Effect of Cerebral Lesions on Continuous Performance Test Responses of School Age Children Born Prematurely

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Examined attention skills, as measured by the Continuous Performance Test (CPT), in a group of 64 children born premature and 40 full-term children, ages 6 to 8 years. Premature children were classified by neonatal cerebral lesions into no lesion, mild lesion, and severe lesion groups. It was predicted that severity of lesion would be associated with CPT performance. While mean differences among the groups of prematures did not reach significance, children with severe lesions made significantly more errors of omission and commission than the full-term comparison group. Children with mild lesions were poorer than full terms in

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errors of commission. Children with no lesions also made more errors of omission and commission than full terms, suggesting attention deficits secondary to prematurity even in the absence of identified brain lesion. With increasing severity of lesion, increasing percentages of each group were found to perform more than 2 SD below the mean in errors of commission. Results suggest that premature children, with and without identified lesions, are at risk for attention deficits.

KEY WORDS: premature infant; longitudinal outcome; neuropsychological measures; attention deficit.

In the last decade, technological advances in the neonatal intensive care nursery (NICU) have resulted in significantly increased rates of survival for very premature infants. Among those medical interventions contributing to these gains include jet ventilation, use of steroids prenatally and postdelivery, and most recently, widespread use of surfactant to enhance lung development in the neonate (Kraybill et al., 1995). These medical interventions are designed to reduce the impact of the many medical complications, especially those relating to respiratory function, that threaten the survival of the premature child. This has resulted in increased survival for smaller and smaller prematures, but it is also this group of infants that is at highest risk for complications that may affect long-term developmental functioning (Bhusan, Paneth, & Kiely, 1993). The question continues to be raised as to whether improved survival is resulting in increasing numbers of children with disabilities.

To better understand the developmental risks to which NICU survivors are subject, but which may not be clear in early childhood, recent longitudinal studies of premature children have extended follow-up examinations to school age. This provides a greater capability to assess those developmental abilities that affect learning. Longitudinal studies also provide predictive information about what types of neonatal complications are associated with what type of later disability. This knowledge may enable health and education professionals to monitor particular areas of development and provide early intervention where appropriate.

The majority of studies of developmental outcome at school age have focused on overall cognitive performance measured by IQ. Relatively good outcome, in terms of intellectual functioning in the average range, can be expected for larger prematures and even for those very premature infants who escape severe respiratory and central nervous system complications (Hack et al., 1994; Teplin, Burchinal, Johnson-Martín, Humphry, & Kraybill, 1991). A number of studies have looked at more specific areas of developmental performance. Findings of these studies suggest that very premature infants are at risk for developmental deficits in the areas of perceptual motor functioning (Jongmans, Hender-
son, de Vries, & Dubowitz, 1993; Saigal, Szatmari, Rosenbaum, Campbell, &
King, 1991), fine motor performance (Klein, Hack, & Breslau, 1989), and show
poorer math and reading achievement than normal birth weight children
(Klebanov, Brooks-Gunn, & McCormick, 1994). These specific deficits may
account for the substantial percentage, nearly 50% of extremely low birth weight
prematures, who experience academic failure or require special education despite
having IQs in the normal range (Hack et al., 1994).

Some studies have looked at the impact of specific neonatal complications
on later development. This research suggests that the greatest risk for later
disability is associated with extensive ischemic cerebral hemorrhage and peri-
ventricular leukomalacia (Volpe, 1991). With improved ultrasonography and
refined Magnetic Resonance Imaging (MRI), cerebral lesions resulting from
these insults are being more carefully defined and their associations with later
disability explored. This has led to studies of comparative performance of prema-
tures grouped according to similar lesion types. Children who have experienced
milder degrees of hemorrhage are not likely to experience any major neurological
or intellectual deficit, and, even for children with severe hemorrhage, outcome is
not uniformly poor (De Vries et al., 1985; Roth et al., 1993).

A number of studies of very low birth weight prematures (Hack et al., 1994;
Szatmari, Saigal, Rosenbaum, Campbell, & King, 1990; Teplin et al., 1991)
have noted particular problems with sustained attention at school age. This has
usually been assessed by teacher and/or parent ratings of behaviors associated
with difficulties staying on task, easy distractibility from a task, or fidgetiness.
Problems with attention certainly could also contribute to the poor school
achievement demonstrated by a sizable proportion of very low birth weight
prematures, despite normal intelligence.

