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ETIOLOGICAL AND NEUROPSYCHOLOGICAL CORRELATES
OF MINOR PHYSICAL ANOMALIES IN
MENTALLY RETARDED, CEREBRAL PALSID
AND NORMAL INDIVIDUALS

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MASTER OF ARTS

THESIS

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September 1981

The undersigned recommend to the Faculty
of Graduate Studies and Research acceptance of the thesis
"Etiological and Neuropsychological Correlates of Minor Physical Anomalies
in Mentally Retarded, Cerebral Palsied and Normal Individuals"
submitted by Marlene Rivier
in partial fulfillment of the requirements for
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ABSTRACT

Minor physical anomalies constitute an important diagnostic tool in the identification of early developmental deviation. Frequencies and patterns of minor anomalies, lateral dominance and verbal and spatial skills were examined in four groups of mentally retarded adults and a normal control group drawn from the staff and residents of the Rideau Regional Centre in Smiths Falls, Ontario. The mentally retarded groups represented four etiological categories: Down syndrome, prenatal, perinatal and postnatal causation. A group of cerebral palsied subjects drawn from the same source was included in the anomalies portion of the study and constituted an additional perinatal group.

Analyses of the frequencies and patterns of anomalies between the groups yielded highly significant results. Control and Postnatal mentally retarded groups manifested significantly fewer anomalies than the other groups and did not differ from one another. The Down syndrome group displayed significantly more anomalies and a more consistent pattern of anomalies than any other group. The Prenatal and Perinatal retarded groups were similar in terms of frequency and pattern of anomalies suggesting that these constitute a single etiological entity which may be at risk to perinatal complications as a function of early genetic or teratogenic factors which also result in malformation. The cerebral palsied subjects had significantly more anomalies than the Controls but did not differ from the Postnatal retarded group. It is more likely that subjects in this group had

sustained CNS damage as a result of independent perinatal events but some individuals did demonstrate evidence of early maldevelopment. These results verify the usefulness of anomalies in the search for etiologies. An anomaly score combining the weighting system employed by Waldrop and Halverson (1971) but not limited to the anomalies included in this popular survey but rather involving a comprehensive open ended anomaly examination is recommended.

In the neuropsychological portion of the study which was limited to Control and retarded subjects, Controls obtained significantly higher Peabody Picture Vocabulary test and Raven's Coloured Progressive Matrices scores but did not differ from the other groups in terms of lateral dominance, all groups showing a strong preference for the right body side. The four retardation groups were indistinguishable from each other using any of the three neuropsychological measures singly or in linear combination. Within the mentally retarded groups anomaly score did not correlate with verbal or spatial score. Level of retardation did not correlate with the verbal-spatial discrepancy score nor did this score differ across the five groups. The degree of lateralization of anomalies was not related to verbal-spatial discrepancy score or the measure of lateral dominance. Both spatial and verbal ability scores decreased with age and years of institutionalization while the verbal score was particularly susceptible to the effects of early and prolonged institutionalization.

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TABLE OF CONTENTS

	Page
ABSTRACT	1
AKNOWLEDGEMENTS	4
TABLE OF CONTENTS	8
LIST OF TABLES	8
LIST OF FIGURES	11
INTRODUCTION	16
The Role of Anomalies in Diagnosis	18
Causes of Malformation	21
Genetic Causes	23
Environmental Causes	24
The Perinatal Component	25
The Development of Anomalies	27
The Head	28
The Eyes	30
The Ears	32
The Mouth	33
The Hands	34
The Feet	35
Malformations and CNS Dysfunction	36
"Stigmata of Degeneration"	37
Early MPA Studies	38
MPA's in Normals	39
MPA's in Hyperactives and Other Clinical Groups	40
Newborn Screening	42
MPA's and Treatment	45
MPA's and Attractiveness	47
Problems in the Perinatal Period and Early Life	48
Mental Retardation	53
Cerebral Palsy	57
The Present Study	62
METHOD	64
Subjects	64
Surveys and Tests Administered	66
Procedure	88
RESULTS	100
DISCUSSION	
REFERENCES	
APPENDIX A: Norms for Selected Body Measurements	
APPENDIX B: Lateral Involvement Score	
APPENDIX C: Lateral Dominance Score	
APPENDIX D: Form Letter	
APPENDIX E: Consent Form for Research	
APPENDIX F: Complete List of Chi Squares	
APPENDIX G: Discriminant Function Analysis with Seven Most Frequent Anomalies	
APPENDIX H: Discriminant Function Analysis with Eye Anomalies	
APPENDIX I: Discriminant Function Analysis with Ear Anomalies	
APPENDIX J: Discriminant Function Analysis with Oral Anomalies	
APPENDIX K: Discriminant Function Analysis with Hand Anomalies	
APPENDIX L: Discriminant Function Analysis with Foot Anomalies	
APPENDIX M: Discriminant Function Analysis with PPVT, CPM and Lateral Dominance Scores	

LIST OF TABLES

Table	Page
1 Mean Score of Groups on Descriptive Variables	55
2 Distribution of Sexes Among the Groups	56
3 MPA Survey and Scoring Weights from Waldrop and Halverson (1971)	58
4 Significant Differences Between the Means on Combined Anomaly Score According to Scheffe's Procedure	67
5 Distribution of Anomalies and Anomaly Types	69
6 Frequency of Individual Anomalies for the Six Groups	71
7 Head Circumference Data for the Six Groups	73
8 Distribution of Additional Anomalies Associated with Significant Chi Squares	74
9 <u>F</u> Matrix from Discriminant Analysis with Seven Most Frequent Anomalies	78
10 Group Membership Predicted from Discriminant Function Analysis	79
11 Mean Scores for Five Groups on Neuropsychological Measures	83
12 <u>F</u> Matrix from Discriminant Analysis with Neuropsychological Variables	85
13 Simple Correlation Coefficients for CPM Raw Score and PPVT IQ with Selected Descriptive Variables	86

LIST OF FIGURES

Figure	Page
1 Means and SD's on Three Anomaly Scores	65
2 Cumulative Frequency on Combined Anomaly Score	68

INTRODUCTION

In recent years there has been renewed interest in minor physical anomalies (MPA's) because of the important role they play as indicators of prenatal developmental error. The presence of MPA's is considered a sign that a more serious deviation in morphogenesis may have occurred (Marden, Smith & MacDonald, 1964). The incidence of MPA's has been examined in a number of normal and clinical groups. While the focus of this research has been on the hyperactive population (Firestone, Lewy & Douglas, 1976; Firestone, Peters, Rivier & Knights, 1978; Halverson & Victor, 1976; Quinn & Rapoport, 1974; Rapoport & Quinn, 1975; Rapoport, Quinn & Lamprecht, 1974; Waldrop & Goering, 1971) other studies have involved normal subjects (Marden et al., 1964; O'Donnell & Van Tuinan, 1979; Waldrop & Halverson, 1971; Waldrop, Pedersen & Bell, 1968), mentally retarded individuals (Firestone et al., 1978; Smith & Bostian, 1964) and a number of other clinical groups (Goldfarb, 1967; Rosenberg & Weller, 1973; Steg & Rapoport, 1975; Waldrop & Halverson, 1971; Walker, 1977).

The following characteristics are typical of the defects selected for study: head circumference outside the normal range, low-set ears, high-steeped palate, hypertelorism (widely spaced eyes), single transverse palmar crease and partial syndactyly (webbing) of the second and third toes. These along with other defects included in the study constitute a small subset of all possible malformations and are used as an index of the degree of divergence from the normal course of development during the first trimester of pregnancy. Research findings indicate that MPA's

can play a significant role in the delineation of etiology, the selection and effectiveness of treatment and as an early screening device. Nevertheless, at present MPA's are entirely overlooked by the majority of researchers and clinical practitioners.

The frequent occurrence of mental retardation (MR) among congenitally malformed individuals (Smith, 1976) along with the discovery of multiple anomalies among individuals with idiopathic MR suggests that the defect in brain function may be due to a congenital anomaly (Smith & Bostian, 1964). The present study attempts to relate MPA's and etiology in four groups of mentally retarded individuals of various etiological backgrounds and compares them to a normal control group. The MR groups consist of a genetic group composed of individuals with Down syndrome and three groups of individuals whose retardation has been attributed to prenatal, perinatal or postnatal events. Both the frequency and patterns of MPA's are examined in these five groups.

Intraindividual differences in the lateralization of defects were also examined with the aid of a right-left laterality score computed for each subject. The relationship of laterality of structural defects to measures of functional laterality or lateral dominance and verbal and spatial skills was also investigated. In addition, the relationship between level of intellectual functioning and anomaly score was examined.

As originally conceived, the study was composed of the aforementioned five groups; however, at the time of data

collection, a group of cerebral palsied (CP) subjects became available and consequently was included in the anomalies component of the study. It was felt that an additional group manifesting an alternative expression of Central Nervous System (CNS) dysfunction, one commonly attributed to perinatal birth injury, would constitute a valuable comparison.

These various investigations help to elucidate the complex relationship between etiology, CNS function and anomalies and to determine the extent to which anomalies can be used to predict patterns of CNS functioning. In order to realistically evaluate the meaningfulness and usefulness of anomalies, it is necessary to first develop an appreciation of their position and importance within the context of anomalous development in general.

The Role of Anomalies in Diagnosis

The term "congenital anomaly" is an all inclusive reference to structural, functional, metabolic, behavioural and hereditary defects present at birth (Persaud, 1977). Structural defects are labelled "malformations" and, although this term is strictly correct when referring to the defects to be discussed here, the more general term "anomaly" is frequently used.

The term "malformation" implies that the defect has arisen during the period of organogenesis of the embryo. Deformations which arise later in fetal development are the result of a degenerative process involving normally formed structures and are thus qualitatively different from malformations (Dunn, 1972). It is important to distinguish deformations such as Talipes equinovarus (typical clubfoot) from malformations because they are typically remediable (Dunn, 1972). Congenital malformations can be classified as gross or microscopic, single or multiple, external or internal, major or minor (Persaud, 1977).

In recent years, malformations have been increasingly regarded as instrumental clues in the delineation of a host of different syndromes (Smith, 1976). These various disorders not only involve deviations of structural morphogenesis but may also manifest themselves in varying degrees of functional deviation. Of particular interest to the psychologist are a variety of neurological and neuropsychological dysfunctions involving sensory, motor, perceptual and cognitive abilities as well as behavioural problems.

A high incidence of MPA's has been found in association with sensory handicaps such as congenital deafness (Waldrop & Halverson, 1971) and perceptual and cognitive problems ranging from academic failure (Rosenberg & Weller, 1973) through learning disabilities (Steg & Rapoport, 1975) to MR (Firestone et al., 1978; Smith & Bostian, 1964). MPA's have also been related to behavioural problems like hyperactivity, characterized by inappropriate motor activity, distractibility and impulsivity (Firestone et al., 1976; Firestone et al., 1978; Halverson & Victor, 1976; Quinn & Rapoport, 1974; Rapoport & Quinn, 1975; Rapoport et al., 1974; Waldrop & Goering, 1971; Waldrop & Halverson, 1971; Waldrop et al., 1968). A high incidence of MPA's has also been found in association with socially withdrawn behaviour among girls (Waldrop, Bell & Goering, 1976; Waldrop & Halverson, 1971), severely disturbed behaviour in children (Steg & Rapoport, 1975) and in childhood schizophrenia (Goldfarb, 1967) and autism (Walker, 1977).

The presence of an individual anomaly is seldom sufficient to arrive at the identification of a specific underlying etiology or disorder: rather, it is the recognition of the overall pattern of anomalies which results in a specific diagnosis (Smith, 1976). Individuals with the same etiological syndrome may exhibit variance in expression as regards the severity of the individual anomalies: but the overall pattern of anomalies remains the same. Intraindividual variance in expression is also not infrequent with varying degrees of involvement of the left versus right sides of the body.

The prolonged and complex development of the CNS makes it particularly vulnerable to teratogenic influences and indeed, CNS dysfunctions such as MR, behavioural aberrations and neurological abnormalities are frequent features of congenital disorders (Smith, 1976). Individuals with the same multiple defect syndrome tend to present a similar pattern of CNS functioning. Thus, the ability to predict future performance may be greatly enhanced through the information derived from a specific diagnosis.

The detection of minor anomalies can be as useful as major malformations in the recognition of specific syndromes (Smith, 1976). In contrast to major anomalies which may have an adverse effect on either the functioning or social acceptability of the individual (Marden et al., 1964), minor anomalies constitute unusual morphological features that are of no serious medical or cosmetic consequence (Smith, 1976). MPA's are easily detectable through gross inspection of the body and oral cavity and are most common in areas of complex and variable features such as the hands, feet and head, especially the face (Smith, 1976).

