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A Neuropsychological Approach For Differentiating the Residual Effects of Neonatal Intraventricular Hemorrhage

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A NEUROPSYCHOLOGICAL APPROACH FOR DIFFERENTIATING THE RESIDUAL EFFECTS OF NEONATAL INTRAVENTRICULAR HEMORRHAGE

by

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Glenn Thomas Goodwin

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by

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It is well documented in the literature that low-birth-weight (LBW) and prematurity are associated with a variety of developmental disabilities. Within this population of LBW children it is estimated that at birth, up to 45% of them experience intraventricular hemorrhage (IVH). Only recently has pediatric research begun to look at the potentially unique effects of IVH, and attempt to separate these out from the effects of LBW in general. The purpose of this study was to investigate the neuropsychological differences that may occur in children with a history of mild or severe IVH, who are now approaching school age. The main objective was to determine whether children, ages 4 and 5, who were diagnosed with a mild IVH at birth would perform differently on a neuropsychological screening from children who were diagnosed with a severe IVH.

Twenty-nine 4- and 5-year-olds born at the University of Utah Medical Center and Primary Children's Medical Center constituted the sample for this study. Potential children were identified through the

medical records, where documentation of incident and severity of IVH was obtained. Descriptive medical data and documentation of other common sequelae of LBW was also obtained from the medical records. Parents of potential subjects were contacted from the respective medical centers, and interested parents were then contacted by the research team and included in the study.

The children were tested on a variety of neuropsychological functions by trained examiners from the Early Intervention Research Institute at Utah State University and from the Neuropsychological Consultation Services in Salt Lake City, Utah. Analysis of this data was used in determining whether or not there were residual differences in the performance of preschool-age children who have a history of IVH at birth.

The results did not indicate significant difference between mild and severe IVH groups in performance on the neuropsychological assessment. Discriminant analysis showed no significant results which did not indicate that group membership could be predicted based upon test performance. Individual subtest analyses also did not indicate a significant difference in performance. Further analysis indicated significant relationships between the presence of other common sequelae of LBW/IVH such as seizure disorder and birth asphyxia, and the neuropsychological test results. Further research is needed to determine the reliability of these findings.

(118 pages)

CHAPTER I

INTRODUCTION

During the past 20 years, the problem of predicting developmental outcome from characteristics apparent in infancy has taken on new interest among the medical and psychology professions. The possibility of early prediction is particularly relevant to the population of low-birth-weight (LBW) infants. These children have been shown to be at risk for a range of developmental disabilities and handicapping conditions (Caputo & Mandell, 1970; Murphy, Nichter, & Liden, 1982; Ross, Schechner, Frayer, & Auld, 1982). Major advances in medical care and the development of neonatal intensive care facilities have greatly enhanced the treatment and follow-up of LBW infants. As a result, the mortality rate has declined, but subsequently it is also becoming progressively more obvious that the same conditions that once caused death in LBW infants are also responsible for a host of adverse neurological, medical, and behavioral sequelae in the survivors (Stewert, Reynolds, & Lipscomb, 1981).

In a recent world survey and review of follow-up studies involving LBW infants, Stewert et al. concluded that the incidence of intraventricular hemorrhage (IVH) is by far one of the most common causes of developmental disabilities. In modern neonatal intensive care facilities, the incidence of IVH in LBW infants (less than 1,500 grams or born after less than 35 weeks gestation) is approximately 40 to 45 percent (Volpe, 1981).

An understanding of neuropathology of IVH has been made possible largely through the use of ultrasound, computerized tomography (CT), and more recently Positron Emission Tomography (PET) (Grants, Borts, &

Schellinger, 1981; Papile, Munsick-Bruno, & Schaefer, 1983; Volpe, Herscovitch, Perlman, & Raichle, 1983). Briefly, periventricular hemorrhage (surrounding the ventricles, but not filling the ventricles) and IVH emanate from the small vessels, pricipally capillaries, in the subependymal germinal matrix, located near the head of the caudate nucleus (Hambleton & Wigglesworth, 1976). Approximately 80 percent of the cases of periventricular hemorrhage rupture through the ependyma and fill the ventricular system. In more severe forms, the hemorrhage extends into the cerebral parenchyma which is often followed by the development of a porencephalic cyst, post-hemorrhagic hydrocephalus, and other complications (Pasternak, Mantovani, & Volpe, 1980). The pathogenesis of IVH is related to several factors concerned with the distribution and regulation of cerebral blood flow, intravascular pressure, vascular integrity, and extravascular environment. These factors combine in the premature LBW infant, particularly in the infant subjected to asphyxial insult, to result in periventricular or IVH (Volpe, 1981).

The prognosis of IVH is best considered in terms of the short- and long-term outlooks. Volpe reports that all the important factors in determining outcome are not clearly understood, but there is a distinct relation between the severity of the hemorrhage and the prognosis. It is known that more severe hemorrhaging generally produces more short-term medical complications and more long-term complications, but the types of long-term disabilities have not yet been clearly established.

The recent contributions by Papile et al. (1983), through the use of CT, have made it possible to classify IVH into four grades, which allow for follow-up based on severity. The classifications are: Grade

I, germinal matrix hemorrhage; Grade II, IVH with normal ventricular size; Grade III, IVH with ventricular dilation; Grade IV, IVH with parenchymal hemorrhage. Grades I and II are considered to be less severe, while Grades III and IV are more severe because of the massive amount of bleeding and ventricular dilation.

It has only been in the last four to six years that longitudinal and follow-up studies have begun to look specifically at the contributions of IVH to developmental deficits and handicapped conditions. This is partly due to the fact that ultrasound and CT as methods of assessment, detection, and diagnosis of IVH are rather new methods. As a result, recent studies that specifically investigate the after-effects of IVH (Gaiter, 1982; Ment, Scott, & Rothman, 1978; Papile et al., 1983; Papile, Munsick, Weaver, & Pecha, 1979; Williamson, Desmond, Wilson, Andrew, & Garcia-Prats, 1982) have typically been with children 36 months or younger.

Almost unanimously, there has been a call for more long-term follow-up at late preschool and early school age to determine the residual effects of IVH. The majority of investigations cited earlier have generally agreed that Grades I and II may or may not result in a significant handicap. While it is known that up to 80 percent of those children experiencing Grades III and IV IVH may exhibit moderate to severe handicapping by the time they are 3 years old, some children in this group appear to be minimally affected (Papile et al., 1983). It is not clearly known which cognitive, physiological, and behavioral functions are the most effected by differences in severity of IVH and which functions have been possibly reacquired due to the plasticity and

equipotentiality of the developing brain (Rourke, Bakker, Fisk, & Strang, 1983).

There emerge two basic questions that need further investigation: (1) are there longitudinal differences in outcomes that occur between mild and severe IVH; and (2) if there are differences, where do these differences occur neuropsychologically? By determining the differentiating effects of IVH, educators and early intervention and rehabilitation programs will be in a better position not only to identify those children at risk, but more importantly, they will be better equipped to plan specific strategies for helping these children.

Follow-up studies up to this point in time have used global measures of intelligence and developmental quotients, neurological examinations, and physiological measures to report data about the effects of IVH. While this has been helpful in identifying how these children are progressing, a major limitation is that this information may not lend itself easily and practically to specific, qualitative descriptions of brain behavior relationships that can be used by those responsible for rehabilitation (Beaumont, 1983; Lezak, 1983; Rourke et al., 1983).

The rapidly developing field of neuropsychology has as its main focus the description and clarification of brain relationships. The neuropsychological approach to assessment emphasizes relating brain dysfunction to observable, empirically described behavioral deficits (Filskov & Boll, 1981). The information gathered from a neuropsychological approach to assessment can be used to (1) establish the existence of any cognitive deficits related to an insult, (2) establish the relative magnitude of this insult in terms of actual

behavioral descriptions, and (3) establish a patient's current functional status to serve as a basis for the design of remedial or rehabilitative therapy, and to monitor progress of treatment and recovery (Beaumont, 1983; Filskov & Boll, 1981).

Statement of the Problem

The data that are currently available on IVH populations are useful in identifying early those children who are at risk. The problem is that there is almost no long-term data which can be used to determine whether IVH results in a unique pattern of severity and type of handicap. The need, then, is for a more longitudinal assessment to be carried out that can provide specific behavioral descriptions of residual effects of IVH in terms of severity and that can be useful in a programmatic way to educators and rehabilitators.

Purpose of the Study

The purpose of the present study was to conduct a neuropsychological assessment of late preschool and early school-age children who had a history of neonatal IVH, in order to determine whether there were residual effects, and to differentiate these effects according to severity of the hemorrhage. The main objective was: **To determine whether children ages 4 and 5 who had been diagnosed by CT and/or ultrasound as having experienced Grades I or II IVH differed neuropsychologically from Grades III and IV IVH and to specify what the differences were.** The following research questions were examined:

A. Will children ages 4 and 5, who experienced Grades I and II IVH as diagnosed by CT and/or ultrasound, differ significantly

on a broad spectrum neuropsychological assessment from children who experienced Graded III and IV IVH?

B. If there were differences between mild IVH (Grades I and II) and severe IVH (Grades III and IV), where did these differences occur across neuropsychological domains?

CHAPTER II

REVIEW OF LITERATURE

Introduction

To better acquaint the reader with the nature of IVH, a description of the evolution and physiological process involved will be presented first. Following this, and because the incident of IVH is almost always associated with LBW, a brief discussion of the longitudinal studies of LBW children in general will be presented. The studies specific to IVH will then be reviewed. The research findings will be integrated using both meta-analytic (Glass, 1976) and narrative methods. The general field of neuropsychology will then be summarized and followed by a review of concepts and issues related to child neuropsychology. Elucidation of some differences that are unique to neuropsychological assessment of children will be included.

IVH

Neuropathology. The primary lesion in IVH is bleeding, principally from small blood vessels into the periventricular germinal matrix. There is a rich arterial supply for this region that is derived from the anterior cerebral artery and the middle cerebral artery via the deep lateral striate arteries. Further arterial contributions are derived from penetrating branches of the middle cerebral arteries and from the internal carotid artery by way of the anterior choroidal artery (Tarby & Volpe, 1982). Volpe states that this vascular supply is prominent from 24 to 32 weeks gestation.

According to both Hill and Volpe (1981), the hemorrhage in infants originates in the germinal matrix overlying the head of the caudate

nucleus at the head of the foramen of Monroe. In the majority of cases, periventricular hemorrhage ruptures through the ependyma into the ventricular system. Volpe (1981) explains that blood typically spreads throughout the ventricles, then passes through the medial and lateral apertures of the fourth ventricle to collect in the basilar cisterns or the posterior fossa. Typically, there are large clots in the occipital horns of the lateral ventricles and within the subarachnoid space of the cistern magna. Volpe states that this particular distribution may result in part from the settling of the blood from slowly flowing ventricular fluid in predominantly supine infants. A diagrammatic representation is shown in Appendix I.

Subsequent to the initial hemorrhage, Tarby and Volpe (1982) report that an obliterating fibrosing arachnoiditis may develop and cause the obstruction to cerebrospinal fluid flow that results in posthemorrhagic hydrocephalus (PHH). In more severe lesions (Grade IV), the periventricular hemorrhage appears to extend into the cerebral parenchyma. In these cases, the development of a porencephalic cyst is a frequent sequelae (Tarby & Volpe, 1982).

Pathogenesis. When considering the pathogenesis of IVH, several factors must be considered that relate to (1) the anatomic and physiologic determinants of the distribution and regulation of cerebral blood flow and pressure within the germinal matrix, (2) the nature of the germinal matrix vasculature itself, and (3) extravascular factors (Tarby & Volpe, 1982). A summary of the pathogenesis is shown in Figure 1.