Although the neuroanatomical correlates of attention are not yet fully
known, dominant theories suggest that many important attentional functions are
localized in frontal regions of the brain. Attention is also represented by an
anatomical network involving many different structures (Van Zomeren &
Brouwer, 1994). In cases of specific brain trauma, such as closed head injury,
problems with attention certainly could also contribute to the poor school
achievement demonstrated by a sizable proportion of very low birth weight
prematures, despite normal intelligence.

Attention deficits in school age children are often seen in conjunction with
hyperactivity, and may be symptomatic of Attention Deficit Hyperactivity Disor-
der. Diagnosis of the disorder often relies heavily on checklist ratings of parents
and teachers. Behaviors associated with hyperactivity may be easier to observe
than those reflective of primary attention problems. In an effort to broaden
assessment strategies for measuring attention deficit, a number of objective,
neuropsychological assessment techniques have been developed. Among the
tasks to assess attention deficits, is the Continuous Performance Test (CPT),
originally developed by Rosvold, Mirsky, Sarason, Bransome, and Beck (1956).
This test has been adapted in a number of variations such that it can be used with
children and adults. There is some controversy as to the ecological validity of these laboratory measures, that is, whether they are predictive of behavior in natural settings (Barkley, 1991). A number of investigators have found correlations between performance on CPT and academic achievement (Gordon, Mettelman, & Irwin, 1994; O’Brien et al., 1992).

Prematures with documented cerebral lesions appear to be a group at particular risk for attention difficulties. Although researchers have begun to look at more specific areas of cognitive function in assessing developmental consequences of prematurity, little has been done to investigate the impact of specific neonatal complications on later cognitive performance. This study was designed to assess attention skills at school age in a group of premature children with well-documented neonatal cerebral lesions. It was hypothesized that degree of attention deficit would be associated with severity of cerebral lesion. An additional interest was the role prematurity in general might play in the development of attention skills in children.

**METHOD**

**Participants**

Subjects were drawn from a group of children born prematurely, enrolled in a collaborative follow-up study by the Hammersmith Hospital and the Institute of Education, London. They were enrolled as infants after delivery at the Hammersmith if they were 34 weeks gestation or less at birth, had no major congenital anomaly, and had three cranial ultrasound examinations in the first week of life. The larger study was aimed at examining the relationship between early neurological status and later development. Performance of the children at 6–8 years of age on measures of neuromotor and perceptual motor functioning is reported elsewhere (Jongmans et al., 1993).

The original cohort consisted of 212 children, 29 of whom were lost to follow-up. No significant differences were found between birth weights and gestational ages of children evaluated at 6 years, and those lost to follow-up. Eleven children were found to be too impaired, due to multiple cognitive, sensory, or motor disabilities, to complete the testing. These children had all sustained severe cerebral lesions in the neonatal period. During the 6-month recruitment for the current study, 64 of the children were between the ages of 6 and 8 years and consented to participation. The children were born between May 1983 and April 1985. No significant differences were found between the children evaluated for the current study and the remaining children tested for the larger study in terms of birth weight, gestational age, or incidence of cerebral lesion. A compar-
A sample of full-term children was drawn from regular education primary school classrooms in the London metropolitan area, representing a similar range of socioeconomic backgrounds to this premature group, primarily lower middle to middle class. The comparison children were matched with the premature sample in terms of age, sex, and ethnicity. Forty full-term children, who by report of school principal and classroom teacher were not having particular academic difficulties, participated in the study. The mean age for the premature sample was 80.6 months and for the full-term group, 81.3 months. The premature sample at birth ranged in gestational age from 26 to 34 weeks and had a mean birth weight of 1227.5 grams. Demographic characteristics of the two groups appear in Table I.