In the case of the severely malformed or impaired individual MPA's are unlikely to play an important role in bringing the individual to the attention of health care professionals. However, the presence of MPA's may aid the practitioner in arriving at a specific diagnosis. The clinical diagnostic value of MPA's is perhaps best appreciated in those cases where major external anomalies are not present. Marden and

co-workers (1964) state that the presence of two and especially three minor anomalies should alert the pediatrician to the possibility that a more serious deviation in morphogenesis may have occurred. Close monitoring of high MPA infants can avert potentially life-threatening crises in those with major internal anomalies.

MPA's can also serve as indicators of CNS anomalies which may be either structural or functional in nature and later express themselves as neurological, neuropsychological or behavioural problems. The detection of potentially high risk infants fulfills an important prophylactic role, permitting early intervention, remediation and the prevention of secondary problems which might otherwise have developed. These advantages must be carefully weighed in light of the possibility that labelling children "high risk" early in life may alter the expectations of and interactions with significant others producing a self-fulfilling prophecy.

In addition to their usefulness in screening normal populations, MPA's have enormous potential in dealing with various clinical populations. Where other more positive evidence is lacking, MPA's are indicative of congenital-biological factors as opposed to experiential ones in the delineation of etiology and consequently, can contribute to the selection and effectiveness of treatment. MPA's also have an important research function in the identification of sources of teratogenic influence and ultimately in the prevention of malformation and their consequences.

Causes of Malformation

Medical advances in the care and treatment of the neonate have produced a significant decline in infant mortality during the last century. The eradication of many causes of infant mortality, however, has resulted in a sharp rise in the infant deaths attributable to congenital malformations from 1 in 35 to 1 in 5 (Polani, 1973). Hospital data indicate that significant anomalies affect between 1 and 6% of newborns (Kennedy, 1967; Polani, 1973) and considerable underreporting is suspected (Polani, 1973). These infants are thought to be a small proportion of all affected conceptuses, the vast majority of which succumb early in pregnancy.

The specific causes responsible for the vast majority of individual instances of malformation remain unknown (Smith, 1976; Willis, 1962). Although a great many disorders attributable to specific environmental and genetic factors have been delineated, the identification of the teratogenic agent operating in a given case continues to be difficult.

Genetic Causes

The majority of recognized malformation syndromes have been attributed to genetic causes (Smith, 1976). It has been important to distinguish cases of nongenetic familial incidence from genuine cases of genetic determination, as a high frequency of an anomaly among family members may reflect the similarity of

their environmental experiences during the prenatal period and throughout life rather than a genetic effect. The presence of an anomaly in several biologically related individuals could be related to maternal, nutritional, toxic, or infective factors and should not itself be considered proof of genetic causation (Willis, 1962).

Genetically based anomalies may be transmitted to offspring with varying probabilities of expression related to the location and characteristics of the deviant genetic material. Autosomal dominant conditions are the easiest to diagnose in that at least one parent is affected, and all heterozygous offspring manifest the disorder. In the event that both parents are affected any homozygous offspring may manifest the anomaly in an unusually severe form (Willis, 1962). Autosomal recessive disorders are more difficult to diagnose due to the role played by heterozygous carriers. In the case of semi-dominant transmission heterozygous individuals may show a mild subclinical form of the condition while homozygous individuals exhibit the severe form. It has been suggested that a number of conditions previously thought to be recessive, such as some of the metabolic anomalies, may be of this type. Chemical studies of the parents of affected individuals have found the predicted mild metabolic changes of insufficient magnitude for treatment to be sought (Willis, 1962).

In addition to conditions associated with the autosomes are those anomalies due to sex-linked genes. A trait is said to

be sex-linked when the aberrant gene is carried either on the large segment of the X chromosome which is not represented on the Y, or on the much smaller differential segment of the Y chromosome. The most common of these are the recessive X-borne anomalies, the classic example being that of the affected son of the heterozygous carrier mother. Dominant X-linked anomalies which are often mis-identified as autosomal dominant (Smith, 1976) are quite rare as are the Y-linked disorders.

In the case of polygenetic determination anomalies may be produced as a result of the interaction of several genes or the effects of one abnormal gene may be modified by others. Anomalies may also be the result of an interaction between genic and non-genic factors. Spontaneous gene mutations are responsible for some instances of abnormal development but do not account for a very large proportion of cases (Willis, 1962).

Dysmorphic development may also result from genetic imbalance due to gross chromosomal abnormalities. Non-dysjunction during meiosis is frequently the cause of abnormal complements of sex chromosomes producing such conditions as Klinefelter or Turner syndrome. Should the chromosomal sorting error occur during the first mitotic division of the zygote a genotype identical to that produced by the first process results. However, if the error occurs after the first cleavage division a mosaic genotype results composed both of normal and abnormal cells.

Chromosome abnormalities may also affect the autosomes. Here again, non-dysjunction is frequently the cause and Trisomy

21 or Down syndrome is one of the conditions commonly produced. Maldivision at the centromere may occur whereby either the short or long arms are lost and occasionally chromosome breakages occur. This may be followed by a rearrangement or translocation of the detached genetic material. If the result is a genetically balanced product a phenotypically normal individual develops. When the individual reaches maturity genetically unbalanced gametes may be produced. Consequently, cases of translocation-related anomalies may be traced to fresh unbalanced occurrences or may have been inherited from a balanced translocation carrier parent. As with the sex chromosomes, mosaicism involving the autosomes may occur depending upon the timing of the error.

Environmental Causes

Environmental factors have begun to attract considerable attention as causes of malformation. Diverse agents have been observed to produce similar malformations while the same agent introduced at different times may have a range of effects upon morphogenesis. It is suggested that differences in susceptibility of various organs or tissues and changes in susceptibility over time act to modify the effects of various environmental teratogens.

Normal morphogenesis is dependent upon an adequate supply of various vitamins, minerals and amino acids. The impact of maternal nutrition on the developing embryo is clearly

demonstrated by the relationship between endemic cretenism and maternal iodine deficiency (Warkany, 1971). Maternal diets deficient in the heavy metals zinc and magnesium have been related to malformations in offspring and manganese deficiencies have been linked to irreversible congenital ataxia (Winick, 1976). Folic acid antagonists such as aminopterin have been used as abortifacients because of their usually lethal effect on human embryos (Thiersch, 1952; Wilson, 1973). In those instances where exposure has not been lethal, malformations have been observed in fetuses and newborns subjected to the drug early in pregnancy (Milunsky, Graef & Gaynor, 1968; Thiersch, 1952).

The use of anti-convulsant medication during pregnancy has been linked with malformation and mental deficiency in children (Aase, 1974; Hanson, Myrianthopoulos, Sedgwick Harvey & Smith, 1976; Hill, Verniaud, Horning, McCulley & Morgan, 1974; Speidel & Meadow, 1972; Zakai, Mellman, Neiderer & Hanson, 1975). Winick (1976) suggested that the underlying mechanism may be one of folic acid antagonism. Smith (1976) has made a similar suggestion regarding the mentally deficient and malformed children born to chronic alcoholic women (Jones & Smith, 1973; Jones, Smith, Streissguth & Myrianthopoulos, 1974; Jones, Smith, Ulleland & Streissguth, 1973).

The preceding examples demonstrate that whether an agent has a beneficial or adverse effect on the mother is not a reliable predictor of its toxicity for the unborn. This point can perhaps be better demonstrated by the embryopathic effects of

a normally non-toxic drug, thalidomide, which produced malformations in a high proportion of infants born to mothers who took the drug early in pregnancy (Lenz, 1962; Lenz & Knapp, 1962; McBride, 1961). The thalidomide incident also underlines the potential danger in relying on animal research in testing the teratogenic potential of an agent; some species, including rats and lower primates, are resistant to thalidomide teratogenesis while certain other species require larger dosages to produce the malformations, and still others do not react in the characteristic manner (Wilson, 1973).

Maternal virus infections have also been implicated as causes of malformation. The incidence of early maternal Rubella infection and the subsequent birth of malformed infants has been well documented (Cooper & Krugman, 1966; Gregg, 1941). In addition to the high incidence of MR among these children there appears to be an elevated risk of autism and behavioural disorders (Chess, 1977). Cytomegalovirus, the most common congenital virus infection is now beginning to be recognized as a serious source of malformation and retardation (Blattner, 1974; Willis, 1962). Recent evidence suggests that hyperthermia may constitute the underlying teratogenic agent in some cases of maternal infection (Smith, Clarren & Sedgwick Harvey, 1978). It was observed that mothers who experienced high fever associated with several different infections during the first half of gestation produced infants with a similar morphological phenotype accompanied by severe mental retardation. The authors conclude

that hyperthermia must be considered a possible underlying teratogen in cases where the pattern of malformations is consistent, independent of the type of maternal infection.

Irradiation is also recognized as a serious threat to the unborn and has in the past been considered an acceptable procedure for therapeutic abortion (Murphy, 1929; Sternberg, 1973). Maternal age (Penrose, 1954), maternal hormonal disturbances such as diabetes, oxygen deficiency due to maternal circulatory disease, anemia and placental disorders have been implicated as causes of malformation (Willis, 1962). In addition, circulatory disturbances in the embryo due to faulty implantation, cardiac abnormalities or abnormal vascular connections with the placenta may also contribute to malformation of the embryo (Willis, 1962).

In a prospective study of over 50,000 pregnancies, referred to as the National Institute of Mental Health Collaborative Perinatal Project, children were surveyed for major and minor anomalies and the analysis of this data along with a host of other variables revealed a number of risk factors (Heinonen, Slone & Shapiro, 1977). The greatest probability or risk of an infant displaying major anomalies was associated with such factors as low birth weight, single umbilical artery, hydramnios (excess of amniotic fluid) and maternal diabetes. A somewhat lesser risk was associated with maternal convulsive disorder and vena cava syndrome. The variable of convulsive disorder is unfortunately, confounded with the effects of

anticonvulsive medication. These authors contend that maternal convulsive disorder represents a significant risk independent of medication effects. Bacterial infection after the fourth lunar month, other maternal endocrine disorders, severe toxemia, male sex, maternal age greater than 40 years and duration of pregnancy less than 9 or greater than 10 lunar months all constituted statistically significant, though lesser risks for major anomalies. As discussed previously the defects associated with bacterial infection after the fourth lunar month should be classified as deformations rather than malformations and are not of interest here (Dunn, 1972; Willis, 1962).

The greatest risk of minor malformation in this Project was associated with birthweight less than 1,500 gm, single umbilical artery and hydramnios. A statistically significant but lesser risk was associated with abruptio placentae (premature detachment of the placenta), maternal urinary tract infection, severe toxemia and congenital malformations in prior siblings.

A study of the incidence of the single transverse palmar crease in newborns (Davis, 1966) revealed a similar clustering of maternal and infant factors. Maternal variables such as age greater than 30 years, multiparity, previous stillbirths, toxemia and hydramnios were all significantly more prevalent among the infants with a single crease. These infants were also significantly more likely to be stillborn, die during the neonatal period, be male, of low birthweight and three times as likely to have other malformations than the group of infants without the single crease.

A study by Toivanen and Hirvonen (1970) reports an association between male sex of offspring and the incidence of toxemia in late pregnancy. The authors also found that the magnitude of the relationship was greater when only severe cases of toxemia were considered. It is suggested that histoincompatibility of the mother and unborn male dependent upon the Y chromosome may be functioning in the development of toxemia.

The Perinatal Component

In the previous studies such variables as low birth weight, prematurity, postmaturity, abruptio placentae, toxemia, multiparity and previous stillbirths appear significantly more frequently among malformed infants than among normals. The association of what are best characterized as perinatal factors with anomalies must be viewed as a consequence of or association with early maldevelopment. Polani (1973) in his study of women who habitually aborted early in pregnancy found a high rate of chromosomal abnormalities in abortuses. He concluded that, with respect to chromosome abnormalities, affected individuals are at risk to spontaneous abortion from the time of fertilization and throughout pregnancy. This hypothesis can be extended to include more subtle genetic and teratogenic effects and may be reflected in a range of pregnancy complications. Thus, it may be useful to consider malformed individuals as being "at risk" from the time of conception or exposure to the source of teratogenic influence

and continuing to be so throughout development. While many abnormal conceptuses are lost early in pregnancy, the survivors of this period may be lost later in pregnancy or may experience premature delivery, complications of birth, neonatal distress and/or neonatal death.

