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Research Paper

# Long-term memory consolidation of new words in children with self-limited epilepsy with centro-temporal spikes

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ABSTRACT

Accelerated long-term forgetting has been studied and demonstrated in adults with epilepsy. In contrast, the question of long-term consolidation (delays > 1 day) in children with epilepsy shows conflicting results. However, childhood is a period of life in which the encoding and long-term storage of new words is essential for the development of knowledge and learning. The aim of this study was therefore to investigate long-term memory consolidation skills in children with self-limited epilepsy with centro-temporal spikes (SeLECTS), using a paradigm exploring new words encoding skills and their long-term consolidation over one-week delay. As lexical knowledge, working memory skills and executive/attentional skills has been shown to contribute to long-term memory/new word learning, we added standardized measures of oral language and executive/attentional functions to explore the involvement of these cognitive skills in new word encoding and consolidation. The results showed that children with SeLECTS needed more repetitions to encode new words, struggled to encode the phonological forms of words, and when they finally reached the level of the typically developing children, they retained what they had learned, but didn't show improved recall skills after a one-week delay, unlike the control participants. Lexical knowledge, verbal working memory skills and phonological skills contributed to encoding and/or recall abilities, and interference sensitivity appeared to be associated with the number of phonological errors during the pseudoword encoding phase. These results are consistent with the functional model linking working memory, phonology and vocabulary in a fronto-temporo-parietal network. As SeLECTS involves perisylvian dysfunction, the associations between impaired sequence storage (phonological working memory), phonological representation storage and new word learning are not surprising. This dual impairment in both encoding and long-term consolidation may result in large learning gap between children with and without epilepsy. Whether these results indicate differences in the sleep-induced benefits required for long-term consolidation or differences in the benefits of retrieval practice between the epilepsy group and healthy children remains open. As lexical development is associated with academic achievement and comprehension, the impact of such deficits in learning new words is certainly detrimental.

## 1. Introduction

Although declarative memory has long been assessed and studied, few studies have focused on long-term memory consolidation in children and adolescents. Yet childhood is a period of life when the encoding and long-term storage of new words is essential for the development of knowledge and learning. The specificity of long-term memory consolidation is that the process takes several days (even weeks) to complete. Sleep plays a crucial role in this long-term consolidation process [1,2]. The current hypothesis is that Slow Wave Sleep (SWS) allows the learning and explicit consolidation of new words via the activation of the hippocampal network, while Rapid Eye Movement Sleep (REM) allows for the transfer of this new knowledge to neocortical structures via interactions between thalamic-cortical and hippocampal-cortical networks. This phase of sleep is thought to be involved in the integration of new words into the existing lexicon [3,4].

In typically developing children, studies have confirmed the benefits of sleep on the consolidation of declarative verbal or visuospatial material [5,6]. For example, it has been shown that the memorization of new words has been shown to increase significantly after a nap or after a

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night of sleep [7–9 10 11 12], thus demonstrating the power and importance of sleep in the long-term memory consolidation of new words in children. While there is a growing interest in long-term consolidation in typically developing children and adolescents, studies of children with neurological disorders are still rare.

In the field of epilepsy, a common complaint - in both adults and children - is memory impairment. Patients typically report forgetting previously learned information to quickly. In the clinical setting, however, this accelerated forgetting rate is difficult to capture with standardised tests as they only include 30–45-minute delayed recall, which does not allow assessment of the long-term (post-sleep) consolidation process.

This accelerated long-term forgetting (ALF) has been studied and demonstrated in adults with epilepsy, with delays ranging from a few hours to several days or weeks (for review, see [13]). In contrast, the question of long-term consolidation (delays $>$ 1 day) in children with epilepsy shows conflicting results. For example, encoding deficits rather than consolidation deficits were observed in children with generalized epilepsy when compared with control children [14], whereas in another study, long-term consolidation was impaired regardless of the initial encoding level [15]. Although most studies of children with focal structural or non-structural epilepsy have found impaired long-term consolidation [16 17 18], one study [19] reported long-term consolidation gains in patients with focal epilepsy (structural or non-structural), suggesting a robust memory consolidation mechanism that is resistant to epileptic interference during sleep. As these different studies include heterogeneous groups of patients with structural vs. non-structural epilepsy, seizures originating from different locations, the interpretation of the results remains difficult, as sleep characteristics differ according to the presence/absence of associated lesions [20]. While the substrate of ALF appears to be located in the hippocampal-neocortical networks and possibly in the extrahippocampal areas, the specific roles of seizures, electrophysiological epileptic abnormalities, sleep, brain damage and/or medication remain uncertain (for review, see [13,21]).

Self-limited epilepsy with centro-temporal spikes (SeLECTS) is a particularly interesting model for studying long-term memory consolidation as it is characterized by a large increase in the frequency of interictal discharges during NREM sleep. Indeed, episodic memory disorders have been increasingly suspected in SeLECTS (for review, see [22]), and ALF has been reported in a heterogeneous group of children presenting with SeLECTS or generalized epilepsy [23]. Furthermore, SeLECTS is often associated with deficits in oral and written language development (see the meta-analysis of [24] and also: [25–28]). Correlations have been found between cognitive deficits and the location of discharges [29,30] and between the frequency of epileptic discharges during sleep and reading deficits have been demonstrated [31]. This evidence suggests a possible link between the slow-wave sleep pathophysiology associated with this epilepsy, the long-term memory consolidation of new words and the difficulties in oral and written language development.