To evaluate the impact of severity of cerebral lesion on attention task performance, the premature children were classified by the characteristics of their neonatal ultrasound. Lesions were classified as periventricular densities (PVD), sometimes called “flares,” cystic periventricular leukomalacia (PVL), or intraventricular hemorrhage (IVH). They were diagnosed as PVD or PVL if unilateral or bilateral periventricular echogenic lesions were present on at least three scans in the coronal and parasagittal plane. If they did not become cystic they were diagnosed as PVD; if they broke down into multilocular lesions they were classified as PVL. Periventricular or intraventricular hemorrhages were graded according to the three-point grading system of Levene (1990). Grade I reflects a small hemorrhage confined to the germinal layer; Grade II, a larger germinal layer hemorrhage extending downwards into the basal ganglia; Grade III, a hemorrhage extending into the brain parenchyma. This classification does not take into account the presence of blood in the ventricles or their size, as does the system of Papile, Burstein, Burstein, and Koffler (1978), the grading used most widely in the United States. A separate notation (Grade IIB) was introduced, in an adaptation of the Levene grading by DeVries et al. (1985) and DeVries, Eken, and Dubowitz (1992), to identify larger hemorrhages where the blood distends the ventricles. Grade I is equivalent in both systems; Grade IIA is the same as Papile et al.'s Grade II lesions; IIB is equivalent to Papile et al.'s Grade III, while Grade III is similar to Grade IV in the Papile system.

The classification of the premature children into groups based on lesion characteristics for the current study consisted of:

- No lesion group (n=22): consistently normal scans.
- Mild lesion group (n=32): Grade I or IIA IVH; PVD “flares”; or mild ventricular dilatation in the absence of hemorrhage.
- Severe lesion group (n=10): Grade IIB or Grade III IVH; or multicystic PVL.

Demographic characteristics, including birth weight, gestational age, sex, ethnicity, and age at testing, of the children born prematurely grouped by lesion...
Table I. Demographics

<table>
<thead>
<tr>
<th></th>
<th>Total group (n = 64)</th>
<th>No lesion (n = 22)</th>
<th>Mild (n = 32)</th>
<th>Severe (n = 10)</th>
<th>Full-term comparison sample (n = 40)</th>
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<tbody>
<tr>
<td>Age at testing</td>
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<tr>
<td>Months</td>
<td>80.6 ± 5.4</td>
<td>81.0 ± 5.3</td>
<td>79.7 ± 4.9</td>
<td>82.7 ± 7.1</td>
<td>81.3 ± 5.6</td>
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<tr>
<td>Sex</td>
<td></td>
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<tr>
<td>Boys</td>
<td>33 (52)</td>
<td>7 (32)</td>
<td>21 (66)</td>
<td>5 (50)</td>
<td>22 (55)</td>
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<tr>
<td>Girls</td>
<td>31 (48)</td>
<td>15 (68)</td>
<td>11 (32)</td>
<td>5 (50)</td>
<td>18 (45)</td>
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<tr>
<td>Ethnicity</td>
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<tr>
<td>White</td>
<td>48 (75)</td>
<td>18 (82)</td>
<td>21 (66)</td>
<td>9 (90)</td>
<td>30 (75)</td>
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<tr>
<td>Black Asian</td>
<td>12 (19)</td>
<td>1 (4)</td>
<td>10 (31)</td>
<td>1 (10)</td>
<td>5 (12.5)</td>
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<td>Birth weight</td>
<td></td>
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<tr>
<td>Grams</td>
<td>1227.5 ± 341.4</td>
<td>1295.4 ± 248.8</td>
<td>1230.9 ± 406.1</td>
<td>1067.0 ± 253.0</td>
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<td>Gestational age</td>
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<td>Weeks</td>
<td>29.2 ± 2.5</td>
<td>30.4 ± 1.7</td>
<td>29.4 ± 2.3</td>
<td>27.7 ± 2.2</td>
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<tr>
<td>Range</td>
<td>26–34</td>
<td>28–34</td>
<td>26–33</td>
<td>26–31</td>
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<td>IQ (estimated)</td>
<td>104.0 ± 13.4</td>
<td>106.1 ± 13.0</td>
<td>106.2 ± 12.5</td>
<td>92.3 ± 11.7a</td>
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*Numbers in parentheses are percentages.

* p < .009.
severity, appear in Table I. While not reaching significance, there was a tendency for children with severe lesions to have been born at lower gestational age and birth weight.

