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Age-related differences in outcomes following childhood brain insults: An introduction and overview

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Abstract

Despite considerable sparing of function following some forms of early brain disease, neural plasticity is far from complete. Many children with early brain insults, including those who sustain traumatic brain injury (TBI), are susceptible to both immediate and long-term neurobehavioral impairments. To introduce this symposium, the present article reviews existing research on the effects of 3 age-related factors on outcomes: age at injury, time since injury, and age at testing. Research findings support the hypothesis that development is more adversely affected the younger the child at the time of brain insult. Although we know less about how outcomes are related to the other developmental factors, there is little evidence that sequelae resolve with age. Potential brain mechanisms responsible for age-related differences are explored and methodological problems are considered. Emphasis is placed on the importance of prospective designs, measurement of developmental change, comprehensive assessments of outcome, and evaluation of factors contributing to variability in outcomes, such as premorbid status, type of brain injury, and environmental influences. Papers in this series demonstrate the utility of these methods and shed new light on developmental processes associated with childhood brain insults. (*JINS*, 1997, *3*, 555–567.)

Keywords: Child neuropsychology, Early brain injury, Child development

INTRODUCTION

The consequences of brain injuries sustained early in life have long been regarded as distinct from the sequelae of brain insults occurring in adulthood. Pathological conditions that would almost certainly lead to severe cognitive dysfunction in an adult, such as severe unilateral brain disease or thinning of the cortical mantel secondary to hydrocephalus, can have quite different consequences for children. Children with early left hemisphere disease, for example, may go on to acquire many age-appropriate language abilities, free from obvious symptoms of aphasia (Heywood & Canavan, 1987). Similarly, early-onset hydrocephalus need not preclude normal or higher intellectual and academic achievements (Smith & Sugar, 1975). The possibility of grossly normal cognitive development in spite of significant early brain injury is consistent with theories of early "plasticity" of the central nervous system (Lenneberg, 1967; Bishop, 1981). Suggestions of plasticity have led some investigators to ask if it is better to have your brain lesion early (Schneider, 1979), and one author to query if the brain is "really necessary" (Lewin, 1980).

Evidence for plasticity, however, is based solely on selected case studies. Review of larger-scale investigations of conditions such as hydrocephalus and infantile hemiplegia show that group means on tests of cognitive ability are depressed relative to normative standards (Levine et al., 1987). In a classic case series, Myer and Byers (1952) described the developmental sequelae of measles encephalitis in 16 children age 1 to 10 years. The investigators observed that the consequences of disease were frequently less evident on IQ testing than on specialized tests of attention, memory, learning, and perceptual abilities. Effects on IQ, however, became more apparent over time, with several of the children in the study showing diminishing IQ scores over follow-up. Adverse long-term consequences were especially apparent in the younger children in the sample, prompting the authors to conclude that "the younger ones had to attempt the acquisition of the more elementary adaptations with defective tools" (pp. 552–553). Hebb (1942) reached a similar conclusion, arguing that early brain damage limits intellectual capacity (Intelligence A) and in so doing con-

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strains the formation of new cognitive products (Intelligence B) over the growth span. The latter proposal has been referred to as the early "vulnerability" hypothesis (Taylor, 1984).

A survey of more recent research on the developmental outcomes of early brain insults fails to provide unequivocal support for either the plasticity or vulnerability hypothesis. Although brain damage sustained prior to birth or during infancy or childhood clearly impacts on development, outcomes vary from child to child. Normal or better cognitive and academic achievement is possible in spite of significant early brain damage. The critical issue, therefore, is not whether there are sequelae, but the extent to which normal development is possible in spite of early brain insult. With attention shifted away from the more extreme positions of plasticity *versus* vulnerability, emphasis can be appropriately placed on how development is affected and on factors associated with the extent of "developmental sparing," such as the type of brain insult and environmental influences (Taylor et al., 1992).

To set the stage for the research advances represented in this symposium, the present article provides a brief overview of research on outcomes of brain injuries sustained either prenatally or at some point during infancy or childhood. Although the research papers in this series pertain to sequelae of childhood TBI, a comprehensive review of age-related influences on outcomes requires examination of studies of diverse forms of early brain disease. At the same time, it is important to emphasize that the impact of age-related factors on outcomes is likely to depend on the etiology of the brain insult. Age-related differences in the outcomes of congenital brain lesions or of brain tumors or CNS irradiation, for example, may have limited implications for children with TBI.

In keeping with previous reviews (Dennis & Barnes, 1994), the consequences of brain damage are evaluated with reference to the factors *age at insult*, *time since insult*, and *age at testing*. Assessment of developmental outcomes requires consideration of each of these factors. Although interest to date has focused primarily on the effects of age at insult, the possibility of either catch-up growth (Feldman et al., 1992; Stiles & Thal, 1993) or progressive deterioration in functioning (Myer & Byers, 1952; Radcliffe et al., 1994) makes it imperative to examine consequences over an extended period of time postinjury (St. James-Roberts, 1979). Given the possibility that sequelae may depend on developmental expectations or the complexity of processing required of the child (Eslinger et al., 1992), it is also important to take age at testing into account in evaluating injury consequences.

