



## Re-examining the crowding hypothesis in pediatric epilepsy

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### ABSTRACT

**Objective:** In adults with left-sided epilepsy, reorganized language may “crowd out” right-hemisphere visual–spatial skills, with relative sparing of language (i.e., the crowding hypothesis). However, this effect has not consistently been demonstrated in pediatric epilepsy studies. The objective of this study was to investigate the crowding hypothesis using a heterogeneous sample of children with intractable epilepsy and typical (left) language dominance or atypical (right or bilateral) language dominance. We examined the relative contributions of seizure onset (before or after age 5), handedness (right versus left), seizure localization (temporal versus extratemporal), as well as language dominance on verbal versus visual cognitive skills.

**Method:** We retrospectively analyzed neuropsychology assessment results from a sample of 91 children who completed presurgical evaluation at the Hospital for Sick Children in Toronto, Canada (34 with typical language, 57 with atypical language, mean age = 12 years). We considered a selection of verbal skills (naming, vocabulary knowledge, verbal abstract reasoning) and visual skills (visual–motor integration, block construction, visual abstract reasoning).

**Results:** Consistent with several previous adult studies supporting the crowding hypothesis, univariate analyses showed that the typical and atypical language groups were comparable on the measures of vocabulary knowledge and abstract verbal reasoning whereas the atypical language group produced lower scores across visual measures. Multivariate analyses (taking into account language dominance and associated factors) showed that language dominance was the strongest predictor of performance on two of three visual measures whereas language dominance was not a significant predictor of performance on most verbal measures. Unexpectedly, both sets of analyses indicated that the atypical language group had poorer naming abilities than the typical language group.

**Significance:** Our data provide some evidence of right-hemisphere functional crowding effects in a heterogeneous sample of children with intractable left-sided epilepsy. Specifically, those with atypical versus typical language dominance showed poorer visual–motor integration and visual–motor problem-solving skills, with comparable scores on certain verbal measures. It is critical that potential crowding effects be considered when interpreting the neuropsychological profiles of children being evaluated for epilepsy surgery.

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## 1. Introduction

### 1.1. Language reorganization in epilepsy

The vast majority of the neurologically intact population is left-hemisphere dominant for language. A greater proportion of those with epilepsy have atypical language dominance, whereby language is represented bilaterally or predominantly within the right hemisphere [1–3]. In the course of typical development, language dominance is established in early childhood (prior to age 5 or 6 years) through mechanisms such as synaptic pruning and increased myelination of white

matter tracts in classical language areas within the temporal and frontal lobes of the dominant hemisphere [4,5]. However, the specialization of typical language areas can be disrupted in the context of early onset epilepsy due to seizure activity itself or to underlying abnormal neural substrates. To functionally compensate for impaired language-relevant regions in the dominant hemisphere, undamaged areas in the contralateral hemisphere may be recruited. The extent of atypical language lateralization varies between individuals and occurs on a continuum, with some individuals having minor right-sided language involvement, some having language represented bilaterally (to varying degrees), and others having strongly right-sided language dominance.

When individuals with epilepsy undergo presurgical candidacy investigations, assessment of language dominance and corresponding language skills is critical when the epileptogenic zone may involve language-relevant brain regions. In these cases, neuropsychological interpretation of verbal versus visual cognitive skills is critical for guiding treatment planning and prediction of language outcomes after surgery,

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as patterns of performance speak to the functional integrity of affected brain tissue. The present study seeks to contribute to our understanding of different patterns of cognitive functioning as a function of typical versus atypical language dominance in children with medically refractory seizure disorder.

### 1.2. The crowding hypothesis

Importantly, bilateral or right-hemisphere language dominance is not necessarily advantageous. According to the crowding hypothesis, the transfer of language functions to the right hemisphere may occur at a cost to typically right-hemisphere (i.e., visual–spatial) functions [6,7]. This functional ‘crowding’ may be attributed to competition for space or to different modes of information processing occurring in a single hemisphere. Arguably, the most compelling support for the crowding hypothesis has come from studies of adults with epilepsy. To our knowledge, the largest-scale study to-date involved 561 patients with left temporal lobe seizures [8]. Patients with right language dominance obtained lower scores than those with left language dominance on several measures of visual–spatial ability (e.g., Wechsler Performance composite subtests, judgment of line orientation, copy of a complex figure) whereas performance on verbal skills (i.e., confrontation naming, verbal fluency, Verbal composite subtests) was comparable between groups. Interestingly, those with bilateral language dominance performed similarly to those with left-dominant language on visual–spatial measures, unless there was also a corresponding shift in handedness. Other studies within the adult literature have similarly found depressed scores on visual (but not verbal) measures for those with atypical language dominance [9–11].