**Measures**

All children were administered the CPT (Loong, 1991). This automated measure is designed for use on an IBM-PC compatible computer. This particular CPT measure was selected because it could be administered on a laptop computer, enabling ease of administration across sites. It has been used as part of broader neuropsychological batteries identifying attentional difficulties in children and adults (Kay & Horst, 1988). This version of the task requires the child to view a series of individually appearing letters, and to strike the space bar whenever the letter A appears directly after the appearance of the letter X. The letter X serves as a warning signal that may or may not be followed by the target stimulus. The task can be set to run for a specific length of time. It is designed for evaluating sustained attention and monitoring. Monitoring refers to a cognitive process in which the individual must be alert to the appearance of target stimuli presented at a high rate, with a high signal to nonsignal ratio (Van Zomeren & Brouwer, 1994).

Errors on CPT fall into two major categories. The first are errors of omission in which the subject fails to hit the key when the A appears. This type of error reflects lapses in attention, distractibility from the task, or slow cognitive processing of the presence of the warning signal. The second type of error is an error of commission. For this type of error, the child strikes the key when the target letter has not been preceded by the signal letter, or in response to a nontarget letter. This usually occurs when the child cannot inhibit the response and may be seen especially in children with impulsivity problems (Barkley, Fischer, Newby, & Breen, 1988).

In an effort to contrast the performance on a standardized attention measure with a behavioral rating scale measure, parents of the premature children were asked to complete the Child Behavior Checklist (CBCL; Achenbach & Edelbrock, 1983). Parents of the full-term comparison children were unavailable for completion of this measure. The CBCL is composed of a number of subscales. For the purposes of the current study, only the Hyperactivity subscale was considered, which measures behaviors relating to immaturity, learning problems, and inattention as well as hyperactivity.

An estimated IQ score based on the British Abilities Scale (Elliot, Murray, & Pearson, 1983) was available for all premature children. This test was administered as part of the larger longitudinal outcome assessment described elsewhere (Jongmans et al., 1993). Although IQ estimate means for the three groups of
prematures were all in the average range, scores for the children with severe
lesions were significantly lower than for the other two groups which were similar
to each other, one-way ANOVA $F(2, 63) = 5.11, p < .009$ (see Table I). The
exclusion of children too disabled to complete the test measures, all of whom
were classified with severe lesions, unavoidably biased the severe lesion group to
more intact children.

Procedure

Families of children in the desired age range, enrolled in the larger follow-
up study, were solicited for their interest in involvement in the current study. If
the families gave informed consent, children were seen either in conjunction with
the follow-up assessment, or at a separate visit.

Children were administered the CPT while seated comfortably at the key-
board. The examiner was a pediatric psychologist, unfamiliar with the child's
neonatal history. Testing was done in a quiet room with only the child and
examiner present. Standardized instructions were given for the CPT task. The
automated task was set at a 5-minute trial, as had been done by the task's
developer in measuring attention of learning-disabled and normal children, with
significant correlations to performance on the Stroop Color-Word Test and the
completed the CBCL during their child’s testing.

RESULTS

To test the hypothesis that severity of cerebral lesion would be associated
with performance on attention skills, mean CPT raw scores were compared
among the full-term comparison sample and the three groups of premature
children. Means and standard deviations for the three groups of premature children
and the full-term comparison group on the two measures of CPT performance are
provided in Table II. CPT-Missing represents errors of omission and CPT-Wrong

| Table II. Means and Standard Deviations of CPT and CBCL |
|------------------|----------|--------|--------|----------|
|                  | Full term| No lesion| Mild | Severe   |
| CPT-Wrong (commission) | 10.5 ± 10.4 | 22.2 ± 29.9* | 27.7 ± 26.5 | 42.6 ± 35.5 |
| CPT-Missing (omission)   | 10.9 ± 7.0   | 15.9 ± 9.0*  | 15.3 ± 8.8   | 18.0 ± 11.0  |
| CBCL-hyperactivity       | —          | 58.1 ± 6.2    | 59.2 ± 5.3    | 58.5 ± 10.7   |

*p < .03, full-term vs. no lesion group.

*p < .014, full-term group vs. no lesion group.
Effect of Cerebral Lesions represents errors of commission. Analysis of covariance, covarying for age at testing, was performed yielding a significant main effect for CPT-Wrong and CPT-Missing, CPT-Wrong: \( F(3) = 6.25, p < .001 \); CPT-Missing: \( F(3) = 3.68, p < .015 \). A significant effect of age at testing was found for CPT-Missing, \( F(1) = 15.15, p < .001 \), but not for CPT-Wrong.