The primary aim of this study was to investigate long-term memory consolidation skills in children with epilepsy using a paradigm that investigates the ability to encode new words and their long-term consolidation. This research takes place in the context of a growing suspicion of memory deficits in the population of children with SeLECTS [22], a suspicion that remains largely unexplored to date using paradigms involving prolonged delays, delays that are nevertheless necessary to highlight an overly rapid decline of the memory trace in relation to the sleep pathophysiology presented by children with SeLECTS.

Therefore, we initially expected to see reduced consolidation gains or even a decrease in consolidation after longer delays in the SeLECTS group compared to the control group as reported in most studies. However, in order to avoid bias in the interpretation of the results obtained in the consolidation measures, we planned to continue the encoding phase until a comparable encoding rate was achieved in both groups (control and clinical). We expected that the children with epilepsy would need more learning trials (compared to the control group) to reach a similar encoding rate.

On the other hand, the literature reports a contribution of the lexical knowledge (for a review, see [9]) but also of working memory skills [32] to the ability to learn new word. Furthermore, a link between the long-term memory and executive-attentional skills has also been demonstrated ([33,34]). We therefore added standardized measures of oral language and executive-attentional skills to explore the involvement of these cognitive skills in new-word encoding and consolidation.

As reported in the literature, we expected the epilepsy group to have more disturbed subjective ratings of sleep than the control group, and thus expected a correlation between sleep questionnaire scores and long-term memory consolidation gains. Finally, we expected to find an association between epilepsy data, particularly disease duration, and consolidation ability.

## 2. Method

### 2.1. Participants

Ten participants presenting with SeLECTS were recruited from the neuropediatric outpatient clinic of the University Hospital of Geneva. The diagnosis of SeLECTS was based on clinical and EEG features. The inclusion criterion for all participants was to be between 8 and 12 years of age, so that the group of children with epilepsy could be compared with a control group of 44 age-matched typically developing children. The following exclusion criteria were applied: 1) refusal to participate by the parent and/or child; 2) inability of the participant to perform the tasks due to sensory (e.g. deafness, blindness) or cognitive impairment; 3) lack/ poor command of the French language. Specific exclusion criteria for the participants in the control group were: 1) neurological disease or medical condition that might affect brain development/ function (e.g. prematurity $<$ 37 weeks of gestation, sequelae of oncological treatments, neurometabolic diseases…); 2) neurodevelopmental disorder requiring speech therapy or special schooling (e.g. developmental language disorder, school learning disorder, autism spectrum disorder); 2) psychiatric disease requiring medication.

Epilepsy data were recorded and included (1) age of seizure onset; (2) duration of active epilepsy, based on EEG features; (3) total number of seizures on a 3-point-scale ($<$5 seizures = 1, 5–19 seizures = 2, more than 20 seizures = 3); (4) severity of EEG trace abnormalities on a 3 point-scale (0 = no irritative activity, 1 = rare epileptic elements, 2 = abundant irritative abnormalities); (5) medication status on a 2-point-scale (0 = no medication, 1 = current antiepileptic medication [ASM]).

The project was approved by the local ethics committee (CCER, Swissethics project ID: 2021-00563). Written informed consent was obtained from all participants (clinical and control).

### 2.2. Experimental paradigm

A task was created to measure the encoding and consolidation skills of new words (pseudowords). The pseudowords were trisyllabic and were derived from real words (e.g: “pantaloppe” instead of “pantalon” [trousers in French] or “elephir” instead of “elephant”) controlled for phonological complexity, word frequency, imageability and concreteness. In the encoding phase, the children listened to a recorded picture story in which the eight pseudowords referred to non-real objects, animals or plants. After listening to the story, the experimenter provided a picture and a description of the properties of each of these new pseudowords in order to ensure that they were correctly semantically encoded (e.g: “This is “*elephir*”. *Elephir* is a delicious syrup. The *elephir* can cure all diseases”).

Systematic encoding was performed for all participants: the experimenter presented each picture of an object/plant/animal associated with its new pseudoword in turn and then showed the pictures to the

participant one at a time to test his or her ability to recall the correct new word. To avoid encoding bias between children with SeLECTS and controls, the encoding phase was continued until 75 % of the pseudowords were correctly encoded for each participant. The procedure was therefore continued until a rate of 6/8 correct pseudoword responses (i.e. appropriate phonological form) was achieved. The number of trials required to reach this threshold was recorded. The number of phonologically altered pseudoword productions during the encoding trials was also calculated.

Two consolidation measures were taken: after a delay of 30 min (T1) and then after an interval of one week (T2). These measures included: (1) a cued visual recall of the pseudowords, in which the participant had to recall the new word when presented with the picture of the object (2) a recognition task in which the experimenter gave the word and the participant had to point to the corresponding picture in a forced-choice set.

### 2.3. Neuropsychological assessment

Several control standardized tasks were selected in order to assess the potential relationhip between oral language and executive-attentional skills and encoding or consolidation processes.

General cognitive level was assessed using the non-verbal reasoning subtest of the Wechsler Intelligence Scale (WISC V: matrix). Oral language assessment included phonology (pseudoword repetition task, ISADYLE), lexical knowledge (KABC II: word naming task) , and a lexical comprehension task (Peabody Picture Vocabulary Test: PPVT , receptive skills (CELF-V: story comprehension) and semantic skills (WISC-V: similitudes). Executive and attentional functions included tasks targeting verbal working memory (WISC-V: MCD = digit span direct order, MCI = digit span reverse order), flexibility processes (Colour Trail Test: CCT), inhibition skills (TEA-CH: contrary worlds), and selective attention (NEPSY II: auditory attention).