The specific aim of this article is to summarize current knowledge pertaining to each of these age-related factors. After a brief review of the current literature on age-related factors, potential mechanisms responsible for age effects are described. Methodological needs and future directions are also discussed, with reference made to the papers included in this symposium.

SUMMARY OF AGE-RELATED EFFECTS

Age at Injury

On the whole, the existing research literature provides much stronger support for the possibility of early vulnerability to CNS insult than it does for early plasticity. Findings from studies of diffuse postnatal lesions, due for example to TBI or cranial irradiation, suggest that cognitive and academic development is more likely to be compromised when insult occurs in infancy or early childhood as compared to middle childhood or adolescence (Shaffer et al., 1980; Chadwick et al., 1981; Fletcher & Copeland, 1988; Packer et al., 1989; Silber et al., 1992; Radcliffe et al., 1994; Anderson & Moore, 1995; Dennis et al., 1995; Levin et al., 1995; Barnes et al., 1996). In the present series of papers, studies by Ewing-Cobbs et al. (1997) and by Anderson et al. (1997) offer further support for the hypothesis that recovery following TBI is less complete in younger children than in older children or adolescents.

Perceptual–motor and spatial skills appear to be particularly susceptible to early insult (Rovet et al., 1988; Banich et al., 1990; Wills et al., 1991; Taylor et al., 1993, 1995b; Anderson & Moore, 1995; Christie et al., 1995; Dennis et al., in press). However, earlier age at insult also has been linked to greater impairments in overall cognitive functioning (Radcliffe et al., 1994; Levin et al., 1995), verbal and written language abilities (Shaffer et al., 1980; Chadwick et al., 1981; Dennis et al., 1987; Ewing-Cobbs et al., 1987, 1989; Chapman, 1995), attention (Kaufmann et al., 1993; Dennis et al., 1995), and metacognitive functioning (Dennis & Barnes, 1996).

Findings from several studies suggest that the deleterious effects of younger age at insult apply only within a restricted age range. Age-related effects have been most clearly evident in comparisons of children younger than age 7 years to older children and adolescents (Oddy, 1993; Radcliffe et al., 1994; Dennis et al., 1995), and of infants and young preschoolers to somewhat older children (Ewing-Cobbs et al., 1989). The relationship between age at insult and outcome is less certain for children who sustain brain lesions during the school-age years. Whereas some researchers have observed greater deficits following TBI in children than in adolescents, findings in this regard are not consistent across studies (Levin et al., 1995; Yeates et al., 1995). Age-related differences, however, may depend to some extent on how outcome is assessed. Recently, Barnes et al. (1996) compared the reading outcomes of children injured prior to age 6.5 years, between 6.5 years and 9 years, and after 9 years. Reading decoding skills were poorer in children who sustained TBI prior to 6.5 years of age than in children injured at later ages, whereas differences between the two older age-at-injury groups were nonsignificant. Reading comprehension, in contrast, was poorer in both younger age-at-injury groups compared to the older group. These findings suggest that the age range over which age-at-injury effects are observed may be wider for later-emerging skills than for skills

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that are mastered at an earlier point in development (Dennis & Barnes, 1994).

Follow-up studies of children with focal lesions are also generally consistent with the early vulnerability hypothesis. Despite considerable sparing of function following early unilateral lesions (Vargha-Khadem et al., 1985, 1992; Levine et al., 1987; Aram & Eisele, 1992; Feldman et al., 1992; Stiles & Thal, 1993), recent findings suggest that these insults do, in fact, have adverse effects on later development. Early left, as well as right, unilateral lesions can result in long-term deficits in lexical–semantic and syntactic processes, with subtle differences in the nature and extent of language impairment depending on the side of the lesion (Stiles & Thal, 1993; Bates et al., 1995; Eisele & Aram, 1995). Visual–spatial impairments are likewise evident following both early and later unilateral right-hemisphere lesions (Woods, 1980; Nass et al., 1989; Vargha-Khadem et al., 1991; Stiles & Thal, 1993).

Studies of unilateral brain lesions that have investigated the relationship of age at insult to outcomes have yielded inconsistent results. Several investigations have revealed more extensive language impairments in persons with later, compared to earlier, unilateral left-hemisphere lesions (Lansdell, 1969; Woods & Carey, 1979; Vargha-Khadem et al., 1985; Levine et al., 1987). In contrast, Aram and Eisele (1994) and Riva and Cazzaniga (1986) found that younger age at insult was related to poorer IQ outcomes in individuals with left-hemisphere vascular lesions. Differences in the type of lesion, age at insult, time postinjury, or the nature of the outcome measures may account for these discrepancies. But there is little doubt that early neural reorganization, whenever it occurs, comes at a long-term developmental cost.

