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Literacy after cerebral hemispherectomy: Can the isolated right hemisphere read?

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ABSTRACT

Objectives: Cerebral hemispherectomy, a surgical procedure undergone to control intractable seizures, is becoming a standard procedure with more cases identified and treated early in life [33]. While the effect of the dominant hemisphere resection on spoken language has been extensively researched, little is known about reading abilities in individuals after left-sided resection. Left-lateralized phonological abilities are the key components of reading, i.e., grapheme–phoneme conversion skills [1]. These skills are critical for the acquisition of wordspecific orthographic knowledge and have been shown to predict reading levels in average readers as well as in readers with mild cognitive disability [26]. Furthermore, impaired phonological processing has been implicated as the cognitive basis in struggling readers. Here, we explored the reading skills in participants who have undergone left cerebral hemispherectomy.

Methods: Seven individuals who have undergone left cerebral hemispherectomy to control intractable seizures associated with perinatal infarct have been recruited for this study. We examined if components of phonological processing that are shown to reliably separate average readers from struggling readers, i.e., phonological awareness, verbal memory, speed of retrieval, and size of vocabulary, show the same relationship to reading levels when they are mediated by the right hemisphere [2].

Results: We found that about 60% of our group developed both word reading and paragraph reading in the average range. Phonological processing measured by both phonological awareness and nonword reading was unexpectedly spared in the majority of participants. Phonological awareness levels strongly correlated with word reading. Verbal memory, a component of phonological processing skills, together with receptive vocabulary size, positively correlated with reading levels similar to those reported in average readers. Receptive vocabulary, a bilateral function, was preserved to a certain degree similar to that of strongly left-lateralized phonological skills [3]. Later seizure onset was associated with better reading levels.

Conclusions: When cerebral hemispherectomy is performed to control seizures associated with very early (in utero) insult, it has been found that the remaining right hemisphere is still able to support reading and phonological processing skills that are normally mediated by the left hemisphere. Our results also suggest the existence of variability in individuals after hemispherectomy, even within groups having the same etiology and similar timing of insult.

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1. Introduction

Reading, the ability to utilize visual representations of letters to access the phonological and semantic representations of words, is traditionally considered a brain function strongly lateralized to the left cerebral hemisphere, LH [1-3]. Vigneau and colleagues in their 2011 meta-review of 128 articles reporting brain activations associated with reading in healthy right-handed adults confirmed that the right hemisphere, RH, on its own, lacks phonological processing abilities that could constitute an important component in reading acquisition, i.e., the RH lacks the ability to map letters to sounds (i.e., to connect orthography to phonology). Phonological processing, while not the only factor...
involved in reading and comprehension, is, nevertheless, the most crucial one utilized in the decoding of words [4]. Substantial evidence indicates that components of phonological processing such as phonological awareness, verbal memory, and speed of naming are critical in reading words and connected text in both average readers and readers with dyslexia [5,6].

While the left hemisphere is demonstrably the seat of reading and phonological processing, the right hemisphere’s precise role in the processing of written language poses a number of questions that have not yet been resolved. Although language competence of the RH is now widely recognized [7], its involvement in reading in healthy populations is traditionally thought to be limited to higher-order skills, such as pragmatics, nonliteral language, and prosody, in addition to some role in semantic interpretation at the single-word level. Interestingly, imaging studies have suggested an increased involvement of the RH in struggling readers — including both those with developmental deficits (e.g., dyslexia) and those having acquired abnormalities (e.g., poststroke) on the left side [8–13]. The compensatory nature of RH involvement in these readers and an understanding of what possible advantages it offers for reading recovery remain unclear partly because of a lack of information regarding the potential of the isolated RH in the development of phonological processing and reading skills. This is where an investigation into the ability of the isolated RH to support reading in individuals after cerebral hemispherectomy becomes critically important, in that it has the potential to reveal both major constraints on the system as well as on its main components. In this study, we report on the reading abilities of 7 individuals who only have an isolated right hemisphere after sustaining perinatal infarct, medically-intractable seizures associated with it, and consequent left cerebral hemispherectomy.

