Linguistic, Cognitive and Affective Development in Children with Pre- and Perinatal Focal Brain Injury: A Ten-Year Overview from the San Diego Longitudinal Project

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Abstract

Over the past ten years, we have made significant progress in addressing key questions concerning deficit and development after early stroke. We found evidence of subtle early impairment and subsequent development in each domain examined. However, the profiles of impairment and development differed across domains. Deficits of language acquisition are initially pervasive in that they are observed following injury to widely distributed brain areas. Spatial analytic deficits exhibit more specific patterns of brain-behavior association, similar to those observed among adults with injury to comparable brain regions. Had we been working in isolation, the separate investigators associated with this project may have reached very different conclusions about the nature of development following early injury. Instead, we were forced to look for ways to resolve the apparent disparity in our cross-domain findings. The model that best fits our data focuses on redefining the nature of early plasticity. Recent animal studies provide strong evidence that plasticity plays a central role in brain development. Brain organization is to a large extent defined by the changes in patterns of connectivity that occur as a result of input to the maturing system. In that sense, the developing brain is a dynamic, responsive, and to some extent self-organizing system. Early injury constitutes a perturbation of normal development. Specific neural resources are lost, and there is consequent impairment of the system. However, it is also a developing system and therefore a system with an exuberance of resources the fate of which are determined in large measure by input. Thus, the magnitude and duration of the initial impairment may well depend on a range of factors such as the timing of insult, extent and location of injury, and specificity of the neural substrate for the function under consideration.

Linguistic, Cognitive and Affective Development in Children with Pre- and Perinatal Focal Brain Injury: A Ten-Year Overview from the San Diego Longitudinal Project

For the past ten years a group of investigators based in San Diego has been studying the effects of pre- and perinatal focal brain injury on the development of linguistic, cognitive and affective functions. The project, which is organized under the auspices of the UCSD Project in Cognitive and Neural Development (PCND), is a large collaborative effort involving investigators from around the world. The project has produced a large and detailed body of data documenting the effects of early localized brain injury on behavioral development. Based upon these data, significant progress has been made toward addressing key questions concerning linguistic, cognitive, and affective deficits and patterns of development following pre- and perinatal brain injury. Since its inception the project's emphasis has been on language and spatial analytic functioning. More recently the scope of inquiry has been extended to include studies of affect. In each of these areas, lesion-specific developmental profiles have begun to emerge. The purpose of the present paper is to provide an overview of findings from this collaborative project within each of these three basic behavioral domains.

When this project began, even the most basic question concerning whether or not it is possible to identify specific deficits associated with early injury was still a subject of debate. Early studies on the effects of focal brain injury emphasized the "resilience" of young children to the effects of early injury and argued that early available mechanisms subserving a transient capacity for plastic change allow children with early injury to develop normal or near-normal cognitive functioning following injuries to the brain that would leave an adult permanently impaired (Alajouanine & Lhermitte, 1965; Brown & Jaffe, 1975; Carlson, Netley, Hendrick, & Pritchard, 1968; Gott, 1973; Hammill & Irwin, 1966; Krashen, 1973; Lenneberg, 1967; McFie, 1961; Reed & Reitan, 1971). These

arguments did not, however, go unchallenged. Other investigators argued that a more fine-grained analysis of behavior showed evidence of persistent cognitive deficit (Day & Ulatowska, 1979; Dennis, 1980; Dennis & Kohn, 1975; Dennis & Whitaker, 1976; Kohn, 1980; Kohn & Dennis, 1974; Rudel & Teuber, 1971; Vargha-Khadem et al., 1983, 1985; Woods, 1980; Woods & Carey, 1979). These apparently contradictory sets of claims suggested a complex interplay between plasticity and specialization of function in the developing brain, but the nature and course of that interaction remained unclear. One limitation of that early work on both sides of the debate was its reliance on retrospective accounts of development in which the outcome of development following early injury is used to infer developmental process.

In order to understand the long-term effects of early neurological insult, it is necessary to investigate processes of recovery and/or compensation as they occur. A prospective approach to the study of development following early injury makes it possible to determine: (1) whether there is <u>early</u> evidence of impairment; (2) whether the profile of impairment in early childhood is the same or different as that observed in adults with similar injury; and (3) whether there is change in the profile over time.

A small number of investigators have adopted this approach to the study of children with focal brain injury. For example, Aram and her colleagues (Aram et al., 1985; Aram et al., 1986; Aram et al., 1983; Rankin et al., 1981) have reported data from cross-sectional studies of children under 5-years of age, providing evidence for global linguistic and cognitive deficits in children with early acquired focal brain injury. Longitudinal follow-ups of these children in the school-age period suggest that these early deficits persist with development (Aram, 1988; Aram & Ekelman, 1988; Aram et al., 1985). These studies are important because they provide strong evidence that early focal brain injury does result in significant functional deficits. However, studies by Aram and other investigators also show that the deficits associated with early brain injury are often quite subtle and may require finer-grained measures to be detected. For example, Riva, Cazzaniga, Pantaleoni, Milani, and Fedrizzi (1987) have uncovered grammatical deficits on the Token Test in LHD

children that are only evident when that test is reanalyzed to extract specific syntactic patterns (see also Dennis & Whitaker, 1976). Similar profiles of early, subtle deficit have been reported for children with frontal lobe injury. Eslinger and his colleagues (Eslinger & Grattan, 1991) report that among younger children the effects of injury to frontal lobe regions may be quite mild. However, they note that with development, patterns of deficit become more pronounced. They suggest that this late emerging pattern may reflect the fact that demands for behaviors mediated by the frontal lobes may become more pronounced as children reach adolescence, thus suggesting a kind of latent deficit profile. This pattern of late emerging deficit has been reported by Levine and her colleagues (Levine, 1993) on measures of IQ. They report a systematic decline in IQ scores beginning in early adolescence. This profile is not confined to children with frontal lobe injury, rather it appears to hold for the focal lesion population as a whole.

A major emphasis in the work from the San Diego project has been its insistence on approaching the study of development prospectively. Such an approach is central to the task of identifying deficit, mapping deficit to lesion site, and tracking possible changes with development. Interestingly, the longitudinal data from different behavioral domains, does not always provide the same answers to these basic questions. As will be described in detail later in this paper, language and visuospatial processing, for example, provide different answers to the questions of initial deficit, of mapping to adult profiles of deficit, and of change over time. The differences in these two domain-specific profiles are striking enough that they might have led an individual investigator working in isolation to posit very different theoretical accounts of developmental change following early brain injury. Yet within the context of this project, we are confronted with the fact that the data have been obtained from the same children. One challenge of this work will be the need to reconcile these differences, and provide a single account of development following early focal brain injury that encompasses what is becoming a diverse and challenging set of findings.

THE POPULATION OF CHILDREN WITH EARLY FOCAL BRAIN INJURY

The studies reported here focus on a group of children with early occurring focal brain injury. The children in this population suffered localized cortical and/or subcortical brain injury in the pre- or perinatal period. While more diffuse brain insult is fairly common, focal brain injury is a comparatively rare disorder in young children. Children with focal brain injury are typically identified in one of three ways: (1) the occurrence of neonatal seizures, (2) documentation of hemiplegia, or (3) routine ultrasound for other medical reasons such as meconium staining, premature birth, etc. The most common cause of localized injury in young children is stroke, either ischemic or hemorrhagic. The identification of lesion site is based on results of neuroimaging using either a CT scan or MRI.

The unifying factor among all the children in our population is the documented presence of injury to a circumscribed region of the brain. The children included in these studies were selected on the basis of the presence of a single, unilateral brain lesion that was acquired prior to, or at birth. Location and size of the lesions were ascertained by obtaining neuro-imaging procedures (MRI or CT scans) on every subject. Individuals were excluded if there was evidence of multi-focal or diffuse brain damage, or if there was evidence of intrauterine drug exposure. Most of the children were born full-term. Finally, on gross assessment, the children in the population do well behaviorally, both individually and as a group. They do not manifest gross cognitive deficits. In fact, they typically score within the normal range on standardized IQ measures, and attend public schools.