Time Since Insult

The effects of time since insult on the outcomes of early brain insults have been less frequently examined than the effects of age at injury. Results from cross-sectional studies have revealed that cognitive weaknesses among children with early brain insults are more prominent in older than in younger age groups. Dennis et al. (1987) compared different age groups of children with congenital hydrocephalus to same-age normal controls on linguistic tasks. According to their findings, the older the age group, the greater the impairments in children with hydrocephalus compared to controls on tasks of efficiency of word finding, grammatical comprehension, and metalinguistic awareness. Wills et al. (1991) found a similar relationship in children with myelomeningocele. In this sample, the older the child at the time of testing, the lower the child's Wechsler Performance IQ and scores on an arithmetic test. In a third cross-sectional study, Banich et al. (1990) examined Wechsler IQ scores in different age groups of children with acquired or congenital hemiplegia. The results from this study showed that time since insult for children with congenital hemiplegia, which is equivalent to age at testing, was negatively correlated with Verbal, Performance, and Full-Scale IQ scores. Similar age differences have been observed in cross-sectional comparisons of children treated with cranial irradiation (Christie et al., 1995; Dennis et al., in press).

The findings from several longitudinal studies also suggest that cognitive and academic skills progress less rapidly with age in some children with early brain insults. Evidence in this regard comes from studies of children with TBI, very low birth weight, hypothyroidism, genetic disorders such as fragile X, unilateral right-hemisphere disease, and exposure to prophylactic cranial irradiation (Hagerman et al., 1989; Fletcher et al., 1990; Rovet, 1990; Marlow et al., 1993; Aram & Eisele, 1994; Radcliffe et al., 1994; Thompson et al., 1994; Anderson & Moore, 1995; Miller et al., 1995). In studies of the sequelae of cranial irradiation treatments and TBI, a lack of age-appropriate cognitive development has been most clearly evident in children who have sustained brain insults prior to age 7 (Radcliffe et al., 1994; Anderson & Moore, 1995). The relative lack of normalization in cognitive and academic skills following TBI in infants and young children stands in marked contrast to the substantial recovery in these abilities observed after TBI in school-age children and adults (Chadwick et al., 1981; Jones, 1992).

Unfortunately, it is not clear if the apparent suppression of normal growth rates after early brain injury reflects deterioration in skills, failure of children to develop at age-appropriate rates, or age-related changes in task complexity. It is also difficult to determine if the adverse consequences of insult become progressively more pronounced over time, or if sequelae remain relatively stable, at least after an initial recovery period. There are several case studies, moreover, that show a pattern of relatively stable if not increasing cognitive abilities over time postinjury (St. James-Roberts, 1981). In a recent study of outcomes in children with congenital hydrocephalus, Brookshire et al. (1995) found relatively constant neuropsychological deficits across a 4-year follow-up interval. There was no evidence in this study that children with shunted hydrocephalus were either catching up to a comparison group over time in verbal and nonverbal abilities, or showing age-related declines in these skills. Different patterns of age-related effects may well be associated with different types of brain insult. Delayed neuropathological changes secondary to cranial irradiation, for example, may help account for the progressive decline in IQ seen in some children treated for cancer (Dennis et al., in press), whereas more static brain lesions may result in different patterns of change over time. Seizure disorder may also contribute to the failure of some groups of children with early insults to maintain age-appropriate progress (Vargha-Khadem et al., 1994). A focus on developmental change, as exemplified by the studies in this symposium, is needed to examine these various possibilities.

Age at Testing

Of the three age-related factors considered in this review, the influence of age at testing is the least well researched. In essence, this factor represents latent or time-lagged se-

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quelae of early brain injury that result from failure to meet new developmental demands. Latent deficits are conceptualized as due to an inability to carry out a new skill or engage in a specific cognitive process, as opposed to a slowed rate of development or a cumulative impairment in functioning. An example of latent effects from the animal literature is the later emerging deficit in delayed response tasks following early dorsolateral frontal lobe lesions in rhesus monkeys (Goldman, 1974). Time-lagged effects in humans are illustrated in a case report by Eslinger et al. (1992), who describe the development of a girl who sustained a frontal lobe aneurysm at age 7 years. Although her childhood years were relatively uneventful, a dramatic increase in social difficulties was noted in adolescence.

Other examples of possible age-at-testing effects include greater verbal memory impairment following TBI in adolescents compared to children (Levin et al., 1988), greater deficits in adaptive behavior and memory in older compared to younger children with shunted hydrocephalus (Holler et al., 1995), the emergence or worsening of behavior problems over time in children who have sustained TBI or other neurological disorders early in life (Brown et al., 1981; Thomsen, 1989; Taylor et al., 1992; Max et al., 1997), and decreases with age in the cognitive abilities of males with fragile-X syndrome (Hagerman et al., 1989; Hodapp et al., 1990). In interpreting the age differences observed in their study, Levin et al. (1988) proposed that advanced memory strategies are especially vulnerable to TBI and that adolescents need to make more use of these strategies to attain "normative" levels of performance. In similar fashion, Eslinger et al. (1992) attributed the changes seen in their patient over time, which continued into adulthood, to a failure to acquire "the executive and self-regulatory processes associated with the frontal lobe . . . at a time when maturation of such processes is critical to psychological development" (p. 768).