This model is in contrast to that of Pasamanick, Rogers and Lilienfeld (1956) who propose a "continuum of reproductive casualty" ranging from death and severe brain damage to minor behavioural and intellectual dysfunction as a function of the severity of birth or pregnancy complication. The former "high risk" model suggests that perinatal complications are a consequence of prenatal genetic or teratogenic events while the latter model regards prenatal and perinatal complications as distinct entities each of which exerts a direct and immediate pathological influence on the CNS of the individual.

It may be however, that these two models apply to two different subgroups who present the same or a similar clinical picture. Certainly an investigation of the incidence of malformation among individuals who have experienced perinatal difficulties is of considerable value in determining the relative influence of these two hypotheses.

The Development of Anomalies

The gestational period is some 10 lunar months long and while no portion of this period can be considered of little consequence to development, the critical importance of the first trimester is often underestimated. This is the period during which a small aggregate of similar cells is transformed into a highly complex organism. While the last two trimesters of pregnancy are marked by rapid cellular proliferation and individual cell growth, the first trimester is characterized by cellular differentiation which occurs at an astounding rate. Indeed, by the end of the first trimester the organ systems and overall morphology of the individual is well established and the fetus has assumed its uniquely human appearance.

Yet the woman may not be aware or convinced that she is pregnant for a good portion of this first trimester and may not begin to modify her behaviour in an attempt to provide an adequate environment for the embryo until much of it has passed. Looking back over the course of the pregnancy she may attach little significance or fail to remember events which have occurred during this period when reporting potentially teratogenic influences. Unfortunately this is the period during which malformations occur and regardless of how ideal the intrauterine environment may be later in pregnancy these effects can not be reversed.

The high incidence of anomalies among various clinical groups underscores the importance of this early period in human development and reinforces the need to increase our understanding of the genesis and significance of anomalies. To this end both the time frame and contingencies involved in anomalous development must be examined.

During the third week after fertilization three distinct layers known as germinal layers exist within the embryo (Willis, 1962). The most external layer or ectoderm will become the nervous, and integumentary systems. The next layer, the mesoderm, will give rise to the musculature, lining of the secondary body cavity, vascular, reproductive and excretory systems and most of the internal skeleton. The innermost layer or endoderm will form the alimentary canal and digestive glands (Balinski, 1975). While this listing is not exhaustive it gives an indication of the nature of the contributions of the various germinal layers. Like the brain many of the anomalies to be discussed derive from the ectoderm.

The development of the body begins in the future head region. The cephalic end remains disproportionately large for some time and very early acquires a favoured blood supply. In the early stages of development the head region is composed of two parts: one is visceral in nature forming the upper end of the alimentary and respiratory tracts, while the second is neural and will differentiate into the brain, its sense organs and supporting structures (Arey, 1965).

The neural plate is the result of a thickening of the dorsal ectoderm at around 19 days (House & Pansky, 1960). The broader anterior end of the plate is destined to become the brain while the narrower caudal part will form the spinal cord. A longitudinal groove appears along the middorsal line called the neural groove. The tissues of the neural plate become elevated into ridges forming the neural folds on either side of the neural groove continuing to rise until they join between the 22nd and 26th days forming the neural tube (Goss, 1973; Smith, 1976).

Even before closure of the neural tube has begun, subdivisions indicative of the three main parts of the brain (the forebrain, midbrain and hindbrain) have made an appearance (House & Pansky, 1960). The nervous system which begins its development and assumes a position of relative importance very early in the gestational period will continue to develop throughout the embryonic and fetal stages. Cell division in the nervous system will continue until birth or shortly after although individual cells and processes will continue to grow until after puberty (Gardner, 1968). Myelination which begins around the 16th week of gestation continues into the first 2 or 3 years of life (Smith, 1976). It is because of this prolonged and complex development that Smith (1976) feels the CNS is especially vulnerable and why CNS symptoms constitute such frequent features of congenital disorders.

The development of anomalies may be the result of any one of several processes. Aplasia or agenesis refers to the failure

of an organ or tissue to develop. Hypoplasia represents the incomplete or arrested development of a structure. The production of abnormalities due to a departure from the normal sequence or pathway of development is termed dysplasia, while hyperplasia refers to an abnormal increase in the number of cells which are arranged in a normal manner.

The anomalies survey introduced by Goldfarb (1967) and modified by Waldrop and co-workers (Waldrop & Halverson, 1971; Waldrop, Pedersen & Bell, 1968) includes 18 MPA's involving the head, face, hands and feet. It is used in the vast majority of MPA research and is used in the current study as part of a comprehensive open-ended anomalies examination. A brief description of the anomalies included in this popular study and their development follows.

The Head

Anomalies in the area of the head are perhaps of most interest because of their obvious proximity to the brain. The head, as has been stated, is an area of early and intense development and by the end of the fourth week it is well defined. It is bent ventrally and expands with the enlargement of the forebrain (Willis, 1962).

Fine electric Hair. Hairs begin to develop early in the third lunar month but do not emerge until the sixth month (Arey, 1965). The first downy coat is called lanugo and is shed just prior to or after birth. It is replaced by vellus which is

itself replaced during puberty although less completely in females. Each generation of hair is coarser and darker than the one that preceded it. In the case of fine electric hair this progression has failed to occur and the hair remains fine and often blonde. Hair that will not comb down is assigned a weighted score of 2 while hair that is soon awry after combing is rated 1 (Waldrop & Halverson, 1971).

Two or more hair whorls. Smith and Gong (1973) consider scalp hair patterning an important clue to early brain development. They state that scalp hair patterning which is determined at 10-16 gestational weeks is secondary to the growth and shape of underlying tissues especially the brain. They found a single hair whorl in 95% of their normal sample. The hair whorl is located anterior to the former position of the posterior fontanel. Waldrop and Halverson (1971) assign a weight of 0 to this anomaly in the computation of their weighted anomaly score.

Head circumference outside the normal range. The development of the cranium including the skull and meninges begins during the fourth and fifth weeks. The overall size of the head is determined by the development of the brain and its skeletal investment. Any head circumference greater than or equal to 1 standard deviation (SD) outside the normal range is rated 1 while any measure greater than 1.5 SD is rated 2. Waldrop and Halverson (1971) recommend positioning the tape measure firmly over whatever points on the forehead just above the supraorbital ridges and occiput which yield the maximal circumference.

The Eyes

The eyes develop from three sources: the forebrain, the surface ectoderm of the head and the intermediary mesenchyme or mesodermal tissue. The optic vesicles become evident as outgrowths of the lateral walls of the forebrain during the fourth week (Willis, 1962). A little later the lens placode arises in the overlying ectoderm from which it eventually detaches itself. In the six week embryo the two primordial eyes are set at a 180 degree angle from one another (Arey, 1965). During the third lunar month the eyes shift from the lateral to medial position (King & Showers, 1969) as the head broadens reducing the divergence virtually to its final dimensions (Arey, 1965).

The eyelids develop as skin folds adjacent to the eyeball at the end of the seventh week. The lacrimal ducts and glands appear during the sixth and ninth weeks respectively. The caruncle, the reddish mass at the inner corner of the eye, is in fact a part of the lower lid which is upraised by the lacrimal duct (Arey, 1965).

Epicanthus. Epicanthus is a condition in which the lacrimal caruncle is either partially or completely covered by a vertical fold of skin. If the caruncle is partially visible a weight of 1 is assigned, if it is completely obscured it is rated 2 (Waldrop & Halverson, 1971).

Hypertelorism. This condition is one in which the eyes are unusually wide-set, that is, where the eyes fail to reach

their final positions. Waldrop and Halverson (1971) assign a score of 1 in cases where the inner canthal distance equals or exceeds 1 SD above the mean and a score of 2 if the distance exceeds 1.5 SD. Smith (1976) contends that in order to identify true cases of hypertelorism, the interpupillary and outerorbital dimensions must also be shown to be increased. The more liberal estimate commonly used is more appropriately termed increased inner canthal distance. This study examines the incidence both of increased inner canthal distance and true hypertelorism and to this end all relevant measurements were taken.

The Ears

The external ears derive from the first branchial groove and the first and second branchial arches bordering it on either side. During the sixth week elevations or hillocks appear, three on each arch bordering on the groove (Arey, 1965). The auricles begin their development under the area of the face in the horizontal rather than ventricle position. As the hillocks develop into the intricate pattern which characterizes the external ear, the auricles begin their ascent up the side of the head until they reach their final position during the third lunar month (King & Showers, 1969). The auricle cartilage does not develop until later in gestation at the beginning of the eighth lunar month.

Low-seated ears. This anomaly refers to a condition where the auricles have not reached their final positions at the sides

of the head. Waldrop and Halverson (1971) measure it by placing the lower edge of a tape measure across the bridge of the nose, the outer corner of the eye and the top of the ear. If the top juncture of the ear is below the line formed by the nose bridge and eye by less than or equal to .5 cm a weight of 1 is given, if greater than .5 cm a weight of 2 is given.

Adherent ear lobes. This anomaly is considered present if the lobe of the ear fails to extend below the lowest point of attachment to the head. If the ear extends straight back it is rated 1, if it extends upward from the point of attachment toward the crown it is weighted 2 (Waldrop & Halverson, 1971).

Malformed ears. If the ears deviate markedly from the normal auricular pattern they are given a weighted score of 1 (Waldrop & Halverson, 1971).

Asymmetrical ears. Ears that differ obviously from each other in shape, size, protrusion or seating on the head are assigned a weighted score of 1 (Waldrop & Halverson, 1971).

Soft and pliable ears. Defective cartilage results in an ear which feels weak and jellylike and does not quickly spring back into position when flopped forward. Waldrop and Halverson (1971) assign a weight of 0 to this anomaly.

The Mouth

By the end of the fourth week the stomodaeum or oral depression is present on the ventral surface of the head below the forebrain. On either side of it lie the maxillary and

mandibular processes. The lower jaw is formed by the union of the two mandibular processes while the upper jaw is formed by the union of the two maxillary processes together with the two medial nasal processes (Arey, 1965). The palate is formed by two shelflike projections from each maxillary process region which grow toward the midplane of the oral cavity. During the seventh and eighth weeks the palatine processes encounter the tongue which is elevated due to the growth of its internal muscle and are forced to bend downward. Later the tongue is withdrawn and the palatine processes are forced upward and back into the horizontal plane. Fusion of the two lateral palatine processes occurs at the beginning of the ninth week and progresses back from the front of the mouth (Arey, 1965).

The tongue consists of two parts: the root which develops chiefly from the union of the second branchial arches and the oral portion of the tongue which occupies the oral cavity. The oral portion is derived from the two lateral swellings and tuberculum impar which are indicated at around the fourth week. The lateral swellings increase greatly in size and during the sixth week the three components fuse forming the body of the tongue. At around nine weeks the various papillae begin to appear as elevations on the tongue giving it its characteristic appearance and texture (Arey, 1965).

High-steepled palate. Should the two palatine processes fail to meet and fuse the result is a condition known as cleft palate (Goss, 1973). However the processes may meet and fuse.

successfully but fail to develop along the correct planes forming the characteristic rounded dome of the palate. The result may be a high-steeped palate to which Waldrop and Halverson (1971) assign a weight of 2 or one with a narrow flat roof assigned a score of 1.

Furrowed tongue. A tongue with one or more deep grooves along its surface is given a score of 1 (Waldrop & Halverson, 1971).

Tongue with smooth-rough spots. Also known as geographic tongue, this condition is due to a localized thickening of the epithelium and is given a weighted score of 1 (Waldrop & Halverson, 1971).

The Hands

The arm bud appears around the 26th day (Smith, 1976) as a lateral swelling and becomes distinct early in the fifth week (Willis, 1962). At around the 38th day the hand plate is formed and the finger rays appear around the 43rd day as cartilaginous forerunners of the skeleton. Initially the digits are held together by webs, the thumb separating early and widely. Separation is complete by the 47th day (Arey, 1965).

Creases are the result of flexional folding of the skin of the developing hand occurring from the seventh to the 14th weeks and can be observed through gross inspection by the 11th week (Popick & Smith, 1970). Thus alterations in crease patterns represent aberrant flexion folding and according to Popick and

Smith (1970) "may be interpreted as secondary to abnormal form and/or function of the early developing hand."

Curved fifth finger. This is a condition where the tip of the fifth finger curves inward toward the other fingers. A markedly curved finger is rated 2 and a slightly curved finger 1 (Waldrop & Halverson, 1971).