LANGUAGE

In order to understand the effects of early focal brain injury on language development, we need a brief reminder of the patterns of language development that would be expected in a normal child.

In the normal course of language development, children show first signs of word comprehension at about 10 months of age and begin to produce first words around their first birthday. Productive vocabulary increases slowly until about 16 to 18 months when vocabulary size increases markedly and rapidly (Fenson et al., 1994). At about 20 months

of age children begin to combine words into short "telegraphic" sentences, and over the course of the next year, they acquire much of the morphology of the language (Brown, 1973; De Villiers & De Villiers, 1972). At about two years and six months (2,6), children begin to combine simple propositions to produce complex sentences and by the child's fourth birthday, she has access to the vast majority of the structures of her language. Language development from this point on entails refining the formal subtleties of morphology and syntax and learning how and when to recruit these different grammatical structures, for example, how to tell a joke, give directions or recount a coherent story. Whereas our studies of early language development focus on the lexicon and grammar, in both production and comprehension, our studies of older children have included the use of narratives both as a context for assessing grammar (specifically morphological production and the use of complex syntax) and also as a discourse genre.

To formulate our first hypotheses regarding possible effects of pre- and perinatal focal brain injury on language acquisition, we started with the extensive literature on language impairment in adults with similar lesions. At this point, we must provide an important caveat: the adult neurolinguistic literature is rich, complex, and fraught with controversy. In addition to more than 100 years of highly relevant work on adult aphasia, the literature on brain and language in adults includes neural imaging studies of normals (using positron emission tomography, functional magnetic resonance, and electrophysiological techniques), lateralization studies with normals (including dichotic listening and visual hemifield presentations) and both behavioral and neurological studies with a wide array of patient groups (e.g., split-brain patients, epilepsy patients, and patients with various forms of dementia). The literature as a whole comprises so many conflicting claims that one could find an *a posteriori* justification for virtually any pattern that we are able to observe in children with focal brain injury. For this reason, we have based our first round of hypotheses on a handful of relatively uncontroversial claims about adult aphasia that appear in virtually every neurology textbook. For example, there is general agreement that the left hemisphere is specialized for most aspects of language in the vast majority of normal adults

(Bryden, 1982; Damasio & Damasio, 1992; Galaburda et al., 1994; Gazzanaga, 1994; Hellige, 1993), although it has become increasingly clear in the last two decades that the right hemisphere also plays a role. In addition, it is generally believed that the perisylvian regions of the left hemisphere are especially important for phonological, lexical and grammatical functions (Damasio, 1989; Damasio & Damasio, 1992; Geschwind, 1972; Rasmussen & Milner, 1977). Furthermore, anterior versus posterior damage along the left Sylvian fissure is reliably (albeit imperfectly) correlated with the contrasting syndromes described by Broca and Wernicke, respectively (Damasio & Damasio, 1992; Goodglass, 1993; Naeser, Helm-Estabrooks, Haas, Aurbach, & Levine, 1984), across a variety of natural languages (Bates & MacWhinney, 1989; Menn & Obler, 1990). These conclusions form the basis for our hypotheses regarding the effects of early left hemisphere injury on language development in children.

As we have just noted, more recent research suggests that the right hemisphere does play a role in language processing, complementing the functions mediated by the left. Specifically, studies have shown that right hemisphere injuries have specific effects on the comprehension and production of humor (Brownell, Michel, Powelson, & Gardner, 1983), metaphor (Brownell, Simpson, Birhle, Potter, & Gardner, 1990), and idioms (VanLancker & Kempler, 1986). They also show deficits in the organization of connected discourse, specifically they have problems with cohesion and coherence in narratives (Garner, 1983; Hough, 1990; Joanette, Goulet, & Hannequin, 1990; Kaplan, Brownell, Jacobs, & Gardner, 1990). These studies have formed the basis for our hypotheses regarding the effects of early right hemisphere injury on language development in children.

Extrapolating from these studies, there was ample reason to assume that the left hemisphere may be innately specialized for core aspects of language, e.g. morphology, and that the perisylvian area is likely to play a particularly important role in the acquisition of such linguistic structures, whereas the right hemisphere might come into play as children begin to use language for a variety of discourse functions. Our initial hypotheses predicted that: (1) children with injuries to the left hemisphere would develop more severe language

impairments overall than those with right hemisphere damage (the left-specialization hypothesis); (2) children with damage to the anterior regions of the left hemisphere, especially the perisylvian area of the left frontal lobe, would develop more severe language production deficits (the Broca hypothesis); (3) children with damage to posterior regions of the left hemisphere, particularly the posterior portion of the left temporal lobe, would develop more severe language comprehension deficits (the Wernicke hypothesis); and (4) children with right hemisphere damage would demonstrate problems in telling a story or using language to make inferences. Although these four broad hypotheses are easy to defend in light of more than 100 years of research on adults with focal brain injury, they have not been supported in the developmental studies carried out by the San Diego group or by other researchers.

Over the course of our ten year study we have gathered a sample of 53 prelinguistic children with unilateral focal brain injury and examined their communicative skills as they developed; another 19 children with the same etiology joined our language studies after the preschool period. Although this is not a large sample by traditional epidemiological standards, to our knowledge it is the largest and most stringently defined sample of children with pre- or perinatal focal brain injury that has been described in this important developmental period. We have indeed found evidence of the importance of the left hemisphere for language learning and use. However, the specific pattern of brain organization that we can infer from these studies is markedly different from initial adult-based expectations.

In the sections that follow, we will describe four studies completed by the San Diego group that span the range from 10 months to 12 years of age. The studies are all cross-sectional, although some of the children have participated at two or three data points, as our history with them developed. Similarly, the earlier studies were carried out with a small number of subjects, with each of the infant studies increasing in size as we built our pool of these very special children. The first three studies describe children from the cohort described above that was identified prior to the onset of measurable language skills. They

were tested longitudinally from prespeech through the period when typically developing children begin to regularly use grammatical sentences. The fourth study is a cross-sectional study of children from 3 to 12 which describes the acquisition of more complex syntax and narrative skills.

Babbling and first words**.** The first study reported by the San Diego group was a multiple case study of five infants studied longitudinally (Marchman, Miller, & Bates, 1991). They were observed at three data points from the onset of canonical babble through 21-22 months of age and compared to ten typically developing children matched for level of language development. Four of the children with focal brain injury had left-hemisphere lesions and one had a right-hemisphere lesion. Two of the left-hemisphere lesions were posterior, all of the other lesions were anterior (including the right-hemisphere lesion). Language comprehension and production, and gesture production were sampled using a preliminary version of the MacArthur Communicative Development Inventory (CDI), a parent report instrument developed by the San Diego group in collaboration with colleagues at the University of Washington, Seattle and Yale University (Fenson, Dale, Reznick, Thal, Bates, Hartung, Pethick, & Reilly, 1993). A 30-minute spontaneous communication sample was used as a context to measure quantity and length of vocalizations, sophistication of syllable structure, and the types of consonants produced.

Marchman et al. (1991) report that all five children were delayed in gesture and word production at all three data points on the CDI. For the children with anterior lesions, however, word production began to move into the normal range at the third data point (between the 18th and 37th percentile for children their age). The two children with left posterior lesions, on the other hand, remained below the 5th percentile for children their age. The anterior-posterior differences also appeared in the spontaneous communication samples. As a group, the children with focal brain injury did not differ from their typically-developing peers on the number or length of vocalizations produced. However, their phonological development paralleled their lexical development. Specifically, the children with focal brain injury produced fewer “true” consonants and a smaller proportion of labial

consonants (e.g., /b/ and /p/) than the typically-developing children, but by the third data point children with anterior lesions had begun to use "true" consonants as frequently as the typically-developing children.