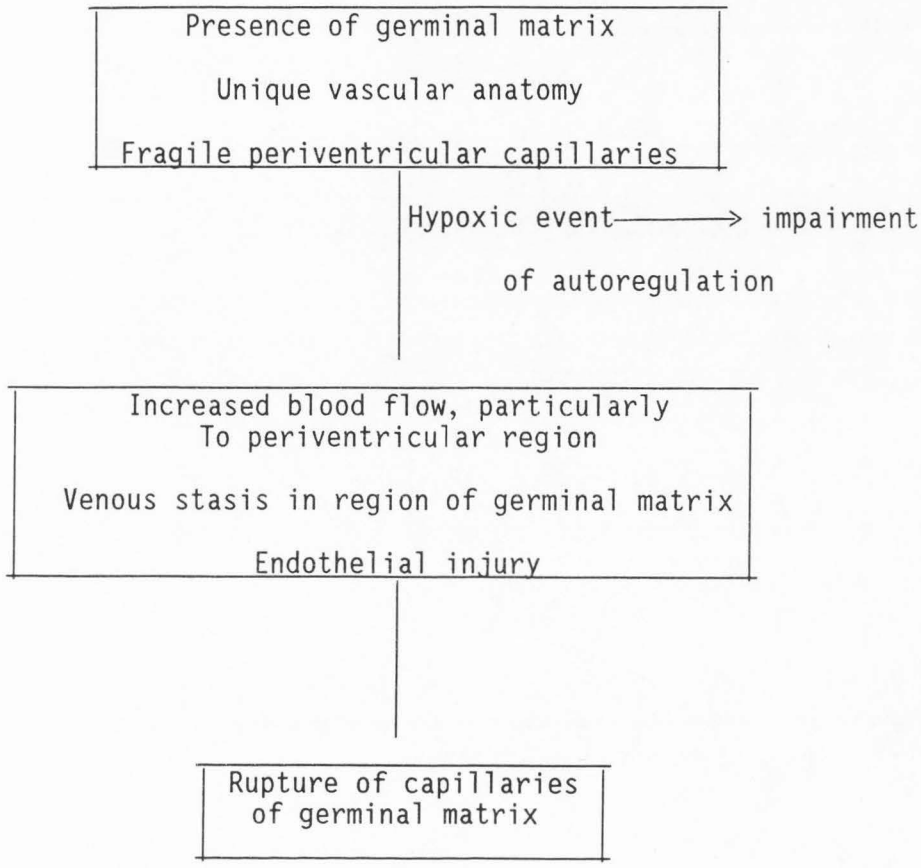

Figure 1: Pathogenesis of periventricular/intraventricular hemorrhage. (Hill & Volpe, 1981)

Anatomic studies (Hill & Volpe, 1981; Tarby & Volpe, 1982; Volpe, 1981) indicate that during the period of greatest susceptibility to IVH the vascular supply to the germinal matrix is particularly prominent. Volpe suggests that a disproportionate amount of the total cerebral blood flow enters the periventricular circulation and established a precarious baseline of high-volume flow.

Elevations in arterial blood pressure demonstrated in experimental observations in newborn Beagle pups (Goddard, Lewis, Armstrong, & Zeller, 1980) and in fetal sheep (Reynolds, Evans, & Reynolds, 1979) have also been observed in the human infant. In the first minutes of

life, increased arterial pressure has been documented during apneic episodes, with spontaneous or handling-induced motor activity, during seizures, rapid eye movement, sleep, exchange transfusions, rapid colloid infusions, and as a consequence of asphyxia. Tarby and Volpe conclude that fluctuations in arterial pressure are important in the pathogenesis of IVH.

The interaction effect of systemic and intracranial factors in increasing cerebral blood flow and the possibility of hemorrhage may be most pronounced in the premature infant with asphyxia (Tarby & Volpe, 1982). In the latter case, three factors combine initially to cause increase in cerebral blood flow: hypercapnia; the "diving reflex," which preferentially shunts blood to the brain; and arterial hypertension (Tarby & Volpe, 1982, p. 1,081). Also, superimposed on these physiological changes may be significant changes in cerebral blood flow secondary to the therapeutic effects.

There are other factors in addition to alterations in capillary pressure produced by arterial factors that may cause or exacerbate the increased pressure within the periventricular capillaries. Elevations of venous pressure may also occur with asphyxia, particularly when associated with hypoxic cardiac failure (Tarby & Volpe, 1982). Hill and Volpe (1981) explain that there is a reversal in the direction of venous flow as the internal cerebral veins are formed at the level of the foramen of Monroe and head of the caudate nucleus. While not unique, the anatomic situation can cause turbulence which may result in increased venous pressure and may accentuate the impact of the above factors.

The nature of the periventricular capillaries in the germinal matrix is also of significance in the genesis of IVH. This area has been characterized as an immature vascular area that may be readily injured by hypoxic insult (Pape & Wigglesworth, 1979). Tarby and Volpe also indicate that extravascular factors may be involved in the genesis of IVH, including the nature of the periventricular region itself. The periventricular germinal matrix is a gelatinous region that appears to provide support for the many vessels that move through it. They explain that the periventricular germinal matrix of the human premature infant has been shown to contain a high level of fibrinolytic activity. This may explain why capillary hemorrhage has the capacity to enlarge into a massive lesion that may extend into the ventricles or into the brain parenchyma.

Clinical features. The clinical features of IVH vary from a catastrophic neurological event to an extremely subtle or silent course (Tarby & Volpe, 1982). The occurrence of periventricular IVH may be accompanied by either of two clinical syndromes. The first is the presentation of a major hemorrhage. This is a catastrophic neurological deterioration that usually evolves in minutes to hours and consists of clinical signs such as deep coma, respiratory abnormalities, generalized tonic seizures, unreactive pupils, absence of extra-ocular movements, and flaccid quadriparesis. Tarby and Volpe also explain that the neurological syndrome is often accompanied by a falling hematocrit, a bulging anterior fontanelle, systemic hypotension, bradycardia, and temperature instability. Acute hydrocephalus may also occur. Many infants fail to survive this event.

The second syndrome is a more subtle deterioration that occurs usually in the infant with a smaller hemorrhage. Tarby and Volpe state that this syndrome tends to evolve over hours to days, often in a saltatory fashion, and is characterized by a change in level of alertness, a decrease in spontaneous and elicited movements, hypotonia, and more subtle abnormalities of eye position and movement. The abnormalities of this second syndrome may be missed or overlooked easily in an infant who is already compromised by the non-neurologic disorders of prematurity.

Mechanisms of brain injury. There are recognized mechanisms of brain injury associated with periventricular IVH (Hill & Volpe, 1981; Tarby & Volpe, 1982; Volpe, 1981). These are shown in Figure 2.

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1. Preceding hypoxic-ischemic insults
2. Increased intracranial pressure and decreased cerebral perfusion
3. Destruction of periventricular white matter
4. Destruction of glial precursors in the germinal matrix
5. Focal cerebral ischemia
6. Posthemorrhagic hydrocephalus.

Figure 2. Mechanisms of brain injury associated with periventricular IVH (Tarby & Volpe, 1982, p. 1,085).

Because IVH is often preceded by hypoxic-ischemic insults, lesions caused by such insults may be expected to be important in determining long-term prognosis (Tarby & Volpe, 1982). Periventricular leukomalacia and selective neuronal injury to brain-stem nuclei as well as to cerebral and cerebellar arteries have been identified to be associated with periventricular IVH.

Tarby and Volpe also indicate that marked intracranial hypertension and impaired cerebral perfusion may be important determinants of long-term injury. In premature infants, the systemic blood pressure may fall precipitously. Thus, in the infant with a severe IVH and marginal arterial blood pressure, even a small increase in intracranial pressure may impair cerebral perfusion.

The destruction of periventricular white matter by intraparenchymal hematoma may also be a cause of focal motor lesions following periventricular IVH. These lesions are associated with tissue destruction and cyst formation (Pasternak et al., 1980; Tarby & Volpe, 1982). The subsequent occurrence of focal motor deficits, most often a spastic hemiparesis, can be correlated with these cystic lesions.

Destruction of glial precursors in the germinal matrix area and focal cerebral ischemia are also associated with periventricular IVH (Tarby & Volpe, 1982). These occurrences need further study and investigation to clarify their subsequent outcomes.

A more frequent after-occurrence of IVH is hydrocephalus or progressive post-hemorrhagic ventricular dilation (Korobkin, 1975; Larroche, 1972; Tarby & Volpe, 1982). The occurrence of progressive hydrocephalus in LBW infants has been shown to be associated with multiple developmental handicaps (Boynton et al., 1985). There is a relatively high correlation between severity of the IVH and the probability of developing hydrocephalus. The ventricular dilation may begin with the lesion, or more commonly begin approximately one to three weeks after the hemorrhage. Tarby and Volpe state that the rapidity with which the hydrocephalus develops is also correlated with

the severity of the causative lesion. The precise relation between ventricular dilation and the genesis of brain injury is largely unknown (Tarby & Volpe, 1982). It is known, however, that ventricular dilation results in deleterious anatomic changes such as axonal stretching and axonal loss. Tarby and Volpe suggest further research to delineate more clearly how ventricular dilation causes brain injury.

Low-Birth-Weight Studies

The incidence of LBW infants comprises about 7 percent of all deliveries (Kitchen et al., 1980). Among this group of LBW infants, it is estimated that 5 to 15 percent develop handicapping conditions of varying degrees (Hunt, Tooley, & Harvin, 1982; Stewert et al., 1981). Recent national and international reviews of LBW follow-up studies suggest that the percentage rate of handicapping is less than 10 percent, and possibly as low as 6 percent (Kitchen et al., 1980; Stewart et al., 1981).

In the 1940s and 1950s, not as much attention was paid to the treatment of LBW infants, and many died. In the late 1950s and early 1960s, much was learned about the normal physiology of the LBW infants and about the conditions that cause death and damage. During this period, however, the incidence of handicapping conditions actually increased, due mainly to inadequate application of new knowledge and iatrogenic disease (Rawlings, Reynolds, Stewert, Strang, 1971, Stewert et al., 1981). From the 1960s on, the survival rates of LBW infants have increased steadily, and the prevalence of handicaps has remained stable and relatively low. This can be attributed to the more rational use of modern knowledge and to increasing sophistication of obstetric and neonatal care (Stewert et al., 1981).

Both clinical practice and longitudinal research efforts have been greatly enhanced by the development of neonatal intensive care units (NICU). It has become more possible to treat more serious medical problems in the neonate and at the same time conduct ongoing research simultaneously. A large proportion of the longitudinal studies of LBW have looked at children who were treated in NICUs.

Methodologically, most longitudinal studies exclude infants of birth weight under 500 grams, as survival of infants under this weight is unusual. Published reports concerning LBW infants usually have an upper limit of 2,000-2,500 grams (Kitchen et al., 1980; World Health Organization, 1978). By definition, the selection of LBW infants for study of mortality and morbidity is made on the criteria of birth weight alone, a measure which is readily available.

From this general area of agreement, the variety of approaches to follow-up of LBW infants makes for a number of difficulties in terms of integrating the findings. One approach taken is to report longitudinal information based on accumulation or pooling of data from various age groups (Drillien, Thomson, & Burgoyne, 1980; Kitchen et al., 1980; Ross et al., 1982; Smith, Somner, & von Teczchner, 1982).

Another approach is to include LBW children in a one-time follow-up study at a specific age (Ment, Scott, Ehrenkranz, & Warshaw, 1982; Noble-Jamieson, Lukeman, Silverman, & Davies, 1982). Kitchen et al. (1980) state that these two approaches make it difficult to compare findings at different age levels because of the differences in methodology. Kiely and Panath (1981) suggest that there needs to be more uniformity among researchers so that more accurate and precise information can be generated.

In spite of differences in approach, there is some useful information being generated. Based on a pilot sampling of 20 studies, most of the children being followed have been treated in NICUs (Stewert et al., 1981). This information is important to know when comparing results across studies where some children may not have been treated in an NICU.

A basic commonality found in some of the major studies that are frequently cited (Drillien et al., 1980; Kitchen et al., 1980) is the reporting of birth weight, gestational age groupings, percentages of handicapping and neurological problems, differences in socioeconomic status, and sex differences. This has allowed for correlation of outcome measures of developmental progress with those variables to determine if possible relationships exist.

A major weakness of LBW studies is that while some studies include a type of control or comparison group (Drillien et al., 1980; Ferrari, Grosoli, Fontana, & Cavazutti, 1983; Nickel, Bennett, & Lamson, 1982; Noble-Jamieson et al., 1982; Siegel, 1982), others do not (Hirata et al., 1983; Hoskins, Elliot, Shennan, Skidmore, & Keith, 1983; Jones, Cummins, & Davies, 1979; Knobloch, Malone, Ellison, Stevens, & Zdeb, 1982). Kiely and Panath (1981) report that no scientific inferences about sequelae among these children can be made unless they are compared with some other group. They explain that the type of comparison group will depend on the nature of the study and the research questions. They suggest that researchers should clearly specify the type of comparison group being used and that results should be interpreted with this in mind.

In terms of measures being used to draw conclusions about longitudinal effects of LBW, the majority of studies in the pilot sample use a variety of tests and measurements. This has been both helpful and confusing. The advantage is that researchers are looking at different characteristics of behavior. The problem, however, is that it is again difficult to make comparisons across studies. The common measures being used are intellectual measures, developmental quotients, neurological examinations, and physiological measures such as post-natal birth weight at different ages and head circumference. Kiely and Panath again address this issue, calling for some conventional format to be established so that future follow-up studies may be comparable with one another.

A final issue addressed by LBW studies is the at-risk infant. In a current environmental intervention program for LBW infants (Ramey, Bryant, Sparling, & Wasik, 1984), the researchers involved strongly suggest that pre-term and LBW infants must be properly screened and identified as appropriate targets for intervention. While they have been able to isolate clusters of perinatal variables, such as IVH, that account for most of the variance in outcome up through 40 months, they emphasize that the actual outcome may change as these children continue to be followed. They recommend longer follow-up to determine whether further improvement occurs or, if not, to determine the best timing for intervention.

IVH Studies

Follow-up studies of LBW children have only recently begun to examine the results of IVH that may be unique to this insult (Gaiter, 1982; McCarton-Daum, Danzinger, Ruff, & Vaughn, 1983; Papile et al.,

1983; Williamson et al., 1982). These studies have generally followed the same format as the LBW studies mentioned earlier.