Single transverse palmar crease. A single crease also called a simian crease refers to the condition where an unbroken line extends fairly straight across the palm of the hand. Waldrop and Halverson (1971) rate this anomaly 1.

The Feet

The leg buds appear around the 32nd day (Smith, 1976) and the foot plate and toe rays are present early in the sixth and seventh weeks, respectively (Willis, 1962). As with the fingers the toes are restricted by webs, the big toe being the first digit to separate and doing so widely. According to Arey (1965) syndactyly or the retention of webbing favours union of the middle digits. The development of the foot is complete by the eighth week.

Third toe longer than second. The third toe being longer than the second is an instance of asymmetrical length of the toes. If the third toe is definitely longer than the second a weighted score of 2 is given (Waldrop & Halverson, 1971).

Partial syndactyly of the two middle toes. In this condition the second and third toes are observed for partial

syndactyly extending to near the lower toe joints. This anomaly is weighted 1 (Waldrop & Halverson, 1971).

Big gap between the first and second toes. This anomaly represents an over-extension or separation of the big toe and is judged to exist if there is "a flat base" across the gap of more than half the width of the second toe" and is assigned a weight of 1 (Waldrop & Halverson, 1971).

Malformations and CNS Dysfunction

CNS anomalies constitute the most common congenital defects found in man, but only a fraction of these abnormal conceptuses remain viable and progress to term (Willis, 1962). The median dorsal region of the embryo appears to be particularly susceptible to teratogenic influence such that failures of closure, separation and skeletal investment of the neural tube are frequent occurrences. Dysraphic failures may be complete (craniorachischisis) affecting the entire length of the neural tube or may constitute a failure of closure at the posterior (rachischisis) and/or anterior (cranioschisis) ends, as closure of the neural tube progresses in a proximal-distal fashion from the neck area of the embryo cranially and caudally. This process is normally complete by 26 days gestation; thus failures of neural tube closure represent relatively early occurring defects (Smith, 1976). Among this group are included such conditions as anencephaly, the most common of human malformations incompatible with postnatal survival, exencephaly, encephalocele and spina bifida (Willis, 1962).

Another class of CNS malformations referred to as holoprosencephaly involves defective forebrain development and subsumed under this heading are conditions such as cyclopia and arhinencephaly (Nishimura & Okamoto, 1976). Iniencephaly, hydrocephalus and hydromyelia, and microcephaly complete the list of general categories of major CNS defects (Nishimura & Okamoto, 1976).

Individuals with these major CNS anomalies can be assigned to a general category of CNS defect on the basis of external appearance alone. Virtually without exception, these various CNS defects are accompanied by a consistent pattern of facial and auricular anomalies and not infrequently involve malformation of the extremities (Nishimura & Okamoto, 1976). Rarely is a major CNS anomaly encountered in the absence of other external malformations, often minor in nature.

If on the other hand, major facial anomalies are considered such as aprosopus (facelessness) one finds that these are routinely accompanied by a diminution of brain size and/or the absence of some brain structures (Willis, 1962). The close correspondence between CNS and facial anomalies is apparent in the example of cyclopia which is classified primarily as a CNS abnormality by some (Nishimura & Okamoto, 1976) while others (Willis, 1962) refer to it as a facial anomaly.

The individual structures of the human body do not develop in a vacuum and their respective development can not be fully appreciated outside a context of mutual interdependence. The alteration of one structure may have far reaching consequences for the developing organism by disturbing the delicate balance existent between many different processes and thus compromising the formation of subsequent structures. The primary anomaly along with the associated secondary defects thus produced are termed an anomalad by Smith (1976). The clustering of anomalies of different temporal onset may constitute, therefore, an

anomalad rather than having resulted from various teratogenic influences or exposure to a single influence over a prolonged period.

"Stigmata of Degeneration"

The diagnostic use of MPA can be traced back to the work of Penrose (1954) and others (Gibson & Frank, 1961) who examined the concentration of what Lombroso (1887) termed "stigmata of degeneration" in persons with Down syndrome and other major congenital defects. While variability in the precise type and number of anomalies in individual cases of Down syndrome have been reported (Levinson, Friedman & Stamps, 1955), of those anomalies typically associated with the disorder minor abnormalities constitute the majority (Smith & Bostian, 1964).

There are relatively few studies of MPA but the efforts of various groups of researchers have contributed to the understanding of the development, significance and utility of minor anomalies.

Early MPA Studies

Marden, Smith and McDonald (1964) screened 4,412 newborns for both major and minor congenital anomalies. Major defects were discovered in 2% of the infants while only 0.7% had multiple major anomalies. Almost 15% of the infants had at least one minor anomaly, but the existence of two or three minor anomalies in a particular infant was rare except in babies with a major

anomaly. Of the 20 individuals with two or more minor abnormalities, 18 had one or more major anomalies. The authors observed that the incidence of minor anomalies increases with the incidence of major anomalies and concluded that two and especially three minor anomalies should be considered suspicious. No deviation was considered an anomaly if it had an incidence greater than 4% but was instead classed as a normal variant. Chromosomal aneuploidy syndromes occurred in only 0.4% of the sample.

Smith and Bostian (1964) examined 50 idiopathic mentally retarded individuals, 50 persons with ventricular septal defect (VSD) a congenital cardiac anomaly, 50 with cleft palate and 100 controls for the presence of 327 congenital anomalies, 72% of which were minor. The frequency of anomalies was highest in the MR group and the most significant difference was in the proportion of MR individuals with three or more defects as compared to the controls. None of the subjects in the control group had three or more anomalies compared to 10% in the cleft palate group, 18% in the VSD group and 42% in the MR group. Chromosome studies of the 21 MR subjects with three or more defects revealed no abnormalities and 78% of the defects in the MR group were classified as minor. One anomaly was present in 21% of the control children, a slightly higher incidence than the 15% in the previously described study (Marden et al., 1964). The area of discovery for 71% of the minor anomalies involved the hand, eye, ear, face and mouth.

The authors concluded that three or more anomalies in an individual appear to indicate a significant abnormality in prenatal development and that since minor anomalies do not present a management problem they are often overlooked as a potential indicator of altered embryonic morphogenesis. The authors go on to state that the discovery of multiple anomalies in individuals with idiopathic MR while not constituting proof, does suggest that the defect in brain function may be due to a congenital defect. This concept constitutes the underlying rationale for much of the MPA research which followed this study.

Goldfarb (1967) reports a study in which normal, schizophrenic and behaviour disordered children were examined for the presence of 21 MPA's. The schizophrenic children exhibited significantly higher stigmata scores when compared to normals. There were also fewer schizophrenic children with no anomalies and more of the children in this group had stigmata scores of five or more. When compared to controls nine of the 21 anomalies occurred significantly more frequently among the schizophrenic children and four of the nine had a significantly higher incidence in the behavioural group. None of the anomalies occurred with a significantly greater frequency among the normal children. Goldfarb interprets these results as evidence of embryonic and fetal maldevelopment in childhood schizophrenia.

MPA's in Normals

Waldrop, Pederson and Bell (1968) utilized a slightly abbreviated form of the MPA survey constructed by Goldfarb (1967) with some modification to the scoring procedure. Those anomalies which had been found to be significantly more frequent among the schizophrenic children were assigned weights of 1 or 2 dependent upon the magnitude of the deviation from normal. Weights of 1 were given to the anomalies which were more frequent though not significantly so among the schizophrenic children and the remainder were assigned a weight of 0. Both a total score (total count of the anomalies) and a weighted score (sum of the 0, 1 and 2 weightings) were computed for each subject, but since the two correlated highly only the weighted score was retained because of its greater range.

The researchers examined two samples of normal 2 1/2 year old nursery school children for the presence of MPA and collected a number of behavioural measures on each child. In order to reduce the risk of chance correlations between the weighted score and behavioural measures, males and females were treated as independent samples and relations were accepted only if similar in the two groups. Unfortunately this procedure would tend to overlook any actual sex differences.

Weighted MPA score correlated positively with such behavioural measures as: inability to delay gratification, nomadic play, frenetic play, spilling and throwing, opposes peer and perseveration. A negative relationship was associated with tractibility. The authors stated that these behaviours are

similar to the cluster associated with hyperactivity and that the more MPA found in a particular child the more likely he was to be aggressive, hyperactive and intractable. A follow-up study of these children some five years later (Waldrop & Halverson, 1971) showed the MPA score and associated hyperactive behaviour to be stable. The high MPA 7 1/2 year olds were also found to be poorly coordinated and lower than average in verbal ability.

A replication of the original study (Waldrop & Halverson, 1971) again found a significant correlation between hyperactivity and the anomaly score for boys but not for girls. Instead, high MPA girls scored high on an intractability-inhibition factor tending to move around less, oppose peers more and to be more perseverative than low MPA girls. These findings have since been replicated by Waldrop and Bell (1976).

O'Donnell and Van Tuinan (1979) also examined behaviour problems in preschool children. They expected MPA score to be related to uncontrolled hyperactive behaviour in boys and withdrawn behaviour in girls as described by Waldrop and Halverson (1971) and Waldrop and Bell (1976). They found that scores on "conduct" and "hyperactivity" factors from a behaviour checklist related significantly to observed activity level, gross motor incoordination and MPA score for boys. For girls the "conduct" factor correlated with activity level and gross incoordination but not MPA's and the "hyperactivity" factor related only to gross motor incoordination. Distractibility was related to MPA score and fine and gross motor incoordination for

boys only. Interestingly social withdrawal was related to activity level and MPA's for boys and not girls in direct contrast to previous findings (Waldrop & Bell, 1976; Waldrop & Halverson, 1971).

Such inconsistencies in findings combined with the findings of others (LaVeck, Hammond & LaVeck, 1980) who have examined the interaction of environmental psycho-social factors and MPA's in hyperactivity serve as reminders that such environmental influences must not be underestimated.

MPA's in Hyperactives and Other Clinical Groups

Utilizing the anomalies survey introduced by Goldfarb (1967) and later modified by Waldrop and co-workers (Waldrop & Halverson, 1971; Waldrop et al., 1968) a number of studies have found a higher incidence of MPA in hyperactive children when compared to normal controls (Firestone et al., 1976; Firestone et al., 1978; Halverson & Victor, 1976; Quinn & Rapoport, 1974; Rapoport & Quinn, 1975; Rapoport et al., 1974; Waldrop & Goering, 1971). Significantly more MPA's have also been found in groups of congenitally deaf children (Waldrop & Halverson, 1971), severely disturbed children (Steg & Rapoport, 1975), autistic children (Links, Stockwell, Abichandani & Simeon, 1980; Walker, 1977), children with learning disabilities (Steg & Rapoport, 1975), retarded children (Firestone et al., 1978) and first grade children who experienced academic failure (Rosenberg & Weller, 1973). These findings are particularly interesting in light of

reports by Chess and co-workers (Chess, 1977; Chess, Korn & Fernandez, 1971) of a high incidence of autism, mental retardation and behavioural disorders in cases of congenital rubella which itself has been linked with anomalous development (Cooper & Krugman, 1966; Greg, 1941). High MPA autistic subjects have been found to have lower IQ scores, more frequent hospitalization and more normal family histories with regards to psychiatric illness, drug abuse and imprisonment in comparison to their lower MPA peers (Links et al., 1980). Increased maternal age has also been associated with autism (Gillberg, 1980) and frequency of anomalies has been observed to increase with maternal age (Links, 1980).

Newborn Screening

Large numbers of newborns have been screened and high and low MPA groups selected for continued study by Burg, Hart, Quinn and Rapoport (1978). These infants were observed at 1 and 2 years by investigators blind for newborn MPA score. At age 1 high MPA males were characterized as more irritable, less adaptable, having lower threshold and more negative mood. At the same age high MPA females were described as less active and showed less approach behaviour. At age 2 high MPA males were rated as less cooperative than their low MPA counterparts and were more irritable and subject to night walking. The high MPA females at this age were rated by a psychologist as exhibiting more negative emotional tone. A subgroup of infants considered irritable at ages 1 and 2 all came from the high MPA group.

Another group of researchers (Waldrop, Bell, McLaughlin & Halverson, 1978) followed 30 males who had been evaluated for MPA's at birth. These boys were observed at age 3 in the nursery school setting for evidence of short attention span, peer aggression and impulsivity. The authors stated that while it was not unusual for low MPA boys to be hyperactive it was quite unusual for high MPA boys not to be hyperactive. They conclude by stating that a subgroup of hyperactive boys with congenital contributors can be identified at birth with considerable accuracy.