A primary purpose of the present study was to examine whether the crowding effect also applies to a pediatric epilepsy sample. Thus far, findings in the pediatric epilepsy literature have been more variable than in the adult literature. Gleissner et al. [12] provided some support for the crowding hypothesis, as their patients with atypical language representation showed poorer visual memory performance than those with typical language representation; however, scores on other visual–spatial measures were comparable between groups. The lack of support for the crowding hypothesis in pediatric epilepsy has been suggested by Billingsley and Smith [13], who found that atypical language dominance was associated with depressed function of both verbal and visual skills. Along these lines, Everts et al. [14] found no association between atypical language dominance and visual–spatial ability. In contrast, beyond the epilepsy literature, supporting evidence for the crowding hypothesis has come from studies involving children with pre- or perinatally acquired left hemisphere lesions and hemiplegia [15] or spastic cerebral palsy [16]. Furthermore, Muter, Taylor, and Varga-Khadem [17] showed that visual–spatial intellectual skills (as measured by Performance subtests on the Wechsler scales) may be selectively impaired over time in children with hemiplegia because of perinatal left hemisphere lesions, despite considerable stability of overall intellectual functioning.

It is important to note that most studies supporting the crowding hypothesis reviewed above had relatively small sample sizes and based their conclusions on broad group comparisons (typical versus atypical language dominance) using either univariate or nonparametric techniques. Such analyses serve as a useful starting point to investigate the crowding hypothesis in patients with epilepsy with typical versus atypical language dominance. However, more rigorous techniques are also needed to examine whether language laterality can uniquely explain observed group differences.

There is a paucity of studies in pediatric epilepsy that have used multivariate techniques to more robustly examine the contributions of atypical language dominance and associated factors on verbal versus visual cognitive skills. Previous studies have shown that individuals with earlier seizure onset, left-sided seizure focus, left-handedness, and extratemporal lesions are more likely to have atypical language

dominance [12,18–21]. Duration of epilepsy has generally not been found to significantly predict atypical language dominance (see review by Dijkstra & Ferrier [22]), which may be attributed to language plasticity occurring during a sensitive period at a young age (i.e., prior to age 5 years). As such, duration of time after this sensitive period would not necessarily be expected to affect language organization and functioning. Therefore, in our study, we consider the impact of early seizure onset (prior to age 5 years) versus late seizure onset (age 5 years or later). At this point, what is unclear is the ability of these aforementioned factors (i.e., handedness, site of lesion/seizure focus, early seizure onset) to predict verbal versus visual cognitive performance and the relative contributions of each factor. Considering multiple factors simultaneously is essential, as it is unknown whether purported crowding effects may be attributed to atypical language dominance per se. Pediatric epilepsy is an appropriate and interesting model to investigate the effects of plasticity proposed by the crowding hypothesis as atypical language dominance is relatively common, and impacts the developing brain in a unique way.

### 1.3. Current study research questions

In light of the reviewed literature, we addressed the following research questions:

1. In a pediatric epilepsy sample, do those with atypical language dominance perform more poorly than those with typical language dominance on visual versus verbal cognitive measures? In previous research [8,10,16], such broad group-level analysis has been the primary statistical approach. We have repeated that strategy here to establish whether our data are in line with previous studies supporting the crowding hypothesis. It has previously been argued that memory functions are not lateralized in children [23,24]. Therefore, we examined nonmemory verbal and visual skills in this study using univariate analyses.
2. What are the relative contributions of seizure onset (prior to or after age 5 years; early versus late), handedness (right versus left), seizure localization (temporal versus extratemporal), and language dominance (typical versus atypical) on verbal versus visual cognitive functions? To our knowledge, no studies in pediatric epilepsy have considered the impact of language dominance and associated factors on visual and verbal cognitive measures using multivariate analyses.