With regard to the predictions posed earlier, these results provided evidence that children with focal brain injury are indeed impaired in the early stages of language acquisition. There was also the first tantalizing suggestion (for this group, at least) that the profiles of impairment are likely to be decidedly different from those of adults with similar lesions, since children with anterior lesions (left and right) began to move into the normal range for word production by 21-22 months of age while those with left posterior lesions remained significantly delayed. Finally, the study yielded some evidence for change over time, at least for the children with anterior focal brain injury.

Early lexical development**.** Thal et al. (1991) used the CDI to extend these findings to 27 children with focal brain injury (14 male and 13 female, including the five children from the Marchman et al. study). The participants were between 12 and 35 months of age and 15 were studied longitudinally (10 at two data points and 5 at three data points). Vocabulary comprehension and production were measured between 12 and 16 months of age using the CDI: Words and Gestures; vocabulary production was only measured using the CDI: Words and Sentences. The results of this study reinforce those of Marchman et al. (1991). Thal et al. found delays for the group as a whole in vocabulary comprehension (for the 12 to 16 month period over which it was measured) and production (throughout the full 12 to 35 month range). Thus, the conclusion that children with focal brain injury are at risk for some form of early language delay was supported.

In addition, results from Thal et al. provided stronger evidence that relationships between behavioral profiles and lesion site during development are not the same as those seen in adults. First, in the age range from 12 to 16 months, significant delays in vocabulary comprehension were found only in children with right hemisphere lesions (RH). Second, particularly severe expressive language delays were seen in children with left posterior lesions (LP), continuing into later data points (17 to 35 months of age).

Children without LP, on the other hand, moved into normal percentile ranges, indicating substantial development over time. Thus, LP appear to be associated with significant delays in expressive language, a pattern that only partially maps onto the profile reflected in adults with focal brain injury.

From first words to grammar**.** Bates, Thal, Trauner, Fenson, Aram, Eisele, & Nass (in press), further extended these findings in 3 studies covering development from 10 - 44 months of age. A total of 53 children participated altogether (36 LH, 17 RH), 27 at one data point only, 20 at two data points, and 6 at all three data points. In substudy 1, the CDI: Words and Gestures was used to examine word production and comprehension, gesture production, and the proportion of comprehended words that were also produced in 26 children between 10 and 17 months of age. The CDI: Words and Sentences was used to examine word production and grammatical complexity in 29 children between 17 and 31 months of age in substudy 2. In substudy 3, mean length of utterance in morphemes was derived from spontaneous language samples for 30 children between 20 and 44 months of age.

In the first substudy, LH and RH were compared using percentile scores on the CDI. Results indicated that more children than expected by chance were delayed in comprehension and word production between 10 and 17 months of age (using binomial tests). A maximum likelihood ratio comparing the number of LH to RH who did or did not fall below the 10th percentile did not reach significance ($p<.10$). However, using binomial tests, Bates et al. (1997) found that more RH than expected by chance fell into the delayed range (below the 10th percentile) but no more LH than expected by chance did so. Even more surprising, none of the children with lesions involving the left temporal cortex (the presumed site of Wernicke's area) were in the risk range for word comprehension. This apparent RH disadvantage for comprehension runs directly counter to the Wernicke's hypothesis, but it is compatible with comprehension results for older children in two other developmental studies (Eisele & Aram, 1994; Trauner et al., 1996) as well as the earlier study reported by the San Diego group (Thal et al., 1991). Thus, in the age range from 10

- 17 months, there is weak evidence for RH specialization for language comprehension and clear disconfirmation of left posterior specialization for language comprehension (the Wernicke hypothesis). Similar analyses of gesture production indicated no significant delays associated with LH or +LT, but did find support for RH disadvantage in gesture production, similar to the findings for comprehension.

There was not a significant left-right difference in word production, nor was there evidence for left temporal involvement on overall word production percentile scores. Note, however, that this null result is confounded by the surprising finding that comprehension deficits are greater in RH children. Hence it was important to control for the number of words that a child knows in order to assess whether there are site-specific effects on the ability to produce those words. To control for this confound between comprehension and production, Bates et al. conducted a second series of analyses looking at the proportion of receptive vocabulary that children are able to produce. This analysis did yield a significant disadvantage for children with left temporal involvement. In other words, a left hemisphere disadvantage for expressive language does emerge when differences in word comprehension are controlled, in the period between 10 and 17 months of age. The fact that this left hemisphere disadvantage comes primarily from children with damage involving the left temporal lobe provides yet another challenge to the Wernicke hypothesis.

In their second substudy of children in the 19 - 31 month range, Bates et al. (1991) carried out comparisons of percentile scores for word production, as well as comparisons for two measures of early grammar: mean length in morphemes of the three longest utterances reported by parents (M3L), and the proportion of total vocabulary comprising closed class words (i.e., grammatical function words). These comparisons produced a number of surprises. First, a significant number of children in this sample continue to be at risk for delays in expressive language between 17 and 31 months of age. There were no significant differences overall between LH and RH for word production or grammar, but children with left temporal lobe damage were at a greater disadvantage for both total vocabulary and M3L. The left temporal disadvantage appears to be even stronger when

there is also damage to the left frontal lobe, a finding that is compatible with hypotheses based on the adult literature. Surprisingly, however, delays were equally serious for children with damage to the right frontal lobe, suggesting that frontal effects are symmetrical in nature during this period of development. There were significant differences between LH and RH on the proportion of closed class (or function) words in their vocabulary, with LH lower than right, but the mean scores indicated that this reflected a right hemisphere advantage (i.e., abnormally high closed class ratios) rather than a left hemisphere disadvantage (i.e., abnormally low closed class ratios).

Finally, in substudy 3 of the Bates et al. (1991) report, free speech samples for focal lesion subjects between 20 - 44 months were compared on mean length of utterance (MLU) in morphemes, in order to obtain a general measure of grammatical complexity in spontaneous speech. The same LH/RH and +LT/-LT comparisons were conducted. As a group, subjects were about 4 months behind normal controls on MLU: about 52% fell in the lowest 10% for their age. LH/RH comparisons did not reach significance although the difference was in the predicted direction (LH lower than RH). However +LT were significantly lower than -LT. Only 31% of the sample with -LT fell into the lowest 10% for their age while 85% of the +LT sample did so (significant by a likelihood ratio, $p < .002$). These results contradict the Wernicke hypothesis, and extend the left temporal findings that appeared before this point. However, in contrast with substudy 2, frontal involvement did not increase the risk for expressive language delays in this analysis, providing little evidence for the Broca hypothesis.

The series of studies presented here on the emergence of language in very young children with early focal brain damage does not follow the pattern we would expect based on lesion site-symptom correlations in adults with focal brain injury. This apparent contradiction may, at least in part, reflect the very different task demands that confront infants and adults in the language domain. Infants and toddlers are learning to comprehend and produce language <u>for the first time</u>. Adults have already acquired their language; their task is to use that knowledge for fluent and efficient language comprehension and

production. It appears that in the acquisition and development of the linguistic system, children draw on a broader array of brain structures. However, the Bates et al. (1996) results do provide evidence that the left temporal lobe is of major importance to the emergence of left-hemisphere specialization for language under normal conditions.