It should be emphasized, however, that latent effects may be difficult to detect. Recognition of these effects requires that the investigator determine if sequelae are specifically associated with the age of the child at testing or with developmental transitions in cognitive processes, as opposed to age at injury or time since injury. It is also relevant to note that time-lagged effects have not been consistently documented. Yeates et al. (1995), for example, were unable to replicate the age differences in verbal memory impairment following TBI observed by Levin et al. (1988).

BASES OF AGE-RELATED DIFFERENCES

To account for the greater impact of acquired brain insults in younger children, researchers have proposed that skills undergoing active development at the time of the insult are more susceptible to disruption than previously established abilities (Ewing-Cobbs et al., 1989; Dennis & Barnes, 1994). Given the rapid changes in linguistic and other cognitive abilities during the early childhood years, this phase of development may be particularly liable to neurologic insult (Ewing-Cobbs et al., 1989; Locke, 1993; Neville, 1993; Chapman, 1995). Potential neural mechanisms underlying age differences in disease sequelae include a greater susceptibility of the immature brain to insult, greater effects of early compared to later insult on subsequent neural development, or neural degeneration following early injuries (Banich et al., 1990; Rovet et al., 1990, 1992; Aram & Eisele, 1994). The possibility of a protracted period of vulnerability to neurologic insult is consistent with the fact that brain development continues throughout childhood (Huttenlocher, 1990; Thatcher, 1991; Stuss, 1992; Anderson & Moore, 1995).

A proposed basis for time-since-injury effects is damage to neural systems responsible for skill acquisition (Rourke, 1988; Aram & Eisele, 1992). Evidence that widely distributed cortical and subcortical systems are important for skill acquisition early in life suggests that the learning capacities of young children may be especially vulnerable to brain injury (Stiles & Thal, 1993; Dall'Oglio et al., 1994). Alternatively, early insults may limit the brain's capacity to develop normally or interfere with the timing of neural development (Banich et al., 1990; Dennis & Barnes, 1994). Increasing deficits over time may also be attributed to disruptions in the child's ability to interact with the environment at ages when these interactions are critical to further development (Fletcher et al., 1984; Greenough et al., 1987; Aram & Eisele, 1994; Fischer & Rose, 1994; Anderson & Moore, 1995).

Latent effects are ascribed to delayed manifestations of early brain insults. According to the "functional immaturity" account of latent effects, the consequences of injury to brain regions that are prefunctional at the time of insult will not be fully apparent immediately postinsult. The sequelae of these lesions will only be realized when the damaged areas are needed to subserve a later developing function (Goldman, 1974; Banich et al., 1990).

The "crowding" hypothesis is a variant of this type of explanation applicable to children with unilateral disease. Crowding is said to occur when one brain region is damaged and another part of the brain takes over the functions of the damaged area (Aram & Eisele, 1992). The intact brain region, in turn, has diminished capacity to subserve the functions for which it was originally intended. In other words, later dysfunction occurs because the brain region that would have subserved a given function has become committed to other functions, rather than because of damage to that area *per se*. The crowding hypothesis typically has been used to explain the effects of early left-hemisphere disease on nonverbal abilities (Satz et al., 1994). The "maturational gradient" hypothesis, which assumes that the left hemisphere is more mature, and thus less compromised by insult than the right hemisphere, has been proposed to account for the apparent precedence given to sparing of verbal over nonverbal skills following left-hemisphere insult. However, evidence for such a gradient is equivocal, and recent findings suggest that crowding effects can be observed follow-

ing damage to either hemisphere (Aram & Eisele, 1992; Levin et al., 1996). Additionally, although shifts in language dominance are more likely when brain damage is sustained very early in life, we do not yet have a clear understanding of the conditions necessary for transfer of function to the nondominant hemisphere, or the extent of hemispheric equipotentiality for verbal and nonverbal abilities (Satz et al., 1994; Vargha-Khadem et al., 1994; DeVos et al., 1995).

METHODOLOGICAL NEEDS

Examination of the Separate Influences of Age-Related Factors

The frequent confounding of the three age-related factors in studies of childhood brain injury is a major obstacle to understanding of their unique effects. If testing is conducted within a limited age range, for example, children with earlier brain insults will tend to be older than children with later insults (Dennis et al., in press). If only the short-term consequences of brain injury are assessed, children who are younger at the time of insult will also be tested at earlier ages than children with later-occurring insults. The factors time since insult and age at testing are similarly confounded in following children with congenital brain disease. With a few exceptions, researchers have typically failed to consider these confounds (Banich et al., 1990; Silber et al., 1992; Aram & Eisele, 1994; Dennis et al., in press). In the present symposium, the studies of Anderson et al. (1997), Ewing-Cobbs et al. (1997), and Yeates et al. (1997) illustrate methods for distinguishing the influences age at injury *versus* time since injury.