A computer search of ERIC, Psychological Abstracts, Biological Index, and Index Medicus was initially carried out to locate a data base of research related to IVH. On all articles reviewed, cross-referencing was also carried out in order to locate all possible primary research articles involving follow-up of children with IVH. Although there were a number of studies investigating children with IVH, these were generally with children no older than 36 months. Outcome measures were usually based on gross physiological measures such as CT-scan and/or global scores of development. There was very little follow-up with older children where more specific developmental and behavioral measures were used, from which conclusions could be drawn about cognitive and intellectual functioning.

There were also few studies which looked at the long-term results of IVH and differentiated these results in terms of severity of IVH. With the application of CT and ultrasound as diagnostic instruments, it has been possible to more clearly assess the presence or absence of IVH as well as the severity (Krishnamoorthy, Shannon, DeLong, Todres, & Davis, 1979; Papile, Burstein, Burstein, & Koffler, 1978). It has thus become more feasible to evaluate children who were diagnosed as having had neonatal IVH and to follow these children with testing to determine how they were functioning as the became older.

Because of the differences that occurred across studies and the difficulty in comparing and integrating the data available, a mini meta-analysis (Glass, 1976) was carried out to better integrate the data from major studies. Briefly summarized, meta-analysis requires

the reviewer to locate either all studies or a sufficiently large representative sample of studies, express the results of each study in a common metric, and then quantify or code various characteristics of each study that may have affected its results. Because the results of all studies are expressed in a common metric, typically obtained results of studies with given characteristics can also be estimated. The reviewer also has available a systematic analysis of the strengths and weaknesses of primary research, which can then be used as a guide in planning future research (the coding instrument used to conduct the meta-analysis appears as Appendix E).

From a sample of 9 primary research studies, from which data will be analyzed, a preliminary meta-analysis was done using follow-up outcome measures based on developmental quotients such as the Bayley Developmental Scales, neurological examinations, and other developmental measures. These studies were longitudinal (accumulation of outcome measures based on evaluation at different times and ages) and follow-up (data collection done only once at a particular age). There were other studies that investigated the performance of IVH children, but they did not provide the kind of data available which could be used in a meta-analysis.

Studies reported diagnosis and classification of IVH based on ultrasound and or CT. Although the descriptive information differed somewhat depending on which instrument was used, the differences in severity could be separated according to the pathophysiology that occurs with varying degrees of severity. For clarity, these comparisons were reported using Papile's et al. (1983) numerical system (Grades I, II, III, IV).

Effect sizes (ES) were computed to represent averages across all studies. An effect size was computed by using the following basic formula: $X_e - X_{c/Sc}$, where X_e = the mean of one group, X_c = the mean of the comparison group, and S_c = the standard deviation of the comparison group. Where means and standard deviations were not available, other formulas developed by Glass (1976) were used. When comparing ES numbers, an ES of 1.00 indicates one standard deviation difference between the two groups being compared. The meta-analysis results are shown in Table 1.

Table 1

Meta-Analysis Results

	Comparison	NES*	ES
1.	Total IVH (Grades I-IV) vs. non-IVH	9	1.12
2.	Grade I IVH vs. non-IVH	8	0.33
3.	Grade II IVH vs. non-IVH	4	0.16
4.	Grade III IVH vs. non-IVH	4	0.73
5.	Grade IV IVH vs. non-IVH	4	1.18
6.	Grade I IVH vs. Grade II IVH	5	0.43
7.	Grade I IVH vs. Grade III IVH	4	0.41
8.	Grade I IVH vs. Grade IV IVH	4	2.11
9.	Grade II IVH vs. Grade III IVH	8	0.43
10.	Grade II IVH vs. Grade IV IVH	4	1.38
11.	Grade III IVH vs. Grade IV IVH	2	0.20

*NOTE: NES indicates the number of effect sizes for both comparisons.

When Grades I and II were combined to represent a mild IVH group and compared Grades III and IV which represent a severe IVH group, differences across studies were found. Effect sizes ranged from 0.15

to 3.71 with an average effect size of 1.45. It may be that these differences were the results of differences in age. It was not possible to break up outcome measures by age groupings because of the differences in methodology of the studies.

When all grades of IVH (I-IV) were compared to LBW but non-IVH groups, an ES of 1.12 results, which indicates just over one standard deviation difference between the groups. This difference came mainly from Grades III and IV being included in this group (Papile et al., 1983).

When comparing Grade I IVH vs. non IVH, and Grade II IVH vs. non-IVH, the differences were much smaller (ES = 0.33 and 0.16). These findings were generally supported by results reported in the 9 sample studies. The differences between Grade III IVH vs. non-IVH and Grade IV IVH vs. non-IVH were substantially larger (ES = 0.73 and 1.18). These ES reflected the differences in severity between mild hemorrhaging (Grades I and II) and more severe hemorrhaging (Graded III and IV). When making comparisons between grades, however, there was some discrepancy among findings. Fitzhardinge, Flodmark, & Ashby (1982) and Papile et al. (1983) indicated no significant differences between Grades I and II, but Williamson et al. (1982) reported a substantial difference (ES = 0.87). Again, these results may have reflected differences in age at time of testing. As expected, there were differences between Grades I and III and Grades I and IV (ES = 0.41 and 2.11), although greater differences occurred between Grades I and IV. There were also similar differences between Grades II and III and II and IV (ES = 0.43 and 1.38). There appeared to be little difference between Grades III and IV (ES = 0.20).

With the exception of a rather moderate difference between Grades I and II, the results of this small analysis confirmed findings being reported in current research. Although based on small numbers of ESs, there appears to be a distinction between mild and severe hemorrhaging in terms of residual effects up through 3 years of age. There is a clinical difference between Grades I and II and Grades III and IV because of the occurrence of ventricular dilation and massive bleeding that occurs with the more severe grades. It is not known, however, how these differences show up over time in terms of intellectual and cognitive functioning.

Based on the findings of the initial review and to provide more clinically meaningful comparisons, Grade I and II were combined to form a mild IVH group and Grade III and IV combined to form a severe group. Six additional studies were located and included in a second meta-analytic review. Table 2 shows the comparisons made based on 15 studies.

Table 2

Final Meta-Analysis Results

Comparisons	NES	MES
Total IVH (mild and severe) vs. non-IVH	17	0.80
Mild IVH (I and II) vs. non-IVH	6	0.20
Severe IVH (III and IV) vs. non-IVH	5	0.92
Mild IVH vs. severe IVH	21	0.78

When all grades of IVH (I-IV) were compared to similar but non-IVH groups, an ES of 0.80 resulted which indicated just over 3/4 of a standard deviation difference between the groups. These findings were again consistent with what has been reported in the primary research. Because there was a disproportionately larger number of mild IVH comparisons represented, and because the difference between mild IVH and non-IVH groups was relatively small (ES = 0.20), the overall comparison of IVH vs. non-IVH may not be as high as expected. The main reason is that a larger number of children with mild IVH survived than with severe IVH. There were less children available with a history of severe IVH which could be included in research studies.

When comparing the mild IVH group with the non-IVH group, the differences were much smaller (ES = 0.20). This was consistent with studies reported where children have been followed through approximately 30 months of age.

Comparisons made between the severe IVH and non-IVH groups resulted in an ES of 0.92 (just less than one standard deviation difference). The previous two comparisons (mild IVH vs. non-IVH and severe IVH vs. non-IVH) were based on smaller numbers of available ESs, and the conclusions must be considered tentative at best.

The final comparison made, and the one most relevant to this study, was based on a larger number of available ESs, and, therefore, represents a more confident findings. An ES of 0.78 was obtained when mild IVH vs. severe IVH groups were compared. A difference of just over 3/4 of a standard deviation suggests a significant difference between mild and severe hemorrhaging as these children continued to

develop. It is not known if this rate of difference will change or remain the same as these children approach school age.

Because of the lack of longitudinal research with children ages 4 and 5 who have had neonatal IVH, there remains a question as to the ability of the developing brain to recover the loss of function caused by an IVH. It is not known to what degree the child's brain can recover from mild or severe IVH. It is, therefore, not possible to predict the types of deficits that may occur residually at preschool and early school age following a history of neonatal IVH.

Because Grades I and II hemorrhage are less severe, and some studies report diminishing symptomology with age, there is a need to follow-up these two groups at the late preschool age to determine if these children remain at risk for minor handicaps (slow learners, LD, ADD, and hyperactives). There is also much more potential for recovery of deficits with Grades I and II, and, therefore, the need to identify and describe any lingering problems.

Grades III and IV may not fare as well, but continued follow-up with these children at late preschool age also needs to be done to determine how these children differ from those with less severe IVH.

Neuropsychology

Clinical neuropsychology is concerned with developing knowledge about brain-behavior relationships and the application of this knowledge to the evaluation and treatment of individuals with behavioral disabilities and disturbances (Benton, 1974; Davidson, 1974; Rourke et al., 1983). Although the field of neuropsychology is a new and developing science, there has been substantial growth in the last 20 years that distinguishes neuropsychological theory and practice from

both psychology and neurology (Filskov & Boll, 1981). Although early work in neuropsychology was done primarily with adults, the newer subspeciality of pediatric neuropsychology has begun to emerge as a distinct approach to the assessment of children (Goldman, Englestein, & Guerry, 1983; Rourke et al., 1983).

The purpose of a neuropsychological approach to assessment is threefold: (a) diagnostic, (b) patient care, and (c) research (Lezak, 1983). Neuropsychology's diagnostic role has diminished somewhat because of the recent development of non-invasive techniques like CT, but its contributions to patient care and research have grown. As mentioned in the introduction, neuropsychological assessment can provide educators and rehabilitation programs with a description of the child's mental capabilities. In addition, it can give an often more important analysis of <u>how</u> the child fails that will tell the therapist or teacher how the child might improve his/her performance. Lezak states that such precise and descriptive information about intellectual, behavioral, and emotional status is essential for careful management of rehabilitation following brain injury.

In the area of research, the precision and sensitivity of a neuropsychological approach provides a valuable tool for investigating small, sometimes quite subtle behavioral alterations, such as those that may follow insults to the brian like IVH. Global indices of development or intellectual functioning are limited in their usefulness because they are typically too global of a measurement. Neuropsychological assessment can break down intellectual domains into sub-functions that are more behaviorally meaningful.

The actual practice of neuropsychological assessment in the United States has evolved mainly out of psychology and is best represented in the battery approach such as the Halstead-Reitan Battery (Beaumont, 1983). This approach uses the same battery with all patients, regardless of the presenting symptomology. The advantage of this approach is that it covers a broad range of functioning.

Contemporaneous with the American developments has been the evolution of a clinical-theoretical, individualized approach in Russian neuropsychology under the leadership of A. R. Luria. This developed through single case studies and emphasized careful, intensive observations. The Luria-Nebraska Battery represents this approach.

A current trend in neuropsychological practice is a blend of both approaches, where the clinician puts together an individual battery from various sources that fits the clinical need most appropriately (Lezak, 1983; Nilsson, 1985; Rourke et al., 1983). This approach is advocated by a number of neuropsychologists because of the inherent differences that occur during different stages of child development (Rourke et al., 1983). The important issue is to select a battery that is appropriate for the age level and that answers the referral or research questions.

Neuropsychological interpretation of test results is also different from standard psychological reporting. For example, if a clinician wishes to use the Bayley Developmental Scales within a neuropsychological battery, he becomes more interested in the subtest scores and what these scores represent in terms of specific brain-behavior relationships, than in the global developmental quotient (Lezak, 1983; Nilsson, 1985; Rourke et al., 1983). This approach,

then, can provide both quantitative data and a qualitative description of a child's performance on a variety of skills.

Child Neuropsychology

Historical developments. Although early work in neuropsychology was done primarily with adults, the newer subspeciality of child neuropsychology has begun to emerge as a distinct approach to the assessment of children (Goldman et al., 1983; Rourke et al., 1983; Taylor, Fletcher, & Satz, 1984). Methods for the psychometric evaluation of children date back to the development of intelligence tests of the turn of the century. Since that time, a multitude of testing procedures have been developed for the assessment of intelligence, academic achievement, language, and perceptual-motor skills. Neuropsychological procedures for children are among the most recent of these developments and have extended from this context (Taylor et al., 1984).

Since the current status of child neuropsychology can best be characterized by tracing its roots, a brief historical review will be presented. According to Taylor et al., the concept of cerebral dysfunction in children has had more impact on current conceptualizations of child neuropsychological assessment than any other single factor. The concept itself seems to have come from observations of relatively distinct deficits in behavior and cognition of children with brain disease and similar deficits in children without established neurological disorders. Taylor et al. explain that those observations have been used to justify the inference of cerebral dysfunction in cases where certain behavioral deficits are present but where definitive neurological disorders cannot be verified. Cerebral

dysfunction is, therefore, based on the conviction that similar behavioral patterns represent similar etiologies rather than on direct proof of abnormal brain status (Taylor et al., 1984).