## 2. Methods

### 2.1. Participants

We retrospectively analyzed clinical data from 110 consecutive cases of children with left-sided focal epilepsy who underwent assessment of language dominance between October 1981 and March 2017 at the Hospital for Sick Children in Toronto, Canada. All patients had medically intractable epilepsy (as defined by failure to achieve seizure control after at least two trials of antiepileptic drugs; (AEDs)) and completed neuropsychological assessment to help determine surgical candidacy. We excluded patients with overall intellectual functioning less than two standard deviations below the population mean ( $n = 16$ ). Lower intellectually functioning patients would be expected to have less variability in their overall profile of scores, thus, reducing the potential to detect possible crowding effects. Three patients were excluded because of their language laterality investigations being unreliable or nonconclusive.

Our final sample consisted of data from 91 patients with left-sided focal epilepsy, 57 with typical (left) language dominance, and 34 with atypical (bilateral or right) language dominance. Children were assessed at the overall mean age of 12.35 years (range = 3.12 to 17.8 years). Patients whose language investigations indicated bilateral, but mostly left-hemisphere language dominance were classified as having typical language representation. Similarly, patients whose language

investigations indicated clearly bilateral or mostly right-hemisphere language dominance were classified as having atypical language representation. Data on language dominance for each patient were gathered from epilepsy surgery conference reports within the medical chart. As recently described by Hermann, Loring, and Wilson [25], assessment practices of language dominance have evolved over time; these changes are reflected in the methods used across participants in our sample, who were seen at our institution over a span of 36 years. Previously standard invasive Wada testing across many epilepsy centers has significantly decreased with the development of valid and reliable noninvasive functional imaging paradigms to assess language laterality [26,27]. As such, in our retrospective clinical sample, language dominance was evaluated using either functional magnetic resonance imaging (fMRI,  $n = 63$ ), magnetoencephalography (MEG,  $n = 4$ ), or Wada/Etomidate speech and memory procedures ( $n = 24$ ). Medical charts were reviewed to collect relevant demographic and medical data, and this information is summarized in Table 1. Retrospective review and subsequent analysis of patient data was approved by the hospital's research ethics board.

## 2.2. Neuropsychological measures

For eligible patients, we extracted assessment data from three visuospatial tasks and three verbal tasks. The three visual tasks included the Block Design and Matrix Reasoning subtests of the Wechsler scales [28–33], as well as the Beery Buktenica Test of Visual–Motor Integration (Beery VMI) [34–36] three verbal tasks included the Vocabulary and Similarities subtests of the Wechsler scales [28–33], and the Boston Naming Test [37]. The Beery Buktenica Visual–Motor Integration Test requires copying increasingly complex line drawings with a paper and pencil. The Block Design subtest involves using colored blocks to match a pictured design and thus, measures visual–spatial construction and problem-solving skills. The Matrix Reasoning subtest measures visual abstract reasoning and requires the patient to complete visual–spatial patterns by selecting the best option from an array. The Vocabulary subtest is a measure of word knowledge for which patients were asked to explain the meaning of words read aloud by the examiner. The Similarities subtest measures verbal abstract reasoning and requires the patient to explain how two words/concepts are alike. For the Boston Naming Test, patients are asked to name line drawings of objects. Not all participants completed all measures, resulting in differing sample sizes. Certain measures may have been discontinued or not administered because of individual differences in cooperation and fatigue, as well as time constraints on the day of the assessment. Further, within the study period, there were changes in clinical practice over time (e.g., variability in the preference of measures included in the assessment battery, clinician changes).

**Table 1**  
Demographic and epilepsy-related characteristics of our sample.

|   | Typical language<br>( $n = 57$ ) | Atypical language<br>( $n = 34$ ) | $p$  |
|---|----------------------------------|-----------------------------------|------|
| Sex (# males)   | 24                               | 23                                | .029 |
| Handedness (# right-handed)   | 54                               | 24                                | .004 |
| Age of seizure onset<br>(mean, standard deviation)                                | 7.14 (4.69)                      | 7.14 (4.50)                       | .999 |
| # onset of seizures prior to age 5 years  | 22                               | 15                                | .662 |
| Age at assessment<br>(mean, standard deviation)                                   | 12.03 (3.52)                     | 12.87 (3.55)                      | .277 |
| Duration of epilepsy at time of assessment<br>(mean in years, standard deviation) | 4.90 (3.68)                      | 5.73 (4.08)                       | .317 |
| Site of seizure focus (#)   |                                  |                                   |      |
| Temporal  | 37                               | 15                                | .91  |
| Extratemporal   | 20                               | 19                                |      |
| Number of AEDs<br>(mean, standard deviation)                                      | 1.58 (.71)                       | 1.76 (.70)                        | .239 |
| Full scale IQ   | 93.65 (12.15)                    | 87.34 (13.00)                     | .03  |