Discourse and grammar from 3 - 12 years**.** Our study of older children is based on narratives elicited from 31 children with FL (13 with RHD and 18 with LHD) between 3,6 and 9,6 and their age and gender matched controls (Reilly, Bates, & Marchman, in press). Narratives represent a complex discourse context in which to examine both core aspects of language, e.g. morphology and syntax (mediated by the left hemisphere in adults) as well as narrative genre skills, e.g. coherence, inferences (mediated by the right hemisphere in adults). In our primary narrative task, the children were asked to look through a wordless picture book, Frog, where are you? (Mayer, 1969) and then, while looking at the book, to tell the story to an adult. Our analyses focused on different levels of narrative production: (1) microstructures: lexical types and tokens, morphology and syntax; (2) macro-structures: narrative components and theme. Our findings support an overall delay in the acquisition and deployment of linguistic structures as well as in the development of narrative skills. In addition, it appears that younger children with left temporal damage have particular difficulty acquiring specific morphosyntactic structures.

To begin, children with focal brain injury produced shorter stories overall than their age-matched normal controls, and they included fewer components of the story. Their stories contained a smaller number of propositions, and they used fewer word types as well as fewer word tokens. With respect to specific lexical measures, there were some changes in lexical output depending on age, but no clear effects of lesion group. Developmental changes included an increase in both the use and range of evaluative terms (e.g. causal inferences and emotional terms), and an increased use of pronouns that are co-referential with a noun in the same sentence. It appears that, by age five, children with focal brain injury are able to keep up with their age mates in vocabulary production during a narrative (story-telling) task.

In contrast with these lexical findings, morphological development continues to lag behind in the children with FL, at least for a while. By age five, neurologically intact children made very few morphological errors; the FL group did not reach the same level of proficiency until age seven. Similar to our findings for the earlier developmental period (i.e. in the emergent stages of language), this selective disadvantage in the acquisition of morphology before age 7 was due primarily to children with left temporal involvement.

We approached syntax in the narratives from two perspectives: frequency of complex sentences and diversity of complex structures. Not surprisingly, children used more complex syntax as they got older. However, children with brain injury lagged behind normal controls across the age range from 3.5 to 12 years. Among the youngest children (3,5-5,0), children with RHD clustered with typically developing children of the same age, whereas for children with LHD, the use of complex syntax was extremely rare. Among the older children (5,0-9,6), the LHD and RHD groups both performed below normal controls, with no sign whatsoever of a difference due to side or site of lesion. Interestingly, if we plot the developmental trajectories for these groups, the LHD group shows the same slope as typically developing children but at a significantly slower rate, whereas the slope for the RHD group is essentially flat. That is, in this cross-sectional study, the older children with RHD appear to use complex syntax with the same frequency as their younger counterparts. Given that complex syntax is one of the primary linguistic mechanisms of integrating and relating events in a story, this profile may be evidence of a broader right hemisphere integrative deficit. Note, however, that there is no evidence here for an RH disadvantage in overall level of performance on language measure. The one peculiarity that we do observe pertains to the pattern of change over time in RH children, and not to their absolute level of performance relative to other children with focal brain injury.

In contrast to this measure of syntactic frequency, our syntactic diversity measure looks at the number of complex sentence types in each child's story, on a scale from 0 - 5. Among the younger children, the four children with left temporal involvement produced significantly fewer complex types compared with the six children whose lesions spare the

left temporal area; however, this profile does not hold after age five, when both RHD and LHD children scored significantly lower than their typically developing controls, with no evidence of any kind for a specific effect of lesion site within the damaged hemisphere.

In addition to shorter stories, the brain injured children include significantly fewer of the story episodes in their narratives. Moreover, the stories told by FL tended to focus on the local story events rather than tying these together by invoking the more global theme of the story. This may indicate a delay in integrating the macrostructure with individual events as well as delay in making inferences about the motivations of the characters. The transition from a sequential description of local events to coherent narrative with an integrating theme occurred by about age 5/6 in the control group; it did not appear consistently until 7/8 in the stories from children with focal brain damage. Again, we see no clear patterns relating to lesion side or site.

Overall, we found delays in the lesion group on both linguistic and narrative measures. In addition, children with left temporal damage appear to be the most vulnerable for the acquisition of new linguistic structures before 5-7 years of age. This emerging profile of delay in narrative skill, morphology and decreased use of complex syntax are reminiscent of the initial delays in language displayed by the FL infants and toddlers (described above). The productive delays that we observe for core linguistic structures do <u>not</u> map onto the lesion profiles observed in adults with analogous injuries (left temporal lesions in adults are more likely to result in comprehension rather than production deficits). However, at the very least, these findings are compatible with the idea that the left temporal lobe plays an important role in the emergence of the left-hemisphere specialization for language that is typically observed in normal adults (i.e., in adults without this history of early brain injury). Finally, these preliminary narrative data suggest that deficits in linguistic abilities are not completely resolved by 5 years of age, as has been suggested; instead, deficits may reassert themselves as the children face new linguistic challenges. What we appear to be witnessing is a dynamic and repetitive process, overall, very much like normal language acquisition, but with a somewhat delayed developmental trajectory.

As we have seen, the data for language development in the focal lesion population yields a number of surprises, contradicting predictions based on more than a century of research on adult aphasia. As we are about to see, the data for spatial cognition in the same population tell another story.

SPATIAL ANALYTIC PROCESSING

The focus of work in spatial cognition has been on a specific subset of spatial processes involved in spatial pattern analysis. Spatial analysis is defined as the ability to specify both the parts and the overall configuration of a pattern. It thus involves both the ability to segment a pattern into a set of constituent parts, and the ability to integrate those parts into a coherent whole. Studies with adults have shown that different patterns of spatial deficit are associated with LH and RH lesions (e.g., Arena & Gainotti, 1978; Delis et al., 1988; Delis et al.,1986; Gainotti & Tiacci, 1970; McFie & Zangwill, 1960; Piercy et al., 1960; Ratcliff, 1982; Swindell et al., 1988; Warrington et al., 1966). Injury to left posterior brain regions results in disorders involving difficulty defining the parts of a spatial array, while patients with RH lesions have difficulty with the configural aspects of spatial pattern analysis. We have found similar patterns of disorder in our studies of young children with early focal brain injury. In the description of the studies to follow, data specifying both deficit and recovery of function are reported. The discussion has been divided by task. Over the course of our study of the focal lesion population it has become clear that not all spatial tasks tap the encoding and integrative functions associated with spatial analysis with equal proficiency. Thus the evidence for the two patterns of disorder are best described by the convergence of data across different tasks.

Spatial Classification. Our study of spatial classification (Stiles-Davis et al., 1985) was the first to explicitly establish a specific disorder of spatial integrative ability in 2- to 3- year olds with RH injury. In this task children were presented with stimulus sets containing two classes of objects, and simply encouraged to play. This procedure elicits systematic class grouping activity in both normal children and children with focal brain injury. The results showed that children with RH injury were selectively impaired in their ability to form

spatial groupings. Specifically, while RH injured children would stack objects or place one object in another, they did not place objects next-to one another to extend their constructions out in space. Normal and LH damaged children regularly placed objects next to each other as early as 24-months. A second task using a temporal measure of classification showed that the RH children were not impaired in their ability to form simple class relations. Thus the impairment on the spatial classification task reflected a primary disorder of spatial grouping rather than a disorder of classification, per se. These findings suggested very limited development of spatial integrative ability for children with RH damage.

