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Early Language Development After Peri-natal Stroke

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Abstract

Early unilateral brain damage has different implications for language development than does similar damage in adults, given the plasticity of the developing brain. The goal of this study was to examine early markers of language and gesture at 12 and 24 months in children who had peri-natal right hemisphere (RH) or left hemisphere (LH) stroke (n = 71), compared with typically developing controls (n = 126). Parents completed the *MacArthur-Bates Communicative Development Inventory (CDI): Words & Gestures* (12 month data point), or the *CDI: Words & Sentences* (24 month data point). Statistical analyses were performed on percentile scores using analysis of variance techniques. At 12 months, there were no differences among groups for Words Understood, Phrases Understood or Words Produced. At 24 months, both lesion groups scored significantly lower than controls on Word Production, Irregular Words, and Mean Length of Sentences, but lesion groups did not differ from each other. In longitudinal subset of participants, expressive vocabulary failed to progress as expected from 12 to 24 months in the stroke group, with no differences based on lesion side. Gesture and word production were dissociated in the left hemisphere subjects. Findings suggest that early language development after peri-natal stroke takes a different course from that of typical language development, perhaps reflecting brain reorganization secondary to plasticity in the developing brain.

Keywords

peri-natal stroke; early language; gesture; MacArthur Bates CDI; plasticity

1. Introduction

It is widely known that damage to the left hemisphere (LH) in adults often leads to severe and long-lasting language deficits in the form of expressive and/or receptive aphasia

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(Benson & Ardila, 1996; Damasio, 1992). Similar damage to the right hemisphere (RH) typically spares propositional language but may have adverse effects on other aspects of communication such as prosody (Ross & Monnot, 2008). In contrast, much less is known about language development following early focal brain damage in infants. Such damage, however, is not uncommon, with an estimated incidence of ischemic peri-natal stroke (IPS) of 1:1500 to 1:4000 live births (AHA/ASA, 2012; Laugesaar et al., 2007; Nelson & Lynch 2004; Schulzke, Weber, Luetschg, & Fahnenstich, 2005). The frequency of IPS is thus similar to that for adult-onset stroke, making it an important area for research, especially given that the consequences of early focal damage may reverberate for decades.

Plasticity is a dynamic and adaptive process that is the foundation of brain development and learning, and in instances of early brain damage, plasticity may prompt alternate neural organization (Stiles, 2000). Children with peri-natal lesions have been reported to demonstrate transient delays in productive and receptive language but are within the normal range for language by school age (Bates, 1998; Bates et al., 1997; Dick, Wulfeck, Krupa-Kwiatkowski, & Bates, 2004; Vicari et al., 2000). Although these children are not aphasic, some studies suggest more persistent language impairments after peri-natal stroke (Aram & Ekelman, 1987; Eisele & Aram, 1994). Little is known about the very early trajectory and pattern of language development after peri-natal stroke, although some studies report differences in language based on hemispheric side of the lesion (Bates, 1992; Riva et al., 1986), while others show no differences based on the side of the lesion (Ballantyne, Spilkin, Hesselink, & Trauner, 2008; Ballantyne, Spilkin, & Trauner, 2007; Feldman, MacWhinney, & Sacco, 2002). The role of gestures in early language development has also received little attention in the peri-natal stroke population. Bates et al. (1997) found both gesture and word comprehension were more likely to be impaired in 10- to 17-month-old infants with right as opposed to left hemisphere damage from peri-natal stroke. They hypothesized that these findings may relate to innate differences in information processing capacities in the 2 hemispheres, with the left hemisphere more suited to processing perceptual detail and the right hemisphere to perceptual integration. If this is the case, then children with right hemisphere damage might have difficulty integrating information that they are in the process of learning. This could include both language and gesture at early stages in learning and development. Bates et al. (1997) suggested that a longitudinal approach to the study of language development might lead to more clarity in terms of mechanisms by which the developing brain might compensate in the face of early injury.

The goal of the current study was to examine early language development in infants and toddlers after peri-natal stroke using both cross-sectional and longitudinal methods, as well as to study the relationship between gesture and language development in this population.