Previous studies have reported on language skills in areas such as syntax, prosody, and semantics following left hemispherectomy [14–20]. Both near-normal and impaired language outcomes have been reported, and heterogeneity of outcomes has been attributed to the effects of specific etiologies and clinical factors that are associated with them [18,21].

To date, only a few studies have investigated reading after left cerebral hemispherectomy, and these previous studies report on a combined total of 7 patients. Two studies performed before the emergence of modern neuroimaging examined 4 adults with isolated RH and suggested that only those who had sustained a very early insult (i.e., before 1 year of age) and developed fluent spoken language could read, although elements of deep (phonological) dyslexia were noted [12,22]. A more recent study by Cummine and colleagues [23] extended these findings by documenting phonological dyslexia with slight deficits in whole-word reading following left-sided resection. Where these two studies reported on individuals who were tested decades after surgery, there is one study that reports on a 15-year-old adolescent who was tested 6 years after his left-sided surgery [20]. The individual described in this study could not read at all perhaps because of the fact that his spoken language development started only following surgery at the age of 9 years. In the only study incorporating brain imaging, Danelli and colleagues [24] tested a 17-year-old, Italian-speaking, young adult who had his left hemispherectomy at the age of 2.5 years. They reported on a unique patient whose hemispherectomy was not intended to control epilepsy, who had normal reading abilities, but whose reading skills were developed only after many years of intensive therapy. This patient, nevertheless, displayed some persistent deficits which were characterized as surface dyslexia. Their imaging data show that a major “left-like blueprint” subserves near-normal reading by the isolated RH with the reduced intensity of activations in the temporoparietal and angular gyrus areas. Taken together, these previous studies indicate that some patients can learn to read after left cerebral hemispherectomy.

To better understand the mechanism of right hemisphere reading, we investigated reading, including nonword reading and the components of phonological processing that have been linked to reading levels in both healthy and struggling readers. As we suggested here, phonological processing is an umbrella term covering distinct components which are all involved in fluent reading. They include the following: (i) phonological awareness (the ability to manipulate phonological structures); (ii) verbal or phonological memory (the coding and temporary storage of phonological information in short-term memory); and (iii) the speed of retrieval or rapid access (fast connections to phonological forms associated with graphic forms) [25]. All these skills, together with vocabulary size, have been shown to reliably predict reading levels in children and adults, including populations with mild mental disability [26].

The LH dominance for these phonological processes develops gradually and becomes a strongly lateralized LH function in late adolescence in proficient readers. This stands in contrast to the case of patients with dyslexia, who show continuous RH involvement [27–29]. Given the very early (perinatal) insult to the LH in the patients we studied, we hypothesized that all participants in our study would, nevertheless, be able to read and develop some mastery of the requisite phonological skills. We also expected that the patients in the present study would present correlations between specific skills and reading ability similar to those of average readers and readers with impaired mental function — namely that their phonological awareness skills would strongly correlate with their individual word-reading ability, while their verbal memory, speed of retrieval, and vocabulary size would correlate with their capacity for processing connected text. We also hypothesized that the size of their vocabulary, a critical component of reading and a bilaterally-distributed function, would be less impaired in contrast to left-lateralized phonological components.

2. Methods

2.1. Approvals and patient consent

The University of South Carolina, Columbia Institutional Review Board and University of California, Los Angeles Institutional Review Board approved this study. Patients and families signed research informed consents and Health Insurance Portability and Accountability Act (HIPAA) authorizations.