To look at the effect of prematurity per se on CPT performance, an ANCOVA, covarying for age at testing, was performed contrasting prematures without lesions with the full-term comparison sample. Again, a significant main effect was found for CPT-Wrong, \( F(1) = 4.977, p < 0.03 \), and CPT-Missing, \( F(1) = 6.411, p < .014 \), with prematures without lesions performing more poorly than the full-term comparison group.

To further illustrate differences between performance of the prematures without lesions and the full-term comparison group as a function of age, regression lines are presented in Figure 1(A and B) looking at performance within each group. For CPT-Wrong there was no significant age regression in either group; full-term comparison group, \( F = 2.23, p = .14, R^2 = .06, B = -.44 \); prematures, \( F = 0.15, p = .70, R^2 = .008, B = -.49 \). Older children did not perform significantly better than younger. For CPT-Missing there is a significant age regression for both groups; full-term comparison \( F = 5.04, p < .03, R^2 = .117, B = -.43 \); prematures \( F = 5.38, p < .03, R^2 = .212, B = -.781 \). The regression slope is steeper for the premature group. While at younger ages, the prematures performed more poorly than full-term children, at older ages they performed similarly to the comparison group.

Because age was a significant covariate for CPT-Missing, and because no standardized age-based norms were available for British children in this age group for the CPT measure, standardized residuals were calculated for raw scores of the premature children based on scores of the full-term comparison children. Standardized residual scores for each of the groups were then compared using the Kruskal-Wallis one-way analysis of variance. Group effects were found for CPT-Wrong standardized residual scores, \( H(3) = 21.849, p < .0001 \), and for CPT-Missing, \( H(3) = 9.095, p < .02 \). To ascertain the specific effect of group on both CPT-Missing and CPT-Wrong standardized residual scores, post hoc comparisons were performed using the Tukey-HSD following a one-way analysis of variance; CPT-Wrong: \( F(3, 100) = 6.299, p < .0006 \); CPT-Missing: \( F(3, 100) = 3.588, p < .016 \).

Results of the post hoc Tukey-HSD procedure (with significance set at \( p < .05 \)) yielded a significant difference for CPT-Wrong standardized residual scores between the full-term group and the mild lesion group, and between the full-term and the severe lesion group. For CPT-Missing a significant difference was found between the full-term comparison group and the severe lesion group. No significant differences were found among the premature lesion groups for either CPT-Wrong or CPT-Missing standardized residual scores.
Fig. 1. Regression line for the prematures with no lesion and the full-term group (A) on CPT-MISSING as a function of age at testing, and (B) on CPT-WRONG as a function of age at testing.
Mean comparisons may be obscured when wide variation exists within groups. Another way to assess relative performance within groups is to look at the percentage within each group performing below the normal range. Figure 2 displays the percentage within each of the premature groups and within the full-term comparison group with standardized residual scores more than 2 standard deviations below the mean of the comparison group on CPT measures.

A consistent pattern of increasing percentages of children performing below the expected range was found comparing the full-term group with the three premature groups. Using a chi-square test for Trends, this reached significance for CPT-Wrong, $\chi^2(3) = 18.42, \phi = .4209, p < .001$. Among the premature groups alone, this also reached significance for CPT-Wrong, $\chi^2(2) = 5.96, \phi = .3052, p < .05$. Differences in percentages of scores outside the expected range for CPT-Missing did not reach significance.

No significant difference was found among mean scores for the premature groups in ratings of hyperactivity on the CBCL by their parents. Correlations between performance on the CPT and ratings on the CBCL Hyperactivity subscale were significant for CPT-Missing ($r = .33; p < .004$). The correlation between CBCL and CPT-Wrong was not significant ($r = .08$).

**DISCUSSION**

The original hypothesis, that severity of cerebral lesion would be associated with poorer performance on the CPT, was partially supported. Although there were differences between full-term children and specific premature groups, differences among the premature groups, themselves, did not reach significance. This may have been due to the exclusion of children too disabled for the test procedure, which contributed to a relatively small severe lesion group, and
unavoidably biased the group to more intact children. The premature sample also showed considerable variability within groups. In looking at the percentages of children in each group performing in the abnormal range, it is clear that the severity of cerebral lesion is associated with an increased risk for abnormal attention, at least in terms of errors of commission.