All participants (control and epilepsy groups) were assessed using the same protocol. The 30 min between the encoding phase and the first recall were filled for all participants first with the non-verbal reasoning task (Matrix, WISC V) to avoid verbal interferences, and then with the selective auditory attention task (NEPSY II), the lexical comprehension task (PVTT), the working memory task (the digit span task, WISC V). The other standardized tests were administered at the second session one week later.

*Questionnaires:* Parents completed the Behavioral Rating Inventory of Executive Functions (BRIEF), which allows for more ecological data. It includes a Global Executive Composite Score (GEC), and two subscales: the *Behavioural Regulation Index* (BRI) composed of inhibition, flexibility, emotional control skills, and the *Metacognitive Index* (MI), including processes of initiation, working memory, planning, organization of material, control [35]. They also completed the validated French Sleep Disturbance Scale for Children (SDSC), which allowed screening for difficulties in initiating and maintaining sleep, sleep breathing disorders, excessive sleepiness, presence of parasomnias, and non-restorative sleep.

### 2.4. Statistical analyses

SPSS version 26 software was used for statistical analyses. Independent samples *t*-tests were used to test for demographic differences (age) between the control and the epilepsy groups.

Normality tests were performed on the experimental and neuropsychological data using the Shapiro-Wilk test. A normal distribution was observed for some control neuropsychological measures (PPVT, MCI, CTT, Isadyle), and standard independent samples *t*-tests could be used for the descriptive comparison of the two groups for these results. The other data were not normally distributed, and group differences were analysed using the Mann-Whitney *U* test.

After checking Spearman rank order correlations (*rhos*) between the different variables, stepwise regression analyses were computed to determine the specific contribution of the cognitive control measures (language, executive and attention tasks) to the experimental memory measures (encoding and long-term consolidation). Benjamini-Hochberg corrections were used to control for false positive rates in multiple comparisons. Correlation analyses were also performed with the sleep and the epilepsy data for the epilepsy group.

Multivariate analysis of variance (ANOVA) with repeated measures was performed to test whether the two groups differed in their encoding skills and consolidation gains between T1 and T2.

## 3. Results

### 3.1. *Participants (Table 1)*

In the SeLECTS group, the EEG data showed that three children had persistent epileptic dysfunction in the centro-temporal region, three had occasional/rare epileptic spikes, and four had a normal EEG at the time of assessment. Most children (8/10) had a bilateral focal dysfunction (past or present), the remaining two children had a right hemisphere centro-temporal epileptic focus.

Regarding the number of seizures presented by the children, two of them had less than 5 seizures reported, six out of ten children had experienced 5 to 20 seizures, and two children presented with more than 20 seizures.

The average duration of the epileptic disorder was 18 months (SD = 15,4) with large differences between children, ranging from 1 to 51 months.

Six children were not taking any medication at the time of the assessment, and the other 4 were treated with a single antiepileptic drug (levetiracetam, clobazam or sulthiame).

Demographic data showed that age was not statistically different between the clinical and control groups.

**Table 1**
Demographic and clinical characteristics of the participants: means (standard deviation SD) and frequencies (percentage).

| | **ECTS Group $n = 10$** | **Control group $n = 44$** | **Significance Test** | ***p*-value** |
|---|---|---|---|---|
| **Age,** in years | 9.878 (SD = 1.529) | 10.15 (SD = 0.375) | $t(52) = 0.557$ | 0.58 |
| **Sex**: F; M | 4; 6 (40 %; 60 %) | 23; 21 (52 %; 48 %) | | |
| **Laterality**: Right; Left | 9; 1 (90 %; 10 %) | 37; 7 (84 %; 16 %) | | |
| **Mother-tongue**: monolingual; bi-trilingual | 5; 5 (50 %, 50 %) | 27; 17 (61 %; 39 %) | | |
| **Onset** age of epilepsy (in years) | 6.64 (1.36) | | | |
| **Duration** of epilepsy (in months) | 17.94 (15.41) | | | |
| **Medication** | 6 | | | |
| No medication | 4 | | | |
| Monotherapy | 0 | | | |
| Polytherapy | | | | |
| **EEG data** | 4 | | | |
| Normal | 3 | | | |
| Few spikes | 3 | | | |
| Abundant epileptic abnormalities | | | | |
| **Number of seizures** | 2 | | | |
| 0–5 | 6 | | | |
| 6–20 | 2 | | | |
| More than 20 | | | | |
| **Epileptic focus** | 2 | | | |
| Right hemisphere | 0 | | | |
| Left hemisphere | 8 | | | |
| Bilateral | | | | |

### 3.2. *Neuropsychological assessment (Table 2)*

The results obtained in both groups were not statistically different for non-verbal reasoning skills, selective auditory attention abilities and executive processes, which were tested either with standardised tests of inhibition and working memory or with an inventory of behavioural executive dysfunction. Only the flexibility process was significantly less efficient in the SeLECTS group than in the control group (CCT, $p < .001$).

However, most oral language skills differed between groups, with the SeLECTS group performing worse than the control group on measures of lexical knowledge (PPVT, $p < .05$), receptive skills (CELF-V: story comprehension, $p < .01$) and verbal semantic skills (WISC-V: similitudes, $p < .05$). Phonological scores obtained in a pseudoword repetition task (ISADYLE) were not statistically different between groups, but poorer short-term auditivo-verbal memory scores were observed in the SeLECTS group, suggesting a poor auditivo-phonological loop (MCD: digit span direct order, $p < .01$).