A further issue with regard to the study of age-related factors has to do with the manner in which age is conceptualized. The use of broad-band age categories is warranted if there is a reason to compare children above and below a preestablished age level. As an example, the above-cited evidence that children younger than 7 years of age are more vulnerable than older children to TBI and cranial irradiation (Radcliffe et al., 1994; Anderson & Moore, 1995; Dennis et al., 1995) would help justify comparisons of these two age groups. Frequently, however, there is little basis for categorizing children into age groups. As illustrated by the findings of Barnes et al. (1996), it is also conceivable that age differences vary for different measures of outcome. In light of these considerations, and to enhance statistical power (Cohen, 1988), it may often be preferable to analyze age as a continuous variable.

Longitudinal Follow-up

A major benefit of longitudinal follow-up is that it permits assessment of developmental sparing in terms of deviations from expected individual developmental trajectories, rather than in terms of group differences at discrete time points after insult (Fletcher et al., 1995). Analyses of individual growth trajectories are more sensitive than cross-sectional comparisons to changes over time, and less subject to recruitment biases. In making cross-sectional comparisons, it is often difficult to know if all age groups are equally representative of disease severity. To the extent that clinical services tend to lose contact with less severely affected children over time, recruitment of children from these sources may yield artifactual age effects (Banich et al., 1990).

Other advantages of longitudinal designs include the opportunity they provide to examine change at the time it occurs rather than retrospectively, to explore cumulative risks or chains of reactions between the child and environment, to chart the course of changes in the child and family over time, and to study correlates of growth or decline (Rutter, 1993; Fletcher et al., 1995). The study by Kinsella et al. (1997) in this symposium demonstrates the validity of post-acute neuropsychological test findings as predictors of long-term deficits in achievement.

A special virtue of prospective recruitment of children with TBI is that it permits the investigator to obtain information about premorbid child and family status soon after injury (Rutter et al., 1980; Rivara et al., 1994). Problems associated with retrospective recall, although potentially an issue even when information is provided immediately after insult, become even more problematic with increasing time postinjury. Information regarding the child and family status prior to the child's brain insult enables the researcher to make a more precise determination of injury consequences. According to findings reported by Yeates et al. (1997) in this symposium, the status of the family prior to insult is also useful in predicting injury consequences.

An additional advantage of longitudinal designs is that they allow examination of the manner in which development is affected by brain insult. The hypothesis that skills that are not yet well developed at the time of insult are more susceptible to disruption than are already established abilities (Dennis & Barnes, 1994) would lead one to anticipate a pattern of disease effects similar to that shown in Figure 1. Hypothetical effects of brain insult on an established skill are illustrated in Figure 1a. Data from studies of children with TBI (Chadwick et al., 1981; Jaffe et al., 1995) indicate that the initial effect of insult at t_1 may be the most dramatic, resulting in a deficit *a* in Figure 1a. Improvements in performance with age would then occur at some linear or nonlinear growth rate *b*. Growth over time in an unaffected child would be predicted based on either practice effects or skill development across the follow-up interval. For a child with a brain insult, however, recovery would also be occurring, and would potentially result in an even steeper slope of change than that found in an unaffected individual. At some point in time, t_2, recovery would be expected to reach an asymptotic level, corresponding to residual deficit *c*. A further possibility is that a child with brain insult may show initial recovery to a level *c*, but then begin to fall further behind as a skill becomes more complex or as new learning is required.

In contrast, the impact of brain insult on a to-be-acquired or developing skill, illustrated in Figure 1b, may not be readily apparent at time t_1 (parameter *a*). The reason for

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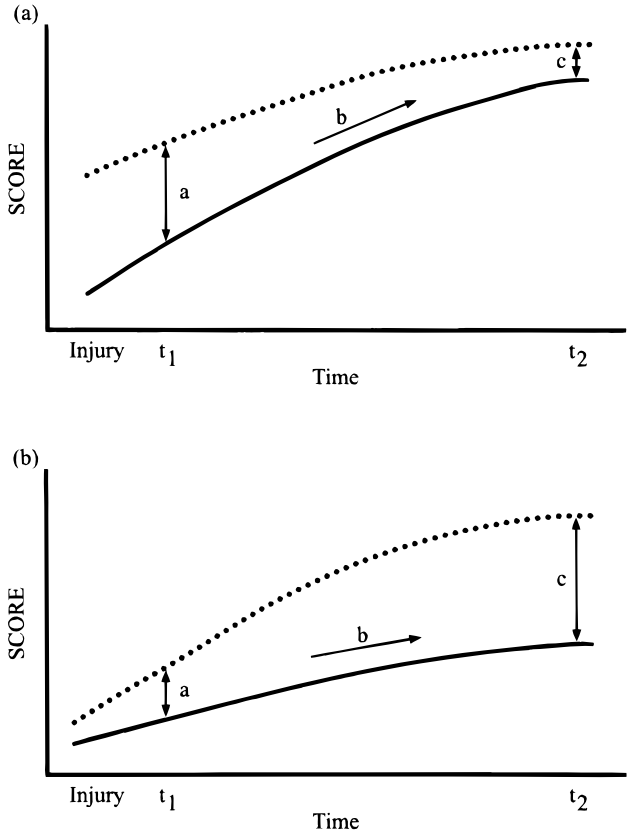

