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Linguistic Outcomes for Hemispherectomized Children

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1. Introduction

This paper reports on linguistic outcomes of a large series of pediatric hemispherectomies and examines some of the factors that may be predictive of language outcome. This work is part of a larger project examining language development following hemispherectomy, to better understand the linguistic capacity of each, isolated, developing hemisphere. We have previously reported on functional category development of a subset of our population (Curtiss & Schaeffer, 1997a, b). In this paper we examine the question of hemispheric plasticity for language development and the effects of age, seizure-related and etiological factors on language following hemispherectomy.

Clinical, experimental, and neuroanatomical data have increasingly converged to indicate that at or even before birth, in the vast majority of individuals, the left hemisphere is prepotent to support language acquisition, that is, genetically programmed to serve as the neural substrate for language (e.g., Gallagher & Watkin, 1996; Molfese & Segalowitz, 1988; Witelson, 1982). However, the picture is not entirely clear regarding the development of cerebral specialization for language or the capacity of the right hemisphere to support language development. Moreover, it is not yet known whether the LH on its own, without the support of the RH can mediate normal and complete language development.

Recent Event Related Potential (ERP) studies of normal children in early stages of overt lexical acquisition and clinical studies of children with unilateral lesions lend support to the view that the left hemisphere is "pre-potent" for language (Aram, 1992; Dennis, in press; Mills et al, 1993; Molfese, 1989). We will refer to this view as the "*prepotency*" view. Importantly, it predicts that even with early damage to the left hemisphere (LH), the right hemisphere (RH) will not support full and normal language acquisition. On a somewhat different view, it has been proposed that despite this initial predisposition of the LH, the RH has an equal potential to subserve language, but the continuing lateralization of language to the LH overrides this potential (Corballis & Morgan, 1978; Kinsbourne, 1974; Lecours & Joanette, 1985; Locke, 1997). Studies of unilateral LH lesions in childhood have been used to support this position as well (Bates et al, 1992; Stiles & Thal, 1993; Thal et al, 1991). Moreover, in addition to a view that the RH has equal potential to subserve language. some of these data have been used to suggest that the RH plays a key role in language development, and if damaged, language development will be impaired. This "*equipotential*" account, then, predicts that with significant early damage to the LH, the initially equivalent linguistic potential of the RH will be realized, that the earlier the damage, the greater the potential which can be tapped, and in addition, that damage to the RH may result in linguistic impairment.

Because so little is understood about the mechanisms responsible for inter- vs. intra-hemispheric language transfer after LH focal lesions (Cohen, 1992; Duchowny et al, 1996; Helmstaedter et al, 1994), the potential of the RH to serve as the substrate for the acquisition of grammar may not be adequately determinable by studies of focal damage in children. It is often unknown whether impaired performance in these cases reflects the best efforts of the damaged LH, the linguistic performance of the RH, or some combination of both. Moreover, findings regarding language transfer often conflict with each other regarding age, etiology, and lesion location. Thus it is the study of language development subsequent to hemispherectomy — the removal of an entire cortical hemisphere — that may best directly address the question of the linguistic potential of the RH.

The specific linguistic effects of hemispherectomy remain an area of some controversy. There have been a number of studies reporting the greater capacity and proficiency of the LH over the right with respect to morphosyntactic comprehension, production, and judgments (Day & Ulatowska, 1979; Dennis & Kohn, 1975; Dennis, 1980a, b; Stark et al, 1995; Vargha-Khadem et al, 1991) and with respect to reading and spelling (Ogden, 1996). Others, (Strauss & Verity, 1983; Riva & Cazzaniga, 1986; Vargha-Khadem et al, 1997) have reported excellent, even normal linguistic abilities after hemispherectomy of either side.

Given that hemispherectomy is performed in treatment of intractable epilepsy, such variable findings may be accounted for only by considering such factors as etiology of damage, age at seizure onset, duration of seizures, and age at surgery in addition to side of damage. However, little research has been carried out specifically addressing the effects of such factors on language.