2.2. Recruitment and clinical variables

In recruiting patients for this study, we made an effort to find individuals whose conditions would allow the isolated right hemisphere (RH) the greatest potential to develop language skills. This selection process excluded individuals with progressive lesions, such as those having Sturge–Weber syndrome or Rasmussen encephalitis. In addition, we excluded individuals in certain etiology groups, such as those with cortical dysplasia and hemimegalencephaly, who will inevitably undergo hemispherectomy, since the integrity of the remaining hemisphere experiencing the said conditions is uncertain. To meet our selection criteria, we selected individuals who had very early, in utero and acquired, insult to the left hemisphere. Additionally, we chose patients who exhibited a high percentage of seizure control following hemispherectomy, since this would suggest that the remaining RH has been spared and has relative integrity. The only etiology group that meets all these combined requisite characteristics is that of children who have undergone left hemispherectomy to arrest seizures associated with perinatal infarct. Hence, all participants with perinatal infarct to their left side were recruited during their participation in a 3-year long concurrent study involving a two-week course of intensive gait therapy (as previously described) [30]. In general, the histopathology results of the seven individuals were consistent with the findings of a middle cerebral artery (MCA) stroke in utero. Clinical history and neuroimaging results were reviewed both presurgically and postsurgically to check for the presence of any remaining visible missed connections between the two hemispheres and on the status of the remaining RH. The RH of
the participants reported on in this study can be described as normal, with no overt signs of any of the mentioned pathologies. The clinical variables in Table 1 were abstracted from the records as previously described[31]. These included age at seizure onset, age at surgery, age at testing, medication history of anti-epilepsy drug (AED) consumption, and the presence of seizure episodes at the time of testing. All participants had undergone psychoeducational testing.

Two participants (1F and 7M) were diagnosed with MCA infarct immediately after birth. The rest of the cohort were all diagnosed with cerebral palsy around 2 years of age. Brain imaging was performed on all subjects, between ages of 2 and 4 years, and the presence of the left hemisphere lesion was confirmed. There was no seizure activity noted at that time. However, they all exhibited a delay with respect to important developmental milestones, such as sitting, walking (no crawling was noted in all children), and the production of the first words. The hemiparesis observed in these children was described as the nearly complete neglect of the affected arm and hand with an increasing degree of impairments in the proximal-distal muscle axis and the absence of voluntary movements in wrist/hand. Some of the children could perform a pincer hold on an object but could not release their grasp. The first words uttered by the children in the cohort appeared around 24 months of age, after which language development was described as normal, with two-word and multi-word utterances deemed as appropriate. The onset of seizures disrupted this development and very quickly became refractory to medications. The kinds of seizures varied greatly, with daily occurrences of up to 250 episodes[32]. The cerebral hemispherectomy procedure was anatomical in participants 2F and 7M and with daily occurrences of up to 250 episodes[32]. The cerebral hemisphere, with two-word and multi-word utterances deemed as appropriate.

All seven participants (females: n = 6, age range: 6–21 years) were from monolingual English-speaking families. Presurgical evaluations of their language abilities were not available probably because of severe seizure activity. Interviews were conducted with the parents of each participant in order to obtain an account of the participant’s language and literacy acquisition and to review their Individual Education Plans (IEPs). All parents stated that, after an initial delay, their children’s language development seemed appropriate from about 24 months of age until seizures became uncontrolled and their language began to deteriorate. Some children could barely speak at the time of their surgery, while others retained a few words and signs. Language recovery was described as fast, and, within 3–4 weeks postsurgery, children had attained their presurgery, preseizure levels. All participants returned to the same grade level without missing a school year, with either no professional intervention or (at most) 1 weekly session with a Speech Language Pathology (SLP) professional. Two participants, 1F and 2F, had started literacy acquisition only after cerebral hemispherectomy, and the remaining five had begun acquiring literacy skills before surgery. However, only two participants, 3F and 5F, could read (Table 1). All participants had age-appropriate speech and comprehension of language at testing, based on the data of previously published assessments[21], although detailed examination revealed subtle syntactic deficits in some of them.

2.4. Reading and other testing

All tests used in this study allow for a standardized and widely-used assessment from early childhood to adulthood. The tests were administered in order to collect information on the participants’ general reading skills, phonological processing (phonological awareness, phonological memory, and rapid naming), word reading and nonword reading, and vocabulary. Individual test scores are presented in Table 1.

2.4.1. Reading: word and word/paragraph

To test word reading, we used the Woodcock Reading Mastery Test, WRMT-III[36], and its subtest of Word Identification and administered this to 5 participants (1F, 2F, 4F, 5F, and 6F). The Word Identification subtest includes reading/pronouncing words in isolation from a word list in an order of increasing difficulty. The raw scores were converted to standard scores with norms of 100 ± SD 15. Standard scores are shown in Table 1.