Fig. 1. Hypothetical developmental changes in established (1a) *versus* to-be-acquired (1b) skills in children with brain insults (solid line) and in unaffected children (broken line).

this is that the skill would not yet have fully emerged, even in an unaffected child. Sequelae, nevertheless, would become more apparent over time as the child with brain insult fails to acquire the skill at the expected rate. In this instance, improvements in performance over time (parameter *b*) would take place less rapidly in the child with brain insult than in the unaffected child, and the former child's deficit *c* at t_2 would thus be greater than the initial deficit *a*.

The major advantage of this conceptualization of sequelae is the emphasis it places on developmental sparing as a complex, multicomponent process. The influence of age-related factors can be examined in relation to each of the several components of this process. Although age is typically considered in terms of performance relative to an "expected" level of functioning at a given point in time (parameter *a* in Figure 1), age-related factors may also be related to rates of change over time (parameter *b*) or to the extent of residual impairment present at the point at which the child's initial recovery reaches a plateau (parameter *c*). Isolating distinct parameters of the developmental impact of brain lesions may be of additional value in exploring biological and environmental influences on outcomes. The paper by Yeates et al. (1997) in this series demonstrates the benefits of this type of approach to longitudinal data analysis.

Some of the problems encountered in doing longitudinal research include the possibility of practice effects, selective attrition, and the influences of study participation on outcomes. Although there is no foolproof method for dealing with the effects of repeated testing (Brooks et al., 1984), one workable approach is to compare changes in the children with brain insults to changes in a comparison group. Attrition is problematic only if it potentially biases study findings. It is therefore important to compare participants who drop out with those who remain involved in terms of background variables and outcomes obtained prior to dropout (Cicchetti & Nelson, 1994; Francis et al., 1994). Suspected biases can then be taken into account in interpreting the results. Attrition is minimized by arranging for ongoing contacts with families, providing clinical assistance and reasonable stipends for participation, and being willing to accommodate to family schedules (Streissguth & Giunta, 1992). Making referrals and recommendations based on assessment results may have a positive influence on children, but interventions can be monitored to explore relationships between service provision and outcomes.

Appropriate Assessments of Outcome

Studies of the consequences of early brain injury fail to suggest a unitary pattern of neuropsychological impairment (Rutter, 1981). Certain skills, however, appear to be particularly vulnerable to disruption following TBI and other childhood brain insults, including speeded performance, memory and learning, visuoperceptual and attentional skills, and executive function (Rutter, 1981; Goldstein & Levin, 1985; Dennis, 1991; Knights et al., 1991; Levin et al., 1993; Taylor et al., 1996). Assessment of these skills is valuable in detecting more subtle degrees of brain damage and in tracking cognitive recovery. Assessment of specific cognitive processes may also provide clues regarding the types of abilities that are most vulnerable to earlier brain insults, or most closely associated with injuries to circumscribed brain regions (Dennis, 1991; Dennis et al., 1995). An example of this approach is provided in the present symposium by Levin and colleagues, who show the value of a specific task in exploring age differences in the vulnerability of executive functions to frontal lobe damage.

Assessments should additionally include measures of behavior, school performance, and academic achievement (Brooks, 1990; Fletcher et al., 1990). One reason to include these assessments is that they may reveal brain-related impairments not evident in traditional neuropsychological testing (Dennis, 1991; Ylvisaker, 1993). A second reason is that environmental factors may have stronger influences on measures of behavior and academic competence than on neuropsychological skills (Taylor & Schatschneider, 1992). Behavior rating scales developed for general use have had mixed success in detecting sequelae of childhood brain disease (Fletcher & Ewing-Cobbs, 1991; Perrott et al., 1991). Consequently, it may be worthwhile to consider behavior ratings developed specifically for children with brain in-

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sults (Rivara et al., 1994; Barry et al., 1996; Roberts & Furuseth, in press). It may also be useful to supplement behavior ratings with interviews and observations (Fletcher & Ewing-Cobbs, 1991; Max et al., 1997).

A particularly vexing measurement problem encountered in following children over time and in comparing different age groups relates to the fact that most outcome measures are age limited. Tests appropriate for infants, for example, do not apply to preschoolers, and preschool test procedures can not be used in assessing older children. One approach to this problem is to use different tests according to the age of the child, and then to treat tests that measure similar constructs as equivalent for the purposes of analysis (Ewing-Cobbs et al., 1989). The major limitation of this approach is that any age-related variation in outcome may be ascribed to differences in test procedures rather than to age differences *per se* (Mulhern et al., 1992). Variance due to type of test may also obscure important developmental effects. A means to contend with this problem is to restrict group comparisons or repeated measures analysis to subsets of data involving uniform test procedures. The major drawbacks of this suggestion are the reduced sample sizes that result, and the researcher's inability to examine changes across broader age ranges. Another possibility is to examine the effect of change in type of test as a variable in the analysis (Silber et al., 1992; Radcliffe et al., 1994). The studies of Ewing-Cobbs et al. (1997) and Anderson et al. (1997) reported in this symposium illustrate current efforts to grapple with this problem.