## 2.3. Statistical approach

Prior to the main statistical analyses, between-group differences on several demographic and epilepsy-related variables were examined using analysis of variance, independent samples t-tests, or chi-squared ( $\chi^2$ ) tests, as appropriate. To address our primary research questions, we started by comparing the typical and atypical language groups on all verbal and visual outcomes using independent samples t-tests. To provide a more rigorous examination of the crowding hypothesis, we also conducted six multiple regression analyses, one for each of our dependent variables (3 verbal measures and 3 visual measures). We entered seizure onset (onset before or after age 5 years), seizure localization (temporal vs. extratemporal), handedness (right vs. left), and language dominance (typical vs. atypical) as predictors in each of the regression models in a single step as we wanted to evaluate the relative impact of each factor. Listwise deletion was used to handle missing data. No patients were identified as outliers and excluded from the regression analyses because of large Mahalanobis distance.  $p$  values of less than .05 were considered significant. To allow for direct comparison across outcome measures, all standardized data were converted to z-scores.

## 3. Results

As seen in Table 1, the typical and atypical language groups were similar on several relevant characteristics, such as proportion of males to females, age at seizure onset, age at assessment, duration of epilepsy, and number of AEDs. There was a similar proportion of patients who had onset of epilepsy prior to the age of 5 years, and there were no significant differences in the proportion of patients with temporal versus extratemporal seizure foci. A greater proportion of patients within the atypical language group were male and left-handed compared with the typical language group. The typical language group also had higher standardized scores on the measures of overall intellectual functioning, with the mean of the typical language group being in the Average range and the mean of the atypical language group being in the Low Average range.

### 3.1. Univariate analyses comparing typical versus atypical language groups

Mean z-scores for all measures for the typical and atypical language groups are presented in Fig. 1, and the results of the t-tests are shown in Table 2.

#### 3.1.1. Verbal measures

Naming scores were significantly higher for the typical compared with the atypical language group, although there were no group differences in performance on the Wechsler Vocabulary or Similarities subtests.

#### 3.1.2. Visual measures

The atypical language group showed significantly poorer performance than the typical language group on all visual measures.

### 3.2. Multivariate analyses

See Table 3 for a summary of all multivariate regression results.

#### 3.2.1. Verbal measures

The overall model predicting naming scores was significant, explaining 31% of the variance. Seizure localization and language dominance were significant predictors, whereas early seizure onset and handedness were not. Specifically, lower naming scores were associated with temporal lobe seizures and atypical language dominance. The overall model predicting vocabulary scores approached (but did not reach) statistical significance ( $p = .06$ ), with only seizure localization being a significant predictor; lower vocabulary scores

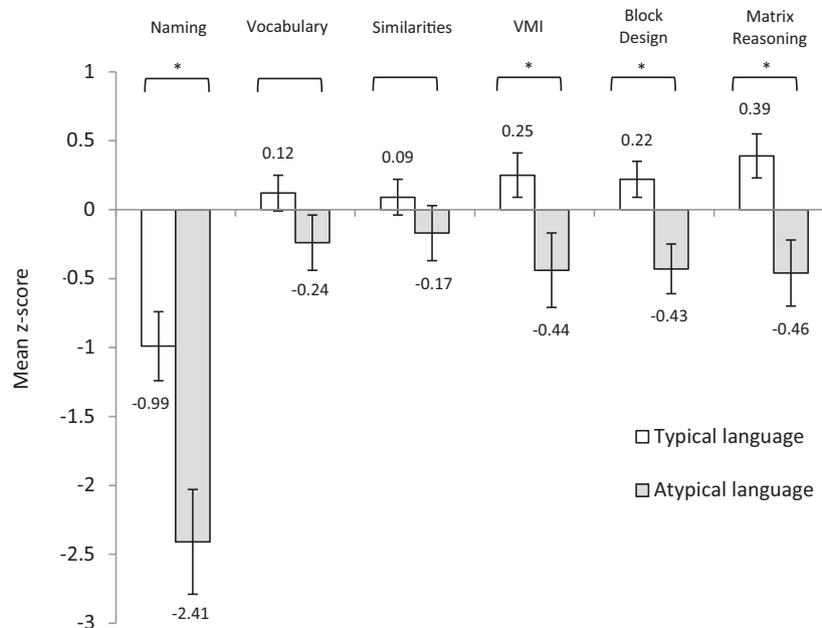


Fig. 1. Mean z-scores for all outcome variables in the typical versus atypical language groups. Note: Significant comparisons are indicated by an asterisk (\*).

