, in the discussion of this review we noticed that several studies may have been underpowered, hence the statistical significance was not reached, resulting in false negative findings. Another shortcoming that was evident across studies was lack of blinding of assessors, which could have introduced an unconscious bias. Moreover, studies have largely included children seen at tertiary hospitals who were candidates for epilepsy surgery. Hence, the findings may not stand for children with less severe TLE that is well-controlled with medication.

The results of the current study, however, offer guidance for future research. Future studies need to involve a large number of patients to avoid false negative findings due to low power and enable examination of the contribution of core epilepsy and cognitive factors on reading in children with TLE. Power analyses should be performed and reported. While blinding of patients to intervention used for epilepsy is not possible, blinding of assessors is, and should be implemented in future studies. Ideally, studies would have prospective longitudinal design and include children with TLE as well as healthy control children. Future studies should consider cognitive theories and the body of knowledge arising from studies of reading in typically developing children, and the use of tests that provide separate scores for reading of different types of words, as this could increase diagnostic accuracy. Finally, it is critical to develop treatments for reading difficulties in children with TLE that would involve early identification of children at risk as well as programs for reading difficulties, as reading deficits alone are associated with adverse academic, vocational, financial, and psychosocial outcomes.

5. Conclusions

The most consistent, although not equivocal, finding across the small number of studies investigating reading in children with TLE is of difficulties with reading accuracy. The cognitive and epilepsy factors associated with these reading difficulties have barely been examined. One study, however, provides statistically strong evidence that deficits in semantic memory (and to a much smaller extent episodic memory) are related to reading difficulties in this patient population. While only two studies examined changes in reading post-temporal lobe surgery, neither found evidence of an improvement and one found evidence of a small, but significant decline in reading accuracy. No study examined efficacy of reading intervention in this patient population. Given the evidence of reading difficulties in children with TLE pre- and post-surgery as well as functional significance of reading for academic progression, employment and income, early identification of children with TLE at risk of reading difficulties and provision of effective treatment is important. Conducting studies that examine efficacy of reading interventions in children with TLE is paramount.

Disclosure of conflict of interest

None of the authors has any conflict of interest to disclose.

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Appendix A

Table 3
Quality assessment: Downs and Black [25] checklist.

Study	Quality assessment criteria: domains and items																												Sum
	Quality of reporting										External validity			Internal validity — statistical and methodological bias							Internal validity — selection bias						Power	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	
Blanchette and Smith [26]	1	1	0	0	2	1	1	0	1	0	0	0	1	0	0	0	0	1	1	1	1	0	0	0	1	1	0	14/28
Camfield et al. [29]	1	1	1	NA	2	0	0	NA	1	0	1	NA	NA	NA	NA	0	NA	1	NA	1	1	1	NA	NA	1	0	0	12/18
Chaix et al. [27]	1	1	1	NA	2	1	1	NA	0	1	0	NA	NA	NA	NA	1	NA	1	NA	1	1	1	NA	NA	1	0	0	14/18
Lah and Smith [8]	1	1	1	NA	2	1	1	NA	1	1	1	NA	NA	NA	NA	1	NA	1	NA	1	1	1	NA	NA	1	1	0	17/18
Lah and Smith [30]	1	1	1	1	2	1	1	0	1	1	1	1	1	0	0	1	1	1	1	1	1	1	0	0	1	1	0	22/28
Vanasse et al. [28]	1	1	1	NA	2	1	0	NA	0	0	0	NA	NA	NA	NA	1	NA	1	NA	1	1	0	NA	NA	1	0	0	11/18

Items. 1: Is the hypothesis/aim/objective of the study clearly described? 2: Are the main outcomes to be measured clearly described in Introduction or Methods section? 3: Are the characteristics of the patients included in the study described clearly? 4: Are the interventions of interest clearly described? 5: Are the distributions of principal confounders in each group of subjects to be compared described clearly? 6: Are the main findings of the study described clearly? 7: Does the study provide estimates of the random variability in the data for the main outcomes? 8. Have all important adverse events that may be a consequence of the intervention been reported? 9: Have the characteristics of patients lost to follow-up been described? 10: Have actual probability values been reported (for example, 0.035 rather than < 0.05) for the main outcomes except where the probability value is less than 0.001? 11: Were the subjects asked to participate in the study representative of the entire population from which they were recruited? 12: Were those subjects who were prepared to participate representative of the entire population from which they were recruited? 13 Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive? 14: Was an attempt made to blind study subjects to the intervention they have received? 15 Was an attempt made to blind those measuring the main outcomes of the intervention? 16: If any of the results of the study were based on 'data dredging', was this made clear? 17: In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case–control studies, is the time period between the intervention and outcome the same for cases and controls? 18:Were the statistical tests used to assess the main outcomes appropriate? 19: Was compliance with the intervention/s reliable? 20: Were the main outcome measures used accurate (valid and reliable)? 21: Were the patients in different groups recruited from the same population? 22: Were study subjects recruited over the same period of time? 23: Were study subjects randomized to intervention groups? 24: Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? 25: Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? 26: Were losses of patients to follow-up taken into account? 27: Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?

All items given 0 or 1 point, except for item 5 which was given 0, 1 or 2 points. Items 4, 8, 12, 13, 14, 15, 17,19, 23, and 24 were not applicable to cross-sectional studies and were marked as NA (not applicable). Total possible score for longitudinal studies was 0 to 18 (4 studies) and for cross sectional studies was 0 to 28 (2 studies). The checklist contains five sub-scales: reporting (items 1–10), external validity (items 11–13), bias (items 14–20), confounding (items 21–26), and power (item 27).

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