In addition, the reading subtest from the Kaufman Test of Educational Achievement K-TEA II Brief was used[37]. This reading score is based on Word Recognition and Paragraph Comprehension with standardized norms of 100 ± SD 15. There are 46 items in the Word Recognition part, which require reading and pronouncing both regular and irregular words (i.e., irregular words being those that do not strictly follow phonetic rules). Most of the 27 items on the Paragraph Comprehension test involve reading a passage and giving oral answers to literal and inferential questions. Some items require a response to commands given in printed statements, e.g., “Turn your head”.

2.4.2. Decoding: nonword reading

To test decoding skills, we used Woodcock Reading Mastery Test, WRMT-III[36] and its Word Attack subtest in 5 participants (1, 2, 4, 5, and 6). The Word Attack subtest assesses phonetic decoding skills through reading aloud increasingly complex nonsense words. The raw scores were converted to standard scores with norms of 100 ± SD 15. Standard scores are shown in Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Participant</th>
<th>Age at seizure onset (years)</th>
<th>Age at surgery (years)</th>
<th>Age at the time of testing (years)</th>
<th>AED</th>
<th>Seizures present</th>
<th>Performance on all tests, 100 ± 15</th>
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AEDs — antiepileptic drugs, PA — phonological awareness, PM — phonological memory, and RN — rapid naming.
2.4.3. Vocabulary, PPVT
The Peabody Picture Vocabulary Test — Third Edition (PPVT-III) was used to test vocabulary knowledge [38]. Peabody Picture Vocabulary Test assesses receptive lexical comprehension and is composed of 17 sets of lexical items that must be matched to the correct pictures. The sets are of increasing difficulty, ranging from a child's typical first words to words that are highly infrequent even among adults. The raw scores were converted to standard scores with norms of 100 ± SD 15.

2.4.4. Phonological processing measures
The two standardized tests were used to measure the components of phonological processing as well as decoding skills. Primarily, the three subtests of the Comprehensive Test of Phonological Processing (CTOPP) were used to assess the three components of phonological processing [39]: phonological awareness (PA), phonological memory (PM), and rapid naming (RN), with standardized norms of 100 ± SD 15. The PA test involves elision and blending words and was administered to assess the awareness and ability to manipulate phonological structures reflecting the capacity to code information phonologically for temporary storage in working memory.3 The PM part assesses the size of short-term verbal storage and included memory for digits and nonword repetition.2 The RN portion estimates the ability to quickly retrieve phonological forms (names) associated with graphic stimuli and included naming digits and letters.3

2.5. Data analyses
Clinical variables and test-performance-derived standard scores were entered into a database and analyzed using descriptive statistics and nonparametric correlations (Spearman, two-tail), comparing reading scores with measures of phonological processing, vocabulary, and clinical variables. Since a p-value based on an equation with fewer than 10 observations is inaccurate, a table of critical values required significance at the .05 level (a directional test) was used to confirm significance.

3. Results
3.1. The cohort description
Histopathology following hemispherectomy confirmed that all participants experienced primary insult to their left cerebral hemisphere before birth. Age at seizure onset ranged from birth to 5 years (median: 4 years); age at surgery ranged from 1 to 10 years (median: 8 years); and age at testing ranged from 10 to 21 years (median: 13 years). All patients except one, 2F, were seizure-free at the time of testing, with 2 taking antiepileptic drugs (AEDs). All but one participant had, at least, 4 years between surgery and testing (range: 4–11 years, median: 6 years), with one child (4F) having 1 year postsurgery.

3.2. Reading
The median scores for all the tests in this study were in the average range (≥80).

3.2.1. Word and paragraph reading, K-TEA
The reading scores were in the range of 70 to 99, median: 80. About 60% of all the participants (4/7) scored in the low average and average ranges (≥80).

3.2.2. Word reading, WRMT-III
Test scores for the entire cohort are shown in Table 1. The word-reading scores tested by the Word Identification subtest were in the range of 68 to 95, median: 81. Three participants, 60% (out of the five tested on this measure), had word reading in the average range (≥89).