were associated with temporal lobe seizures. As a trend, atypical language dominance was associated with lower vocabulary scores as well. The overall model predicting similarities scores was nonsignificant, although temporal lobe seizure onset was again significantly associated with poorer performance.

### 3.2.2. Visual measures

The overall model predicting VMI performance was significant, explaining 25% of the variance. Early seizure onset and atypical language dominance significantly predicted lower VMI scores. The overall model predicting block design scores was significant, explaining 14% of the variance. Only language dominance was a significant predictor, with typical language dominance associated with better performance. The overall model predicting matrix reasoning scores was significant, explaining 30% of the variance. Only handedness was a significant predictor, with left-handedness associated with lower scores.

## 4. Discussion

The relationship between cognitive performance and language lateralization is not yet well understood in children with epilepsy, with varying patterns of visual versus verbal cognitive performance shown in previous studies. The crowding hypothesis is a theory about the effects of neuroplasticity, which states that the transfer of language to the right hemisphere due to early left hemisphere injury ‘crowds out’ original right hemisphere visual–spatial functions. Early studies supporting the crowding hypothesis were conducted with adults, with the few pediatric studies yielding more variable results. Indeed, it is conceivable that the reorganization or crowding of functions

would be a protracted process, and the impact of potential right hemisphere crowding on the developing brain has yet to be fully elucidated. In children with seizures, proper interpretation of neuropsychological test results in the context of language lateralization, and the site of seizures is critical for presurgical evaluations to inform the risk of functional loss.

The objective of the present study was to examine the crowding hypothesis in a pediatric epilepsy sample, while taking into account language dominance and associated factors (i.e., early epilepsy onset, handedness, seizure localization). Most of the research supporting the crowding hypothesis relies on broad (univariate) comparisons between atypical and typical language-dominant samples, which do not consider the impact of other factors that may be contributing to the pattern of verbal and visual performance. We conducted univariate analyses to allow for comparison with previous investigations and offered additional multivariate findings.

Preliminary analyses showed that our atypical language group had a greater proportion of males, a finding consistent with one other pediatric study [21], and opposite to that of Helmstaedter et al. [38] and Kurthen et al. [39] whose samples had a higher proportion of females with atypical language dominance. Interestingly, it has been proposed that females have a shorter timeframe than males within which language can be transferred to the right hemisphere [40]. Thus, males may have a greater capacity to reorganize, potentially explaining the sex differences in atypical language prevalence in our sample. Although there has been some controversy about sex differences with respect to the crowding hypothesis, these have not been frequently documented in the child or adult literature. Moreover, a greater proportion of the atypical language group were also left-handed, consistent with the suggestion that left-hand dominance may be a characteristic feature of patients with right-hemisphere language representation [12]. Our finding that patients with atypical language dominance had mildly depressed intellectual functioning (on average) compared with those with typical language dominance is also in keeping with several previous investigations [10,13,15,41], and could indicate generally reduced neural resources in individuals with atypical language representation. It should be noted, however, that the difference in overall IQ between language groups in our sample was very subtle (less than half a standard deviation) and does not adequately explain the pattern of effects observed in our data.

Table 2

t-Test results comparing the typical with atypical language groups on all outcome variables.

| Outcome variable          | t     | p    | 95% confidence interval |
|---------------------------|-------|------|-------------------------|
| Naming (n = 61)           | −3.27 | .002 | −2.29, −0.55            |
| Vocabulary (n = 79)       | −1.52 | .132 | −0.83, 0.11             |
| Similarities (n = 81)     | −1.09 | .278 | −0.73, 0.21             |
| Beery VMI (n = 45)        | −2.35 | .024 | −1.29, −0.10            |
| Block Design (n = 81)     | −2.96 | .004 | −1.10, −0.21            |
| Matrix Reasoning (n = 44) | −3.06 | .004 | −1.41, −0.29            |