2. Methods

2.1 Subjects

One hundred ninety-seven infants and toddlers, ages 10 to 25 months, participated in the study. This included 71 children with peri-natal stroke and 126 typically developing control participants. Within the focal lesion group, 51 subjects had LH damage and 20 had RH damage. Participants were part of a larger study of early language development in young children with peri-natal stroke. Of the 71 children with peri-natal stroke, 47 (66%) were diagnosed within the peri-natal period and 24 (34%) were diagnosed later in infancy either when the presence of a hemiparesis was noted, or the child had a seizure, and an MRI scan showed evidence of a remote cerebral infarct (presumed peri-natal stroke). Only children with a single, unilateral lesion due to a peri-natal stroke were included as focal lesion subjects, thus, children with a bilateral stroke or stroke occurring more than 28 days after birth were excluded. In the peri-natal stroke group, inclusionary criteria were: unilateral

stroke; gestational age ≥ 36 weeks; and diagnosis documented by review of medical history and neuroimaging data, such as Magnetic Resonance Imaging (MRI) or Computed Tomography (CT). The location of the lesion was confirmed by a clinical neuroradiologist who was blinded to subject status. Most of the participants had large middle cerebral artery distribution lesions that included frontal, temporal and parietal cortex on the affected side. The exclusionary criteria included intrauterine drug exposure or any condition that could have caused global or evolving brain damage such as severe hypoxia. Children with perinatal stroke were recruited through pediatric neurologists in San Diego County.

For the control group, the inclusionary criteria were: gestational age ≥ 36 weeks and normal neuro-developmental history. The exclusionary criteria included the presence of any neurological or developmental disorder. The control children had normal medical histories and scored within the normal range on standardized measures of cognition and language. The typically developing (TD) controls were recruited through the University of California, San Diego (UCSD) hospitals and clinics as well as the San Diego community through advertisements and flyers.

There were approximately equal numbers of males and females in all groups studied. Approximately one-third of the participants in this study were also participants in a previous study using the CDI (Bates et al., 1997), though at the time, their CDI data set was not fully collected.

2.2 Measures

The MacArthur-Bates Communicative Development Inventories (CDIs) (Fenson et al., 1993) were used in this study. These inventories are widely-used, well-standardized, parent-report questionnaires designed to assess the early language skills of infants and toddlers, including comprehension, vocabulary, grammatical skills, and nonverbal gestures/actions. The CDIs have two separate forms, an infant form for ages 8 to 16 months, and a toddler form for ages 16 to 30 months. The infant form, CDI: Words and Gestures (CDI-WG) yields age-based percentile scores for specific indices including Phrases Understood, Words Understood, Words Produced, Early Gestures, Later Gestures, and Total Gestures. The toddler form, CDI: Words and Sentences (CDI-WS) yields age-based percentile scores for specific indices including Words Produced, Irregular Words, and Mean Length of 3 Longest Sentences.

2.3 Procedure

For this study, parents of children between 10 and 13 months of age (12-month data point) received and completed the infant form (CDI-WG), and parents of children between 22 and 25 months of age (24-month data point) received and completed the toddler form (CDI-WS). Inventory completion time was approximately 10–20 minutes.

2.4 Analyses

The infant and toddler forms of the CDI (Words and Gestures, Words and Sentences) were analyzed separately using SPSS (version PASW 18). In order to determine whether our perinatal stroke group was hetero- or homogeneous, we first analyzed if there were differences in performance that were related to time of diagnosis (peri-natal versus later diagnosis). These analyses were performed using independent t-tests, with time of diagnosis as the independent variable, and the indices of each CDI as the dependent variables. Following this determination, for CDI-WG, one-way ANOVAs were performed, with group (LH, RH, Control) as the independent variable and specific index as the dependent variable. CDI-WG indices examined were the percentile scores for: Phrases Understood, Words Understood, Words Produced, Early Gestures, Later Gestures, and Total Gestures. For CDI-WS, one-way

ANOVAs were performed, with group (LH, RH, Control) as the independent variable and index as the dependent variable. CDI-WS indices examined were the percentile scores for: Words Produced, Irregular Words, and Mean Length of 3 Longest Sentences. Post-hoc analyses were conducted, controlling for Type 1 error, using Bonferroni (when variances were equal) or Dunnett's T3 (when variances were unequal) statistical tests.