MPA's and Treatment

Results of a study by Ferguson and Trites (1980) suggest that MPA's may be useful in the selection of treatment. These authors were looking for measures that might predict response to stimulant-drug therapy in hyperactive boys in a double-blind crossover study. They found that boys diagnosed as brain damaged according to the results of a neuropsychological assessment had a higher rate of response to Ritalin than those with no evidence of brain damage. Boys with abnormal EEG's also showed a higher rate of response to medication. Other variables which consistently differentiated responders from non-responders were: rated as less attentive, more impulsive, higher MPA scores, younger age and lower IQ's.

This study is suggestive of an association between MPA and brain damage but more importantly, it verifies the value of the

anomaly score in the selection of treatment. While high MPA individuals may be quite responsive to biologic treatment, low MPA individuals may be more amenable to a psycho-social approach. Attention to such variables as anomaly score may be helpful in sorting out apparent inconsistencies from study to study in the evaluation of various treatment strategies.

MPA's and Attractiveness

If the presence of a high number of MPA's resulted in an unusual appearance, a child's social interactions would be affected and atypical behaviour may be expected. In order to determine whether or not these high MPA children are indeed "funny looking" Rapoport and Quinn (1975) asked two individuals to rate full-face colour photographs of children on a four-point, bipolar scale. While there was high agreement between the raters on attractiveness there was no significant relationship between weighted MPA score and attractiveness ratings. The same, however, would not be expected to hold true in the case of major anomalies which may have a considerable impact on appearance.

Problems in the Perinatal Period and Early Life

Rapoport and Quinn (1975) report that hyperactive children with MPA scores of 5 or greater were significantly more likely to be seen as problems before the age of 3 years. These authors also report an association of head-banging in infancy with high MPA scores.

High stigmata score hyperactive children are more likely to be the product of pregnancies associated with obstetrical complications (Quinn & Rapoport, 1974) and there is a higher incidence in these cases of miscarriages and stillbirths in other pregnancies (Rapoport & Quinn, 1974). It seems unlikely that differential reporting of obstetrical problems in the low and high MPA groups could account for these differences.

Taft and Goldfarb (1964) have reported "evidence of reproductive casualty" among schizophrenic children, a group for whom elevated MPA scores have been reported (Goldfarb, 1967). They found the incidence of prenatal and perinatal problems to be 69% higher for schizophrenic boys and 56% higher for girls when compared to their sibs and control children.

Links et al. (1980) found increased MPA scores and pregnancy complications in autistic children in comparison to same sex siblings although MPA scores and pregnancy complications did not correlate directly. The authors suggest that pregnancy complications and anomalies may be the result of unknown factors which also play a role in the etiology of autism.

Many recent studies (Ellenberg & Nelson, 1979; Finer, Robertson, Richards, Pinnell & Peters, 1981; MacDonald, Mulligan, Allen & Taylor, 1980; Mulligan, Painter, O'Donoghue, MacDonald, Allen & Taylor, 1980; Rothberg, Maisels, Bagnato, Murphy, Gifford, McKinley, Palmer & Vannucci, 1981; Towbin, 1978) verify the importance of perinatal factors in consequent neurodevelopmental sequelae most notably MR and CP. The focus of

much of this research has been on perinatal asphyxia. Asphyxia is most frequently associated with prematurity and low birth weight (MacDonald et al., 1980; Rothberg et al., 1981) but also presents a significant problem with full-term infants (Finer et al., 1981) and actually may be associated with a higher risk of mortality in affected term infants in comparison to pre-term peers (MacDonald et al., 1980). It is unfortunate that these researchers have not as a matter of routine examined infants for evidence of dysmorphic development.

Mental Retardation

Considerable overlap exists between those factors associated with the production of malformations (Willis, 1962) and those thought to be responsible for the clinical condition referred to as mental retardation (Berg, 1974). MR is frequently mentioned in association with malformation disorders (Smith, 1976) and a relatively high incidence of malformation has been detected in the MR population (Firestone et al., 1978; Smith & Bostian, 1964) particularly in the Down syndrome subgroup (Gibson & Frank, 1961; Levinson et al., 1955; Penrose, 1954). The overlap is not complete since many malformed individuals develop to average and above average intellectual levels (Smith, 1976) and many instances of MR have been traced to post-embryonic causes such as encephalitis, trauma and anoxia (Berg, 1974).

MR has been defined as "subaverage general intellectual functioning which originates during the developmental period and

is associated with impairment in adaptive behaviour" (Heber, 1961). It is suggested that MR be viewed not as a disease entity itself but as a symptom of some other aberrant process (Berg, 1974). Like anomalous development the specific causal agent responsible for abnormal mental development is identifiable with certainty only in a minority of cases (Berg & Kirman, 1950).

Lewis (1933) sub-divides the MR population into a group composed of normal variants, that is, the lower extreme of the theoretical distribution of intelligence who are usually mildly affected, and a second group of organically diseased variants who are usually more severely affected. It is this latter group that is of interest here.

The severely affected are defined as those whose IQ's are below 50 and who therefore fall in the moderate, severe and profound ranges of MR. Severe subnormality affects some 3.7/1000 in the young adult population and of these between 1/4 and 1/3 have Down syndrome (Kushlick & Blunden, 1974). Crome (1960) reports that upon post-mortem examination the great majority of these severely defective individuals demonstrate widespread and varied cerebral pathology and other investigators (Leisti & Iivanainen, 1978) have reported evidence of hypothalamic dysfunction associated with general cerebral involvement.

A recent study (Moeschler, Bennett & Cromwell, 1981) examined computerized tomographic (CT) scans in a group of moderately to severely retarded individuals with no known etiology. While the vast majority of subjects had CT scans which

were interpreted as normal a sub-group, independent of CT scan findings, composed of approximately half the subjects emerged containing individuals with many "minor dysmorphic features." The absence of demonstrable brain pathology in large numbers of MR subjects has been perplexing however, the microanatomic work of Purpura (1974) surrounding what has been termed "dendritic spine dysgenesis" in MR individuals has given new direction to the search for neuroanatomic and neurophysiologic mechanisms in MR.

Anomalies have long been noted in the Down syndrome population and at one time constituted the sole means of diagnosing this disorder (Penrose, 1954). In later years Smith (1971; 1976) made a more precise accounting of the pattern of malformation associated with this and other recognized MR syndromes. The observation of relatively high MPA scores in the idiopathic MR group (Moeschler et al., 1981; Smith & Bostian, 1964) is of particular interest. To date the research has looked mainly at the frequency of anomalies in this and other groups and little attention has been paid to which defects are most prevalent in a given population in order to identify defining characteristics or patterns. Minor anomalies have largely been overlooked as a potential clinical guide in the delineation of etiology in MR. The combination of a detailed history and MPA survey may be most helpful in this regard.

Cerebral Palsy

CP is a complex of motor disturbances characterized by spasticity, athetosis, rigidity, tremor and/or ataxia of a non-progressive nature arising at some time between conception and two years of age (Towbin, 1960). The prevalence rate has been estimated at between 1.6 and 5 per 1,000 individuals under 21 years of age (Molnar & Taft, 1973).

Unlike MR the nature of brain lesions associated with CP in relation to specific neurological manifestation (spasticity etc.) are known (Marks, 1974; Towbin, 1960). Regions of involvement include areas 4 and 6 of the cerebral cortex, the pyramidal and extrapyramidal systems and more rarely the cerebellum.

Although early research concentrated on mechanical birth injury as the main etiology in CP this notion has now been largely discounted (Illingworth, 1964; Towbin, 1960). Low birth weight and prematurity (preterm delivery) have been identified as important risk factors (Ellenberg & Nelson, 1979) and considerable attention has been paid to asphyxia as a causal agent. The neuropathologic effects of asphyxia have been described as they manifest themselves in term and preterm infants (Towbin, 1970; 1978). However as Illingworth (1964) points out the asphyxia may itself be due to depression of the respiratory center by a "prenatal developmental defect." Indeed an increased incidence of anomalies has been reported in CP's (Roboz, 1962) especially in those afflicted with MR (Illingworth, 1964). An

association between CP and MR has long been recognized (Molnar & Taft, 1973).

The Present Study

Current research indicates a high incidence of anomalies among a number of clinical groups and a frequent association of MR and congenital malformation. Anomalies have been clearly shown to be a consequence of early developmental deviation and as such constitute a valuable diagnostic tool. The delineation of an early prenatal cause through the anomaly examination is important to family planning, the identification of teratogens and ultimately to prevention. Anomalies have also proven useful in the selection of treatment and its subsequent effectiveness. Anomalies play an important role in the identification of high risk infants through newborn screening which with the appropriate follow-up and early intervention will help to ameliorate the primary problem and prevent the development of secondary problems. It is, however, necessary to evaluate the procedure with a known population and to explore the many types of information that can be derived from it.

The present study seeks to evaluate the clinical usefulness of anomalies in the determination of etiology in MR and CP. In addition the relationship between intraindividual differences in lateral involvement and measures of lateral dominance, and verbal and spatial skills is examined. Finally a determination of the relationship between anomalies and level of intellectual functioning in MR individuals is made.

Currently the diagnosis of etiology in MR relies heavily on the social and medical history. Much of the information is supplied by parents and other individuals as late as middle childhood when institutionalization of the child is being considered and when the memories of important early events may be obscured. As well, information from various sources may be found to be contradictory at a point in time when verification is no longer possible. There may also simply be a paucity of relevant information concerning the individual's past and little solid evidence to point to a specific cause. The use of an anomaly survey is helpful in evaluating the relative importance of prenatal factors and in addition to the information contained in the history can result in a more reliable diagnosis.

The present study examines the frequency and pattern of anomalies in four groups of retarded adults, a group of CP individuals and a group of normal controls. The MR groups represent four etiological categories: Down syndrome, prenatal, perinatal and postnatal causes of retardation. Initially the six groups were compared on the frequency of anomalies.

The Down syndrome subjects constitute the most homogeneous group, their condition being due to a verifiable chromosomal defect. They also are the group traditionally linked with a cluster of congenital anomalies (Penrose, 1954) and were expected to have a high incidence of anomalies. Although the incidence of anomalies in this group has long been a topic of discourse little attempt has been made to statistically evaluate the relative

importance of various anomalies in discriminating the Down syndrome individual from normals. One of the aims of this study has been to identify those anomalies which constitute the least variant features of Down syndrome and best discriminate this group from others especially the Prenatal MR group.

The other three MR groups are more heterogeneous and are linked together within their groups more by the timing of the etiological event than by the specific event involved. The Prenatal MR group was composed of individuals considered likely to have undergone a teratogenic event and were expected to have an elevated incidence of anomalies. It is important to examine the nature of anomalies associated with the more heterogeneous Prenatal MR group. By identifying those anomalies that are most frequently found in this and other clinical groups and are most effective in discriminating these groups from normals, the predictive value of newborn screening is greatly enhanced.

The Postnatal MR and normal Control groups were assumed to have developed normally during the prenatal period and were expected to have a low incidence of anomalies. Due to the less than complete reliability of the history a degree of error was expected in the assignment of MR subjects to groups, such that, the Postnatal MR group might exhibit somewhat more anomalies than the Control subjects from whom they theoretically should not differ.

In terms of frequency of anomalies the Perinatal MR group is most interesting. According to the "continuum of reproductive

casualty" model (Pasamanick et al., 1956) the perinatal birth complication is directly responsible for the brain damage which results in MR and the level of anomalies in this group should not differ from that of the Postnatal MR or Control groups. This is in contrast to what might be termed the "high risk" model which would suggest that conceptuses which have been exposed to a teratogenic influence are predisposed to a range of pregnancy complications from abortion and death to complications of delivery and the neonatal period. According to this model the Perinatal MR group is identified with the Prenatal MR group and should exhibit a high incidence of anomalies. While the majority of subjects in this group were predicted to belong to the "high risk" category it was considered possible that a subgroup of individuals might have been the victims of direct perinatal events and that the mean for this group would lie between those of the Prenatal and Postnatal MR or Control groups. The CP group constituted an additional test of this hypothesis as CP is generally regarded as a manifestation of CNS damage sustained during the perinatal period.

In addition to the anomaly survey which was administered to each subject, a measure of verbal skills, the Peabody Picture Vocabulary test (PPVT) (Dunn, 1965), a measure of spatial ability, the Coloured Progressive Matrices (CPM) (Raven, Court & Raven, 1977) and the Reitan-Klove Lateral Dominance or functional laterality examination described by Reitan and Davison (1974) was also administered to the MR and Control subjects.