Block Construction. In order to elaborate the spatial classification findings, we conducted a large study focused specifically on the ways in which 3- and 4-year-old children with focal brain injury spontaneously organize blocks into spatial groupings (Stiles & Nass, 1991; also see Stiles-Davis, 1988 for data on normal children). The study included two experiments. The first was a cross-sectional examination of 20 children tested at ages 3 and 4 (five children with RH injury and five with LH injury were included at each age). The second experiment was a longitudinal case study report of 6 children (three RH and three LH) tested at both ages 3 and 4. The longitudinal data were intended to provide converging evidence for developmental patterns observed in the cross-sectional experiment. The data from both experiments were evaluated using eight measures of spatial grouping activity. The results showed that focal brain injury affected grouping activity for children with both the RH and LH injury. Overall, performance of both groups was below that of normal children at 3- and 4-years of age. The profiles of deficit differed, however, for the two lesion groups. Children with RH injury were impaired on all measures of spatial construction at age 3. By age 4, development was observed on low-level measures assessing children's ability to combine pairs of objects; however, impairment was still observed on more global measures of organization. The behavior typical of this pattern of results was one in which children systematically placed blocks one-by-one into disordered heaps. In contrast, while children with LH injury at age 4

continued to produce fewer local level relations, they showed a more normal pattern of development in the kinds of global structures they produced. Like normal 4-year-old children they generated arches, enclosures and symmetries. The findings for both the RH and LH groups were consistent for the cross-sectional and the longitudinal experiments. The pattern for the RH group extends our findings of spatial integrative deficit early in the preschool period. The findings of impaired development for the children with LH injury is the first report of spatial deficit in this group.

In a follow-up study, children were given a more structured task in which they were asked to copy a series of modeled constructions (Stiles, Stern, Trauner, & Nass, 1996). This study was designed to allow a more detailed examination of both the products and the process of block construction. In this study, both children with LH and RH injury showed evidence of impairment. Children with LH injury initially showed delay on the task, producing simplified constructions. By the time they were 4-years of age, they showed in interesting dissociation in performance. Most of the children were able to produce accurate copies of the target constructions, however the procedures they used in copying the forms were greatly simplified. This dissociation between product and process persisted at least through age 6. RH children were initially delayed, then later produced disordered, poorly configured constructions. At this time the procedures the children used to generate their ill-formed constructions were comparable to age-matched controls. However, by the time these children were 6-years of age their profile of performance changed. By that time they were able to accurately copy the target construction, but like their LH injured peers, they used simple procedures to generate these constructions. This study suggests that there is indeed impairment in spatial processing following early injury, and there is compensation with development. However, close examination of how spatial constructions are generated suggests persistent deficit. These findings have been replicated in a second study of American and Italian children with localized brain injury (Vicari et al., in press). This also demonstrated that children with isolated subcortical injury show the same profiles of deficit as children with cortical involvement.

Drawing. Our study of drawing in the focal lesion population has shown the children with RH injury initially have considerable difficulty drawing organized pictures (Stiles-Davis et al., 1988). In a simple free drawing task, children were asked to draw a house. By age 3.5 to 4, normal children produce well organized houses, with an outer form representing the building and appropriately positioned inner features representing doors and windows. By age 5 the house drawings of children with LH injury are indistinguishable from those of normal controls. However, during the late preschool period drawings of children with RH are disordered and lack integration. The lack of organization suggests deficits in the ability to integrate parts to form a coherent whole. This is consistent with Swindell and colleagues' (1988) characterization of drawings by adult patients with RH injury as, "scattered, fragmented, and disorganized...subjects often overscored lines and added extraneous scribblings" (p. 19).

This notable impairment in drawing among the children with RH injury does not persist. Our longitudinal studies have shown considerable improvement with age. Improvement in the organization of their drawings is striking, but the drawings also exhibit striking similarity over time. This similarity may reflect the development of graphic formulas. Graphic formulas are common in the normal development course of drawing. Children begin to use graphic formulas from their earliest drawings (Stiles, 1995) and their use persists through adulthood. Thus the development of graphic formulas would not be an abnormal feature of drawing among children with RH injury. The development of formulas may, however, serve as a useful compensatory strategy. Mastery of specific graphic formulas would allow the children to represent common objects, while minimizing the spatial processing demands. If the children's improvement on the drawing task is achieved through the compensatory strategy of graphic formula production, then they should be more dependent on formulaic representation than normally developing children. Reliance on graphic formulas was tested using a task developed by Karmiloff-Smith (1990) in which children are asked to first draw a house, and then an impossible house (Stiles et al., 1997). The most common solution to this task among normal children is to distort the

spatial configuration of the house. Data from children with LH injury are indistinguishable form those of normal controls. However, in our longitudinal sample of 5 RH children tested every 6- to 12-months for a period from 3- to 6-years, configural distortion was not used. Instead the children derived a number of non-configurational solutions for solving the problem, including verbal descriptions (drawing an identical house and then describing something impossible inside), formula substitution (drawing another formulaic object and asserting it was a house), reduction (putting a dot on the page and saying the house is very small), and invisibility. Once again, these data indicate that while these children are developing and their performance on specific spatial tasks improves, the processes by which they master these tasks may differ from those of normally developing children. This suggests a pattern of specific, subtle, and persistent deficit in spatial processing.

Processing Hierarchical Forms. Another set of studies considered here focuses on a particular class of stimuli, hierarchical forms. This task has provided particularly strong data on the spatial processing deficit for children with LH injury. Any visually presented pattern can be conceived of as a structured hierarchy consisting of local level elements and more global level assemblies. One example of a simple hierarchy is the hierarchical form stimulus. It consists of a large letter composed of appropriately arranged smaller letters, such as a large H made up of small Ss. Hierarchical stimuli have been used in studies of normal children (Stiles-Davis et al., 1988; Dukette & Stiles, in press), and of both normal (e.g., Kinchla & Wolf, 1979; Martin, 1979; Navon, 1977; Palmer, 1980; Palmer & Bucher, 1981) and neurologically involved (Delis et al., 1988; Delis et al., 1986; Lamb et al., 1989, 1990; Robertson & Delis, 1986) adults. They have proven to be sensitive measures of spatial pattern analysis in the normal adult and child populations. They have also been used successfully to identify differential patterns of spatial deficit in adults with focal left and right posterior brain injury. Specifically adult patients with right posterior injury have difficulty processing the global level of the form, while patients with left posterior injury have difficulty with the local level.

Studies of normal adults suggest that processing of information at the global and local levels of the pattern are not symmetrical. Hemifield and functional MRI (fMRI) studies (Martinez et al., 1997) suggest that the RH is more efficient at processing global level information than local level information. By contrast the LH appears to be equally efficient at processing information at both levels of the pattern hierarchy. Hemifield data show that when targets are presented to the left visual field/right hemisphere, response time to identify targets at the global level are faster than when targets are presented at the local level. No differences in reaction time were observed for global and local targets presented to the right visual field/left hemisphere. Data from fMRI studies using hierarchical form stimuli showed asymmetrical activation patterns for local targets with greater activation in the LH, and symmetrical activation for global targets. Activation sites in this study were in homologous left and right inferior temporal regions.

Data from one study of hierarchical form processing among children with LH or RH brain injury are consistent with the pattern of data outlined above. In this task children were asked to study and remember a hierarchical pattern. After a brief distracter task they were asked to reproduce the form from memory. Children in the early school-age period showed a marked dissociation of performance. Children with LH injury were able to reproduce the global level of the target forms, but were impaired in their reproduction of local level elements. Children with RH injury, though less accurate than their age-matched controls, were able to reproduce both levels of the pattern. This profile of results is consistent with the data from the normal adult subjects. If injury to the LH leaves only the RH spatial processing system, then local processing should be impaired. However, if injury to the RH leaves the LH processing system, then subjects should be able to process both levels of the pattern.

The last study may appear to contradict the model of spatial analytic processing described at the beginning of the section. The original model suggested a double dissociation, with the RH responsible for global processing and the LH for local processing. However, if a model of processing dominance were substituted for the

dissociation model all of the available data can be accounted for. By the dominance model both hemispheres would be capable of processing both local and global level information, but they would differ in the level of proficiency with which each processes information at the two levels. Thus, the RH would be a more efficient global processor and the LH a more efficient local processor. If a particular task were relatively easy at one level, then either hemisphere could handle the information; but if the task differentially taxed one level of processing only the dominant hemisphere could effectively complete the task. If, in the case of the hierarchical forms task, local level processing were more difficult than global level processing, only the LH could efficiently carry out the task. Slight, but consistently slower RTs to local level targets among normal adult subjects supports this view. In contrast to the hierarchical forms task, other tasks discussed in this section may selectively tax the more global, integrative functions. Thus block construction or drawing may place a disproportionately large burden on integration, while taxing the encoding or segmentation functions only minimally. If this were the case this would account for why some tasks appear to be better indices of RH dysfunction, and others of LH dysfunction.