**Table 3**  
Regression results for all outcome variables.

| Dependent variable   | Predictors           | B (95% confidence interval) | t     | p     |
|--|----------------------|-----------------------------|-------|-------|
| <b>Naming</b> (n = 61)<br>R = 0.56<br>R <sup>2</sup> = 0.31<br>F = 6.38 (p < .001)           | Early seizure onset  | 0.23(−0.60,1.05)            | 0.55  | .59   |
|  | Seizure localization | −1.36(−2.14,−0.58)          | −3.49 | .001  |
|  | Handedness           | 0.10(−1.30,1.50)            | 0.15  | .89   |
|  | Language dominance   | 1.72(0.82,2.62)             | 3.81  | <.001 |
| <b>Vocabulary</b> (n = 79)<br>R = 0.34<br>R <sup>2</sup> = 0.11<br>F = 2.36 (p = .06)        | Early seizure onset  | −0.15(−0.60,0.30)           | −0.66 | .51   |
|  | Seizure localization | −0.58(−1.0,−0.14)           | −2.63 | .01   |
|  | Handedness           | 0.06(−0.61,0.73)            | 0.18  | .86   |
|  | Language dominance   | 0.49(−0.003,0.99)           | 1.98  | .051  |
| <b>Similarities</b> (n = 81)<br>R = 0.29<br>R <sup>2</sup> = 0.08<br>F = 1.69 (p = .16)      | Early seizure onset  | −0.28(−0.73,0.18)           | −1.20 | .24   |
|  | Seizure localization | −0.48(−0.92,−0.04)          | −2.17 | .03   |
|  | Handedness           | −0.13(−0.81,0.55)           | −0.39 | .70   |
|  | Language dominance   | −0.41(−0.09,0.92)           | 1.63  | .11   |
| <b>Beery VMI</b> (n = 44)<br>R = 0.51<br>R <sup>2</sup> = 0.25<br>F = 3.52 (p = .015)        | Early seizure onset  | −0.59(−1.14,−0.04)          | −2.18 | .04   |
|  | Seizure localization | 0.41(−0.14,0.97)            | 1.51  | .14   |
|  | Handedness           | −0.48(−1.25,0.29)           | −1.26 | .22   |
|  | Language dominance   | 0.80(0.18,1.42)             | 2.61  | .01   |
| <b>Block Design</b> (n = 82)<br>R = 0.38<br>R <sup>2</sup> = 0.14<br>F = 3.22 (p = .02)      | Early seizure onset  | −0.20(−0.64,0.24)           | −0.90 | .37   |
|  | Seizure localization | −0.19(−0.62,0.24)           | −0.89 | .38   |
|  | Handedness           | 0.49(−0.15,1.13)            | 1.51  | .13   |
|  | Language dominance   | 0.57(0.09,1.06)             | 2.35  | .02   |
| <b>Matrix Reasoning</b> (n = 44)<br>R = 0.55<br>R <sup>2</sup> = 0.30<br>F = 4.12 (p = .007) | Early seizure onset  | −0.35(−0.97,0.28)           | −1.12 | .27   |
|  | Seizure localization | 0.03(−0.49,0.56)            | 0.12  | .91   |
|  | Handedness           | 0.89(0.01,1.77)             | 2.04  | .048  |
|  | Language dominance   | 0.45(−0.19,1.10)            | 1.42  | .16   |

Taken together, our univariate analyses provide support for the crowding hypothesis and are consistent with results from several previous studies. Critically, we found that the atypical language group had poorer performance than the typical language group across our selected visual–spatial measures. Vocabulary knowledge and verbal abstract reasoning skills (as measured by the Wechsler Vocabulary and Similarities subtests) were comparable between our typical and atypical language groups. This result is predicted by the crowding hypothesis, which prioritizes the development of language functioning at the expense of visual–spatial skills. We also found that the typical language group obtained higher confrontation naming scores than the atypical language group. This result is consistent with another pediatric study from our center [42] but differs from an adult study, which found that naming performance was similar in those with typical and atypical language dominance [8]. Such a contrast in findings highlights that results from adult studies cannot necessarily be extrapolated to pediatric samples. Specifically, lateralizing effects (e.g., visual–spatial crowding) shown in adults might not similarly present in children or may be more nuanced or subtle. Our univariate analyses suggest that although visual–spatial crowding may occur in children with left-hemisphere seizures and atypical language dominance, certain language skills (such as naming) might not be spared as has been shown in adults [8]. Notably, closer inspection of our data also indicates that the poorer naming performance of the atypical language group is largely driven by patients with temporal lobe seizures, for whom naming deficits have been well documented (reviewed e.g., Bell et al. [43]).