Smith (1976) describes intraindividual variance in expression whereby the left and right body sides exhibit differential involvement as regards the frequency of anomalies. Of the 18 anomalies in the Waldrop and Halverson (1971) survey, 10 may be manifested unilaterally or bilaterally and these in addition to any other unilaterally expressed anomalies were used to compute a structural laterality score for each subject.

Studies of the validity of neuropsychological testing (Guertin, Ladd, Frank, Rabin & Hiester, 1966; Ladd, 1964; Klove, 1959, 1974; Klove & Reitan, 1958; Morrow & Mark, 1955) have shown that individuals with left cerebral hemisphere lesions perform more poorly on verbal tasks while individuals with right hemisphere lesions have greater difficulty with spatial tasks. By examining the pattern of test scores it is possible to identify the impaired hemisphere with a high degree of accuracy. Utilizing the functional laterality or lateral dominance score and verbal and spatial ability score data an attempt was made to predict the structural laterality score, that is, the body side most affected by anomalies.

The relationship between anomalies and level of intellectual functioning in MR was also examined whereby anomaly score was correlated with CPM and PPVT scores. An investigation of the pattern of performance on the PPVT, CPM and lateral dominance examination was also undertaken.

Mathews (1974), in his review of neuropsychology and MR, states that results on the Wechsler-Bellevue scale (Wechsler,

1939) indicate a Performance Quotient (PQ) greater than Verbal Quotient (VQ) discrepancy for MR subjects. A more recent study (Calvert & Crozier, 1978) suggests that VQ-PQ discrepancies on the Wechsler Adult Intelligence Scale (Wechsler, 1955) are related to full scale IQ for MR individuals with the lower IQ groups having VQ greater than PQ, little discrepancy in the middle groups and PQ greater than VQ in the higher IQ groups. In the Calver and Crozier study four of the groups fell in the mild to borderline range while the fifth fell in the moderate range constituting on the whole a relatively high functioning sample. The Wechsler scales rely heavily on motor ability and expressive language skills which may particularly disadvantage low functioning MR individuals. The two tests selected for use in the present study rely neither on motor ability nor expressive language skills.

METHOD

Subjects

The six groups each contained 12 subjects for a total of 72 male and female clients and staff of the Rideau Regional Centre, a large residential treatment facility for MR persons located in Smiths Falls, Ontario. The subjects included in the study were those who met the etiological criteria set for the various groups, agreed to participate in the study and in the case of clinical subjects for whom the appropriate consent could be obtained from legal guardians.

The Down syndrome group. The Down syndrome group was composed of individuals who had been so diagnosed by a physician excluding those for whom a cytogenetic examination indicated a mosaic genotype.

The Prenatal MR group. This group consisted of subjects whose history indicated that a teratogenic influence may have been operating early in pregnancy or who possessed a major anomaly. This would include cases of threatened abortion during the first trimester, maternal illness, toxemia or malnutrition and an unexpectedly high incidence of MR in an otherwise normal family. Excluded from this group were any individuals who had been identified as belonging to a recognized genetic syndrome.

The Perinatal MR group. This group was composed of individuals who had experienced gestational disorders such as prematurity or postmaturity or complications of delivery. McKay

(1969) suggests the following factors as being important in the identification of infants who have sustained mechanical or hypoxic birth injuries: premature rupture of the membranes, prolonged or precipitate delivery; low weight for gestational age, use of forceps, breech extraction, cyanosis, convulsions, jaundice and failure to feed well.

The Postnatal MR group. The Postnatal MR group consisted of individuals whose development was described as normal up until the occurrence of such events as traumatic head injury or viral infection.

The CP group. This group consisted of individuals who possessed a severe physical handicap the degree of which had precipitated their institutionalization to a greater extent than any perceived intellectual deficits. In fact these individuals would be described as minimally impaired in terms of cognitive functioning in comparison to the other four clinical groups, CP constituting by far their major handicap.

The Control group. The Control group consisted of volunteers from among the staff who agreed to participate in the study.

Table 1 presents the data for the six groups on age, and years of institutionalization and age at institutionalization for the five clinical groups.. The six groups did not differ significantly on age nor did the five clinical groups differ on years spent in an institution or the age at which they entered an institution. Table 2 presents the number of males and females in

Table 1

Mean Scores of Groups on Descriptive Variables

		Group					
		Control	Down Syndrome	Prenatal MR	Perinatal MR	Postnatal MR	CP
Age (Years)							
Mean		26.00	32.58	32.42	30.33	32.92	30.50
SD		6.08	5.78	9.51	5.42	5.40	12.30
<u>n</u>		12	12	12	12	12	12
Years Institutionalized							
Mean	-	-	19.50	20.42	20.17	17.75	14.58
SD	-	-	8.71	6.64	4.71	9.16	8.20
<u>n</u>	-	-	12	12	12	12	12
Age Institutionalized							
Mean	-	-	13.08	12.00	9.17	15.17	15.92
SD	-	-	12.14	5.64	4.65	8.09	9.72
<u>n</u>	-	-	12	12	12	12	12

Table 2

Distribution of Sexes Among the Groups

Sex	Group					
	Control	Down Syndrome	Prenatal MR	Perinatal MR	Postnatal MR	CP
Male						
$\frac{n}{\text{Row \%}}$	5 11.63	7 16.28	9 20.93	11 25.58	4 9.30	7 16.28
Column %	41.67	58.33	75.00	91.67	33.33	58.33
Female						
$\frac{n}{\text{Row \%}}$	7 24.14	5 17.24	3 10.34	1 3.45	8 27.59	5 17.24
Column %	58.33	41.67	25.00	8.33	66.67	41.67

Total Males

 $\frac{n}{\text{Row \%}}$ = 43 $\frac{\%}{\text{Column \%}}$ = 59.72

Total Females

 $\frac{n}{\text{Row \%}}$ = 29 $\frac{\%}{\text{Column \%}}$ = 40.28

each of the six groups. Due to the difficulty in finding subjects who met the etiological criteria of the various groups it was not possible to select equal numbers of males and females and the groups did differ in terms of the distribution of the sexes, $\chi^2 (5) = 11.37, p < .05$. It was later determined that sex did not correlate with the anomaly or other dependent measures and consequently it was not treated as a covariate.

Surveys and Tests Administered

The evaluation of each subject consisted of a survey of external physical anomalies noting lateral involvement and an assessment of lateral dominance, verbal and spatial skills.

Anomalies survey. Three anomaly scores were computed for each subject. The first, referred to as the weighted anomaly score was derived using the Waldrop and Halverson (1971) survey and scoring weights of 0, 1 or 2 presented in Table 3. The anomalies involved and criteria have been previously described in detail. Norms for head circumference (Appendix A) were provided by Nellhaus (1968) and the measurement was obtained by placing a metric tape measure across whichever points on the occiput and supra-orbital ridges yielded the maximal circumference. Inner canthal and outer orbital dimensions (Appendix A) were measured using a geometric compass equipped with rubber tips for safety and were compared to norms published by Laestadius, Aase and Smith (1969). Interpupillary distance was determined according to the method described by Pryor (1969) and was compared to norms provided by him (Appendix A).

Table 3

MPA Survey and Scoring Weights from Waldrop and Halverson (1971)

HEAD

Fine electric hair:	
Very fine hair that will not comb down	2
Fine hair that is soon awry after combing	1
Two or more hair whorls	0
Head circumference outside normal range:	
More than 1.5 SD's	2
1.0 to 1.5 SD's	1

EYES

Epicanthus:*	
Where upper and lower lids join the nose	
Deeply covered	2
Partly covered	1
Hypertelorism:	
Approximate distance between tear ducts	
More than 1.5 SD's	2
1.0 to 1.5 SD's	1

EARS

Low-seated ears:*	
Point where ear joins the head not in line with corner of eye and nose bridge	
Lower by more than 0.5 cm	2
Lower by 0.5 cm or less	1
Adherent ear lobes:*	
Lower edge of ear extends	
Upward and back toward crown of head	2
Straight back toward rear of head	1
Malformed ears*	1
Assymetrical ears	1
Soft and pliable ears*	0

Table 3 continued

MOUTH

High-steeped palate:	
Roof of mouth	
Definitely steeped	2
Flat and narrow at the top	1
Furrowed tongue (one with deep ridges)	1
Tongue with smooth-rough spots	0

HANDS

Curved fifth finger:*	
Markedly curved inward toward other fingers	2
Slightly curved inward toward other fingers	1
Single transverse palmar crease*	1

FEET

Third toe longer than second:*	
Definitely longer than second toe	2
Appears equal in length to second toe	1
Partial syndactyly of the two middle toes*	1
Big gap between the first and second toes*	1

*May be manifested unilaterally or bilaterally

The anomaly survey conducted in the present study was a comprehensive one not limited to the anomalies selected by Waldrop and Halverson (1971). All anomalies recognized by the examiner were noted and two further anomaly scores were computed in addition to the weighted score. The total anomaly score constituted a frequency count of all anomalies observed in a single subject. The combined score incorporated the information included in both the weighted and total anomaly scores. Thus, a weight of 1 was assigned to each and every anomaly encountered with the provision of applying a weight of 2 to several anomalies as per Waldrop and Halverson (1971) when present in a severe form.

Structural laterality. It is theoretically possible for many anomalies to manifest themselves unilaterally as has been noted in Table 3 for the Waldrop and Halverson anomalies. A measure of lateral involvement or structural laterality ranging from 1 (completely left-sided) through 11 (unlateralized) to 21 (completely right-sided) was computed for each subject (Appendix B). With a score of 11 as the starting point, 1 point was subtracted for each anomaly manifested on the left body side and 1 point was added for each right-sided anomaly to arrive at the structural laterality score.

Lateral dominance. Lateral dominance or functional laterality was assessed using the Reitan-Klove Lateral Dominance examination as described by Reitan and Davison (1974). The subject is asked to mime various tasks such as "Show me how you

hammer a nail" and the observer notes the side of the body used to execute the task. Seven of these items involve the hands, two the eyes and two involve the feet. Due to the difficulty encountered by the MR subjects in carrying out the two items involving the eyes, these items were replaced for the MR subjects with two trials of sighting down a paper tube which was presented to the subject at hand level and on the mid-line. A functional laterality score ranging from 1 (completely left dominant) to 11 (completely right dominant) was computed for each Control and MR subject (Appendix C).

Verbal ability. An estimate of verbal ability was provided through administration of the PPVT (Dunn, 1965). In this test a stimulus word is said aloud by the examiner and the subject is asked to indicate which of four line drawings "best tells the meaning of the word."

Spatial ability. Spatial ability was assessed with the book form of the CPM (Raven et al., 1977) and raw scores were converted to standard scores with a mean of 100 and an SD of 15 with the aid of information provided by C. W. Dils (personal communication). This permitted direct comparison with PPVT IQ scores. In this test the subject is presented with an incomplete visual pattern and is asked to select the stimulus from the set of six patterns below it which completes the main pattern. Although the CPM is intended for use with children, Dils (1960) recommends it for general clinical use especially with individuals suspected of having impaired intellectual functioning

because it is shorter, easier and more attractive than the standard adult version (Raven, 1960).

Procedure

Over 200 files were reviewed in an effort to select subjects for the study. Following this a covering letter (Appendix D) and a consent form (Appendix E) together with a stamped self-addressed envelope were sent to the parents or guardians of prospective clinical subjects. Consent was also obtained from individual subjects prior to their inclusion in the study.

Each subject was accompanied by the investigator to a quiet area where the PPVT, CPM, lateral dominance examination and anomaly survey were administered after a short period during which rapport was established. The order of presentation was adjusted in order to facilitate optimal performance for each subject. For instance, the anomaly survey was administered last to Control subjects who tended to find this aspect of the data collection most anxiety laden. Some retarded persons are very conscious of test performance due to previous failure experiences and so in these cases the two ability tests were left to the end. The lateral dominance examination tended to be the least threatening procedure and was generally administered first. After the data collection all subjects were given the opportunity to ask questions and at the close of the session clinical subjects were escorted back to their wards. Information

regarding the results were made available to any subjects or authorized persons who expressed such an interest.

RESULTS

The examination of the anomaly data was conducted using three types of statistical analyses. Initially a series of ANOVA's were performed in order to examine differences in the frequency of anomalies between groups. Subsequently multiple Chi Square analyses were carried out in order to examine the incidence of individual anomalies among the groups. Finally multivariate analyses consisting of several discriminant function analyses to assess patterns of anomalies in the various groups and several multiple regressions were performed.