Neglect. Adults with right hemisphere lesions often exhibit evidence of extrapersonal neglect on the side contralateral to the lesion. That is, such individuals may ignore objects in their left visual fields, even in the absence of an obvious visual field defect. In one of the newest initiatives within our project, we have begun to study this well-known phenomenon in children with early focal brain damage. Preliminary results indicate that children with RH damage do exhibit contralateral spatial neglect, similar to what is observed in adults after RH strokes. Further studies are underway to more precisely characterize the extent and patterns of extrapersonal neglect in our study population, and to determine whether a complementary form of contralateral spatial neglect is displayed by children with LH damage (a relatively rare finding in the literature on unilateral neglect in adults).

In summary, the data from these studies of the FL population show that early brain injury does result in selective deficits of spatial functioning. These deficits, like those observed among adult patients, are specific and conform to important aspects of spatial

pattern analysis. Thus from an early point in development, we see instantiated at the level of brain substrate important and differentiated aspects of the spatial analytic system. However, documentation of selective deficit does not necessarily imply a simple structure-function mapping, or the loss of such mapping. While the patterns of deficit observed in children are consistent with the patterns observed in adults, they are also considerably more subtle and we have preliminary data to suggest that they can be compensated for more readily. We may therefore be observing selective loss within a well defined, but dynamic and developing system for spatial analysis. Thus, while the building blocks for the spatial analytic system appear to be in place from an early age and are susceptible to the effects of early brain injury, there is still a considerable degree of flexibility or plasticity which results in much more subtle forms of deficit and may allow for functional sparing later in development.

AFFECT

Affect represents a new area of study for our center, thus we have just begun to investigate the neural underpinnings of this communicative system. However, our initial findings in two areas of affective behavior are tantalizing. In one line of work, we have begun to investigate the development of affective facial expression. A second line of work focuses on vocal prosody.

Affective facial expression. During a child's first year, affective facial expression plays a significant role in mother-child interaction (e.g. Stern, 1977) By their first birthday, as first words emerge, normally developing infants are fluent affective communicators, consistently using specific facial configurations both to express and to interpret emotional state (Stenberg & Campos, 1990; Hiatt, Campos, & Emde, 1979; Klinnert, Campos, Sorce, Emde, & Svejda, 1983; Stenberg, Campos, & Emde, 1983; Fox & Davidson 1984, 1988; Malatesta et al., 1989; Fox, 1994). Because facial expression emerges so early in life, its development in infants with focal brain damage provides a promising context in which to investigate the developing neural substrates of emotions as well as to ascertain the degree to which the young infant brain is specified for these particular behavioral functions.

Given the paucity of detailed neurodevelopmental data on spontaneous affective expression, either observational or experimental, our best model stems from adult neuropsychological research. Evidence from normal adults and adult stroke patients suggests that the right hemisphere plays a critical role in the processing of emotional information, both in the facial and vocal channels (Borod, 1993; Pizzamiglio, Caltagirone, & Zocolotti, 1989; Bryden & Ley, 1983; Ross, 1981; Ross & Mesulam, 1979, see Borod, 1993 for a review). Patients with RH injury have been found to be "inexpressive" (Ross & Mesulam, 1979; Borod, Koff, Lorch, & Nicholas, 1985; Blonder et al., 1993) and aprosodic (Ross, 1981). Complementary research with school-aged children who suffered perinatal brain damage (Tranel et al., 1987), indicate that children with RH injury also have difficulty voluntarily displaying emotion, and have been characterized as "inexpressive" (Denckla, 1983); they also have difficulties in elicitation and discrimination tasks for emotional expression (Voeller, 1986). These findings would predict that children with RH injury would show depressed affect expressivity compared to normals. In addition, data from the adult literature suggest that valence, i.e., whether an emotion is positive or negative, plays a critical role in the organization of emotion with the left hemispheres mediating positive emotions and the right responsible for negative emotions (Gainotti, 1969, 1972; Sackheim et al., 1982; Natale & Gur, 1983). More recently, data based on EEG studies of affective responsiveness (Ahern & Schwartz, 1985; Fox & Davidson, 1984, 1988; Davidson & Fox, 1982; Dawson, 1994; Fox, 1994) suggest that the valence dichotomy may be reflected solely in the frontal lobes. Together these findings would suggest that children with posterior LHD would show normal affective profiles; and children with posterior RHD will show decreased positive affect both facially and vocally. In contrast, children with isolated right frontal damage will display decreased negative affective profiles (which may in fact present as a very cheerful child) whereas those with left frontal damage will show decreased positive and increased negative responsiveness.

To test these hypotheses, we have examined both positive and negative affective expression in 12 infants (6-24 months) with pre- or perinatal unilateral focal brain damage

(6 RHD and 6 LHD) and their age and gender matched controls (Reilly, Stiles, Larsen, & Trauner, 1995). Infants were videotaped in free and semi-structured tasks with the mother and with an experimenter. Interactions were microanalytically coded using Ekman and Friesen's Facial Action Coding System (1978). Our results from the cross-sectional data demonstrate a consistent pattern of affective expression: both normal babies and babies with posterior left hemisphere damage exhibit the full range of affective expressions appropriate to the elicited situations. In contrast, the infants with right hemisphere damage, especially those with posterior involvement, showed marked affective impairment in the expression of positive, but not negative emotion. Interestingly, longitudinal data from the one infant with isolated right frontal damage showed no such impairment, whereas comparable data from the infant with left frontal damage showed enhanced negative affect and depressed positive affect. Overall, these data are consistent with the adult neuropsychological findings that the right hemisphere plays a critical role in affective expression (Borod et al., 1985; Borod, 1993). More specifically, one of the few adult studies based on naturalistic data (Blonder et al., 1993) also found that adults with RHD expressed more negative and less positive facial affect than either patients with LHD or controls. In addition, the infant data maps onto the findings of electrophysiological studies (Fox & Davidson, 1984, 1988; Dawson et al., 1992; Fox, 1994) implicating the frontal lobes in the mediation of approach/avoidant emotions. In sum, the infant profile appears to be quite similar to that found in adults with homologous lesions. These results suggest that for affective expression, brain organization is specified very early on. We are currently collecting data to investigate the degree these profiles persist in development.

Prosody. Our preliminary studies of older children with focal brain damage used experimental tasks and focused on meta-affective abilities. In adults, damage to the right hemisphere (RH) produces deficits in the comprehension and expression of affective meaning in language or affective prosody. Left hemisphere (LH) damage may cause difficulty with the understanding and use of the more linguistic aspects of prosody (e.g., contrastive stress). We have begun to look at comprehension and expression of affective

and linguistic prosody in the FL population. In one study (Trauner et al., 1996) 13 children with LH injury, 15 with RH injury and age matched controls ranging in age from 5 to 20-years were tested on tasks involving comprehension and expression of affective prosody, and to a lesser extent on tests of linguistic prosody. Children with LH lesions performed more poorly than controls on tests of linguistic, but not affective, prosody. Individuals with RH lesions demonstrated difficulties in the comprehension and expression of both affective and linguistic cues. These results are consistent with those found in adults with acquired focal brain damage (Ross, 1981; Tucker, Watson, & Heilman, 1977; Kolb & Taylor, 1981; Benowitz et al., 1983; Borod et al., 1985; Borod, 1993). Looking across these studies, we have evidence of affective profiles in the first year of life which differ according to lesion site and later evidence of site-specific prosodic differences from school aged children and adolescents. These initial studies present a developing affective profile that is consistent with that of adults with comparable damage.