We have attempted to begin to address these questions by studying the language of a large series of hemispherectomied children and analyzing which of a number of clinical factors was predictive of spoken language outcome. Our central questions were first, what is the linguistic capacity of each isolated developing hemisphere and second, what is the effect of specific clinical factors on language development after hemispherectomy? Our hypotheses are listed in (1) below:

(1) Hypothesis 1: *Children who have undergone left hemispherectomy are expected to show marked deficits, particularly with respect to grammatical development, compared to their right hemispherectomy counterparts*
Hypothesis 2: *Early surgery is expected to lead to better language outcome, particularly for left hemispherectomies*
Hypothesis 3: *Late onset of seizures is expected to have far less impact on spoken language for the R hemis than the left*
Hypothesis 4: *Duration of seizures will be inversely related to quality of language development*
Hypothesis 5: *Seizure control will be inversely related to linguistic outcome*
Hypothesis 6: *Developmental pathology will be associated with a poorer linguistic prognosis than acquired pathology*
Hypothesis 7: *Gender will prove of little consequence in predicting linguistic outcome*

2. Subjects

Our subject population consisted of 49 children who had undergone hemispherectomy as part of the UCLA Pediatric Epilepsy Surgery Research Program. (See Peacock et al, 1995 for more details) Patients were included in our sample if, among other criteria, they had catastrophic childhood epilepsy, their seizures were resistant to antiepileptic medications, they had surgery before 18 years of age, they were monolingual speakers of Standard American English or were in a Standard American English environment, and they were patients for whom follow up information was available.

A breakdown of the subject population by side of damage, age at seizure onset, age at surgery, disease etiology, and gender is presented in Table 1.

Table 1

Pt. No/Sex	Lang. Rank	Surg/Side	Seizure Onset	A/S (yrs)	Diagnose/Pathology	Seiz. Relief
1F	4.5	Left	6	9;6	RE	no
2M	3	Left	Birth	8;6	INF + CD	yes
3F	3	Left	Birth	6;8	CD +Other	no
4M	3	Left	10 mo	6;2	INF	yes
5F	3.5	Left	Birth	4;0	INF + Other	yes
6M	2.5*	Left	Birth	1;5	CD + Other	no
7F	4*	Left	Birth	1;5	CD	yes
8M	3*	Left	2 mo	0;8	CD + Other	yes
9F	3	Left	3 wks	11;5	INF + Other	no, 1seiz/mo
10M	5	Left	6 mo	9;8	INF	yes
11M	0	Left	11 mo	9;0	INF	no
12F	4	Left	Birth	6;8	INF + Other	yes
13F	4	Left	5;7	5;11	RE	no
14M	3.5	Left	2;5	5;5	RE	yes
15M	3	Left	2;11	5;3	VE	no
16M	3.5	Left	3;4	4;7	RE	yes
17M	0	Left	Birth	3;9	HC	no
18M	0	Left	Birth	3;4	CD	no
19M	3*	Left	Birth	2;10	CD	yes
20M	3.5*	Left	1 week	2;9	CD	yes

21M	1.5*	Left	3 mo	2;7	CD + Other	no
22M	2.5*	Left	6 wks	1;8	CD + Other	yes
23F	1*	Left	Birth	1;8	CD + Other	no
24M	4*	Left	Birth	1;5	CD	yes
25F	5*	Left	1 mo	1;3	SW	yes
26F	2*	Left	2 mo	1;0	CD	yes
27F	0*	Left	1 week	1;3	CD + Other	no
28M	1*	Left	1 week	1;0	CD	yes
29F	3*	Left	2 wks	0;5	CD	yes
30M	0*	Left	Birth	0;3	CD + Other	yes
31F	5	Right	12	17;3	RE	no
32F	5	Right	5	14;1	RE	no/short szs
33M	4	Right	Birth	7;9	INF	yes
34F	5	Right	4;5	5;11	RE	yes
35M	4	Right	2	3;5	RE	yes
36F	2.5	Right	2 mo	5;1	CD + Other	no
37F	3	Right	4 mo	4;3	POR	yes
38M	5	Right	2;6	4;3	CD	yes
39M	1	Right	9 mo	3;8	CD	no
40M	0*	Right	2 wks	2;11;	CD + Other	no 1seiz/2-3 wks
41F	1*	Right	6 mo	2;5	CD	yes
42M	4*	Right	8 mo	2;2	INF	yes
43F	0*	Right	Birth	2;2	CD	no
44M	0*	Right	Birth	1;5	CD + Other	no
45F	1*	Right	Birth	1;1	CD + Other	no, 1seiz/day
46F	0*	Right	4 mo	0;10	CD + Other	yes
47F	0*	Right	1 mo	0;10	SW + Other	no
48F	0*	Right	1 mo	0;8	VE	no
49F	3*	Right	5 mo	0;9	CD	yes