Three separate ANOVA's were conducted using the three anomaly scores: weighted, total and combined. The means and the SD's are presented in Figure 1. As expected the groups differed on each of the scores: weighted, $F(5, 66) = 9.61, p < .0001$, total, $F(5, 66) = 18.48, p < .0001$, and combined, $F(5, 66) = 19.33, p < .0001$.

Several orthogonal contrasts were planned in advance and the nature of the relationships between the groups was essentially the same for the three groups as seen in Figure 1. The combined score encompassed the information contained in the other two scores while maximizing the differences between the groups, thus in the interest of expediency only the results for this score are reported henceforth.

Initially the mean of the Down syndrome, Prenatal MR, Perinatal MR and CP groups was contrasted with that of the

Figure 1

Means and SD's on Three Anomaly Scores

C CONTROL
 DS DOWN SYNDROME
 PR PRENATAL MR

PE PERINATAL MR
 PO POSTNATAL MR
 CP CEREBRAL PALSY

MEANS

Control and Postnatal MR groups. As predicted the combined mean of the Control and Postnatal MR groups was significantly lower, $t(66) = 4.65$, $p < .0001$. As expected the means of the Control and Postnatal MR groups did not differ significantly from one another while the Down syndrome subjects had significantly more anomalies than the Prenatal MR group, $t(66) = 3.25$, $p < .006$.

Interestingly of the two perinatal groups, the CP's had significantly fewer anomalies than did the Perinatal MR group, $t(66) = 2.83$, $p < .02$, although this difference was not evident using the weighted score.

Additional post hoc comparisons utilizing the Scheffe procedure yielded three homogeneous subsets, each subset containing no pair of means which differed significantly from one another. The first set consisted of the Control, Postnatal MR and CP groups. The second consisted of the CP, Perinatal and Postnatal MR groups and the third was composed of the Prenatal and Perinatal MR groups. Table 4 presents the differences between the means of the various groups on the combined anomaly score.

On inspection of Figure 2 the six groups can be assigned to one of two basic categories. The first category manifests relatively few anomalies and consists of the Control, Postnatal MR and CP groups while the second consisting of the Down syndrome, Prenatal and Perinatal MR groups has a greater frequency of anomalies. These basic differences are further highlighted in Table 5. The contrast between the two categories

Table 4

Significant Differences Between the Means on Combined
Anomaly Score According to Scheffe's Procedure

	Group					
	Control	Down Syndrome	Prenatal MR	Perinatal MR	Postnatal MR	CP
Control		9.58*	6.33*	4.67*	1.92	1.83
Down Syndrome			3.25*a	4.91*	7.66*	7.75*
Prenatal MR				1.66	4.41*	4.50*
Perinatal MR					2.75	2.84b
Postnatal MR						.09

a t test, $p < .006$

b t test, $p < .02$

* $p < .05$

Figure 2

Cumulative Frequency on Combined Anomaly Score

Table 5

Distribution of Anomalies and Anomaly Types

	Group						TOT
	CONT	DOWN SYN	PRE MR	PERI MR	POST MR	CP	
Total Anomalies	32	121	89	70	46	43	401
%	8	30	22	18	11	11	100
Total Anomaly Types	11	28	25	30	18	13	35
%	31	80	71	86	51	37	-

Note. Includes only those anomalies affecting more than a single subject.

is enhanced when the variety of anomalies observed within the individual groups is considered, also shown in Table 4. The Down syndrome, Prenatal and Perinatal MR groups displayed a high proportion of the 35 individual anomalies observed in the study while the Control, Postnatal MR and CP groups manifested considerably fewer of the individual anomaly types.

The frequency of individual anomalies across the six groups was compared using the Chi Square statistic. These data are presented in Table 6. A complete listing of the Chi Square data by region of the body is provided in Appendix F. Of the 35 analyses conducted 11 or 31% were significant, well beyond the 1.75 that would be expected on the basis of chance at the .05 level of probability.

The 11 anomalies that reached statistical significance were manifested in various regions of the body. The analysis of the head circumference data, $\chi^2 (20) = 49.19, p = .0008$, presented in Table 7, revealed some rather clear differences. The majority of subjects in the Control, Postnatal MR and CP groups demonstrated head circumference measurements within 1 SD of the mean for their age group, while the majority of Down syndrome subjects had reduced head circumferences and the Prenatal and Perinatal MR groups tended to have increased head measurements. Table 8 provides data on the distribution of the other significant anomalies. Such anomalies as upslanting palpebral fissures, $\chi^2 (5) = 32.73, p = .00001$, microthalamia, $\chi^2 (5) = 11.65, p = .04$, furrowed tongue, $\chi^2 (5) = 26.87, p = .00006$,

Table 6
Frequency of Individual Anomalies for the Six Groups

	Group						TOT
	CONT	DOWN SYN	PRE MR	PERI MR	POST MR	CP	
Increased inner canthal distance*	3	8	10	10	7	10	48
Adherent ear lobes	7	8	9	5	6	6	41
Head circumference inc/dec*	5	10	7	7	4	5	38
Clinodactyly of 5th finger*	5	9	7	2	6	7	36
Big gap between 1st and 2nd toes*	3	8	4	5	1		21
High-steeped palate	1	6	5	2	4	2	20
Clinodactyly of toes	1	4	7	4	1	2	19
Prominent ears**		7	3	3		1	14
Irregular spacing of teeth		4	2	3	2	1	12
Abnormally short great toe	1	3	4		3		11
Assymetrical length/size of toes	3	1	1	1		5	11
Abnormal shape of teeth		4	3	1	1	1	10
Deep crease on sole between 1st and 2nd toes***		7		3			10
Scapha helix incomplete	2	1	5	1		1	10
Epiqanthus		5		1	2	1	9
Assymetrical ears			4	2	2	1	9
Single palmar crease**	1	5		1			7
Abnormal eyebrows (e.g., synophrys)		2	3	1	1		7

Table 6 continued

	Groups						TOT
	CONT	DOWN	PRE	PERI	POST	CP	
	SYN	MR	MR	MR	MR		
Other palatal anomalies	2	3	2				7
Malformed ears	1	3	3				7
Upslanting palpebral fissures***	6						6
Malformed toenails	3	1	1	1			6
Furrowed tongue***	5						5
Downslanting palpebral fissures			2	1	1		4
Microphthalmia*	3			1			4
Single crease on 5th finger	2			1	1		4
Multiple/unusual hair whorls				1	2		3
Other tongue anomalies			1	2			3
Body hirsutism	1	1	1				3
Low-set ears			1	1	1		3
Large lower lip	2			1			3
Short broad fingers**	3						3
Partial syndactyly of 2nd and 3rd toes			1	2			3
Fine hair	1	1					2
Low posterior hairline			1	1			2

Note. Includes only those anomalies occurring in two or more individuals.

* $p < .05$

** $p < .01$

*** $p < .001$

Table 7

Head Circumference Data for the Six Groups

	Group						
	CONT	DOWN SYN	PRE MR	PERI MR	POST MR	CP	TOT
Reduced							
-1.5 SD or Less							
Frequency	0	2	0	0	2	2	6
%	0	16.7	0	0	16.7	16.7	8.3
-1 to -1.5 SD							
Frequency	2	8	1	1	1	2	15
%	16.7	66.6	8.3	8.3	8.3	16.7	20.8
Normal							
-1 to 1 SD							
Frequency	7	2	5	5	8	7	34
%	58.3	16.7	41.7	41.7	66.7	58.3	47.2
Increased							
1.5 SD or Greater							
Frequency	2	0	0	1	0	1	4
%	16.7	0	0	8.3	0	8.3	5.6
1 to 1.5 SD							
Frequency	1	0	6	5	1	0	13
%	8.3	0	50	41.7	8.3	0	18.1

Table 8

Distribution of Additional Anomalies Associated
With Significant Chi Squares

	Group						TOT
	CONT	DOWN SYN	PRE MR	PERI MR	POST MR	CP	
Increased inner canthal distance	2	0	0	1	2	1	6
Severe	1	8	10	10	5	9	43
Upslanting palpebral fissures	0	7	3	3	0	1	14
Prominent ears	0	7	3	3	0	1	14
Furrowed tongue	0	5	0	0	0	0	5
Clinodactyly of 5th finger	5	6	2	2	4	7	31
Severe	0	3	0	0	2	0	5
Single palmar crease	1	5	0	1	0	0	7
Short broad fingers	0	3	0	0	0	0	3
Big gap between 1st and 2nd toes	3	8	4	5	1	0	21
Deep crease on sole between 1st and 2nd toes	0	7	0	3	0	0	10

Note. Anomalies designated severe were assigned a weight of 2 according to the Waldrop and Halverson (1971) survey.

single palmar crease, $\chi^2 (5) = 17.88$, $p = .005$ and short broad fingers, $\chi^2 (5) = 15.65$, $p = .008$, occurred virtually exclusively among the Down syndrome subjects. Clinodactyly of the fifth finger in its more exaggerated form (weight of 2), $\chi^2 (10) = 18.91$, $p = .04$, a big gap between the first and second toes, $\chi^2 (5) = 16.74$, $p = .005$, a deep crease on the sole of the foot between the first and second toes, $\chi^2 (5) = 28.80$, $p = .00005$, and prominent ears, $\chi^2 (5) = 18.86$, $p = .002$, also tended to distinguish the Down syndrome group from the others. Markedly increased inner canthal distance (weight of 2), $\chi^2 (10) = 23.94$, $p = .008$, tended to be more prevalent among the Down syndrome, Prenatal MR, Perinatal MR and CP groups.

The last set of analyses of the anomaly data involved the use of multivariate procedures. In order to examine patterns of anomalies across the groups several discriminant function analyses were conducted utilizing a step-wise technique. Only those variables which met the entry criterion, that is obtained a univariate "F to enter" greater than one were included in the various equations thereby disregarding those variables which did not make a significant contribution to the discriminant process. These variables may have had exceedingly low frequencies or may have been so prevalent in all of the groups that they provided little discriminative value. The number of variables that can be included in such an analysis is limited in direct proportion to the number of subjects. Consequently the anomalies were analysed in discreet groups according to such criteria as region of the body.

The first discriminant analysis involved the seven most frequent anomalies. Of these, six met the criteria for entry into the analysis. Three discriminant functions were removed before an insignificant amount of variance associated with the true source of differences among the groups (i.e., non-error variance) remained. The first function was associated with a canonical correlation of .74, the remaining functions having canonical correlations of .61 and .48 respectively. The first function with a Wilks' Lambda of .20 and associated $X^2(30) = 104.56$, $p < .001$, selected the Down syndrome subjects primarily on the basis of reduced head circumference scores and secondarily on the presence of a high-steeped palate, clinodactyly of the fifth finger and big gap between the first and second toes. The second function with a Wilks' Lambda of .44, associated $X^2(20) = 53.60$, $p < .001$, contrasted the Control and Postnatal MR groups with the Prenatal and Perinatal MR groups utilizing the anomalies increased inner canthal distance, clinodactyly of the toes and big gap between the first and second toes which were particularly prevalent in the latter two groups. The last significant function with a Wilks's Lambda of .70, associated $X^2(12) = 23.62$, $p < .03$, discriminated the CP subjects from the Control and to a lesser extent the Down syndrome and Prenatal MR groups based largely on the presence of increased inner canthal distance, decreased head circumference and absence of the anomaly big gap between the first and second toes. The values associated with the various discriminant functions are provided in Appendix G.

The anomaly adherent ear lobes did not meet the criteria for entry into the analysis although it was the second most frequent anomaly observed in the study, afflicting almost 60% of subjects across the groups. Most of these were manifested in their milder form (i.e., ear extends straight back from point of attachment with a weight of 1, as opposed to extending upward from the point of attachment toward the crown, with a weight of 2) and possibly in this mild form should be considered a normal variant rather than an anomaly.

Table 9 consists of an F matrix derived from the multivariate analysis demonstrating the differences between the groups. The only groups that were not successfully discriminated from each other were the Control and Postnatal MR groups, the Prenatal and Perinatal MR groups and the Postnatal MR and CP groups. Comparing the results of this analysis with the former univariate analysis (Table 3) it is evident that the differences between the groups are more enhanced using a multivariate approach.

Table 10 compares actual and predicted group membership from the discriminant function analysis. Utilizing the multiple discriminant function procedure with only seven of the 35 anomalies found in the study it was possible to correctly predict group membership in 61.11% of the cases in contrast to 36.11%, 30.56% and 33.33% using the weighted, total and combined scores, respectively.