From this concept of cerebral dysfunction has come the basic premise of the continuum hypothesis, which suggests that there is an isomorphism between disorders of behavior and disorders of brain. This idea has been widely criticized (Benton, 1973; Rutter, 1982). However, the idea that functional signs can provide a basis for making CNS inferences about children, even when the relationship to those signs to the CNS is not documented, has had an insidious influence on neuropsychological approaches to children. Taylor et al. state that neuropsychological assessments of children continue to make unverified inferences about CNS solely on the basis of test results and behavioral observations. This factor must be considered when evaluating and interpreting data from child neuropsychological assessments.

A second influence on the development of child neuropsychology has been adult neuropsychology. The assumption that certain skills represent more direct reflections of cerebral status than other skills has significantly influenced the approach to child neuropsychological assessment (Taylor et al., 1984). This influence is represented by:

> ...(a) the continued search for measures differentially seen to cause dysfunction in children, (b) the frequent use of competent-achievement discrepancies in diagnosing learning problems, and (c) the emphasis on models of adult brain function for interpreting psychometric test results. (p. 212)

Taylor et al. add that because of the difficulties in conducting brain-behavior studies in children (due in part to the low frequency of non-diffuse brain lesions in children), adult models of brain behavior organization have sometimes been assumed prima facie to apply to

children. These adult models have served as a source of hypothesis concerning patterns of behavioral dysfunction in children.

Aside from the problems associated with the wholesale application of adult models to children, reliance on adult models has been useful in several areas (Taylor et al., 1984). The application to children of modes of neuropsychological interpretation developed initially for adults is one example. Interpretive modes based on levels of performance, pathogenic signs, lateralization of deficits, and differential patterns of performance across multiple testing procedures have proven helpful in understanding potential brain-related disorders in children (Rourke et al., 1983).

A second example is the emphasis of adult neuropsychology on various aspects of memory, language, and motor skills observed in brain-damaged adults. This has brought about an awareness of the organization and complexity of higher cognitive functions. The development of the Halstead-Reitan approach and other experimental and clinical approaches to neuropsychology has led to a growing recognition of the diversity of effects of brain injury on behavior (Taylor et al., 1984). Rourke et al. indicate that the application of these approaches to children has yielded important discoveries. The value of neuropsychological tests for distinguishing subvarieties of learning disabilities is representative of these findings. This awareness has a direct bearing on the present study. It is not enough to conclude that children suffering from IVH at birth may or may not develop learning disabilities. Of greater importance is being able to indicate subvarieties of possible learning disabilities that may be occurring residually.

Implications for child neuropsychological assessment. The historical factors mentioned above have led to a variety of neuropsychological approaches to children. One approach is to apply modified versions of adult-oriented tests to children or to create tests that attempt to measure abilities analogous to those tapped by adult neuropsychological batteries (Taylor et al., 1984). An example is the Luria-Nebraska Children's Battery (Golden, 1981).

A second approach is to apply neuropsychological interpretations to more traditional procedures for children (e.g., the WISC-R), sometimes in conjunction with tests developed specifically for neuropsychological assessment. Clinicians using this second approach vary considerably in terms of tests used (Taylor et al., 1984).

A third approach employs measures derived in part from research on cognitive development. This approach represents the greatest departure from adult-derived methods and from the influence of the concept of cerebral dysfunction. Taylor states that the primary concern of this approach is with the age-related organization of children's abilities.

All these approaches emphasize the relationship of test results and behavioral observations to brain status. However, a major problem in defining child neuropsychological assessment in this manner is that few brain-behavior relationships have been established in children (Rutter, 1982). An exclusive emphasis on brain-behavior relationships leads to vague and misleading concepts, such as cerebral dysfunction, or to an over-reliance on methods and models of brain function derived from adult studies (Taylor et al., 1984).

The foregoing discussion of the development and current approaches in child neuropsychology indicates that the researchers and clinician

must be both conservative and cautious when interpreting data from child assessment. Taylor et al. suggests a functional approach to child neuropsychological assessment that fit appropriately within the purpose of this study. This approach is described in terms of four basic postulates. The following postulates comprise the working assumptions of child neuropsychological assessment and help to clarify its unique standing vis a vis other modes of child assessment.

1. Neuropsychological evaluation of a developmental disability consists of (a) a descriptive analysis of the presenting problems (i.e., the child's manifest disability), (b) assessment of a limited set of basic skills or competencies intrinsic to the child (i.e., the child's basic competencies), (c) consideration of socio-cultural variables likely to be more extrinsically determined (i.e., moderator variables), (d) evaluation of the relationship of different biological indices to the child's performance.

2. Although the manifest disability is a product of deficits in basic competencies, the impact of these weaknesses on the child's ability to learn and behave as expected is dependent to some extent on the above-noted extrinsic factors or moderator variables. These factors include the child's ability to compensate for his/her weaknesses, the attitudes of the child towards learning, and the stimulation and encouragement provided by the family and school.

3. Although covariation of basic skills within individuals is usually high, dissociations between skills are characteristics of many disabled children. Such contrasting levels of skill are related to either congenital neurological variation or to outright neurological disorder. The study of the child who exhibits variations in basic competencies is of value in refining our understanding of the nature of these competencies and how they are deployed in more complex activities.

4. The CNS influences the manifest disability via the limits it imposes on these basic competencies. However, because both the manifest disability and the basic competencies are affected by moderator variables, the CNS can only be considered one of several influences. (Taylor et al., 1984, p. 216)

According to this model, there are four types of influential variables: the first represents the child's manifest disability; the second represents the behavioral and cognitive correlates of the

disability; the third represents environmental, social, and instructional factors that determine how the child copes with his/her skill weaknesses; and the fourth represents the status of the CNS and other biological factors.

Development following from an injury. The extent of recovery from insults to the brain is central to the rationale of the present study. This issue has unique relevance to child neuropsychological assessment. The issues of equipotentiality and plasticity of the developing brain are major concerns in the practice of child neuropsychology and have led to the emerging rationale that links assessment and intervention for the purpose of achieving positive changes in the adaptive behavior of brain-injured children. The capacity for the development of function following brain injury early in life reflects the plasticity of the brain.

In terms of IVH, acquisition of functions follows insult to the brain early in development is the more relevant issue rather than reacquisition of function. The brain acquires functional capacity during development. Early lesions, such as IVH, may hamper that process. The degree to which significant and positive behavioral adaptation following brain impairment occurs depends on a number of factors (Rourke et al., 1983). These factors include location of the lesion, size of the lesion, development of the lesion, exposure to environment stimulation, and demographic variables such as age and sex.

Rourke et al. indicate several physiological and psychological processes that may in part account for recovery and acquisition of functions following brain injury early in life. Regenerative

sprouting, collateral sprouting, and denervation supersensitivity have been identified as restorative physiological processes.

In regenerative sprouting, if an axon in severed, the part beyond the cut dies (anterograde degeneration). The proximal part and the soma of the neuron either may die (retrograde degeneration) or remain alive. In the latter case, the severed axon may develop sprouts. According to Rourke et al., this process has been shown to occur in the brain after distinct neurons are damaged, but it is not clear whether the regenerated connections are functionally effective. Rourke et al. state the development of scar tissue seems to hamper the regenerative process, since it has been observed that the removal of scarring may be followed by continued growth of axonal sprouts.

On the other hand, collateral sprouting from intact axons neighboring an injured area tend to invade the damaged sites and to form new terminals. Rourke et al. explain that the collateral's invasion seems to be triggered by the denuded synaptic sites which proclaim their need of connection. Certain cognitive and emotional deficits in children following brain injury may be the consequence of redirected axonal growth. Some functions may be spared at the expense of the normal development of other functions.

A third mechanism refer to a biochemical process called denervation supersensitivity. Rourke et al. again explain that the destruction of neurons, through anterograde degeneration, deprives the postsynaptic membrane of its input. It has been observed that postsynaptic sensitivity to chemical transmitters increased in response to denervation. Rourke et al. state that supersensitivity may manifest itself in increased electrical activity in the severed area. Because

in the brain the supersensitivity recedes at the time that regenerative and collateral sprouting occur, one might infer that the biochemical changes following denervation stimulate the sprouting processes and that these changes play a role in the acquisition of functions following IVH.

Following an early insult like IVH, there may also be other restorative mechanisms involved in recovery. One model suggests that healthy tissue has the capacity to rearrange its functional subservience. This rearrangement may be through the vicarious functioning of some intact brain regions. It has also been suggested that the intact parts of the damaged brain form new interregional connections to subserve fresh behavioral systems (Rourke et al., 1983).

Because of the mechanisms involved in recovery and other factors, such as age at time of lesion and extent of damage, there may be both small and large differences in behavioral and cognitive measures in children with differing severity of brain injury. The behavioral aberrance following early brain injury may initially appear mild. Rourke et al. state, however, that appearances are deceptive. More severe effects often show up as the child gets older. For example, a child may "grow into a deficit" when functions normally subserved by the destroyed tissue become increasingly crucial for the behavioral repertoire as development progresses (Rourke et al., 1983, p. 92).

It may also be that an initial pattern of deficits is replaced by other deficits. Rourke et al. found attentional rather than cognitive deficits particularly apparent in young brain damaged children. Specific cognitive deficiencies are present in young children with a

history of brain injury, but their manifestations may be masked by the more generalized and diffuse effects of attentional deficits.

Rourke et al. summarize this point by ascertaining that the effects of brain damage sustained during childhood may appear early and disappear, appear early and last, or be apparent only after a delay. The developmental pattern depends on such factors as the sort of tissue destroyed, the environment, and the growth and differentiation of the brain.

These issues are unique to the neuropsychological assessment of children. In the case of possible residual effects of IVH, there is an obvious immediate impact on the brain. The relevant question is whether or not such an insult will have further delayed impact or no impact at all as the child develops. In general, the elimination of immature structures seems to have less dramatic behavioral consequences than does the elimination of mature structures. However, effects of early lesions are quite variable and dependent on a number of factors already indicated. The issue of follow-up then, with children who have experienced early trauma or insults to the brain, become an important part of the approach taken in child neuropsychology because of the notions of plasticity and developmental recovery.

Summary

IVH is one of the most important adverse neurological events of the newborn period. It is very common and can be quite severe. Longitudinal studies of LBW children in general indicate that LBW and prematurity are related to subsequent developmental problems. Among those LBW infants who suffer IVH, the short- and long-term outcomes are

related to the severity of the hemorrhage and the ability of the brain to recover from such an insult.

There is a growing body of literature suggesting some developmental problems associated with less severe IVH and more significant and permanent developmental problems following severe IVH. It is also known, however, that follow-up comparisons between survivors of mild and severe IVH tend to indicate marked differences in some cases, but indicate little differences in others.

The use of neuropsychological assessment, when applied to this population of children, can provide a unique contribution to the presently available literature. By looking at an older group of children and examining more specific cognitive functions, a greater understanding of the recovery and future of these children will be available.

CHAPTER III

METHODS

This study was conducted as a cooperative effort between this investigator and Utah State University's Early Intervention Research Institute (EIRI), David Nilsson, Ph.D. (child neuropsychologist) at the Neuropsychological Consultation Services, Primary Children's Medical Center (PCMC), and the University of Utah Medical Center. Children born from 1980 to 1981 were eligible for the study. Both medical centers had a complete medical record on each child describing the incident of IVH, how it was diagnosed (ultrasound and/or CT), the severity of IVH, the type of treatment received in the NICU, as well as family history and medical data.

Sample

Twenty-seven of the 29 children in the final sample came from the Salt Lake area. Two children had moved out of the state of Utah since 1980-1981. Medical records available for each child eligible for the study were made available from both medical centers. The medical centers serve as the major referral source for infants with life-threatening conditions. Children eligible for the study met the following qualifications:

1. Birth-weight less than 2,700 grams, but not less than 800 grams.
2. Gestational age less than 36 weeks.
3. Diagnosed IVH by ultrasound or CT.
4. Must be currently 4 to 5 years old.

Potential children, based initially on information obtained from the medical records, were grouped into a mild IVH category (Grades I and II) and a severe IVH category (Grades III and IV).

Verification that children were still living was obtained through the State Department of Vital Statistics in the respective states. This verification was established before any contact was made with the parents of potential subjects. The names and birthdates of potential subjects were sent to the Department of Vital Statistics where a death search was made to verify if any potential subjects had died since 1980-1981.

The parents of potential children eligible for the sample were then contacted with an initial mailing from the respective medical center. A copy of this letter is found in Appendix B. This mailing contained information on the nature and purpose of the study. A request for parents to include their child in the study was made by the director of the NICU where the children had been treated after birth. Parents who indicated an interest in the study be returning an enclosed postcard were then contacted by the researchers to present the purpose of the study in more detail. Parents were further briefed on the nature of the study and given more information relating to its importance. Parents were requested to participate in the study, questions were answered, and informed consent was explained to each interested parent. An example of the phone-call work sheet used when contacting parents is shown in Appendix C. Parents who decided to include their child in the study were contacted by the Neuropsychological Consultation Services or the EIRI to schedule an

appointment for testing. Twenty-five subjects were obtained from this initial effort.

A second mailing from the respective medical center was sent to parents who had not responded to the initial mailing. The same process of recruitment was carried out with parents who responded to this mailing. Two more subjects were contacted from this effort.