As displayed in Table 1, seizure onset ranges from birth to 12 years, with a mean age of 51.1 months for the R hemis. and 48.56 months for the left. Etiologies of the epilepsy include both developmental and acquired courses: 1) cortical dysplasia, CD (26 patients); 2) Rasmussen's encephalitis, RE (8 patients), 3) viral encephalitis, VE (2 patients); 4) Sturge-Weber syndrome, SW (2 patients); 5) infarct, INF (9 patients); 6) hydrocephalus, HC (1 patient); 7) porencephalic cyst, POR (1 patient). The 'Seizure relief' column shows the degree of seizure control achieved postsurgically, and 'A/S' column indicates age at surgery. It should be noted that even for those children who continue to have seizures,

significant seizure relief was achieved. Persisting seizures suggest a bilateral focus. Those children too young to talk (TYTT)[1] at the time of surgery have an asterisk.

3. Postsurgical linguistic evaluation

Only language production was considered in this analysis. Postsurgical data on the children's language production were collected by means of the MacArthur Communicative Development Inventories (Fenson et al., 1990), or via language sampling, as developmentally appropriate or possible. A question specifically asking for speech onset age was added to the MacArthur for our use. Language samples were collected by means of the Story Game from the Kiddie Formal Thought Disorder Scales (Caplan et al, 1989) or via naturalistic conversation with the examiner interviewing the patient on topics including family, friends, school, birthday, TV shows, and favorite activities. These samples were recorded, transcribed and then analyzed for their grammatical and lexical content using CALC.[2]

Based on these data, we assigned each child a Spoken Language Rank (SLR), using a five point scale, as shown in (2) below.

(2) 0 = no speech
1 = has a few words (fewer than 20 words)
2 = has more than 20 words but no word combinations
3 = constructs short telegraphic utterances
  a. *Helping the monkey*
  b. *He brown*
4 = is a fluent speaker, but does not yet have the target grammar
  a. *Because Sammy was growned up first, so he's the biggest and I growed up and Chris growed and Ruben was last.*
5 = has the target grammar
  a. *I forgot to tell them what I wan*
  b. *I hope I have my iron cast off*
  c. *I hope it's off by Thanksgiving because I live to downhill ski*

Some children's language appeared to fall between numerical ratings, and they received ranks reflecting these intermediate states (e.g., 3.5).

These rankings provided a global index of linguistic outcome. As the mean time post-surgery was 5.28 years for the left hemis and 6.31 years for the R hemis, these rankings represent at least a medium-term outcome.

4. Results

Statistical analyses were performed in order to examine the relationship between SLR and side of surgery, age at seizure onset, age at surgery, seizure control, duration of seizures, and type of damage (developmental or acquired). Gender as a factor was also examined.

Table 1 presents a breakdown of the post-surgical SLR and age at evaluation for our subject population Note that at the time of evaluation, no children included in the sample were too young to be expected to talk in the course of normal language development (3 years).

4.1. Side of surgery

Our first hypothesis was that the children with left hemispherectomy would be expected to have lower SLRs than their R hemispherectomy counterparts. However, there was no significant correlation between side of surgery and language outcome indexed by SLR (left group mean, 2.60, right mean, 2.26; F' = 0.1777, p > 0.5162). Side of surgery was not predictive of SLR for the TYTT group, either (p>0.1162). Both of these are surprising findings and run counter to our hypothesis.

4.2. Age factors

We had hypothesized that early surgery would lead to better language outcome, particularly for L hemis, and that late onset of seizures would have far less impact on spoken language for the R hemis than the left. There was a strong correlation between both age at surgery and SLR (p>0.0004), and age at seizure onset and SLR (p<0.0018). However this relationship did not hold for both right and L hemis. For the L hemis, there was no significant correlation between either age at surgery (F=1.985, p> 0.1146) or age at seizure onset and SLR. In contrast, both age at surgery and age at seizure onset were significantly correlated with SLR outcome for the R hemis (p<0.0018 and p<0.0113, respectively).

Examining Table 1in detail, we can see that the R hemis show first, an association between early seizure onset and lower SLR and second, later seizure onset and higher SLR. The same pattern is not displayed by the L hemi group.

A similar pattern is evidenced between age at surgery and SLR for the R hemi group, and is again a pattern distinct from that of the L hemi group.