A subgroup of the total participants ($n = 59$; 12 LH, 7 RH, 40 Control) had *both* an infant and toddler CDI completed. Longitudinal assessments were conducted on this subgroup using paired-samples t-tests and correlational analyses using the False Discovery Rate (FDR) procedure to adjust for multiple comparisons.

3. Results

Within the peri-natal stroke group, there were no significant differences in performance that were related to time of diagnosis. Thus, in all subsequent analyses, the peri-natal stroke group was considered homogeneously, with no distinction based on whether the stroke was diagnosed in the peri-natal period or in later infancy.

3.1 Infant Form: CDI-WG

The mean CDI-WG percentile scores for the LH Lesion, RH Lesion, and Control groups are shown in Table 1. The groups did not differ significantly on Phrases Understood, Words Understood, or Words Produced. ANOVA yielded significant between-group differences on the indices of Early Gestures, Later Gestures, and Total Gestures. Post-hoc analyses on these indices indicated that the LH group performed similarly to controls, whereas the RH group performed more poorly than did the LH group on all three indices of gesture. Moreover, the RH group performed more poorly than controls on Later Gestures and Total Gestures.

3.2 Toddler Form: CDI-WS

The mean CDI-WS percentile scores of the LH Lesion, RH Lesion, and Control groups are shown in Table 2. Significant between-group differences were found on the indices of Words Produced, Irregular Words, and Mean Length of 3 Longest Sentences. Post-hoc analyses on these indices indicated that both the LH and the RH groups performed significantly more poorly than controls, and that there were no LH versus RH between-group differences.

3.3 Longitudinal Cohort

Within-group correlations between indices from the Infant and Toddler forms are shown in Table 3. In the control group, Words Produced at 12 months was significantly correlated with Total Gesture at 12 months and Words Produced at 24 months, and Total Gestures at 12 months was significantly correlated with Words Produced at 24 months. These correlations were not observed in the LH group. In the RH group, only Total Gestures at 12 months correlated significantly with Words Produced at 24 months.

Figure 1 shows the longitudinal trajectories for the LH, RH, and control groups. Children in the focal lesion groups declined in percentile scores on Words Produced between 12 and 24 month data points. This decline in trajectory was significant for children with RH lesions and approached significance for children with LH lesions. Both LH and RH groups had significantly lower percentiles on Words Produced than did controls at 24 months but not at 12 months (Figure 1).

4. Discussion

This study yielded several important findings. First, early indicators of language development in infants and toddlers with unilateral brain damage show a different pattern from what might be expected if the brain were “hard-wired” for left-hemisphere dominance for language at birth. That is, at one year of age early language does not differ significantly in either focal lesion group compared with controls, and by 2 years of age both LH and RH damage are associated with significant delays in language production compared with controls. Thus, neither the earliest language indicators (at 12 months) nor the side of the lesion predicted the trajectory of language development in children with unilateral brain damage. This is quite different from the adult model of language in which the left hemisphere is crucial for maintenance of normal language function in most individuals, and adults with left hemisphere strokes are likely to have significant aphasia. Previous studies by a number of investigators (e.g., Bates et al. 2001; Thal et al., 1991) have shown a similar pattern of lack of difference in language based on the side of the lesion. However, other studies (e.g., Eisele & Aram, 1994; Reilly, Bates, & Marchman, 1998) indicate that there are some differences in linguistic competence between LH- and RH-damaged children. These differences, however, are subtle and are found in older children after more complex aspects of language such as morphosyntax have developed. At the early stages of language development that we are examining in the present study, single-word use and comprehension may require both sides of the brain to acquire in a typical manner, and damage to either side necessitates brain reorganization.