In order to fulfill the proposed sample size for each group, it was necessary to recruit 2 more subjects from the neighboring states of Wyoming and Idaho. The same procedure was used in contacting these subjects. A final sample size of 13 for the mild IVH group and 16 for the severe IVH group was obtained.

At the time of testing, parents signed the informed consent form after all final questions had been answered. A copy of the informed consent form is provided in Appendix D. A follow-up appointment was also scheduled in order to provide the parents with the results of the testing. The final follow-up session consisted of briefing the parents on the child's performance based on the test data. Questions were answered and further explanations were provided as necessary.

A total of 21 subjects were tested through the Neuropsychological Consultation Service. Another six subjects were tested in their homes by a member of the research team at EIRI. The other two subjects from Idaho and Wyoming were also tested by a member of the research team from EIRI. Arrangements for testing these eight subjects were made by the EIRI research team.

Design

The children were assigned to each group based on diagnosis of IVH. Grades I and II formed the mild IVH group, and Graded III and IV

formed the severe group. Each group served as a comparison for the other in order to appropriately answer the research questions. The rationale for this stems from studies by Papile et al. (1983), Volpe (1981), and on a previously mentioned study by Williamson et al. (1982).

An attempt was made to include an equal number of 4- and 5-year-olds in each group to control for differences that may occur because of maturation. Each group represented a mixture of socioeconomic status as classified by Hollingshead, to account for any differences in history that may have been inherent in the two groups.

All children were treated in NICUs to control for early post-natal differences. It is known from past studies (Stewert et al., 1981) that children treated in NICUs usually have a better chance at recovery from post-natal complications than those who have not been in NICUs.

Instrumentation

Because there has been no follow-up done on survivors of IVH at ages 4 and 5, it was necessary to use a broad-spectrum screening that covered a variety of neurobehavioral functions and combination of functions. A group of tests was combined to form a neuropsychological battery that is clinically appropriate for assessment of residual effects of IVH. This battery was selected on the basis of a review of current practice in child neuropsychology (Filskov & Boll, 1981; Goldman et al., 1983; Nilsson, 1985; Rourke et al., 1983; Rutter, 1982).

Two types of data were collected for each child in the sample. The first type of information was taken from the child's medical record. The second type of data came from the results of the

neuropsychology battery. An outline of the instruments included in the battery is shown in Figure 3.

Assessment Device	Age Range	Brief Description
McCarthy Scales of Children's Abilities (MSCA)	2-1/2 to 8-1/2	5 subtests measuring verbal, perceptual performance, quantitative, memory, motor, and general cognitive
Raven's progressive Matrices (RPM)	3+	Abstract and Conceptual Thinking
Peabody Picture Vocabulary Test (PPVT)	2 to adult	Receptive Vocabulary
Preschool Language Scale (PLS)	1-1/2 to 7	Receptive/Expressive

Figure 3: Outline of instrumentation.

The McCarthy Scales of Children's Abilities (MSCA). The MSCA was designed to satisfy the need for a single instrument that could be used to determine general intellectual level as well as a child's strengths and weaknesses in important abilities (McCarthy, 1972). Scores derived from systematic observation of a variety of cognitive and motor behaviors are provided for six scales: verbal, perceptual-motor, quantitative, general cognitive, memory, and motor. The scales are appropriate for children from 2-1/2 through 8-1/2 years of age. The content of the tasks is suitable for both sexes, as well as for children from various ethnic, regional, and socioeconomic groups. The material and questions are game-like and non-threatening (McCarthy, 1972).

The MSCA is applicable for assessing the strengths and weaknesses of handicapped children since the battery includes a number of easy

tasks which were designed for young children. During the early stages of development, studies with mentally retarded and normal children explored the upper and lower ranges for which the tasks were appropriate and the extent to which they discriminated among successive age levels (McCarthy, 1972).

The Verbal Scale assesses the child's ability to express himself verbally and also assesses the maturity of his verbal concepts. Verbal ability, as measured in other traditional scales (WISC-R), has usually proven to be a good predictor of academic achievement.

The Perceptual-Performance Scale assesses the child's reasoning ability through the manipulation of materials. These are game-like tasks which do not require the child to speak. The child demonstrates such skills as imitation, logical classification, and visual organization in a variety of spatial, visual-perceptual, and conceptual tasks.

The Quantitative Scale was designed to measure the child's facility with numbers and his understanding of quantitative words. The item content is closely related to children's interests, and each item requires only a single step rather than a sequential process. This scale attempts to assess the child's number aptitude rather than to explore the upper limit of his computational skills.

The Memory Scale assesses short-term memory. The pictorial memory and tapping sequence tests present auditory and visual stimuli simultaneously; the verbal and numerical memory tasks provide auditory stimuli only. This assessment of memory in two modalities requires both verbal and non-verbal responses, and, using a variety of stimuli

(pictures, musical tones, words, and numbers), allows for extensive evaluation of short-term memory.

The Motor Scale was designed to assess the child's coordination as he performs a variety of gross and fine motor tasks. A child's motor index reflects his developmental level and is a vital adjunct to the overall picture revealed by the general cognitive index.

The General Cognitive Scale is made up of all the tests in the verbal, perceptual performance, and quantitative scales. The scale was a whole provides a measure of the child's cognitive functioning at a given point in time.

Preschool Language Scale (PLS). This is an instrument widely used as a diagnostic and screening instrument capable of systematically appraising the early stages of language development. The scale is especially useful for evaluating maturational lags, strengths, and deficiencies as they pertain to developmental progress.

The two parts of the PLS are based on the natural dichotomy between auditory comprehension and verbal ability (Zimmerman, Steiner, & Pond, 1979). The scale consists of a series of auditory and verbal language tasks, each of which is assigned to a certain age level. According to Zimmerman et al., all items in the PLS have been selected on the premise that in any language, a child's auditory comprehension and verbal ability develop according to capacity, maturation, and life experiences in a spiraling, sequential advancement. This progressive sequence is a catalyst for each stage of the child's cognitive, emotional, and psychological development.

The PLS is also useful for teachers in that it offers a detailed survey of a child's early language comprehension and use. Examination

of the results should provide useful indications of the child's strengths, emerging skills, lags, and deficiencies in receptive and expressive language.

Raven's Progressive Matrices (RPM). The RPM provide a means to assess a person's present ability to think clearly, irrespective of past experiences or present ability for verbal communication (Ravens, 1977). The colored progressive matrices, which is an additional set of problems used with younger children, was constructed to assess in greater detail the ability to complete continuous patterns which, towards the end of the set, change first in one and then in two directions at the same time. A second set of problems requires the ability to see discrete figures as spatially related wholes and to choose a figure which completes the missing part. A third set contained problems requiring abstract thinking.

Before the capacity to form comparisons and reason by analogy has matured, or in cases where it has become impaired, the progressive matrices will indicate the degree to which a person's capacity for observation and thinking has developed, or the level to which it has deteriorated. After the capacity to reason by analogy has matured, the matrices can show where a person's intellectual capacity lies relative to other people of the same age.

Peabody Picture Vocabulary Test (PPVT). The PPVT is designed primarily to measure receptive (hearing) vocabulary (Dunn & Dunn, 1981). It has been found useful for a number of school, clinical, and research purposes. Since the PPVT is a reasonably good measure of scholastic aptitude, it should also be useful as an initial screening

device in scanning for bright, low-ability, and language impaired children who may need special attention.

Not requiring subjects to read or write makes the scale especially fair for non-readers and other persons with written language problems (Dunn & Dunn, 1981). Also, because neither pointing or oral responses are essential, even severely handicapped individuals are able to be tested.

The PPVT has also been used widely in experimentation and research. The wide range of difficulty reduces the possibility of floor or ceiling effects, which is important in longitudinal studies. Because of its shortness and simplicity, examiners should use caution in generalizing, since its value is primarily as a receptive vocabulary test.

Data Collection

Descriptive medical data was collected from the medical records. Based on a review of current literature and on consultation with the neonatologists at PCMC and University of Utah Medical Center, the following information was collected: sex, age at time of testing, gestational age, and birthweight. Information was also collected on the following sequelae that commonly occur with LBW and/or IVH: seizure disorder, birth asphyxia, post-hemorrhagic hydrocephalus, apnea, hylane membrane disease, and hyperbilirubinemia. Other information was collected on the type of treatment that occurred in the NICU following an IVH. Three medical procedures were relevant: whether or not the infants received an exchange transfusion, ventriculoperitoneal shunt, or lumbar puncture.

The test protocols were administered and scored by trained examiners. The examiners were "blind" about all previous information for each child, including severity of IVH. Scoring and completeness of administration was checked by the research team project coordinator. Consultation was provided by Dr. Nilsson and the EIRI with administration, scoring, and interpretation. All data was recorded by subject I.D. number. A flow-chart of each phase of the study is presented in Appendix E.

CHAPTER IV

RESULTS

Two types of data were collected and analyzed. First, demographic data were collected from the medical records. Second, and because IVH typically occurs within the context of LBW, medical data indicating the presence or absence of other LBW sequelae were also collected from the medical records. These data were analyzed in terms of their relationship to the performance of the mild and severe IVH groups on the neuropsychological testing. The second type of data collected were based on the outcome measures of each of the scales used in the neuropsychological assessment battery. These data were analyzed to answer the primary research question. The demographic data for the 29 subjects is shown in Table 3.

Table 3

Demographic Characteristics of the Sample

Variables	Mild IVH (N = 13)			Severe IVH (N = 16)		
	Mean	SD	%	Mean	SD	%
Sex: male			62			65
female			38			35
Age at testing (mo.)	54.0	4.5		57.5	7.1	
Gestational Age (wks.)	30.5	2.8		31.1	3.5	
Birthweight (grams)	1495.4	473.3		1526.7	521.9	

Medical data, collected from the subjects' medical records, is shown in Table 4. This data represents common sequelae that typically occur along with LBW and IVH. Post-hemorrhagic hydrocephalus and porencephalic cyst do not usually occur with just LBW; they are sequelae that follow the occurrence of severe IVH. The percent of occurrence of each sequelae for the mild and severe IVH group is indicated.

Table 4

Medical Characteristics of the Sample

Sequelae	Mild IVH (n = 13)		Severe IVH (n = 16)	
	No.	%	No.	%
Apnea	9	69	10	63
Birth Asphyxia	1	8	4	25
Seizure Disorder	1	8	4	25
Hyperbilirubinemia	11	85	10	63
Hylane Membrane Disease	13	100	12	75
Post-Hemorrhagic Hydrocephalus	2	15	9	56*

* = Significant difference ($p < .05$)

It is also known that aggressive treatment of IVH, once the clinical signs are evident, can have differing effects in terms of the long-term prognosis. Two forms of treatment that are commonly performed in the NICU when the hemorrhage becomes extensive are lumbar

puncture and ventriculoperitoneal shunting. The lumbar puncture is used both as a prophylactic intervention in treating post-hemorrhagic hydrocephalus and as a treatment in the management of post-hemorrhagic hydrocephalus. Ventriculoperitoneal shunts are used as a last measure in controlling the progression of hydrocephalus. The incidence of these two treatments for the mild and severe IVH groups is shown in Table 5.

Table 5

Incidence of Treatments to Control Immediate Effects of IVH

Procedure	Mild IVH (n = 13)		Severe IVH (n = 16)	
	No.	%	No.	%
Lumbar Puncture	0	0	11	69*
Ventriculoperitoneal Shunt	1	8	4	25

* = Significant difference ($p < .05$)

Primary Analysis of the Neuropsychological Assessment

Two methods were used to compare the results of the neuropsychological testing. A discriminant analysis was performed to determine if the mild and severe IVH groups could be distinguished on the basis of the test scores. Discriminant analysis is employed to statistically distinguish between two or more groups. These groups are defined by the research situation. The analysis aspect of this technique provides

a measure of success with which the discriminating variables actually discriminate between the two groups (Kerlinger, 1979; Nie, Hull, Jenkins, Steinbrenner, & Bent, 1975).

The second analysis used was the t-test of significance. A neuropsychological approach to assessment is predicated upon individual comparisons of a variety of functions. The t-test provides a method for statistical analysis of the differences between the means of each group on each measure.

The results of the discriminant analysis of mild and severe IVH groups and the neuropsychological testing yielded no statistical significant (chi-square = 21.16, d.f = 19, $p < .3$). It was not possible to distinguish performance on the neuropsychological testing based on severity of the hemorrhage. Prediction of group membership (mild or severe IVH) could not be made based on these test results.

Individual t-test analysis of each scale used in the neuropsychological testing further indicated no significant difference between the mild and severe IVH groups. The mean scores of the McCarthy Scales and the results of the analysis are shown in Table 6. As shown in Table 6, there was no significant differences found on any of the scales of the McCarthy. Although there was no statistically significant differences found between the two McCarthy scales, the severe IVH group actually performed slightly better on most of the scales than the mild IVH group. More specifically, it is known that severe hemorrhaging typically causes more severe motor handicaps. These results indicate that even on the McCarthy motor subscale, there was no significant difference between the mild and severe groups.