On the sleep questionnaire (SDCS), the global score was below the clinical cut-off for both groups and showed no statistical differences between the control and SeLECTS groups. However, detailed analysis of the different subscales revealed significantly more parasomnias symptoms in the epileptic group compared to the control group ($p < .05$).

### 3.3. *Experimental new word learning task*

Encoding skills: Statistical analysis showed significant differences in encoding efficiency between the SeLECTS group and the control group. The SeLECTS group required more than 6 trials to reach the fixed 75 % correct encoding criteria, while the control group needed only around 4 trials ($p < .05$) (Table 3). An ANOVA with repeated measures was performed using the first 4 encoding trials to investigate the rate of encoding over the successive trials in both groups. The results showed significant improvements in encoding over the four trials ($F = 47.487$, $p = .000$). Additionally, there was a significant interaction between the encoding rate and the groups (encoding x groups: $F = 3.441$, $p = .018$), suggesting reduced encoding skills in the epilepsy group compared to the control group (Fig. 1).

The clinical group also showed significantly more phonological alterations in the pseudowords to be learned compared to the control group ($p < .01$) (Table 3).

Consolidation skills:

- *Comparison of group performances*

The SeLECTS group recalled significantly more pseudowords at T1 compared to the control group performances. However, there was no significant difference in performance between the two groups at T2. Additionally, recognition scores were also significantly better in the SeLECTS group than in the control group, at both T1 and T2.

- *Long-term consolidation skills*

An ANOVA with repeated measures was performed to examine the cued recall measures at T1 and T2. The results showed no statistically significant differences for consolidation ($F = 2.971$, $p = .091$). However, significant differences in consolidation gains were found between the two groups (interaction group x consolidation: $F = 4.325$, $p = .043$). In other words, whereas the control group showed improvement in consolidation over time (recalling 2.7 words and 3.77 words at T1 and T2 respectively), the epilepsy group did not demonstrate the same improvement (recalling an average of 5.1 words recalled at T1 and 5.0 words at T2).

The ANOVA with repeated measures performed on the recognition scores at T1 and T2 revealed no significant effect of consolidation ($F = 0.934$, $p = .338$) and no interaction between the variables (group x consolidation: $F = 0.344$, $p = .560$). These results suggest that there was no difference between the groups in their consolidation skills or in the evolution of their consolidation scores over time.

**Table 3**
Results obtained in the experimental memory task: mean score (standard deviation) and statistical analyses for groups performance's comparison.

| | ECTS Group $n = 10$ | Control group $n = 44$ | Mann Whitney $U$ | $Z$ score | $p$-value |
|---|---|---|---|---|---|
| **Encoding** | 6.2 | 4.43 | 317.500 | 2.202 | **0.028*** |
| Total number of trials to reach 75 % correct responses | (2.3) 1.68 | (1.86) 0.58 | 353.300 | 3.003 | **0.003**** |
| Mean number of phonological alterations per encoding trial | (1.04) | (0.61) | | | |
| **Recall** | 5.1 | 2.7 | 375.500 | 3.505 | **0.000***** |
| T1 | (1.287) | (1.924) | 293.500 | 1.653 | 0.098 |
| T2 | 5.0 | 3.77 | | | |
| | (1.247) | (2.281) | | | |
| **Recognition** | 7.9 | 5.57 | 333.000 | 2.727 | **0.006**** |
| T1 | (0.31) | (1.63) | 305.000 | 2.304 | **0.021*** |
| T2 | 8.0 | 6.98 | | | |
| | (0.00) | (1.50) | | | |

* significant $p$-value $< 0.05$; ** significant $p$-value $< 0.01$; ***significant $p$-value $< 0.001$.

**Table 2**
Results obtained in the neuropsychological assessment: standard scores, percentiles, indexes or raw score (standard deviation) and statistical analyses for groups performance's comparison.

| Cognitive process (test/questionnaire used) | ECTS Group (n = 10) | Control group (n = 44) | Significance Test | Mann Whitney $U$ | $Z$ score | $p$-value |
|---|---|---|---|---|---|---|
| Non-verbal reasoning (WISC V: matrix) | SS = 12.20 (1.663) | SS = 11.07 (2.415) | | 276.500 | 1.271 | 0.204 |
| Phonology (Isadyle), total score | 10.6 (0.966) | 11.61 (1.755) | $t(52) = 1.758$ | | | 0.085 |
| **Lexical comprehension index (PPVT)** | 112.11 (11.559) | 120.45 (8.982) | $t(51) = 2.418$ | | | **0.019*** |
| **Stories comprehension (CELF V)** | SS = 9.7 (3.302) | SS = 12.2 (2.348) | | 120.500 | −2.243 | **0.025** * |
| **Semantic abstraction (WISC V: similitude)** | SS = 11 (2.211) | SS = 12.93 (2.366) | | 125.500 | −2.128 | **0.033*** |
| **Short-term memory (WISC V: MCD)** | SS = 9.0 (1.886) | SS = 11.48 (2.592) | | 102.000 | −2.657 | **0.008**** |
| Working memory (WISC V: MCI) | SS = 10.3 (2.163) | SS = 11.84 (2.702) | $t(52) = 1.681$ | | | 0.099 |
| Auditive attention (NEPSY II) | SS = 10.44 (3.245) | SS = 9.98 (2.758) | | 229.500 | 0.760 | 0.447 |
| **Flexibility (CCT, interference score)** [a] | 1.919 (0.496) | 1.068 (0.604) | $t(52) = -4.135$ | | | **0.000***** |
| Inhibition (TEA-CH: contrary worlds) [a] | PC = 68 (22.01) | PC = 66.14 (21.724) | | 235.500 | 0.347 | 0.729 |
| Executive behavior-global score (BRIEF GEC) [a] | PC = 60.2 (28.193) | PC = 60.95 (26.25) | | 193.000 | -0.170 | 0.865 |
| Executive behavior: Emotional regulation (BRIEF IRC) [a] | PC = 72.4 (21.986) | PC = 66.08 (25.299) | | 231.500 | 0.765 | 0.444 |
| Executive behavior: metacognition (BRIEF MI) [a] | PC = 50 (34.264) | PC = 57.18 (29.227) | | 179.500 | -0.497 | 0.619 |
| Sleep Questionnaire: total score (SDSC) [a] | 38.8 (6.161) | 37.45 (8.812) | | 270.500 | 1.127 | 0.260 |
| **Sleep questionnaire; parasomnia score (SDSC)** [a] | 13.2 (3.736) | 10.75 (3.404) | | 313.500 | 2.095 | **0.036*** |