A related measurement issue is that even tests with the same or similar content may not measure the same processes in younger and older children (Fletcher et al., 1984; Stiles & Thal, 1993). Changes over time in the degree of impairment due to brain insult may thus reflect age-related differences in what tests measure, rather than any real improvements or declines in the sequelae of brain insult over time. Appreciation of the cognitive processes that contribute to test performance is thus essential.

Examination of Factors That May Be Confounded With Outcomes

Developmental difficulties following early brain insults may not be due to the brain insult itself, but to other preexisting or concurrent conditions. Sequelae can only be assessed by considering confounds, such as congenital conditions, neurological disorders other than the brain lesion of interest, or suboptimal environmental circumstances. Comparison of affected children to normal siblings or to unaffected children from similar socioeconomic backgrounds is one method for isolating the sequelae of brain insult (Taylor et al., 1992, 1996; Grimwood et al., 1995). To assess sequelae of TBI, several investigators have advocated for inclusion of an other-injury group, such as children with orthopedic injuries only (Rutter et al., 1980; McKinlay & Brooks, 1984; Goldstein & Levin, 1985; Oddy, 1993). The advantage of comparing children with TBI to children with non-CNS traumatic injuries is that it allows the investigator some degree of control over the risks associated with accidental injury, the effect of the accompanying non-CNS trauma on the child, and the influence of environmental stressors, such as hospitalization experiences, missed school, and family distress, on outcomes (Brown et al., 1981; Lescohier & DiScala, 1993; Taylor et al., 1995a).

Information pertaining to the child's cognitive, academic, and behavioral functioning prior to injury is especially relevant in evaluating the consequences of TBI. In light of evidence of above average rates of preinjury behavioral and academic problems in at least some subgroups of children with TBI (Oddy, 1993; Goldstein & Levin, 1985), data on premorbid functioning is useful in interpreting group differences in outcomes (e.g., severe TBI *vs*. moderate–mild TBI, or TBI *vs*. non-CNS injury). Two recent studies failed to find higher-than-normal rates of preinjury problems in children with TBI (Donders, 1992; Prior et al., 1994). Nevertheless, assessment of outcomes relative to preinjury functioning permits more precise determination of injury sequelae. Estimates of premorbid functioning can be based on sociodemographic indices, the results of group-administered school testing, or ratings of preinjury behavior and school performance completed by parents and teachers (Levin & Eisenberg, 1979; Rutter et al., 1980; Rivara et al., 1994; Taylor et al., 1995a; Yeates & Taylor, 1997). The effect of injury can then be examined in terms of differences between these estimates and postinjury ratings or test performances. An alternative method for reducing confounds between preinjury status and injury outcomes is to screen out children with preexisting problems (Fletcher et al., 1990).

Evaluation of the Nature and Severity of Brain Insult and of Other Individual Factors

Because age differences in the consequences of early brain disease depend on the nature and severity of brain insult, it is important for researchers to define the types of brain insults sustained by children in the sample and, if possible, to describe the size and location of brain lesions. Sequelae may be restricted to subgroups of children who sustained the most severe insults (Shaffer et al., 1980; Chadwick et al., 1981; Levin et al., 1995; Dennis & Barnes, 1996). The level of injury severity needed to produce measurable sequelae may even be age dependent. Data reported in this symposium by Gronwall (1997), for example, raise the possibility that younger children are more susceptible to milder TBI than older children. A further reason to investigate the nature of the brain damage is that the neuropathological consequences of some types of insults may vary with the age of the child (Packer et al., 1989; Anderson & Moore, 1995). In the latter instance, differences in pathophysiology, rather than in neural organization, may be responsible for age-related variations in outcomes.

The severity of the insult can be assessed in terms of the child's neurological status during the acute phase of the injury or disease, as has been the case in studies of meningitis (Taylor et al., 1992; Grimwood et al., 1995), or, for children with TBI, in terms of the degree of coma, period of unconsciousness, or interval of posttraumatic amnesia (Ewing-Cobbs et al., 1990). Other markers of pathology include the amount of irradiation treatment given to a child with cancer (Silber et al., 1992) and the locus and or extent of brain damage evident in imaging studies (Chadwick et al., 1981; Dennis et al., 1981; Fletcher et al., 1992). As demonstrated by Levin et al. (1997) in the present symposium, quantitative neuroimaging studies hold considerable promise in this regard.