Looking only at the TYTT group, again we find that age at seizure onset was significantly related to SLR only for the group with right-sided surgery (p<0.0097).

These results thus only conformed to our predictions in part. As predicted, R hemis with late seizure onset and late surgery had higher SLRs, but the association between early surgery and poorer outcome for the R hemis was not something we had hypothesized, nor was the lack of a relationship between age at surgery or age at seizure onset and outcome for the L hemispherectomy group, findings suggesting a less-than-straightforward relationship between age factors and linguistic outcome.

4.3. Duration of seizures[3]

We hypothesized that duration of seizures would be inversely related to SLR, and for the group as a whole, we found that duration of seizures was inversely correlated with SLR (p< 0.0262). However, contrary to our hypothesis, this relationship was significant only for the R hemis (p< 0.0176). Duration of seizures was not predictive of SLR for the L hemis (p> 0.4008) or the TYTT subgroup (p> 0.4513).

4.4. Seizure Control

Seizure control was a significant predictor of SLR for the group as a whole (p< 0.0023), and for both left and right hemispherectomies (LH p< 0.0306, RH, p< 0.0498). It was also a significant predictor of SLR for the TYTT group (p< 0.0055). However, upon examination of other factors, one finds that this effect is largely or entirely an effect of seizure control on language performance in the group with developmental pathology. The group with acquired pathology shows no significant relation between seizure control and language rank. Thus the two groups evidence a clear disparity with respect to the effect of seizures on linguistic outcome, and our hypothesis that seizure control would be inversely related to linguistic outcome regardless of side of damage was supported only for those children with developmental damage.

4.5. Etiology of pathology

Related to this finding, we hypothesized that developmental pathology would lead to a poorer outcome than acquired pathology. Contrary to this hypothesis, there was no significant difference in the relationship between etiology of neuropathology and SLR[4]. Moreover, both age at surgery and seizure control were strong predictors of SLR for both groups (for the DG, F = 10.91, p< 0.0003; F = 6.37, p= 0.0108 for the AG). These findings, then, do not support our hypothesis. The only difference in outcome was the relationship between seizure control and etiology and not etiology alone.

4.6. Gender

As hypothesized there was no significant correlation between gender and SLR for any of the groups.

5. Summary

To summarize, many of our predictions were not supported by our findings. Our first hypothesis was not supported. We failed to find a significant correlation between side of surgery and linguistic outcome in terms of the global qualitative and quantitative characteristics of speech production indexed by SLR. Hypothesis 2 was also not supported. Earlier surgery did not lead to higher SLR for the L hemis as predicted. Moreover, contrary to our predictions, early age at surgery led to lower SLR in the R hemispherectomies. Hypothesis 3 was supported by our findings. Late seizure onset did have less negative impact on language in the R hemis, in that late onset age was associated with high SLR. Hypothesis 4 was only partly confirmed. Duration of seizures was not predictive of SLR for the L hemis, only for the right. Hypothesis 5 was also only supported in part. Seizure control was inversely related to language outcome only for those children with developmental pathology. Along similar lines, contrary to hypothesis 6, we did not find lower SLRs in the developmental group except when poor seizure control was factored in. Hypothesis 7 was confirmed. Gender was not related to language outcome.

6. Discussion

Many of our findings were not as we predicted. Three of our results were particularly unexpected. First was our finding that L hemispherectomy was not more predictive of poor SLR or to put it in reverse, that R hemispherectomy was not more consistently associated with *better* language outcome. In fact, almost one-third (31.8%, 6/19) of the R hemis in our sample have no productive language at all, even 6 years post-surgery, compared to 16.67% of the L hemis. This finding appears inconsistent with much of the clinical literature on hemispheric specialization for language in children (e.g., Aram et al, 1995; Aram et al, 1985; Eisele and Aram, 1993; Krashen, 1972; Woods and Teuber, 1978; Woods and Carey, 1979; regarding focal lesions, and Dennis & Whitaker, 1976, 1977; Dennis, 1980a, b; Gott, 1973; Lovett, Dennis & Newman, 1986; Zaidel, 1973; Gadian et al 1996; Helmstaedter et al, 1997; Vargha-Khadem and Polkey, 1992 regarding language following hemispherectomy).