Table 6

Means and Standard Deviations of the McCarthy for Mild and Severe IVH

Scales	Mild IVH (n = 13)	Severe IVH (n = 16)
McCarthy Scales		
General Cognitive		
M	79.3	81.1
SD	33.3	-39.1
Verbal		
M	42.6	44.6
SD	18.2	21.3
Perceptual-Performance		
M	35.6	36.8
SD	17.1	19.8
Quantitative		
M	40.3	40.8
SD	16.2	20.4
Memory		
M	42.3	42.0
SD	16.2	20.5
Motor		
M	30.5	32.6
SD	15.7	15.8

The mean scores for the Peabody Picture Vocabulary Test (PPVT) and the Ravens Progressive Matrices (RPM) are shown in Table 7. No significant difference was found between the mild and severe IVH groups on these measures. The PPVT measures receptive vocabulary and the RPM measures abstract and conceptual thinking.

Table 7

Means and Standard Deviations of the PPVT and RPM for Mild and Severe IVH

Scale	Mild IVH (n = 13)	Severe IVH (n = 16)
PPVT		
M	84.0	82.8
SD	33.7	38.6
RPM		
M	8.3	9.1
SD	6.0	6.0

The last set of comparisons analyzed were the results of the Preschool Language Scale (PLS). Three comparisons were derived from this measure: a verbal language quotient, auditory comprehension, and verbal ability. As shown in Table 8, no significant differences were found between the mild and severe IVH groups on these measures of language ability.

Table 8

Means and Standard Deviations of the PLS for Mild and Severe IVH

Scale	Mild IVH (n = 13)	Severe IVH (n = 16)
PLS		
Language Quotient		
M	94.8	86.8
SD	33.4	40.0
Auditory Comprehension		
M	96.3	88.1
SD	33.0	40.2
Verbal Ability		
M	93.2	84.9
SD	34.6	39.7

Relationship of Medical Data to Performance

The basic question of interest in the study was to determine whether there were significant differences in performance between the mild IVH group and the severe IVH group on the neuropsychological assessment. The results of the primary analysis yielded no significant difference between the groups. It seemed necessary then, to determine if there were significant relationships between other sequelae of LBW/IVH and the test results, that could have accounted for the lack of significant findings.

Pearson Correlational Coefficients were computed between the neuropsychological test results and the medical characteristics of the

sample listed earlier. As shown in Table 9, significant correlations were found between those subjects that had documented episodes of seizure disorder in the early post-natal period and performance on all measures. These correlations ranged from .35 to .51. Other significant correlations, although not as strong, were found between

Table 9

Pearson Correlational Coefficients Between Other Sequelae of LBW/IVH and Neuropsychological Test Performance

	A	BA	SD	HBR	HMD	PHH
McGenCog	.09	.21	.44C	-.09	-.08	-.03
McVerbal	-.03	.21	.35B	-.10	-.07	-.01
McPerformance	.27A	.18	.47C	-.13	-.08	-.09
McQuantitative	.09	.22	.46C	-.10	-.10	-.01
McMemory	-.06	.21	.39C	-.12	-.07	.06
McMotor	.20	.24	.43C	-.14	-.09	.00
PPVT	.00	.33B	.46C	.06	-.12	-.09
PLSLQ	.00	.34B	.45C	.06	.12	-.05
PLSAC	.04	.33B	.45C	-.09	-.16	.05
PLSVA	-.05	.34A	.45C	-.01	-.06	.05
RPM	.27A	.01	.51C	.01	.01	-.06

Note: A = Apnea, BA = Birth Asphyxia, SD = Seizure Disorder, HBR = Hyper-bilirubinemia, HMD = Hylane Membrane Disease, PHH = Post-Hemorrhagic Hydrocephalus, Mc... = McCarthy Scales

A = $p < .10$, B = $p < .05$, C = $p < .01$

those subjects that experienced birth asphyxia and performance on the PPVT and the PLS. The lowest correlation on these language related measures was .33 for the PLS verbal ability and the highest was .34 for the PPVT. Other significant correlations were found between those subjects diagnosed with an apneic episode and their performance on the RPM (.27) and on the McCarthy Performance subtest (.27). There were no significant correlations between test performance and hyperbilirubinemia, hylane membrane disease, or post-hemorrhagic hydrocephalus.

These results indicate a relationship between a history of both seizure disorder and birth asphyxia and performance on the neuropsychological testing. The presence or absence of neonatal seizure disorder has the strongest correlations with outcome measures on the neuropsychological assessment.

Although not within the parameters of this study, it is important to report how the IVH children are performing when compared to normal children. On all measures, both the mild and severe IVH groups performed significantly lower than normal children in the same age group. When compared to the normative data of the standardization samples for the instruments, both groups are performing at close to one standard deviation lower than normals.

The greatest difference in performance when comparing the IVH groups to normal children, is seen on the McCarthy motor subtest. The mean of the standardization sample is 50 and the standard deviation is 10. The mild IVH group had a mean of 30.5 and the severe IVH group had a mean of 32.6. Both IVH groups performed close to two standard deviations lower than the normal children.

CHAPTER V

DISCUSSION

This discussion will first of all summarize the findings of this study. Specific implications of the results will be presented. Following this, the strengths and weaknesses of design and methodology will be discussed. Limitations of the study will then be presented and their relationship to the current findings will be discussed. Suggestions for further research will then be indicated based on the overall review of the study.

Summary of the Findings

The results did not indicate that there is a difference between mild and severe IVH groups in their performance on the neuropsychological testing. On all measures, the analysis did not yield any significant findings. When compared to the scores of a normative sample, however, both IVH groups performed below that of normals. Based on these results, one general conclusion that could be drawn is that the severity of an IVH at birth does not predict children's cognitive performance as they approach school age. Residual effects of IVH have a more profound effect earlier on, but may not continue to have the same effect as the child develops. More obvious gross motor deficits may continue to be exhibited, but cognitive functioning may not show the same degree of deficit. The plasticity of the developing brain may be able to make-up for the cognitive effects of the hemorrhage over time, such that less obvious differences are seen with continuing development.

The issues of plasticity and equipotentiality are major issues to be considered in analyzing the findings of neuropsychological assessment with children. It has been well documented in the literature that the immature brain has the ability to recover from severe insults like IVH (Rourke et al., 1983). IVH in the newborn is typically a germinal matrix or basal ganglia hemorrhage, which has primarily more deleterious effects on gross motor functioning. Secondary effects to the brain as a whole are increased intracranial pressure and decreased cerebral perfusion, destruction of periventricular white matter, destruction of glial precursors in the germinal matrix, focal cerebral ischemia, and axonal stretching and tearing. It is quite possible that as this population of children develop and approach school age, the secondary effects of the IVH, which early on may have a significant effect on cognitive or intellectual ability, may now have less obvious manifestation. The brain may have been able to recover from the effects of a severe bleed in such a way that the neuropsychological measures used were not able to pick up any significant differences in intellectual performance.

In furthering this point, it is important to mention again that the current literature indicates that while more severe hemorrhaging typically results in more severe handicapping, some children with severe IVH have been shown to do as well as children with mild IVH and also as well as similar LBW children without a history of IVH (Gaiter, 1982; Papile et al., 1983). Specifically, a study by Gaiter (1982), which was used in the meta-analysis, produced findings that are similar to the findings of this study. In her study, IVH infants of differing severity were compared to an equally matched group of control infants

without IVH. These subjects were administered the Bayley Mental Development and Psychomotor Scales. The infants were tested initially at 12 months and then at 18 months. The results showed that altogether, motor dysfunction was the most characteristic abnormality present in the IVH infants at both 12 and 18 months. This finding has also been supported by Fitzhardinge et al. (1982) and Williamson et al. (1982).

More importantly related to the findings of this study was that there were no significant differences in cognitive performance between the IVH sample and the control babies in the Gaiter (1982) study. Nine of these infants had Grade II IVH (mild) and ten had a Grade III IVH (severe). No Grade IV IVH (most severe) infants were included in this study. In spite of this difference in samples, Gaiter's conclusion was that the presence of a hemorrhage has a more negative affect on neuromotor functioning than on mental abilities.

At 18 months, Gaiter's sample continued to show no significant differences in cognitive performance. The IVH infants appeared to be almost one month ahead of the control infants in social behavior and seemed to have caught up with the control sample in other areas. The major finding of Gaiter's study was that at 12 months there was a significant difference in the motor performance of the IVH and control infants; cognitive functioning was essentially the same. At 18 months the differences in global motor functioning were less evident than at 12 months, but cognitive functioning continued to show the same lack of significant differences as the 12 month testing. Although motor performance is still more significantly affected even at 18 months,

cognitive performance seemed to show less residual effects both at 12 months and at 18 months.

In the current study, the measures used were primarily measures of cognitive functioning. Except for the Raven's Progressive Matrices, all other subscales had a very high degree of correlation with each other (.80-.99). The instruments appear to have measured similar neuropsychological functions or functions that are highly rated. The results then, seem to indicate a continuing trend of recovery that is consistent with some of the previous findings shown in younger children, where increasingly less difference has been shown in cognitive performance as these children continue to develop. These findings seem to provide some evidence of the fluidity of neurological disorganization in the early history of children having experienced IVH. Even with severe hemorrhaging the brain may have the potential to recover from secondary effects of IVH.

In spite of the fact that the results do not indicate differences in performance between the mild and severe IVH groups, it is important to look at the findings from a neuropsychological approach and examine the results for potential clinical significance. On the McCarthy scales, the severe IVH group actually performed better than the mild IVH group on all subscales. The greatest difference, although not statistically significant, was on the general cognitive and verbal subscale. The most surprising finding was that there was not a significant difference between the mild and severe IVH groups on the McCarthy motor subscale. The finding is not supported by the current literature. There may have been confounding factors in the two groups that resulted in this lack of significant difference. The mild IVH

group may have had more significant motor handicapping that resulted from other sequelae of LBW and Prematurity. This factor was not considered when recruiting subjects for the study.

On the Peabody Picture Vocabulary Test (PPVT), which is a reasonably good measure of scholastic aptitude, there was a difference of only two standard score points between the groups. It is interesting to note that the PPVT is highly correlated with the McCarthy (.91), and may be measuring the same neuropsychological domain as the McCarthy. On the Ravens Progressive Matrices there were no statistically significant differences, but the mild group scored slightly higher than the severe group. The Ravens, however, does show a strong correlation with the McCarthy general cognitive scale (.84), and would seem to suggest that it also measures a similar domain as the McCarthy. As indicated by Ravens (1977), the progressive matrices were designed to measure abstract and conceptual thinking.

The Preschool Language Scale provides a language quotient and a differentiation between auditory comprehension and verbal ability. Although no statistical differences were shown, the largest qualitative difference between the mild and severe groups was on this measure of language ability. What is interesting to note about this is the high correlation between this subscale and the McCarthy general cognitive subscale (.95). These findings may indicate the need for more fine discrimination in the area of auditory comprehension.

The secondary findings from this study, based on the correlations between the presence or absence of other LBW/IVH sequelae and test performance, showed that there is a significant relationship between neonatal seizure disorder and performance. The correlations of .35 -

.51 suggest that children with a history of seizure disorder did poorer on their test performance than those children who did not have a documented seizure disorder. Although a causal relationship cannot be inferred, this finding indicates that the residual effects of this disorder may have lingering effects at preschool age.

A more relevant issue is that the severe group had a greater incidence of seizure disorder than the mild group (25% and 8%, respectively). Although this did not show up as a statistically significant difference, it would be expected that this may have further impaired the severe IVH group in their performance. The results, however, did not show this to be the case.

There was also a significant correlation found between the incidence of birth asphyxia and performance on the PPVT and PLS (.18 - .34). Although not as strong a relationship as shown with seizure disorder, children who had documented episodes of birth asphyxia seemed to do poorer on their performance. Again, there was a greater incidence of birth asphyxia in the severe IVH group (25%) than in the mild IVH group (8%). This difference was not shown to be statistically significant, and it did not seem to have a significant additive effect on the performance of the severe group.

The severe IVH group did have a significantly higher incidence of post-hemorrhagic hydrocephalus (PHH) than the mild IVH group ($p < .05$). Consequently, the severe IVH group also had a significantly greater number of lumbar punctures in attempts to treat and manage the hydrocephalus ($p < .05$). It was expected, based on previous findings (Ment et al. 1982), that the severe IVH group would perform more poorly not only because of the severity of the IVH, but because of the greater

incidence of PHH and its subsequent effects. There was, however, no significant difference found between the groups' performance in spite of the greater incidence of PHH in the severe IVH group.

In general, there was no evidence shown from the results that the lack of significant findings was due to differences in the medical characteristics of the group as described by the data collected from the medical records. There may have been other differences between the groups that were not identified within the parameters of the study. At the present time, it is not known what these other differences are, and how they could potentially effect the findings. Based on the information and findings of this study, however, the results appear to confirm at least some of the findings of previous follow-up that indicate some recovery of cognitive functioning with continued development.

In spite of the lack of significant differences found between severity of IVH and test performance, it is again important to note that this population of LBW children are still performing well below average when compared to normal birthweight children. These results indicate that both IVH groups are still behind their normal age mates. It is not known whether this difference will continue to be evident as these children continue to develop. More research will be needed as these children move into the first and second grade to determine how IVH at birth affects academic performance.