* significant $p$-value $< 0.05$; ** significant $p$-value $< 0.01$; ***significant $p$-value $< 0.001$.
[a] higher score indicates greater difficulties. SS = standard score; PC = percentile.

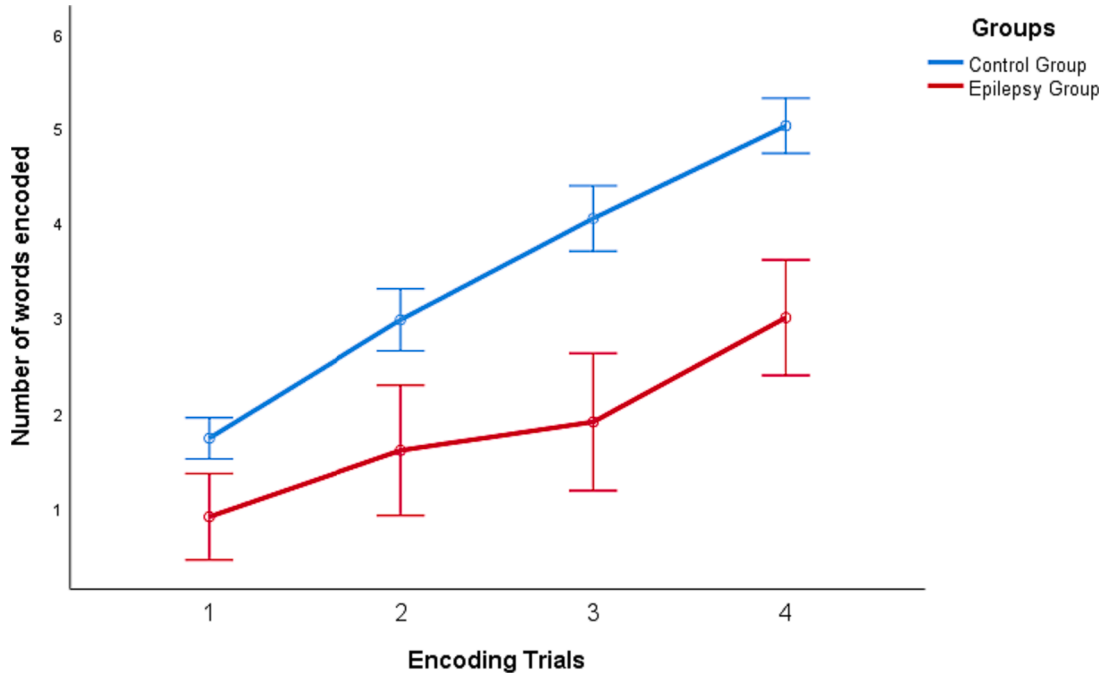


**Fig. 1.** Encoding curves of the epilepsy group and the control group over the first 4 trials.

Correlations between the neuropsychological results, epilepsy data, sleep questionnaire and experimental memory measures (Table 4)

- Correlation and regression analyses with all participants (including both the control and epilepsy groups)

***Encoding skills:*** the study found a negative correlation between encoding skills and both lexical knowledge (PPVT: $p$ =.002) and verbal working memory score (MCI, reversed digit span: $p$ =.007). This suggests that children with poor lexical knowledge required more encoding trials to achieve the 75 % correct pseudoword criteria. Multiple comparisons were corrected using the Benjamini-Hochberg procedure (Table 4) and only the lexical knowledge measure remained significantly correlated with encoding skills (adjusted $p$-value: $p$ =.048).

Stepwise regression analyses were also performed (with PPVT, MCI). The results showed a unique contribution of the lexical knowledge measure (PPVT) to the encoding skills ($p$ =.001), explaining 20,5% of the variance.

As computing correlations with the whole group of participants can result in biased results (Simpson's Paradox), separate analyses were also conducted for each group. The lexical knowledge measure (PPVT) was the only analysis considered due to its significant association with the encoding skills. Negative correlations remained significant when computing PPVT data for the control group only (PPVT $p$ =.013) but failed to reach significance when computing data for the epilepsy group only (PPVT: $p$ =.094). However, upon inspection of the associations, similar trends were observed in both the controls and epilepsy groups. This suggests that the lack of statistical significance may be attributed to the reduced number of participants in the epilepsy group (Fig. 2).