Second, the trajectory of language development in children with focal brain damage diverges from that of typically developing children between the first and second year of life. Whereas early language indicators at 12 months are comparable to those of typical controls, the children with focal brain damage drop well below expected by the second year. Regardless of the side of the lesion, language appears to “stall” by the second year of life. In fact, Words Produced at 12 months does not correlate with Words Produced at 24 months in the brain damaged groups, indicating a drop-off from the expected trajectory. We hypothesize that in the face of early injury, the brain is developing alternate patterns of neural connectivity, and has not yet developed connections robust enough to handle the language burst that typically occurs at this age. If this is the case, it is possible that the language burst may occur later than in typically developing children. Alternatively, there may not be a rapid period of productive language development, but rather a slower, more protracted course as alternate connections are set up. Indirect evidence for this latter hypothesis comes from work of Bates et al. (1997) showing that children with peri-natal stroke are delayed in mean length of utterance (MLU) at 3 years of age, but are at control levels by 5–8 years old. Further longitudinal studies are required to determine which pattern the children with early focal brain damage will follow as language progresses; i.e., will there be a change in the slope of language acquisition between 2 and 5 years of age, or will there be a slow, steady improvement over time to the point of linguistic competence, or at least functionality.

Third, children with right hemisphere damage are delayed in gesture use at one year compared with typically developing toddlers as well as those with left brain damage. Studies of adults with strokes demonstrate a very different pattern, in that adults with left hemisphere strokes are more likely to have impairments in gestural use than do those with right brain lesions (Goldenberg, 2001; Haaland et al., 2000; Weiss et al., 2001). Our results may reflect the different processing styles of the 2 hemispheres that have been demonstrated in the visual spatial domain both in adults and in children with focal brain damage (Stiles et al., 2008; Delis, Robertson, & Efron, 1986), and that has been hypothesized to play a role in language development (Bates & Dick, 2002); that is, the left hemisphere preferentially

processes perceptual detail whereas the right hemisphere processes the integration of information. If the right hemisphere is damaged, the developing brain may have more difficulty integrating gestures as meaningful stimuli and this may be responsible for the delay in gesture use in the RH group.

Fourth, interesting associations and dissociations between words and gestures occur in children with early focal brain damage as compared with controls. Although words and gestures are correlated with each other in typically developing children at 12 months, they appear to be dissociated in children with unilateral brain damage at 12 months. One possible explanation for this observation is that gesture and language may require closely linked but non-overlapping neural circuits, and that the links between the different circuits may be disrupted in children with focal brain damage. Earlier studies by Bretherton and Bates (1984) and Bates and Dick (2002) provide support for this hypothesis.

Further, gesture at 12 months correlates with words produced at 24 months in TD and in RH lesion groups. This finding would not be surprising for TD children following the expected trajectory of language development. When this trajectory is disrupted, however, it would also not be surprising that there would be a dissociation between gesture and language for the reasons discussed above regarding non-overlapping neural circuits. Although we see this in the LH damaged children, this is not the case for the RH children. There may be a different explanation for the gesture/word correlation in RH children, however. If the global/local processing hypothesis discussed above is correct, then we might expect that the child with an RH lesion might have difficulty integrating not only gestures but also oral language into meaningful stimuli. In that case, we would expect a correlation between gesture and language.

Two additional findings are of note. First, no differences in early language development were observed based on time of diagnosis (either at birth with an acute peri-natal stroke, or later in infancy [presumed peri-natal stroke]). Second, there was a disproportionate number of leftmore than right-sided lesion participants in our study. Numerous studies have reported similar left-sided predominance for peri-natal stroke. The reasons for this are not clear, although two commonly used explanations are that hemodynamic differences caused by a patent ductus arteriosus may favor left-sided strokes (Sreenan et al., 2000), and that the left common carotid artery has a more direct route to the brain if a clot is present (deVries et al., 1997).

In summary, the data presented in this study show an interesting pattern of early language development in the face of a unilateral brain injury early in life. The results underscore the role of plasticity in the developing brain. The data demonstrate that in the face of early brain insults, a different trajectory of language development occurs, presumably reflecting brain reorganization such that an alternative means of learning language can take place. This information not only provides information about the manner in which language develops in the face of early injury, but also informs clinicians caring for children with early focal brain damage with knowledge that can be helpful for parents as well as guide interventions.

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Highlights

The pattern of language development differs for children with focal brain damage.

Gesture and vocabulary are dissociated after early focal brain damage.

The typical vocabulary “burst” may not occur in toddlers with focal brain injury.

Figure 1.
Longitudinal data for Words Produced (percentile scores on the MacArthur-Bates CDI) at 12- and 24-month data points for typically developing controls ($n = 40$) and children with left hemisphere lesions ($n = 12$) and right hemisphere lesions ($n = 7$).