Strengths and Weaknesses in Design and Methodology

Strengths. A major strength of this study was the availability of subjects from more than one hospital setting. Kiely and Panath (1981)

indicate in their article on suggestions for design, analysis, and reporting in follow-up studies of LBW babies, that most studies that have been done were based on a single hospital sample. In the various geographical areas, such samples may well represent a complete population study of LBW children, but rarely is evidence provided to support this point. They state that geographically-defined population studies seem to be a much sounder principle. Inferences from samples to population groups would be more secure and inter-hospital comparisons would be possible. As indicated in Chapter III, the subjects in this study came from two hospitals, but were within the same geographical region. Inferences can be made to the population within this geographical region and future research could be done comparing the difference in performance between two hospital populations. The inclusion of subjects from two hospitals would seem to strengthen the findings of the present study by allowing for a greater degree of generalizability.

A second area that is cited by Kiely and Panath (1981) as important in follow-up studies with LBW children is age at time of testing. They state that one of the major flaws of many follow-up studies is that intelligence testing and neurodevelopmental diagnoses are done at an early age. This is done most often in the first two years of life. With children so young, one cannot get a valid and reliable evaluation of developmental functioning. They recommend that every effort should be made by researchers to follow LBW children up to age four and preferably to age seven.

In the present study it was decided to investigate an older group of children because of the issues raised by Kiely and Panath, and

because the current literature in follow-up with IVH children has typically been done with children 36 months or younger. The findings of this study are different in some respects from findings reported in the literature where studies used younger children. Continued follow-up with these children will be carried out to determine the reliability of these results.

As indicated in Chapter II, previous follow-up studies done with IVH children have used gross measures and indicators of development. These have typically been limited by the use of one test such as the Bayley Developmental Scales, or other measures of neurological and physiological functioning. The use of a neuropsychological approach to assessment in the present study allowed for a variety of functions to be measured. It also allowed for comparison of subtest functions, which provide a more qualitative look at a child's performance. Gaiter (1982) used a similar approach in her follow-up study of IVH children by looking at developmental subscale data from the Bayley. Although the results did not indicate a difference in performance between the mild and severe groups in the present study, analysis of a variety of functions allows for more specific conclusions to be drawn. The results did not indicate a difference when looking at global measures like the McCarthy general cognitive scale, nor a difference on other subtest functions such as those assessed by the Preschool Language Scale.

Weaknesses. Some caution should be used in making conclusions based on the results of the present study. There are a number of limitations and potential threats to internal validity that could account for the findings. One area of limitation is the choice of

comparison group used. Kiely and Panath (1981) again indicate that a major problem in study design is determining the proper comparison group to which the IVH child should be compared. No scientific inferences about sequelae can be made unless they are compared with some other group. The type of comparison group depends on the purpose of the study.

The rationale for using differences in severity of IVH as the major comparison rather than using a control group of matched subjects without IVH, was that it is already well documented in the literature that LBW children who suffer IVH typically have a higher incidence of severe handicap than the general population of children. However, if one is interested in outcome not only in terms of whether the new technology used in the NICU has been damaging or not, but also in terms of the etiological factors underlying LBW, Kiely and Panath indicate that a control group of normal children becomes extremely important. The limitations of this study related to this issue are that comparisons were not made between differences in severity of IVH and similar children without IVH.

Another area addressed by Kiely and Panath is the issue of social class and socioeconomic status. An effort was made to include a mixture of socioeconomic status in each group. This was attempted by making inferences about social class based on the employment of the father or mother of each child. This information was obtained from the medical record. However, it is not known whether this information was complete enough to determine heterogeneity of social class within each group. It is possible that the mild IVH group had a greater number of low social class subjects than the severe group. Previous studies

cited by Kiely and Panath indicate that low social class is associated both with perinatal difficulties and with childhood morbidity (especially lower IQ and mild mental retardation).

The sample size in this study represents a major limitation in terms of generalizability. Because of the size of the sample, within group differences could have confounded the results obtained in performance. Investigators planning future follow-up of IVH children should also make every attempt to keep track of these children from an early age rather than to attempt locating subjects four and five years later. Also, follow-up services within the hospital should keep track of children who were treated in the NICU in order to make the availability of greater numbers of subjects more feasible.

Another possible limitation of the design was the combination of Grades I and II as a mild IVH group and Grades III and IV as a severe group. The rationale for defining the two groups in this way was based on previous research suggesting small differences between Grades I and II and between Grades III and IV. The meta-analysis cited in Chapter II suggests differences of less than 1/2 of a standard deviation between Grades I and II and Grades III and IV. In contrast, differences between mild IVH as defined in this study and severe IVH indicate over 3/4 of a standard deviation difference (ES = 0.78).

The main limitation, however, is that it is not known how many of each Grade of IVH were represented in the two groups. If a greater number of Grades II and III were included rather than Grades I and IV, the groups may have been more similar than expected. This represents a potential threat to internal validity. If an equal number of each grade were included in each group, it would be possible to have

represented both ends of the severity spectrum--very mild and very severe.

Although it has been argued by different researchers that the classification system of IVH into Grades I-IV is less useful clinically than previously thought, it would strengthen the results of the present study of inter-grade comparisons had been carried out. Based on the design of this study, it is not known how this factor influenced the findings.

The lack of more thorough description of the medical characteristics of the two groups represents another limitation in methodology. More medical information could have been collected in order to more clearly describe the other sequelae of LBW. It is known that other sequelae of LBW, such as bronchial pulmonary dysplasia, can have an effect on the performance of IVH children (Gaiter, 1982). There are a number of other medical complications that commonly occur with LBW and IVH that may have influenced the findings. For example, the incidence of bronchial pulmonary dysplasia (BPD) is a common sequelae that typically occurs with very low birthweight babies and can compound the existing clinical picture. This information would be important to obtain. Another example of other medical complications that could be obtained is the incidence of porucephalic cysts with severe IVH children, presence or absence of hypertension, and the incidence of cerebral palsy. If the mild IVH group had a greater incidence of other medical problems other than the ones described in this sample, it could have suppressed their scores and accounted for the lack of significant differences obtained.

Another area that represents a potential threat to internal validity is the differences in environment that were experienced by the two groups. It is not known whether children were enrolled in early intervention or developmental programs or whether some of the children were just discharged from the hospital with routine follow-up. If the severe IVH children, because of the severity of their condition, were enlisted in special programs, they may have been able to demonstrate more significant recovery and thus perform as well as the mild IVH group which may not have been enrolled in special education programs because of their apparent lack of severity. It is not known whether early intervention with this particular population of children results in enhanced development and better recovery of function. Future research in follow-up of IVH children should make every effort to identify the types of special programs these children have been in, so that this potential threat to internal validity is ruled out.

Two final issues that represent possible limitations of this study have to do with the functions measured and the instrumentation. Based on the inter-test correlations mentioned earlier, it appears that the subscales, with the exception of the Ravens, were all measuring highly-related areas of cognition. While the advantages of this area was the variety of cognitive functions measured, the limitations are that the instruments did not measure other areas, such as fine motor functioning, where it has been documented that there are differences between severity of IVH. The choice of instrumentation was an improvement over previous research in that grater variety of functions were measured, but the tests may have been too concentrated in one area. Continuing research with IVH children should address this issue

by including a greater number of instruments that measure varieties of motor functioning as well as cognitive functioning.

Indications for Future Research

Follow-up of children with a history of IVH is still a growing area of research. The findings of this study that suggest no differences in cognitive performance between mild and severe IVH groups does add some new and unexpected findings to the current literature. The major contributions of this study are the use of a neuropsychological approach to assessment, the older age group of these children as compared with previous research, and the attempt to look at differences in severity that may be more clinically meaningful than intra-IVH grade differences. Further research is needed to demonstrate the reliability of the current findings. In planning continued follow-up with this population of children, there are a number of areas, based on the design and findings of this study, that should be considered.

The first area is selection of samples. It is highly recommended that every effort be made to include larger sample sizes, so that within group differences are minimized. Furthermore, attempts should be made to include equal numbers of each grade of IVH so that the continuum of severity is balanced in the groups being compared. It is also important to gather as much information from the medical records as possible so that the medical characteristics of the IVH groups are well described. This medical information can then be used to look at the potential effects of other sequelae of LBW as well as IVH. In addition, future studies should also indicate the type of medical problems that have occurred since the children were discharged from the NICU. Children who have profound medical problems at birth typically

continue to have medical complications. Documentation of these post-NICU complications should be made to provide a more accurate picture of a child's current status.

Documentation of past experience in special education programs should also be obtained so that the effects of early intervention can be examined in terms of its relationship to outcome. The parents of children included in the study can provide information on whether or not the children have been in a special education program. Then, information on the type of program can be obtained from the facility where the child is enrolled.

Given that this study looked at an older group of IVH children and the results were not entirely consistent with previous findings using younger children, continued follow-up with this age group is recommended. Replication of the present findings is needed in order to strengthen the inferences being made that the residual effects of IVH have less influence on cognitive functioning as a child develops. It would also be helpful to continue following the same group of children for a period of five years to determine the longitudinal reliability of the current results. Two questions then need to be answered: (1) Can the current findings be replicated with a similar group of IVH children at the same age? (2) Will the lack of apparent differences in performance between groups of mild and severe IVH children continue to hold true as they grow older?

In addition, as more information is gathered on this population of children, an attempt should be made to develop a profile of how IVH children are performing. Profiling how IVH children perform on a variety of difficult functions would give educators a consistent method

to plan intervention. It would also provide a means to describe more completely the behavior and neuropsychological functioning of IVH children.

Another area to be considered in future research with this population of children is the continued use of a neuropsychological approach to assessment. The current study provided some enhancement in assessment as compared with previous studies, but finer discrimination is needed in examining more subtle differences that may be occurring in children with a history of IVH at birth. Although developmental quotients, neurological examinations, and psychological measures will continue to be important in looking at the longitudinal effects of IVH, continued neuropsychological assessment of this population can also provide additional information that can be useful in expanding the data base on research in this area.

A final issue that deserves attention is the need for continued integration of the current research in this area. In the present study, the use of meta-analytic techniques helped to quantify the current state of the literature so that potential trends in recovery could be identified. There are, however, a number of other questions that can be answered by continuing to use meta-analytic approaches in reviewing the literature. Among these are the analysis of different age groups from birth to age four and five in order to more clearly specify the differences in performance that have been previously reported. Further analysis of the types of IVH samples being used and how that relates to outcome can also be more clearly examined by the use of meta-analysis.

The meta-analysis reported in the review of the literature was based on both a small number of studies and a small number of effect sizes. As mentioned earlier, the findings are at least tentative. The results of the meta-analysis, however, do suggest that there are differences in performance of children with mild and severe neonatal IVH, at least up through 36 months of age. The results of the present study, which used an older group of children, did not concur with these findings. More primary research with IVH children and continued integration of the literature needs to be done to determine whether the incidence of neonatal IVH will continue to have residual effects on a child's growth and development.

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APPENDICES

Appendix A
Meta-Analysis Coding Instrument

CODING INSTRUMENT FOR LOW-BIRTH-WEIGHT STUDIES

(authors/year) (title)

INTRODUCTION

	1. Study ID#
	2. Year
	3. Type of Study: (1 = longitudinal with comparison group 2 = longitudinal without comparison group 3 = one time follow-up with comparison group 4 = one time follow-up without comparison group 5 = single subject)

SAMPLE

	1. Mean age at time data collected (if composite of different ages, put age at last measure)
	2. Were children treated in a NICU?
	3. How does study break-up gestational age groupings? (1 = less than 40 weeks 2 = less than 35 weeks 3 = less than 30 weeks 4 = breaks up age groupings into smaller increments 5 = just gives mean age for all subjects)
	4. How does study break-up birth weight groupings (1 = less than 2000 grams 2 = less than 1500 grams 3 = 1200-1500 grams 4 = 1000-1200 grams 5 = less than 1000 grams 6 = just gives mean weight for all subjects)

5. Size of Sample

6. SES (1 = high, 2 = middle, 3 = low, 4 = mixed)

_____(how SES determined)

% of each

1	2	3

8. Sex %

m

f

9. % of sample with no handicap, or considered normal

10. % of sample with major handicap (IQ or DQ less than 70)

11. % of sample with minor handicap (IQ or DQ 71-84)

12. How does study classify different types of handicaps

13. % of sample with gross neurological problems

14. % of sample with minor neurological problems

15. How does study distinguish types of neurological problems

16. Is sample from a single institution or hospital?

IVH

1. Does study mention IVH?

   If yes, explain briefly how

2. Does study compare residual effects of IVH with an equally matched group(s) without IVH?

3. Does study mention differences in severity of IVH?

4. How is severity of IVH classified?
   (1 = Papile's System--based on CT scan
   2 = Same as Papile, but based on Ultrasound
   3 = Based on ultrasound, but a different classification system
   4 = other

5. What % of children in the study had IVH?

6. Does study compare outcome measures of different grades of IVH?

7. Does author make recommendations about specific types of interventions or rehabilitation programs based on the measures used to explain residual effects of IVH?