A finding of additional importance is the significant difference between prematures without lesions and the full-term comparison group. This suggests that even in the absence of detected cerebral lesion, very premature children may be at risk for attention deficit. While this may be a contributor to the poor school achievement found among very premature children with normal intelligence (Hack et al., 1994), further research is needed to determine if these attention deficits are likely to interfere with academic skill acquisition in the classroom setting. Addition of attention measures to the many collaborative perinatal follow-up studies currently in progress could serve as a vehicle for attempted replication of the current findings and to explore their relationship to academic performance.

CPT is generally considered one of the best measures of sustained attention (Mirsky, 1989). It is sensitive to lesions in the brain stem, reticular activating system, and prefrontal cortex. It is possible that as yet unidentified insult, or lesions that cannot be detected with current imaging techniques, may occur secondary to extreme prematurity that results in subtle neurological dysfunction. In keeping with the anatomical network system theory of attention, even subtle insult might affect the sensory integrative nature of the network. The pattern of CPT errors in this study of prematures suggests that the problems lie both in poor inhibition of inappropriate response, and in slow response or lapses of monitoring function when a response is called for.

The regression line for CPT omission errors as a function of age, demonstrated in Figure 1A, suggests that premature children, even without cerebral lesions, may be delayed in acquiring attentional functioning relative to full-term peers. The data suggest that while at younger ages the premature group is performing more poorly than the comparison group, there is a steeper regression for this group and at older ages their performance is more similar to full-term peers. Age effects are generally seen in performance on sustained attention tasks like CPT. Performance generally improves through school age and levels off in later childhood (Greenberg & Waldman, 1993). Prematurity may contribute to delays in maturation rather than to a persistent impairment. Longitudinal evaluation of the premature children as they approach adolescence may clarify this issue. If prematures are lagging in maturation of attentional processes, educational resource support through this period, or even medication, may help prevent early school failure.

It is of interest that this study showed an association between CPT omission errors and parental rating of hyperactivity but not for hyperactivity and commis-
sion errors. Hyperactivity is usually associated most closely with impulsive behavior that results in commission errors rather than omission errors (Barkley et al., 1988). However, the opposite findings were produced in the current study. This may be due to the fact that the Hyperactivity subscale of the CBCL also includes measurement of behaviors of immaturity, inattention, and learning problems. In general, this group of prematures did not have very elevated scores on the Hyperactivity subscale as compared with norms for American children. A limitation of the study was the lack of CBCL data on the full-term group.

It appears that the sustained attention skills measured by CPT are somewhat different from the behavioral characteristics measured by parent ratings. This finding was similar to that of Teplin et al. (1991) who found no difference between extremely low birth weight prematures and full-term controls on parent ratings of hyperactivity, but did find prematures to show deficits in teacher ratings of selective attention.

While the small size of the severe lesion group, and exclusion of the children with severe lesions who could not perform the tasks, may have contributed to a failure to find group differences among the premature children on CPT measures, this fact also suggests that developmental outcome for children with severe lesions is not uniformly poor. It has become apparent that the presence of extensive periventricular cysts is a marker for poor outcome (De Vries et al., 1985; Kuban & Leviton, 1994), but that children who experience severe hemorrhage alone may still have reasonably good developmental outcomes.

Recent innovations in neonatal care may be both improving infant survival, and contributing to a reduction in the incidence of more severe cerebral insults (Philip, Allan, Tito, & Wheeler, 1989). Findings of the current study suggest that children born prematurely who experience mild or even no cerebral insult may still need to be considered at risk for attention difficulties and might require support in the early school years to improve academic performance. Developmental follow-up and monitoring, through the preschool and early school age period, may be important for all children born very prematurely to insure early identification of problems with attention. Pediatric psychologists may play an important role in encouraging that hospital-based developmental follow-up programs for NICU graduates continue beyond infancy, and/or that families of premature children seek evaluation under their state’s Individuals with Disabilities Education Act (IDEA) Part H and Part B auspices.

REFERENCES


Effect of Cerebral Lesions