There have only been a few pediatric studies that have specifically addressed the crowding hypothesis, with the investigation by Billingsley and Smith [13] arguably being the most comparable to the current study. Similar to that study, we also examined several verbal and visual intellectual skills, but with important differences in sample characteristics and statistical approach. The current sample was much larger than that of Billingsley and Smith, which permitted greater power in our statistical analyses. Moreover, our typical and atypical language groups were matched on a greater number of relevant characteristics (i.e., age at assessment, sex, number of AEDs, and duration of epilepsy), including age of seizure onset, thus not requiring us to covary this predictor in our analyses. Billingsley and Smith found that their typical language group showed better performance on several verbal and visual intellectual tasks, although these conclusions were largely drawn from statistical trends, in light of their relatively small sample (N = 14). Given our larger

sample size, we based our conclusions exclusively on statistically significant results. Notably, one of Billingsley and Smith's few statistically significant findings included better verbal reasoning performance (as measured by the Similarities subtest) for the typical language group, which was not replicated in our analyses. However, other differences between the two study samples may also help to account for varying results, such as our inclusion of patients with both temporal and extratemporal left-hemisphere seizure foci, as opposed to patients with left temporal lobe epilepsy only.

An important contribution from our study is our use of multivariate analyses to simultaneously examine the impact of language dominance and associated factors (i.e., seizure localization, early seizure onset, handedness) on verbal versus visual cognitive skills. Such an approach provides a more rigorous test of the crowding hypothesis in that we can make stronger conclusions about whether the variability in our data is due to group differences in language dominance per se.

Overall, our multivariate analyses provide some support for the crowding hypothesis. On two out of three visual measures (Beery VMI and Block Design), language dominance was the strongest predictor of performance, even when considering early seizure onset, seizure localization, and handedness in the models. There were instances in which language dominance-associated factors also emerged as significant predictors in the regression models, but there was no consistent pattern. Specifically, early seizure onset was associated with lower scores on the Beery VMI, and left-handedness was associated with lower matrix reasoning scores. Given the lack of consistency in these findings, these may be idiosyncratic results from our sample, although future studies would be helpful to determine whether they can be replicated. With respect to the verbal skills examined, seizure localization was the strongest predictor of performance across most measures. Consistent with the univariate analyses, language dominance was not a significant predictor of vocabulary knowledge or verbal abstract reasoning. Interestingly, however, language dominance was the strongest predictor of naming scores (even beyond seizure localization), which is not predicted by the crowding hypothesis.

#### 4.1. Limitations

There are several limitations that should be considered when interpreting the findings from our study. First, we acknowledge that language dominance exists on a continuum, in keeping with fMRI

literature [26,44], although we only examined language dominance as being a dichotomous variable (typical versus atypical), consistent with previous studies on the crowding hypothesis. As this was a retrospective study using data that were collected for clinical purposes, we do not have fine-grained metrics of language lateralization that would allow for analyses of language dominance as a continuous variable; indeed, this would provide an even more robust investigation of the crowding hypothesis. As noted earlier, clinical procedures for determining language dominance have also changed over time with the advent of more sophisticated and noninvasive imaging methods. Thus, different methods were used to determine language lateralization in our sample. Our results may have also been somewhat underpowered for some analyses because of reduced sample sizes secondary to missing data. From our clinical database, we selected the verbal and visual cognitive measures that had the largest sample sizes, although we acknowledge that the skills measured by these tasks do not comprehensively assess or represent all verbal or visual abilities.

#### 4.2. Conclusions

We provided some evidence of neuropsychological crowding effects in a pediatric epilepsy sample. Specifically, our data showed that patients with a left-sided seizure focus and atypical (right or bilateral) language dominance performed more poorly than patients with typical language dominance on certain measures of visual–motor construction and problem-solving skills, suggestive of right-hemisphere functional crowding. Vocabulary knowledge and abstract verbal reasoning abilities were similar between the typical and atypical language groups, indicating relative sparing of those language skills. These results should be considered when interpreting the neuropsychological profiles of children being evaluated for epilepsy surgery.

#### Conflict of interest

The authors have no conflicts of interest to declare.

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