Analysis

1. Can an effect size be computed?

2. Data from which mean difference ES was calculated
   1 = means and SD
   2 = means and published test SD
   3 = t ratio/Fratio from one-way ANOVA or exact probability
   4 = F ratio from mixed model ANOVA
   5 = ANCOVA F ratio
   6 = non-parametric test statistic except chi square
   7 = chi square
   8 = probability estimate for t test or one-way ANOVA
   9 = proportions (probit transformation)
   10 = other

DESIGN and MEASURES

1. Type of comparison group (1 = normal birth weight or SFD
   2 = low birth weight
   3 other_____

2. Is comparison and experimental group equally matched?

   If yes, list variables used in matching

3. Type of Measures used for experimental group (1 = IQ or DQ scores
   2 = Psycho-Ed
   3 = Physiological measures
   4 = Neurological Exam
   5 = Clinical opinion
   6 = Non-professional opinion
   7 = Composite_____

4. Adequacy of descriptive information provided about:
   (1 = complete information, 2 = somewhat sketchy,
   3 = inadequate information)

   A. Subject variables

   B. Methodology

   C. Design and Analysis

5. Was data collector blind to subject groups?

6. Threats to Validity

   A. Maturation

   B. History

   C. Testing

   D. Instrumentation

   E. Statistical Regression

   F. Selection Bias

   G. Experimental Mortality/Attrition

   H. Description of sample/methodology/ design and analysis

   I. Other_____

   0 = not a plausible threat
   1 = potential minor problem
   2 = plausible alternative explanation which could account for substantial amount of the results
   3 = by itself could explain all of the outcome

7. General index of validity
   (1 = high.....5 = low; code from conventions)

REVIEWS OF LOW BIRTH WEIGHT STUDIES

Coding Instrument

(author/year) (title)

1. In what way does the article qualify as a review article? (check all that apply)

_____a) "Review" is in title (or similar heading such as "survey").
_____b) Reviews 5 or more articles or studies.
_____c) Author(s) refer to it as a "review" in the text.
_____d) Other_____

_____2. How many previous reviews of outcome of infants of Low Birth Weight are cited by the author as reviews? (indicate with "R" in references)

_____3. Does reviewer critique previous reviews?
Yes = 1, No = 2

Summarize major points of critique:

_____4. Does the review article describe the procedures used to locate or delimit the studies which were used in the review to draw conclusions?
Yes = 1, No = 2

_____5. What is the actual number of longitudinal or follow-up studies used in the review to draw conclusions about the outcome of Low Birth Weight children?

6. Summarize conclusions drawn about common methodological weaknesses in existing studies of Low Birth Weight children.

7. Summarize the major conclusions of the review.

Appendix B
Initial Contact Letter

October 10, 1985

Dear

The Primary children's Medical Center is collaborating in a retrospective study with the Early Intervention Research Institute at Utah State University. The primary purpose of the study is to undertake a developmental follow-up of a sample of infants who were patients in the Neonatal Intensive Care Unit at Primary Children's Medical Center during 1980.

The purpose of the study will be to ascertain the current developmental status of those low birth weight infants who were born in 1980 and 1981. Since your child was in our Neonatal Intensive Care Unit during this time, I am asking your permission to have the research institute contact you, explain the purpose of the study to you, and give you the opportunity to participate in the study if you so desire.

If you want the research team to contact you, please let me know by returning the enclosed postcard by _____ and your name can then be released to the team and they will contact you.

Please be assured that all information concerning you and your child will be kept confidential, and only group results will be reported should you agree to participate in the study.

Sincerely,

Jack Dolcourt, M.D.
Medical Director for Infant Care Services

JD:meh

Enclosure

October 10, 1985

Dear

In a previous letter you were informed that the University of Utah's Medical Center is collaborating in a retrospective study with the Early Intervention Research Institute at Utah State University. The primary purpose of the study is to undertake a developmental follow-up of a sample of infants who were patients in the Neonatal Intensive Care Unit at the University of Utah's Medical Center during 1980. Since I have not received a response card from you, I am sending this second letter.

The purpose of the study will be to ascertain the current developmental status of those low birth weight infants who were born in 1980 and 1981. Since your child was in our Neonatal Intensive Care Unit during this time, I am asking your permission to have the research institute contact you, explain the purpose of the study to you, and give you the opportunity to participate in the study if you so desire.

If you want the research team to contact you, please let me know by returning the enclosed postcard by _____ and your name can then be released to the team and they will contact you.

Please be assured that all information concerning you and your child will be kept confidential, and only group results will be reported should you agree to participate in the study.

Sincerely,

Gary Chan, M.D.
Medical Director for Infant Care Services

GC:meh

Enclosure

Appendix C
Protocol for Phone Call to Parents

IVH RETROSPECTIVE STUDY

Protocol for Follow-Up Phone Call to Interested Parents

Purpose of the Study

1. Follow-up of infants treated in the Neonatal ICU at PCMC and University of Utah.
2. Interested in looking at the developmental outcome of these children at late preschool age and approaching school age.
3. We will be investigating how children have recovered from medical complications that frequently occur with prematurity.
4. We expect to continue following these children over the next few years to determine the longitudinal effects of prematurity.

Neuropsychological Assessment

1. We will be assessing each child's qualitative performance on a variety of intellectual functions: memory, speech, language, physical abilities, thinking process, etc.
2. As a result of this assessment, we will be able to better identify a child's strengths and weaknesses intellectually.
3. This will be valuable information for parents and educators.

Services to be Provided

1. Free testing of your child.
2. Testing will be done by a licensed clinical psychologist.
3. A one-time only assessment that should take approximately 2-3 hours.
4. Free follow-up session where the results of the testing will be reported and explained to you.
5. A copy of the test report.
6. Will pay milage (.20 per mile) for out-of-town subjects.

Consent/Confidentiality

1. All family and children's names will remain confidential.
2. You may withdraw from the study at any time without prejudice.

Procedures

1. The doctor's office (neuropsychology) will contact you to set-up the date of testing.

2. They will call you the day before to confirm the appointment.

3. The follow-up visit will also be scheduled for you at the time of the testing.

Appendix D
Informed Consent Form

INFORMED CONSENT FORM

This certifies that I have been informed of the purpose of the proposed developmental follow-up which involves the follow-up of my child in a retrospective study comparing children who experienced intraventricular hemorrhage at birth. I understand that the risks to my child are minimal and that the potential benefits include my acquiring a better understanding of my child's developmental status.

I understand that there will be a neuropsychological assessment of my child done by a licensed psychologist. The assessment will include a test of intellectual functioning and achievement, a test of physical and motor skills, and an instrument to measure language ability. The total testing time will be approximately two hours. I also understand that any records kept on my child will remain confidential, and that I may request and receive the results of the study.

If I decide to withdraw from the study, I understand that I may do so without prejudice. I also understand that the continued developmental follow-up of my child may be available on a yearly basis until my child reaches the age of nine.

If I have any questions, I may contact Glenn Goodwin, Project Coordinator, at (801) 752-1247 at any time. I also understand that I may contact Glendon Casto, Ph.D., at (801) 750-2000 in those cases where a problem cannot be discussed with Mr. Goodwin.

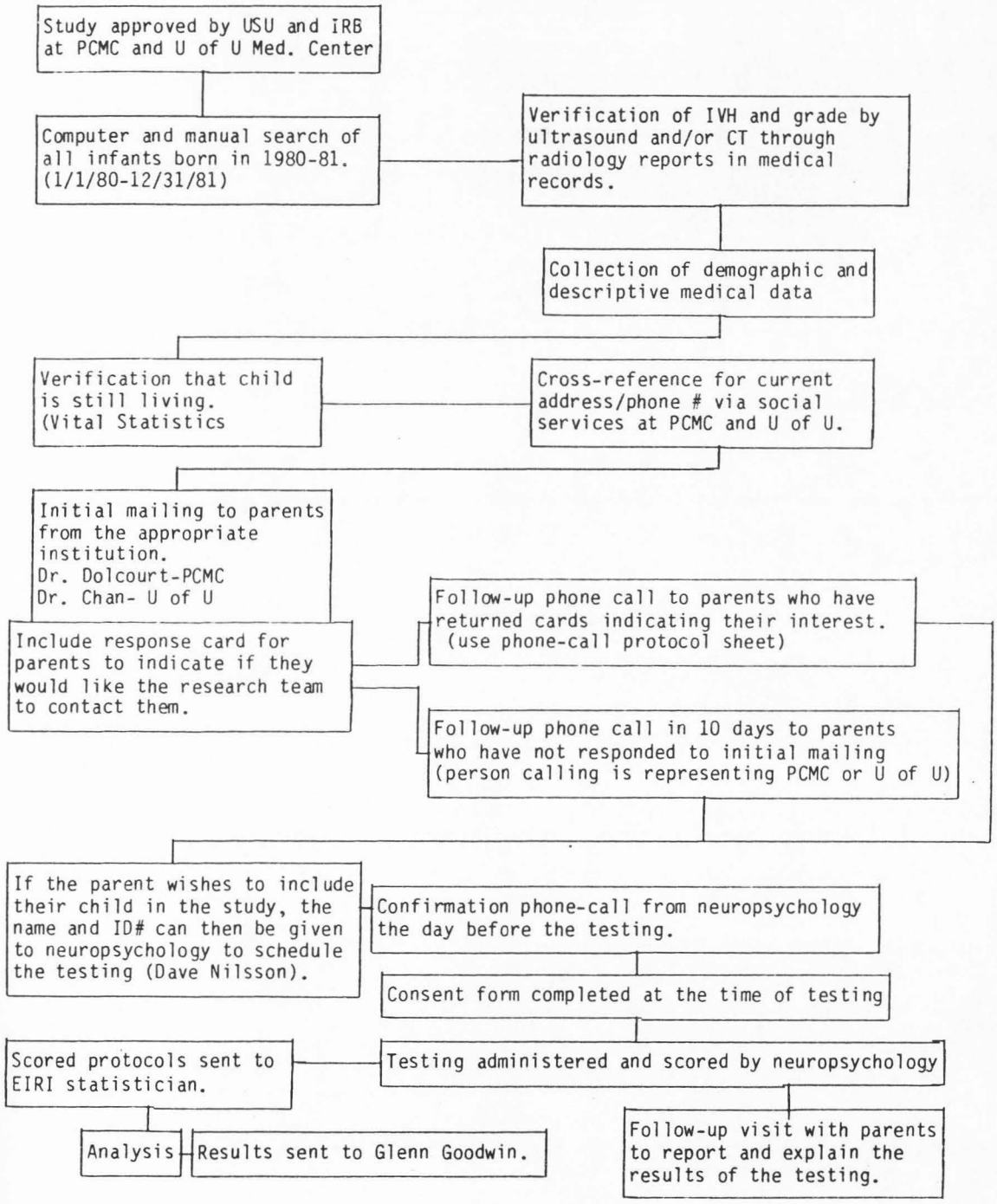
_____ _____

Parent Signature Date

Appendix E
Flow Chart of Procedures

IVH RETROSPECTIVE STUDY

Flow Chart of Procedures



Appendix F
Thank You Letter to Parents

Appendix G
Interest Correlations

Interest Correlations

	McV	McP	McQ	McG	McMem	McMot	PPVT	PLSac	PLSva	Plsiq	R
McV	1.00										
McP	0.84	1.00									
McQ	0.95	0.91	1.00								
McGen	0.97	0.93	0.98	1.00							
McMem	0.96	0.86	0.95	0.96	1.00						
McMot	0.84	0.96	0.92	0.93	0.87	1.00					
PPVT	0.90	0.80	0.90	0.91	0.87	0.79	1.00				
PLSac	0.91	0.88	0.95	0.95	0.95	0.89	0.92	1.00			
PLSva	0.92	0.84	0.94	0.94	0.95	0.87	0.92	0.97	1.00		
PLSlq	0.92	0.86	0.95	0.95	0.95	0.88	0.93	0.99	0.99	1.00	
R	0.77	0.85	0.83	0.84	0.77	0.78	0.76	0.77	0.76	0.76	1.00

Note. McV=McCarthy Verbal; McP=McCarthy Performance; McQ=McCarthy Quantitative; McG=McCarthy General Cognitive; McMem=McCarthy Memory; McMot=McCarthy Motor; PPVT=Peabody Picture Vocabulary Test; PLSac=Preschool Language Scale/auditory comprehension; PLSva=Preschool Language Scale/verbal ability; PLS/lq=Preschool Language Scale/language quotient; R=Ravens.

Appendix H
Articles Used in Meta-Analysis

ARTICLES USED IN META-ANALYSIS

Boznski, M. E., Nelson, M. N., Genaze, D. R., Chilcote, W. S., Ramsey, R. G., Clasen, R. A., O'Donnell, R. J., & Meir, W. A. (1982). Longitudinal follow-up by ultrasound of intracranial hemorrhage and ventricolomegaly in relation to developmental outcome in infants weighing ≤ 1200 grams at birth. The second special Ross Laboratories conference on perinatal intracranial hemorrhage (Vol. II, pp. 1153-1175). Columbus, OH: Professional Services Dept., Ross Laboratories.

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