SUMMARY AND CONCLUSION

We have provided a brief overview of results from the first large-scale prospective study of behavioral development in children with early focal brain injury. It has taken more than ten years to accumulate a large enough database to justify the (tentative) conclusions presented here. It also goes without saying that all of these findings will need to be replicated in other laboratories. Furthermore, because our findings are still primarily cross-sectional in nature, they must be tested and extended in longitudinal work. With those caveats in mind, we want to underscore that research with this population has yielded a number of surprises, including results that are not always compatible with the view of brain organization that one typically finds in surveys of lesion studies in human adults. We end this chapter with three lessons from research with this population, followed by three questions that are left unanswered by this work.

Lesson #1: Against predeterminism**.** The idea that the mind-brain is organized into distinct faculties or "modules" goes back to the 18th century, to the phrenological proposals of Gall and Spurzheim. This phrenological perspective is often accompanied by a

developmental corollary: familiar patterns of brain organization for higher cognitive functions can be found in the mature adult because those patterns were there from the beginning, as innate properties of the human brain. The fact that children in this population outperform adults with homologous injuries can be used to argue against any strong form of predeterminism, predestination, or preformationism. All of the findings that we have reviewed in this chapter point in the same direction: children with early focal brain damage ultimately reach levels of performance well ahead of those observed in adults with homologous injuries. To be sure, brain damage is not a good thing, and children who have suffered some form of focal brain injury typically perform (as a group) reliably below normal controls, sometimes in relatively predictable patterns depending on their site and side of injury. However, our developmental findings suggest that these initial biases are imperfect, indirect, "soft constraints" that can be overcome.

Lesson #2: Against equipotentiality**.** When studies of children with early brain injury first appeared in the neuroscience literature, they were sometimes used to argue in favor of a *tabula rasa* view of the mind-brain, a view on which cortical tissue is, initially, capable of taking on an infinite number of functions, with no bias toward any particular cognitive domain. In its strongest form, the equipotentiality hypothesis is flatly impossible: if it were true, there would be no way to explain why familiar forms of brain organization are observed so often in the neurologically intact adult brain. For example, current estimates are that the left hemisphere plays a special role in the mediation of language in 95 - 98% of normal individuals. Why would this ratio emerge, over and over again, if the two hemispheres were initially unbiased? If one were to flip a coin 100 times, one would be quite surprised if heads came up 98 times, and even more surprised if the same ratio held on the next 100 flips. It would, in fact, be difficult to avoid the inference that the coin is biased. We are forced to a similar conclusion in the study of brain organization for language, spatial cognition and affect, i.e. there must be some kind of bias present from the beginning of life in order to explain the well-documented patterns of left- and right-hemisphere specialization that adults display in these domains. By carrying out prospective

studies of linguistic, cognitive and affective development, we have uncovered subtle but specific patterns of deficit and delay that work against any strong and simple form of the equipotentiality hypothesis. Some form of cortical specialization (or "cortical preference") is clearly there from the beginning of life, although it can give way to an alternative "division of labor" when things go awry. Our challenge for the future is to specify the nature of those early biases, and the developmental processes by which alternative forms of brain organization emerge over time.

Lesson #3: Children are not adults**.** The patterns of lesion-symptom mapping that we have uncovered in our work differ markedly from the patterns revealed in adult neuropsychology literature. In all the domains that we have studied to date, there are quantitative differences in the effects of homologous injuries on children and adults: the effects on children are generally more subtle (i.e. not as severe, compared with performance by normals in the same age range), and performance improves markedly over time -- sometimes to the point where (at least on casual inspection) the deficit seems to have disappeared altogether. These quantitative differences provide further evidence for a conclusion that has emerged in the last 20 - 30 years of research in developmental neurobiology: the developing brain is highly plastic, and alternative forms of brain organization are possible for the "same" behavioral task (although there is emerging evidence that the processes associated with these alternative forms of may differ from those observed with typical organizational profiles).

Within the language domain, the differences are also qualitative. We outlined four simple hypotheses derived from more than 100 years of research on adults with unilateral brain injury: (1) left hemisphere specialization for most linguistic tasks, (2) left frontal specialization for expressive language (i.e., the Broca hypothesis), (3) left temporal specialization for receptive language (i.e., the Wernicke hypothesis), and (4) right hemisphere specialization for some discourse functions. We did not find unequivocal support for any of these hypotheses, and some of them were flatly contradicted by our results.

For example, none of our infants with left temporal lesions were in the bottom 10th percentile for word comprehension; in fact, although results are probabilistic in nature, there is some reason to believe that right hemisphere damage is a greater risk factor for comprehension. These findings run against the Wernicke hypothesis, and against left hemisphere specialization for basic language functions. In line with the adult literature, we do find evidence that children with left hemisphere damage are more delayed in expressive language. However, this finding is only evident from 10 months of age (the dawn of language) up to but not beyond 5-7 years. Furthermore, the effect is coming primarily from children with left temporal involvement (against the Wernicke hypothesis). Frontal involvement is an additional risk factor between 19 and 31 months of age, but in this time window it doesn't seem to matter whether frontal damage occurs in the left or the right hemisphere (against the Broca hypothesis). Some time after 5-7 years of age, we no longer have any evidence for differences due to side of lesion (left vs. right) or intra-hemisphere site of lesion (frontal or temporal). The right hemisphere cases display a flatter developmental profile in the use of complex syntax for narrative purposes, in line with the idea that the right hemisphere may be specialized for discourse. However, there are no significant differences between the left and right hemisphere groups in absolute level of performance after 5-7 years of age. The only firm conclusion that holds in our data for older children with congenital lesions is that brain damage does exact a cost, lowering the group profile below normal controls -- though still well within the normal range.

Although we have no ready explanation for these quantitative and qualitative differences in patterning, these findings do remind us of an important point: the children in our prospective studies are encountering language and other higher cognitive functions for the first time. What we are looking at is, in essence, the effect of early focal brain injury on the learning process. Our results suggest that the brain mechanisms responsible for language learning are not the same mechanisms that govern the maintenance and fluent use of language in normal adults. In other words, we do not believe that language literally moves (bags packed) from one brain region to another across the course of development. Rather,

the learning process may recruit brain areas that are no longer needed once the learning itself is complete, and the task in question has become a routine part of daily life. This conclusion is, in fact, compatible with recent studies of learning and processing in normal adults using positron emission tomography (PET) and functional magnetic resonance brain imaging (fMRI) -- studies that show differential patterns of brain activity for the same task in novices compared with experts (Raichle, 1994), and differential patterns of activity in the same individuals as a new task is mastered and/or as the same task is administered with increasingly difficult and complex stimuli (Just et al., 1996).

These conclusions are easy to defend, in light of our own work and many other studies in the literature. However, as we have noted, they raise more questions than they answer. Let us end by posing three of the most puzzling questions that we now face.

Question #1: Why is language more plastic than spatial cognition or affect? Our results for spatial cognition and affective expression are, as noted, qualitatively similar to the lesion-symptom patterns that have been reported for brain-injured adults. In the spatial domain, right hemisphere injury seems to be associated with a deficit in the integration of information over relatively large spatial scales; by contrast, left hemisphere injury (especially to left temporal cortex) results in a deficit in the extraction of pattern detail. In the affective domain, variants of the left-right differences observed in brain-injured adults are also observed in very young children (e.g. flattening of facial and vocal affect in some cases of RH damage). By contrast, our findings for language development are not at all compatible with the classic aphasia types observed in adults. Deficits in word comprehension and gesture appear to be associated with right rather than left hemisphere damage. Deficits on the production of words and grammar are greater in our LH sample, as we might expect from adult aphasiology. However, the intrahemispheric patterns observed in children are quite different from those observed in adults, including an asymmetrical left posterior (temporal) effect on both vocabulary and grammar, and an additional frontal effect on expressive language that is observed to an equal degree with right frontal and left frontal involvement. More puzzling still, none of these side or site

specific effects are observed in our cross-sectional findings after 5-7 years of age, even though our older children have exactly the same congenital etiology as the younger cases. This is not true for our extensive school-age studies of spatial cognition. Why are the findings for language so different from our findings for spatial cognition and affect? And why does language appear to display more plasticity than other lateralized cognitive and communicative functions?