12-Month Data: Mean percentile scores of the LH Lesion, RH Lesion, and Control groups on each index of the *CDI: Words and Gestures*, and significance values

Table 1

CDI: Words and Gestures	Mean Percentile Score $\pm$ SE			ANOVA (<i>F</i> , <i>p</i>) and Post Hoc (<i>p</i>)			
	LH Lesion (<i>n</i> = 28)	RH Lesion (<i>n</i> = 14)	Control (<i>n</i> = 85)	ANOVA	LH vs CH	RH vs CH	LH vs RH
Phrases Understood	41.54 $\pm$ 5.5	30.04 $\pm$ 6.4	41.74 $\pm$ 3.0	1.11, NS	---	---	---
Words Understood	42.91 $\pm$ 5.8	25.89 $\pm$ 5.4	39.07 $\pm$ 3.2	1.64, NS	---	---	---
Words Produced	33.96 $\pm$ 5.3	32.57 $\pm$ 6.8	39.61 $\pm$ 2.8	.76, NS	---	---	---
Early Gestures	56.50 $\pm$ 6.0	35.32 $\pm$ 9.4	51.99 $\pm$ 3.0	2.52, .084	NS	NS	.092
Later Gestures	42.13 $\pm$ 5.8	20.96 $\pm$ 4.6	48.49 $\pm$ 2.9	6.52, .002	NS	.000	.019
Total Gestures	46.81 $\pm$ 5.6	23.14 $\pm$ 6.1	46.40 $\pm$ 3.0	4.55, .012	NS	.011	.030

Note: Statistically significant ($p < .05$) and trending ($p < .10$) *p*-values are bolded. Post hoc tests utilized were either Bonferroni (when variances were equal) or Dunnett's T3 (when variances were unequal) to control for Type I error.

---designates where no post-hoc tests were performed due to the non-significant ANOVA

Table 2

24-Month Data: Mean percentile scores of the LH Lesion, RH Lesion, and Control groups on each index of the *CDI: Words and Sentences*, and significance values for between-group comparisons.

CDI: Words and Sentences	Mean Percentile Score $\pm$ SE			ANOVA (<i>F</i> , <i>p</i>) and Post Hoc (<i>p</i>)		
	LH Lesion (<i>n</i> = 35)	RH Lesion (<i>n</i> = 13)	Control (<i>n</i> = 81)	ANOVA	LH vs Ctl	RH vs. Ctl
Words Produced	22.50 $\pm$ 4.4	23.15 $\pm$ 7.2	41.56 $\pm$ 2.7	8.65, <.001	.001	.044
Irregular Words	28.42 $\pm$ 3.6	24.42 $\pm$ 5.7	42.65 $\pm$ 2.1	9.13, <.001	.002	.007
Mean Length of 3 Longest Sentences	19.87 $\pm$ 4.2	22.38 $\pm$ 6.1	39.93 $\pm$ 3.0	8.57, <.001	.001	.068

Note: Statistically significant ($p < .05$) and trending ($p < .10$) *p*-values are bolded. Post hoc tests utilized were either Bonferroni (when variances were equal) or Dunnett's T3 (when variances were unequal) to control for Type I error.

Table 3

Longitudinal Subgroup: Correlations between select 12- and 24-month indices within the LH Lesion, RH Lesion, and Control groups.

Indices Compared	Correlation, Significance Level*		
	LH Lesion (<i>n</i> = 12)	RH Lesion (<i>n</i> = 7)	Control (<i>n</i> = 40)
Total Gesture 12 mos to Words Understood 12 mos	.643, .039	.429, .317	.470, .009
Words Produced at 12 mos to Total Gesture 12 mos	.354, .272	.404, .317	.462, .009
Words Produced at 12 mos to Words Produced 24 mos	.362, .272	.354, .343	.540, .000
Total Gestures 12 mos to Words Produced 24 mos	.393, .272	.818, .039	.359, .039

* Significance Level is the adjusted p-value (aka q-value) using the False Discovery Rate (FDR) procedure to adjust for multiple comparisons.

Note. Significant correlations are shown in bold font.