Note that the correlation between encoding and phonological skills just failed to reach significance for the whole group of participants ($p$ =.052).

***Delayed recall*** (T2) correlated with verbal working memory (MCI, reversed digit span: $p$ =.037) as well as phonological skills (ISADYLE: $p$ =.008). In other words, children with stronger working memory and phonological skills were more likely to recall more pseudowords after a week's delay. However, these correlations failed did not reach significance after Benjamini-Hochberg correction for multiple comparisons (Table 4).

Stepwise regression analyses (MCI and ISADYLE) showed that phonological skills only predicted the delayed recall score (p =.016) and accounted for 10,6 % of the variance.

Furthermore, the number of phonological errors produced during the encoding phase was found to be correlated with the interference index, as measured by a flexibility task (CCT; $p$ <.05).

No significant correlations were found between the experimental

**Table 4**
Spearman's rho correlations between the experimental memory measures and the cognitive skills and adjusted $p$-value after correction for Multiple Comparisons.

| | **Lexical comprehension (PPVT)** Spearman rho [adjusted $p$-value [1]] | **Phonological skills (Isadyle)** Spearman rho [adjusted $p$-value [1]] | **Working memory (MCI)** Spearman rho [adjusted $p$-value [1]] | **Flexibility (CCT interf)** Spearman rho [adjusted $p$-value [1]] |
|---|---|---|---|---|
| **Encoding** | **r = -0.419, *p* =.002** [*p* =.048]** * | r = -0.266, $p$ = 0.52 [$p$ =.208] | **r = -0.363, *p* =.007**** [$p$ =.064] | r = -0.216, p =.117 [$p$ =.309] |
| nb trials | r = 0.106, $p$ =.448 [$p$ =.682] | r = -0.005, $p$ =.971 [$p$ =.971] | r =.021p =.880 [$p$ =.925] | **r =.317p =.020*** [$p$ =.12] |
| nb errors | | | | |
| **Recall** | r = 0.090, $p$ =.521 [$p$ =.682] | r = 0.024, $p$ =.863 [$p$ =.925] | r = 0.073, p = 559 [$p$ =.682] | r = -0.181, p =.190 [$p$ =.38] |
| T1 | | | | |
| T2 | r = 0.080, $p$ =.569 [$p$ =.682] | **r = 0.355, *p* =.008**** [$p$ =.064] | **r = 0.285, p =.037*** [$p$ =.17] | r = -0.081, p =.559 [$p$ =.682] |
| **Recognition** | r = 0.093, $p$ =.506 [$p$ =.682] | r = -0.101, p =.467 [$p$ =.682] | r = 0.110, p =.428 [$p$ =.682] | r = -0.209, p =.129 [$p$ =.309] |
| T1 | | | | |
| T2 | r = -0.020, $p$ =.887 [$p$ =.925] | r = 0.196, p =.155 [$p$ =.338] | r = 0.236, p =.086 [$p$ =.264] | r = -0.234, p =.088 [$p$ =.264] |

* significant $p$-value < 0.05; ** significant $p$-value < 0.01; ***significant $p$-value < 0.001.

[1] adjusted $p$-value (Benjamini-Hochberg correction for Multiple Comparisons).

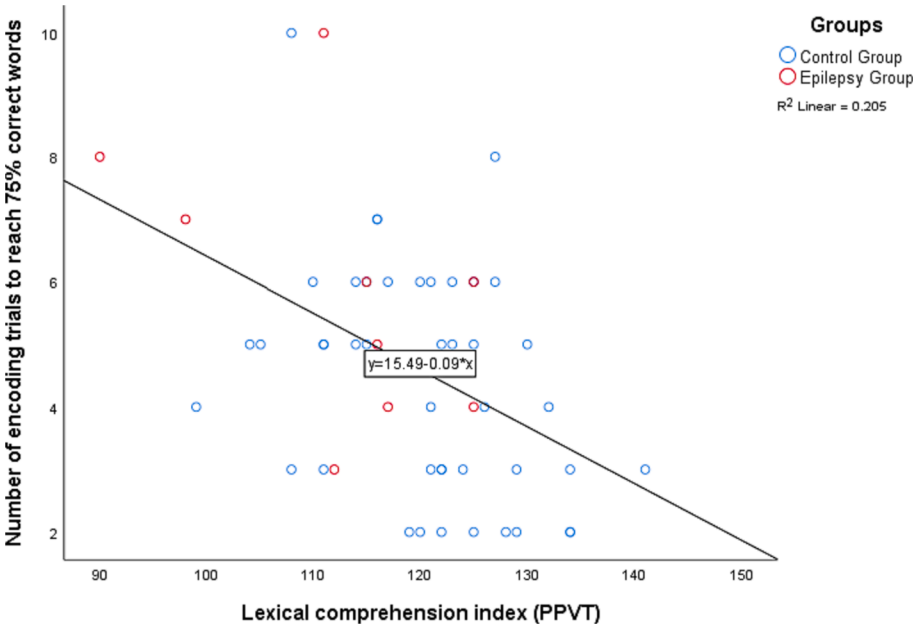


**Fig. 2.** Correlation analysis between the encoding skills and the lexical knowledge of the participants.

measures (encoding, recall, and recognition) and the sleep data, including the parasomnia index.

- Correlation analyses for the epilepsy group only:

There were no significant correlations between the experimental measures of encoding, recall, and recognition, and the epilepsy data including the duration of the disease, number of seizures, severity of the abnormalities in the EEG and age at onset.