It is possible that language is more plastic than other behavioral functions simply because it is a phylogenetically recent phenomenon. Perhaps there has not been sufficient time for language to evolve into a fixed and irreversible neural system. Although we acknowledge this possibility, we suspect that this is not the answer. Language is different from the other systems that we have studied to date in a number of crucial respects, with implications for the nature and plasticity of the neural systems that subserve it. First, language is the system that we use to express meaning; indeed, the boundaries of language include semantics as well as grammar and phonology. Because meaning encompasses all of our experience, the system that we have evolved to encode those meanings must by definition must include information derived from widely distributed neural systems. Perhaps for that reason, language can never retreat to a compact region of the brain, no matter how much phylogenetic time we are given to evolve a "mental organ".

But what about linguistic form, independent of meaning? Could there be a tightly bounded, predetermined region that handles phonology and/or grammar? In principle, this is certainly possible, and to a limited extent it has to be true -- at least for speech sounds. The basic input-output architecture used by speech appears to be a universal property of the human brain, including the system that runs from the ear to the auditory nerve and its termination points in auditory cortex, and the set of cortical and subcortical areas that are involved in the planning and execution of speech production. As Sigmund Freud pointed out long ago in his seminal book on aphasia (Freud, 1953), it is quite likely that, under default circumstances, the continuous sheets of cortex that subserve the rest of language will organize around these basic input-output "hot spots", leading to the familiar pattern of

broad perisylvian specialization for language. At the same time, we now know that this pattern can appear in either hemisphere after early brain injury, and we also know from recent neural imaging studies of normal adults that homologous areas of activation are observed on both sides of the brain in many language tasks, although the activation is typically greater on the left (Just et al., 1996).

This brings us to a central issue in the definition of "language areas": are these regions specialized for speech and language only (i.e. as special purpose mechanisms -- Fodor, 1983), or is it the case that language "borrows" perceptual and motor systems that also do other kinds of work? At the moment, most of the evidence points to the latter option. For example, a recent fMRI study demonstrated that, in addition to carrying out linguistic functions, the various subcomponents of Broca's participate in the planning and execution of one or more non-speech tasks (Erhard et al., 1996). Similar results have been reported for the left temporal regions that are the putative site of Wernicke's area. In short, although it is possible that some aspects of language processing are carried out in highly localized brain regions, those regions may subserve a wider range of function. This may be one reason why these areas show so much plasticity: language is a problem that the brain solves with a range of different general-purpose tools, and for that reason, a number of different solutions are possible.

This brings us to a related point: if language is a parasitic system, running on hardware that evolved for other purposes, it is fair to ask whether the lesion-symptom patterns that we have observed in language, spatial cognition and affect are related in some way? For example, we have noted that RH children show a relatively flat profile in the development of complex syntax. Is this language profile related to the information-integration deficits observed in spatial cognition, and/or to the diminished facial and vocal affect that is sometimes reported for the RH population? Do the same affect and/or integration problems observed in RHD contribute in some fashion to the delays in word comprehension displayed by RH children in the early phases of development? In fact, learning what a word means for the first time is a multimodal integration problem, requiring the child to put

together information from many different sources including the auditory signal, the visual and tactile properties of the thing-to-be-named, as well as social-emotional cues that yield information about the parents' attitude and intentions toward the word and its meaning. In the same vein, we may ask whether the deficits in perceptual analysis associated with left temporal lesions are implicated in some way in the expressive language delays that children with such lesions display between 10 and 60 months of age. The evidence suggests that left temporal cortex is especially well-suited to the extraction of pattern detail, temporal as well as spatial. This fact may give left temporal cortex a "competitive edge" in the language learning process. But why should this "edge" appear most clearly in expressive language, rather than comprehension? We have suggested elsewhere (e.g., Stiles & Thal, 1993; Bates et al., in press; Elman et al., 1996) that learning-to-produce actually requires a much more fine-grained form of perceptual analysis than learning-to-comprehend, because the child must pull enough detail out of the acoustic signal to permit the construction of an intelligible motor template. In other words, understanding what "giraffe" means in context requires far less analysis of the signal than saying the word "giraffe" for the very first time. Of course these suggestions are still quite speculative, but it is a place to start -- which brings us to the next question.

Question #2: What is a "bias"? We have suggested a compromise between the warring claims of equipotentiality and predeterminism, in which different regions of cortex start out not with innate knowledge, but with "soft constraints", innate predispositions to process information a certain way. This is what Elman et al., (1996) refer to as "architectural innateness", as opposed to "representational innateness". Because of its initial predispositions, a particular region of the brain may be recruited to carry out specific aspects of (for example) a linguistic or visual-spatial task, in the same way that a tall child is recruited into the game of basketball. On this view, the division of labor that we see in the adult brain is the product of development rather than its cause. This approach is compatible with findings in developmental neurobiology over the last two decades, suggesting that cortical specialization is driven by activity and experience, in the default

situation and in the alternative situations that arise after early brain injury (for reviews, see Stiles, 1995, in press; Elman et al., 1996, Chapter 5). However, we still know very little about the features of different cortical regions that are responsible for these initial predispositions. What do we mean, in concrete neurocomputational terms, when we say that a region is specialized for information integration, or for the extraction of fine-grained pattern detail? Unfortunately, very little is currently known about the neural microcircuitry of the developing human brain. For example, are there concrete, measurable differences from region to region or hemisphere to hemisphere in cell density and cell types within and across cortical layers, the distribution of neurochemicals, and so forth? What are the computational consequences of such differences, if they exist? We know what questions to ask, but there are very few answers available right now, and our conjectures about innate predispositions for learning cannot be turned into testable hypotheses until such information becomes available.

Question #3: Why does plasticity sometimes fail? We end by pointing out that there are populations of children with deficits in language, cognition and communication that do not display the extraordinary plasticity evidenced by children with early focal brain injury. Examples include children with Specific Language Impairment (SLI), autism, and several different forms of mental retardation including Williams Syndrome and Down Syndrome. All of these populations are currently under study in our San Diego research center, using many of the same behavioral and electrophysiological measures that we administer in our focal lesion studies. On almost every measure, our focal lesion children eventually surpass the other clinical groups, even though recent neural imaging studies of SLI, autism, Williams Syndrome and Down Syndrome provide no evidence for frank lesions of any kind. It seems evident from these comparisons that some forms of early brain injury lead to severe and persistent long-term deficits, without the profiles of recovery and/or compensation that we observe in the focal lesion group.

Why does plasticity fail in these cases? There are several possibilities: (1) diffuse, bilateral “microlesions” that are invisible in neural imaging studies but are nevertheless so

pervasive that they preclude normal development, (2) abnormalities in the cytoarchitecture arising during neurogenesis and/or migration, (3) abnormalities in control of synaptogensis, apoptosis or other regulatory mechanisms in brain development, and/or (4) neurochemical abnormalities affecting either basic metabolic processes or neurotransmitter production. Although these possibilities are no more than sheer speculation today, they may lend themselves to a rigorous test through the combined application of structural and functional brain imaging techniques.

To summarize, we have raised more questions than we have resolved in this chapter, but some lessons have been learned, and there are good reasons to hope that our new questions will be answered. Interdisciplinary research is difficult, requiring time and patience. But our experience to date suggests that this collaborative approach is well worth the effort.

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