This finding is consistent with some clinical reports, however. There are other reports in the literature studying one or a few individual cases, each, of good language outcomes after left-sided damage. Ogden (1996) for example, reports fluent speech in both hemispheres after hemispherectomy; Isaacs et al (199) found that side of damage was not predictive of outcome; Stark et al (1995) report that neither side showed deficits in lexical production; Feldman et al (1992) report that by age 24 months, children with left and right-sided perinatal damage showed comparable language to normals on several linguistic indices; and Curtiss and Jackson (1989) and Vargha-Khadem et al (1997) report cases of fluent, complex language abilities after L hemispherectomy. In our own sample, a number of our L hemis have SLRs of 4 or 5 (7/30 or 23.3%), reflecting fluent, grammatically rich and complex speech, and a few young L hemis appear to be on the road to developing mature, normal grammars, although in each case, phonetic fluency appears to be problematic. Our findings therefore imply a surprising degree of plasticity and RH potential for language development and in this respect support the second view, the "*equipotentiality*" view.

In addition, consistent with reports by others of language impairment following damage to either hemisphere in a few focal lesion cases (Thal et al, 1991; Stiles & Thal, 1991) our findings on such a large sample provide strong evidence of the involvement of the RH in <u>early</u> stages of language acquisition. Perhaps consistent with Molfese (1989; 1990) and Mills et al's (1993) ERP studies on lexical processing in infants, we speculate that the RH may play a crucial role both in storing and processing prosodic and metrical structure as a means of cracking the linguistic code, and in making an initial determination of lexical and phrasal boundaries. Perhaps as Locke suggests, the RH plays a key role in learning and storing lexical items which the LH, either simultaneously (e.g., Golinkoff & Hirsh-Pasek, 1997; Gerken, 199?) or at a later stage, utilizes for grammatical analysis and computation (Locke, 1997).

However, the literature notes a specialization of the LH for computation of syntactic and phonological structure in particular, (e.g., Aram et al, 1995; Eisele & Aram, 1993; Dennis & Whitaker, Dennis, 1980a, b; Stark et al, 1995; Vargha-Khadem et al, 1991; Vargha-Khadem & Polkey (1992) and closer examination of grammatical performance may reveal the expected hemispheric differences in our population as well. Indeed, investigation of functional category development in the speech of 13 of the children in our hemidecorticate sample revealed better performance by the R hemis with both I and D-system elements (Curtiss & Schaeffer, 1997a, b). The picture regarding the effect of side of surgery on linguistic function is clearly a complex one. .

A second surprising result is the lack of a significant correlation between age factors and SLR for the L hemis. Counter to the results of many other studies and our own predictions, the children with earlier LH damage did <u>not</u> predictably develop more language. Other factors such as seizure control and etiology clearly played a role in defining which children were those who would or would not show good spoken language outcomes. The principle that the earlier the damage the better the developmental outcome is clearly too simplistic here.

Our finding that the older the child with RH damage the better the language outcome *is* consistent with our hypothesis, however. The later the RH damage, the more fully the neural substrate for language in the LH is established, and the greater opportunity the RH will have had to play its role. However, while our findings indicate that the RH may play a critical role at an early point in language development, they do not disconfirm the LH as the seat of language in most major respects.

Together with our results on age and side of surgery, our findings regarding duration of seizures, seizure control and etiology make clear that predicting which children can be expected to have the best linguistic prognosis following hemispherectomy is anything but straightforward[5].

We are now examining this large population more fully regarding the details of grammatical development and in particular, whether the RH can construct a normal mental grammar, constrained by UG. It is our hope that this work will contribute to our understanding of the potential for the instantiation of UG in each hemisphere and in a larger sense, the potential of each hemisphere to construct a normal mental lexicon and grammar and the circumstances under which it will do so.

Endnotes

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1. Using a conservative measure of speech onset, we included all children younger than three years at the time of surgery in our "too young to talk" group. The group comprised 19 children.

2. CALC (Computerized Analysis and Language Coding System) is a detailed morphological and syntactic analysis based broadly on a minimalist framework of syntactic theory.

3. From onset to surgery.

4. Gordon et al. suggest that Rasmussen's may actually be a developmental pathology rather than acquired. If so, then our results regarding the effect of disease etiology could be expected to change substantially.

5. We did not explore extent of lesion. All children had pervasive damage (hemispherectomies). Also, it has been suggested that extent of lesion and cognitive outcome do not correlate.

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