## 4. Discussion

Overall, the study results showed impaired encoding in children with SeLECTS. Additionally, the epilepsy group showed reduced long-term retention gains in the recall condition compared to the control group, after controlling for encoding level. However, no significant differences were observed in the recognition task. Lexical knowledge, verbal working memory skills and phonological skills contributed to the encoding and/or recall skills, and interference sensibility index was associated with the number of phonological errors during the pseudoword encoding phase. No correlation was found between epilepsy data and the cognitive and memory skills, or between sleep data and experimental memory measures. The SeLECTS group scored lower than the control group in standardized tests for oral language, short-term verbal memory, and cognitive flexibility. Additionally, the epilepsy group reported more parasomnias in the sleep questionnaire than the control group. No difference in scores between groups were observed for non-verbal reasoning skills, auditory attention and most executive measures.

Regarding encoding measures, the SeLECTS group showed impairments both in the qualitative and the quantitative aspects of learning compared to the control group. Specifically, the epilepsy group required significantly more trials to learn the new words, and the analyses performed on the encoding scores over the successive trials confirmed reduced encoding skills in the patients compared to the control group.

Previous studies have reported reduced encoding skills in children with generalized epilepsy [14]. However, to our best knowledge, our study is the first to investigate new word encoding skills in children with focal epilepsy, specifically SeLECTS, and to identify such a deficit. The number of trials required to accurately encode new words was negatively correlated with the children's general lexical knowledge and with verbal working memory skills, as assessed by standardized tests. It may be questioned whether the epilepsy group's impaired oral language skills could explain the observed decrease in verbal encoding skills. Controversial data has been reported regarding the role of oral language impairments in episodic verbal memory skills. However, recent studies on episodic verbal memory in children with specific language impairment have shown that verbal short-term/working memory (rather that language skills) plays a predominant role, affecting specifically the initial stage of the verbal encoding process (for a review, see [36]). Furthermore, a recent study found that working memory was the primary predictor of new word learning skills in healthy children, surpassing lexical knowledge [32]. These findings have practical implications and should prompt adjustments to pedagogical and therapeutic environments to reduce working memory load during encoding tasks.

Further analysis showed that the SeLECTS group also struggled with the qualitative aspects of encoding, making many phonological errors during the learning phase. This observation suggests that SeLECTS children have difficulties with the ability to encode the exact phonological features of new words. Literature commonly reports global language delays and/ or weaknesses in children with SeLECTS, affecting both the expressive and receptive skills (for review and metanalysis, see [24]. The study's findings confirm the semantic difficulties previously reported in the literature (for review and *meta*-analysis, see [25]), as the children with SeLECTS had significantly lower scores in the lexical comprehension, story comprehension and verbal semantic abstraction tasks compared to the control group. The phonological measures used in this study (pseudowords repetition task) did not reveal any differences between the epilepsy and control groups, although the participants with SeLECTS displayed a very high number of phonological errors in the new word learning task. It is possible that this standardized phonological task was not sensitive enough to detect difficulties in the SeLECTS group. It is also possible that children with SeLECTS have poor phonological representations rather than phonological programming deficits. Further studies on SeLECTS should assess more detailed, precise and complex phonological skills, including complex phonological programming and phonological representation skills. The phonological encoding skills may be modulated by an executive component, as the mental flexibility skills negatively correlated with the number of errors produced during the encoding phase. Although executive involvement in new word

learning, particularly inhibition, has been reported in children with developmental language disorders [37], the specific role of interference, inhibition or flexibility skills in this particular phonological learning process remains unclear.

The study's second major finding concerns the long-term retention after controlling for encoding. The epilepsy group displayed higher recall and recognition scores compared to the control group, which was unexpected.

This may be due to the many repeated encoding trials they underwent to reach 75 % correct encoded words (up to ten trials for some of them), which could have resulted in deeper encoding and easier recall. Presenting the material repeatedly may indeed induce overlearning (and thus reduced forgetting rate) [38]. However, setting the criterion setting under 100 % correct in word list-learning score (as proposed in this study) seems to reduce the risk of overlearning [39]. It is also possible that the higher recognition scores in the epilepsy group reflect a greater dependence on the semantic recognition system through familiarity (rather than pure episodic memory) in the epilepsy group. In addition, differences between the control and SeLECTS group may have been induced by the assessment environment, as children with epilepsy were assessed in a quiet consultation room at the university, while control participants were tested at home for most of them.

However, the analysis of the long-term consolidation measures revealed that the children with SeLECTS displayed differences in retention gains after a one-week delay in the recall condition compared to the control group. It is important to note that the consolidation measures in the recognition condition did not show a different evolution with time between both groups, but this may be due to a ceiling effect as SeLECTS children recognized nearly all words previously encoded at T1. Interestingly, the number of items recalled did not decrease with time in the epilepsy group, but rather remained stable between T1 and T2 in our study. Thus, the consolidation measures did not show the expected retention gains in the SeLECTS group. However, the number of words recalled or recognized did not however decrease after one week, suggesting that there was no accelerated forgetting in our SeLECTS group, as reported in previous studies either in verbal or visual tasks [16 17,18].