3.3. Decoding, WRMT-III
The Word Attack subtest scores were in the range of 65 to 98, median: 92. Only one participant did not reach an average score. The four remaining individuals, 80% (out of the five tested on this measure), had scores equal to or higher than 81.

3.4. Vocabulary, PPVT
Vocabulary scores ranged from 70 to 99, median: 80. Five participants, 70%, had scores in the low average and average ranges (≥84).

3.5. Phonological processing, CTOPP
Phonological awareness, PA, scores varied among individual participants in a range of 79 to 112, median: 85, with 70% of the participants scoring in the average range. Phonological memory, PM, scores ranged from 70 to 109, median: 88, with 56% of all the participants achieving average scores. Rapid naming, RN, scores ranged from 70 to 112, median: 88, with 56% scoring in the average range.

3.6. Correlations
3.6.1. Correlation between word reading and phonological awareness
The Word Identification scores correlated with PA (r = 0.975) but not with the Word Attack scores (r = 0.051). There was no correlation between the two subtests (r = 0.3).

3.6.2. Correlation between paragraph reading and phonological processing components
Significant positive correlations were found between reading scores and measures of PM (r = 0.857) and vocabulary size (r = 0.74). Correlations between reading scores and measures of rapid naming did not reach significance (r = −0.29).

3.7. Reading and clinical variables
Correlations between reading scores, K-TEA, and age at surgery/testing did not reach significance (r = 0.41 and 0.29, respectively). The association between the reading scores and age at seizure onset (r = 0.724) reached the critical value of r = 0.72 required for significance.

4. Discussion
In modern Western society, the ability to process written language (i.e., reading) is a key determinant of one's ability to access information and participate in societal activities. Hence, it is important to understand and consider the capacity of the RH to support both spoken language and written language when discussing outcomes of cerebral hemispherectomy. In typical development, reading emerges with progressive left-brain lateralization and remains a strongly lateralized function throughout the lifespan, with the RH contribution traditionally described as being limited to one-word semantic access and visual word recognition. The fact that a number of studies have demonstrated...
that the RH is utilized by populations having reading deficits raises the question of whether the role of RH is only compensatory or whether it can independently support reading on its own when the LH is not available [9,40].

The findings of previous research that has investigated these questions (with a total of 7 patients across all these published studies) suggest heterogeneity in reading abilities following left hemispherectomy [19,20,22–24]. However, the etiologies that led to hemispherectomy for the patients reported on in these previous studies were quite varied and included patients with progressive disorders (Rasmussen encephalitis and Sturge Weber syndrome) and one with a brain tumor. Since the effects of etiology on language outcomes are widely acknowledged [18,21], we, therefore, chose to focus on multiple patients who had undergone cerebral hemispherectomy for the same etiology, namely, perinatal infarct. Even within the same etiology, the clinical variables in our sample were heterogeneous. However, more importantly, clinical examination of the patients in our study found their remaining RH to be normal, a finding that was corroborated by the ability to control seizures following hemispherectomy in 6 out of 7 of our patients. We, thus, have a reason to believe that we investigated the RH potential in cases wherein unfolding lateralization to the dominant hemisphere had likely been arrested before it had a chance to “claim” language and that the patients’ reading ability was supported by a relatively intact RH.

Despite these relatively homogeneous clinical factors, not all of our participants acquired reading successfully. Four participants, 60%, were found to read and comprehend in the average range (≥80, standard score), while the remaining 3 individuals scored below average (70–76, standard score). The word-reading measure showed similar results with 3/5 participants scoring in the average range and 2 individuals receiving scores of 68 and 73. This finding suggests that the isolated RH has the potential to support reading. However, it also suggests that early insult of the LH by itself (leaving the RH dominant for language acquisition) does not automatically guarantee the full development of this potential in every individual.