The consequences of early brain injury may also be related to factors such as sex and social status (Taylor et al., 1992). In some instances, the sequelae of early neurological insults have proved to be sex dependent, or sequelae have varied in relation to social factors (Taylor et al., 1993; Bendersky & Lewis, 1994; Breslau, 1995). Investigation of age differences may thus require that the latter factors be taken into account.

Consideration of Environmental Influences

Justification for examining environmental influences on development following childhood brain insults is provided by studies showing that brain insults in children can have negative consequences for their families (Waaland & Raines, 1991; Taylor et al., 1995a; Rivara et al., 1996; Wade et al., 1996). Family adversity, whether it is preexisting or stems from the injury itself, is associated in turn with problems in child functioning after insult (Brown et al., 1981; Casey et al., 1986). Additional justification for examining social influences on sparing is provided by studies of laboratory animals indicating that early experience affects brain organization, and that manipulation of the postlesion environment influences subsequent learning capacities (Greenough et al., 1987; Kolb, 1989; Neville, 1993; Fischer & Rose, 1994). Until recently, however, few studies of children have included detailed and systematic assessments of family or other environmental variables (St. James-Roberts, 1979, 1981; Fletcher et al., 1984). The study by Yeates et al. (1997) represents an effort to address this shortcoming.

Environmental factors to consider include family distress and burden associated with the child's condition, family functioning, and the resources the child and family have at their disposal to cope with their needs (Waaland & Raines, 1991; Carlson-Green et al., 1995; Taylor et al., 1995a; Rivara et al., 1996). Sociodemographic variables, parent psychological adjustment, and patterns of family interactions may be useful in identifying families at greatest risk for difficulties adjusting to brain insults in children. Family variables may be of additional value in identifying children at risk for adverse long-term cognitive or behavior problems (Wade et al., 1995; Yeates et al., 1997). Related research involving children with chronic illness suggests the need to evaluate contextually relevant family stressors, such as disruptions in family routines caused by the child or the strain on parents associated with the child's medical needs (Taylor et al., 1995a; Rivara et al., 1996).

The pattern of relationships between social variables and different outcome measures may provide clues as to which aspects of development are most subject to environmental modification. Environmental factors may be especially important determinants of outcomes that are highly experience-dependent, such as syntactic development, academic achievement, and behavioral adaptation (Taylor et al., 1992; Taylor & Schatschneider, 1992; Greenough et al., 1987; Neville, 1993). Discovery of associations between environmental factors and outcomes would suggest ways in which to work with the child and family to promote more positive outcomes. An additional benefit of evaluating the post-injury environment is that it assists the researcher in sorting out the primary consequences of brain insult from secondary, environmentally mediated, sequelae (St. James-Roberts, 1979; Goldstein & Levin, 1985; Rutter, 1993).

DISCUSSION AND CONCLUSIONS

Any viable explanation for the finding that sequelae of brain insults are more pronounced or enduring in younger children than in older children or adolescents must be able to account for two seemingly contradictory observations. The immature brain appears to be more vulnerable to injury, but considerable sparing of function is also possible, and implies a high degree of neural plasticity early in life (Aram & Eisele, 1992; Vargha-Khadem et al., 1994). The major conclusion of this review is that plasticity is incomplete. Although developmental sparing can occur, the plurality of studies in this area indicate that brain insults have more significant long-term consequences for infants and young children than for school-age children or adults. Current findings further suggest that the sequelae of childhood brain lesions either remain relatively constant over time since insult, or worsen. With the exception of early focal lesions (Feldman et al., 1992; Stiles & Thal, 1993) and initial recovery from acute insults (Chadwick et al., 1981; Jaffe et al., 1995), there is no evidence for a lessening of the effects of injury with age. Declines in functioning over age, when they occur, may reflect a slowness in the rate of acquisition of new skills, greater difficulties in higher-level, compared to lower-level, cognitive abilities, or even pathophysiological processes.

While the picture might seem bleak for individuals who have sustained brain insults early in life, long-term sequelae vary substantially depending on the nature of the insult, the manner in which outcome is assessed, and experiential factors (St. James-Roberts, 1979). Considerable sparing or attenuation of deficits over time is possible under some circumstances (Feldman et al., 1992; Stiles & Thal, 1993; Dall'Oglio et al., 1994). Moreover, our current knowledge on age-related influences is limited and we are only beginning to come to terms with the methodological flaws of previous research in this area. Due to frequent confounds

between age at insult, time since injury, and age at assessment, as well as other limitations of study design, only tentative conclusions can be drawn with regard to the unique effects of age-related factors on developmental outcomes.

The practical goals of research on developmental sparing following early brain insults are to enhance our understanding of which children are at risk, the type of risks they face, and how to optimize their development. Theoretical aims are to identify sources of variability in outcomes, developmental differences in brain–behavior relationships and in neural reorganization following brain damage, and the contribution of biological and social factors to sparing (Rourke, 1988; Aram & Eisele, 1992; Dennis & Barnes, 1994; Fletcher et al., 1995; Taylor et al., 1995a; Dennis, in press). The current symposium demonstrates a number of efforts to further progress in these directions.

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