Whereas the contribution of sleep (especially NREM sleep) is well-known in the long-term consolidation process through the off-line reactivations in hippocampal-neocortical circuit, and is typically associated with enhanced long-term retention [40], the role of retrieval practice in this long-term retention has also been evidenced [41]. Research has indeed demonstrated that several retrieval trials are associated with enhanced long-term retention compared to single retrieval trial in healthy participants. In this sense, retrieval could constitute a fast route to memory consolidation, as "repeated reactivations in hippocampal-neocortical circuits afford an opportunity to integrate an initially hippocampus-dependent memory into the co-activated neocortical knowledge structures, similar to replay events during NREM sleep" [42]. Additionally, increased connectivity between the hippocampus and the ventromedial prefrontal cortex has been evidenced, either after sleep [43] or after retrieval practice [44], suggesting similar contributions of retrieval and off-line reactivation (during sleep) to long-term memory consolidation. According to this "retrieval effect", the clinical group (who had more retrieval opportunities during their numerous encoding trials) should have better long-term retention compared to the control group, who had fewer retrieval trials due to their quicker encoding of new words. Therefore, the lack of retention improvement observed in the epilepsy group after a one-week delay may indicate either an off-line consolidation deficit during NREM sleep, or differences in the benefits of retrieval practice between participants with SeLECTS and healthy children. It is unclear whether the difference between 6 retrieval trials in the clinical group and 4 retrieval trials in the control group to achieve 75 % correct encoding truly results in a "retrieval effect" difference in the long-term retention. Further exploration is warranted. Additionally, the observed gain between T1 and T2 in the control group may be due to this retrieval effect rather than sleep-induced long-term consolidation.

These data confirm that children with SeLECTS, are at high risk for long-term memory consolidation weakness or deficit. The participants in this study did not present with an active epilepsy and/or abnormal EEG, which may account for the less severe consolidation impairments observed here compared to the deficits reported in previous studies. The absence of statistical correlations between the epilepsy data and the memory and cognitive measures is also likely due to this factor.

The study has limitations due to the small sample size of children with epilepsy and the heterogeneous duration of epilepsy. Additionally, the EEG data only included a subjective evaluation of the number of epileptic spikes, based on the clinical experience of the senior neuropediatrician, and the EEG was not performed concurrently with the experimental study. Therefore, interpretations between the cognitive and epilepsy data should be approached with caution. The lack of precision in the available epilepsy feature may have contributed to the absence of associations between epilepsy and cognitive data reported in the results. To clarify the correlations between electrophysiological and memory data, future studies should include sleep EEG concomitant with cognitive testing, using standardized index to measure the number of spikes.

However, despite the small group size and short duration of epilepsy in some children, the results demonstrate significant differences in both encoding and consolidation. In addition, the SeLECTS group exhibited poor encoding and long-term consolidation skills, despite most of the children being in remission, with a normalized EEG or with very rare epileptic spikes in the EEG. Although the literature reports favorable long-term neuropsychological outcome [45], our results suggest that memory dysfunctions may persist even months or years after remission of the epilepsy. Another explanation could be that the relation between SWS and memory consolidation is not similar in healthy participants and in clinical participants, as has been shown in groups of epileptic patients with accelerated forgetting [46] and in patients with neurodevelopmental language disorders [47].

The data collected from the sleep questionnaire showed no significant differences between the epilepsy and control groups, except for parasomnias. Additionally, no association was found between the sleep data and the long-term consolidation measures, although previous literature reports a higher frequency of sleep quality deterioration (measured by questionnaires) in children with epilepsy compared to those without epilepsy [48]. The relationship between epilepsy and sleep is complex, with reciprocal interactions, often leading to a vicious circle. Epilepsy causes sleep disturbance, and sleep disturbance, in turn, increases the likelihood of seizures. Children with active SeLECTS thus typically exhibit alterations in sleep patterns, both on an electrophysiological (EEG) level and in terms of sleep quality, as reported by questionnaires. Future studies should thus include further analyses to explore the relationship between sleep parameters and memory consolidation in patients with SeLECTS. Recent data has shown that children with SeLECTS exhibit microstructural sleep abnormalities, specifically reduced NREM sleep instability in terms of cyclic alternating pattern compared to healthy children (for review, see [49]). Therefore, it is important to analyze the microstructural parameters besides the macrostructural level.

While long-term consolidation of new words is typically modulated by a child's lexical richness in healthy children (for a review, see [9], our study found no correlation between lexical knowledge and consolidation measures. Instead, delayed recall skills were linked to working memory and phonological mastery, as assessed with a pseudoword repetition task. These results are consistent with the functional model that links working memory, phonology and vocabulary in a fronto-temporo-parietal network [50]. Given that SeLECTS involves perisylvian dysfunction, it is not surprising that there is an association between impaired sequence storage, phonological representation storage and new word learning.

## 5. Conclusion

In summary, it seems that children with SeLECTS require more repetitions to encode new words and struggle with encoding the phonological forms of words. Once the words are encoded, children with SeLECTS retain what they have learned, but they do not show enhanced recall skills after a one-week delay, as observed in the control participants. It is unclear whether the results suggest differences in sleep-induced benefits necessary for long-term consolidation or differences in retrieval practice benefits between the epilepsy group and healthy children. In real-life settings such as school or daily life, where new words are not repeated frequently, this dual impairment in encoding and long-term consolidation may lead to a significant learning gap between children with and without epilepsy. As the development of vocabulary is linked to understanding and to academic achievement [51], the negative effects of difficulties in learning new words are clear.

## CRediT authorship contribution statement

**C. Mayor:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Visualization, Methodology, Investigation, Formal analysis, Conceptualization. **C. Moser:** Investigation, Project administration. **C. Korff:** Resources.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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