Our finding that the entire cohort’s standard scores on PA were in the range of 79 to 112 suggests, surprisingly, that they have mastered phonological awareness despite the widely accepted notion that the RH does not have access to phonology. The results of phonological decoding, the nonword-reading test, with 4/5 participants scoring a standard score of 90 and the highest median among all tests, 92, further confirmed that the RH can successfully support phonological processing. The PA scores correlated with word-reading scores in a manner similar to that of a neurologically-intact healthy children. In a manner similar to that of a neurologically-intact brain, phonological memory and vocabulary measures, but not rapid naming, correlated with the word/paragraph-reading test scores [41]. We had expected that vocabulary (on the account of its usual bilateral cortical distribution) would be better preserved in patients with isolated RH than normally left-lateralized abilities such as phonological processing [18], but this prediction was not supported, as we found similar levels of performance on all measures.

To summarize our behavioral findings, we found that components of phonological processing (with the exception of rapid naming) and vocabulary levels correlated with reading which is supported by the isolated RH in a manner similar to what has been reported for reading in other populations with both hemispheres. This supports the findings from the brain imaging case study by Danelli et al. [24] and from our own data, showing that the reading networks in the isolated RH are following “a blueprint” of its left counterpart.

Although etiology is an important clinical factor, it may not be the only variable affecting patients’ cognitive outcomes, and variables such as seizure onset, medication history, and integrity of the remaining hemisphere need to be studied in more depth. The variability in reading scores in our cohort was not associated with clinical variables such as age at surgery and testing. Seizure onset at an older age only correlated with better reading results. This suggests that early seizures may disrupt development of both cerebral hemispheres, while a more mature brain brings some degree of resilience limiting the negative effects of seizure activity.

The variability of the results (i.e., some participants obtaining average or subaverage scores for both word reading and nonword reading, while others scored high on one or another) does not allow for any definitive conclusions regarding the model of functional reorganization that occurs in the isolated right hemisphere. For example, the Equipotentiality model would predict spared reading ability for both words and nonwords paired with preserved phonological awareness, and, indeed, three participants (2F, 4F, and 6F) did reach average scores on all these measures. In contrast, the Hemispheric Specialization model would predict poor skills across all categories, as was found for participant 5F. Finally, the Hierarchy of Specialized Functions model would predict preserved word-reading capacity in contrast with nonword-reading capacity. Our remaining participant, 1F, showed the opposite pattern with her nonword reading being the only score in the average range (standard score of 92) and other scores being less than that. Individual variability found within our patient cohort may, thus, be similar to the variability one would expect to find in a healthy population, and this may help explain the results we found in this study.

4.1. Limitations and future directions

Our study has a number of potential limitations that should be taken into account when interpreting these results. Based on the fact that postsurgical language and literacy, as well as hemiplegia levels, were similar to presurgical ones, we assumed that the RH had been supporting language early on in isolation in all our participants. However, we do not have imaging studies to firmly establish this as a fact. In addition, our word/paragraph-reading test included both isolated-word and connected-text stimuli, but in future studies, we think that only connected-text (paragraph)-reading measures should be explored. Finally, although our research presents the largest single sample reported so far, the cohort that we tested is still too small to make any sweeping conclusions about the correlations we found. Future research needs to explore the potential of the RH with respect to reading capability for hemispherectomy patients within each major etiology class and determine reading and phonological processing skills following different insult mechanisms and diverse clinical variables associated with each etiology.

5. Conclusions

Despite these limitations, our findings do suggest that, under some circumstances, the isolated RH has the potential to develop near normal reading ability. Furthermore, in supporting readings, the RH uses at least some of the building blocks that would be used by its left counterpart in healthy children. In a manner similar to that of a neurologically-intact brain, phonological memory and vocabulary in some patients with isolated RH have been identified as being potentially related to reading outcomes. In the same vein, phonological awareness was shown to be correlated with word-reading skills. Seizure onset at an older age was associated with better reading in our group, and this finding would need to be confirmed within other etiology groups. Taken altogether, our findings motivate further investigations in order to understand both the limitations and the strengths of the isolated RH. This knowledge may help in the development of interventions that might improve reading and other language skills in these populations and other populations with brain injury that disproportionally rely upon the RH following developmental or acquired lesions.
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Conflict of interest

None of the authors has conflict of interest.

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