Table 9

F Matrix from Discriminant Analysis
with Seven Most Frequent Anomalies

	Group					
	Control	Down Syndrome	Prenatal MR	Perinatal MR	Postnatal MR	CP
Control		10.01*	3.98*	3.75*	1.89	4.13*
Down Syndrome			7.53*	9.05*	5.06*	5.26*
Prenatal MR				1.06	3.19*	3.66*
Perinatal MR					3.73*	3.38*
Postnatal MR						.88

* $p < .01$, $df(6,61)$

Table 10

Group Membership Predicted from Discriminant Function Analysis

Actual Group	Group					
	Control	Down Syndrome	Prenatal MR	Perinatal MR	Postnatal MR	CP
Control						
$\frac{n}{\%}$	10 83.3	0 0	0 0	1 8.3	1 8.3	0 0
Down Syndrome						
$\frac{n}{\%}$	0 0	9 75	0 0	1 8.3	1 8.3	1 8.3
Prenatal MR						
$\frac{n}{\%}$	0 0	1 8.3	8 66.7	0 0	0 0	3 25
Perinatal MR						
$\frac{n}{\%}$	1 8.3	0 0	2 16.7	8 66.7	0 0	1 8.3
Postnatal MR						
$\frac{n}{\%}$	2 16.7	1 8.3	2 16.7	1 8.3	3 25	3 25
Cerebral Palsy						
$\frac{n}{\%}$	0 0	0 0	2 16.7	0 0	4 33.3	6 50

In order to compare the groups on anomalies occurring in specific regions or structures of the body several additional analyses were conducted. Anomalies associated with the hair had a rather low frequency and did not produce a single significant discriminant function. An analysis of anomalies associated with the eyes produced two significant discriminant functions with canonical correlations of .83 and .51. The first function with a Wilks' Lambda of .22, associated $X^2(20) = 98.80$, $p < .001$, identified the Down syndrome subjects using in descending order of importance upslanting palpebral fissures, microthalamia (small eyes) and epicanthus. The second function with a Wilks' Lambda of .71, associated $X^2(12) = 22.37$, $p < .04$, discriminated the clinical groups from the Controls relying largely on increased inner canthal distance. Values associated with the discriminant functions are provided in Appendix H.

Two significant functions were produced in an analysis of ear anomalies with canonical correlations of .53 and .39. As in previous analyses the first discriminant function with a Wilks' Lambda of .51, associated $X^2(20) = 44.77$, $p = .001$, identified the Down syndrome group based largely on the variable prominent ears. The second discriminant function with a Wilks' Lambda of .70, associated $X^2(12) = 23.33$, $p < .03$, discriminated the Prenatal MR group from the others using the variables incomplete scapha helix and asymmetrical ears. Appendix I presents the values associated with the two discriminant functions for the ear anomalies.

An analysis of oral anomalies produced one discriminant function with a canonical correlation of .72 and Wilks' Lambda of .38, associated $\chi^2 (25) = 63.05$, $p < .001$. The single significant function identified Down syndrome subjects. Most valuable in this regard was the anomaly furrowed tongue and in descending order of importance other palatal anomalies, high steeped palate and large lower lip. Values associated with the discriminant function can be found in Appendix J.

More peripheral anomalies, those affecting the hands and feet, were also examined. The analysis of hand anomalies resulted in one significant discriminant function with a canonical correlation of .65 and Wilks' Lambda of .52, associated $\chi^2 (15) = 43.22$, $p < .001$. This function again discriminated the Down syndrome group from the others and loaded strongly on three anomalies: short broad fingers, clinodactyly of the fifth finger and single transverse palmar crease. Values associated with these discriminant functions can be found in Appendix K.

The foot anomalies produced two significant discriminant functions with canonical correlations of .72 and .48. As expected, the first function with a Wilks' Lambda of .28, associated $\chi^2 (30) = 82.81$, $p < .001$, discriminated the Down syndrome group from the others utilizing mainly the variables deep crease on the sole of the foot between the first and second toes and big gap between the first and second toes. The second function with a Wilks' Lambda of .57, associated $\chi^2 (20) = 36.37$, $p < .02$, maximally discriminated the CP subjects from the

Prenatal and Postnatal MR groups. The anomalies short great toe and partial syndactyly of the second and third toes were associated with the MR groups while asymmetrical length and/or size of the toes identified the CP subjects. Appendix L presents the values associated with the two discriminant functions for the foot anomalies.

Multiple regression analyses indicated that the frequency of anomalies did not differ for males and females nor were high anomaly clinical subjects likely to have been institutionalized at an earlier age than their lower anomaly peers.

The second aspect of the study involved the examination of several neuropsychological measures. As previously stated the CP group was not included in this portion of the study due to the obvious inappropriateness of administering the lateral dominance test and the inordinate amount of time required to obtain the verbal and spatial ability measures from these severely physically impaired individuals. Table 11 presents the means and SD's for the five remaining groups on the PPVT, CPM and lateral dominance scores. Significant univariate F ratios were associated with both the PPVT, $F(4, 55) = 33.26, p < .0001$ and CPM, $F(4, 55) = 23.33, p < .0001$, scores while that of the lateral dominance score did not achieve significance. All groups demonstrated a strong preference for use of the right body side although the clinical groups tended to be more variable and somewhat less right dominant. While the Control group was clearly distinguishable from the MR groups on the PPVT and CPM

Table 11

Mean Scores for Five Groups on Neuropsychological Measures

Group	Neuropsychological Measures		
	PPVT IQ	CPM IQ	Lateral Dominance
Control			
Mean	112.50	114.50	11.25
SD	15.85	12.96	1.06
Down Syndrome			
Mean	18.50	24.33	8.50
SD	20.68	20.64	3.23
Prenatal MR			
Mean	30.25	47.25	10.00
SD	26.27	35.43	2.92
Perinatal MR			
Mean	37.08	42.83	8.17
SD	25.47	29.16	3.74
Postnatal MR			
Mean	37.00	44.25	8.33
SD	22.35	19.74	3.37

Note. Lateral dominance scores range from 1 (completely left dominant) to 12 (completely right dominant).

scores no differences were found between the MR groups on either of these measures.

A step-wise discriminant function analysis was conducted on the PPVT, CPM and lateral dominance data in order to determine whether some linear combination of the variables might reveal differences between the MR groups. This analysis produced one significant discriminant function with a canonical correlation of .85 and a Wilks' Lambda of .27, associated $X^2(8) = 73.37$, $p < .001$. The lateral dominance measure did not meet the criterion for entry into the analysis as the "F to enter" was less than one. Values relating to the discriminant function are provided in Appendix M. Utilizing the PPVT and CPM scores it was possible to discriminate all of the Control subjects, however it was still not possible to distinguish between the MR groups. Table 12 presents an F matrix derived from the discriminant analysis demonstrating the group differences.

Several regressions were carried out in order to examine the relationship between neuropsychological, descriptive and anomaly variables. A correlation of .64 was obtained between the PPVT and CPM scores. Both PPVT and CPM scores decreased with age in the Control and MR groups, $R = .51$, $F(2, 57) = 10.12$, $p < .01$. When only the MR groups were examined a significant relationship was found between the descriptive variables years institutionalized, age and age institutionalized and PPVT, $R = .40$, $F(3, 44) = 2.87$, $p < .05$, and CPM, $R = .44$, $F(3, 44) = 3.56$, $p < .05$, scores. As can be seen in Table 13, in the case of PPVT

Table 12

F Matrix from Discriminant Function Analysis
with Neuropsychological Variables

	Group				
	Control	Down Syndrome	Prenatal MR	Perinatal MR	Postnatal MR
Control		56.19*	40.24*	35.97*	35.62*
Down Syndrome			2.53	2.25	2.38
Prenatal MR				.96	.76
Perinatal MR					.02

Note. The lateral dominance measure did not meet the entry criterion thus the analysis was limited to the PPVT and CPM scores.

* $p < .01$, $df(2, 54)$

Table 13

Simple Correlation Coefficients for CPM Raw Score
and PPVT IQ with Selected Descriptive Variables

	Test Score	
	CPM	PPVT
Control and MR Groups		
Age	-.49	-.35
MR Groups Only		
Age	-.36	-.15
Years Institutionalized	-.36	-.40
Age Institutionalized	.04	.25

scores the effect of age was completely overshadowed by the deleterious effects of lengthy and early institutionalization. Table 13 also shows that both age and years institutionalized exerted a negative influence over CPM scores. The CPM raw score was employed in analyses involving the age variable, as the method of scoring CPM protocols involved adjustments for age within the adult range.

No relationship could be ascertained between the structural laterality score (the extent to which anomalies were unilaterally observed) and the functional laterality or lateral dominance of individuals. Nor was there any relationship between structural laterality, lateral dominance, PPVT and CPM scores or the discrepancy between the latter two scores. When analysis was restricted to the MR groups no relationship was found between the frequency of anomalies and PPVT or CPM scores.

The frequency of discrepancies in favour of either the verbal or spatial measures among MR subjects as a whole did not differ significantly. Neither did the actual verbal-spatial discrepancy score differ among the five groups nor did it correlate with level of intellectual functioning or more specifically level of retardation (profound, severe etc.) although there was a tendency for large discrepancies especially those in favour of the spatial score to be more frequent among MR subjects than Controls.

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DISCUSSION

The results of the study in general, verify the usefulness of anomalies in the delineation of etiology. Differences between the groups were apparent in overall frequency of anomalies, the frequency of individual anomalies and were particularly evident utilizing multivariate analysis to discriminate between the groups on the basis of anomaly patterns.

The Down syndrome group constituted the most reliable MR group in terms of subject selection and homogeneity due to the verifiable nature of the etiology. Predictably these subjects exhibited the highest frequency of anomalies and could be discriminated from all the other groups. The lowest obtained anomaly score in this group exceeded the highest anomaly score in the Control group.

The Control and Postnatal MR groups representing normal embryogenesis did not differ significantly from one another in frequency of anomalies. A degree of error was expected in the selection of Postnatal MR subjects on the basis of history and would account for the slight increase, though statistically insignificant, in the rate of anomalies in this group as compared with Controls.

The Prenatal MR group composed of subjects assumed to have undergone some unknown genetic or teratogenic event demonstrated a significantly elevated incidence of anomalies although significantly lower than the Down syndrome group. The Prenatal

MR group was intermediate between the Down syndrome and Control, CP and Postnatal MR groups.

The two perinatal groups of MR and CP subjects allowed consideration as to whether these CNS sequelae relate directly to perinatal events or whether the perinatal complications are themselves secondary to some earlier genetic or teratogenic event which places the individual at risk. The Perinatal MR group demonstrated a significantly elevated incidence of anomalies and was indistinguishable from the Prenatal MR group in frequency of anomalies. This would support the hypothesis that these constitute high risk individuals who were predisposed to perinatal complications.

The CP group had significantly fewer anomalies than the Perinatal MR group, significantly more than the Controls and did not differ from the Postnatal MR subjects. This would indicate that, in contrast to the Perinatal MR group, CP is more likely to constitute the direct consequence of perinatal events independent of any prior risk factor. However, the intermediate results of this group (i.e., more anomalies than the Controls) combined with the presence of high anomaly subjects in this group suggests that for some CP individuals early prenatal factors do play an important role.

The present study also examined the relative merits of using the Waldrop and Halverson (1971) MPA survey as opposed to a more comprehensive open ended examination in the study of anomaly frequencies. The Waldrop and Halverson survey applies the term

hypertelorism to what is more precisely termed increased inner canthal distance in that only inner canthal distance is measured. In the present study two additional measurements, interpupillary and outer orbital distances were taken as recommended by Smith (1976) to identify true cases of hypertelorism in addition to increased inner canthal distance. While increased inner canthal distance constituted the most frequently observed anomaly the considerably rarer hypertelorism was not detected in a single subject. The latter term represents a more serious mid-line facial defect and should not be as liberally applied as it is in much of the current MPA literature.

Two more of the Waldrop and Halverson survey anomalies (soft and pliable ears and tongue with smooth-rough spots) were not observed. The anomalies two or more hair whorls and third toe longer than the second were subsumed under the more general categories of multiple or unusual hair whorls and asymmetrical length/size of the toes, respectively. The anomaly adherent ear lobes in its milder form affected approximately 60% of subjects across the six groups and should perhaps in this mild form be considered a normal variant, although this will have to be verified in future research. In addition to the anomalies arising from the Waldrop and Halverson survey, 19 other anomalies were detected in a minimum of two individuals. It would appear that restricting the examination of subjects to the survey anomalies places an unnecessary artificial limitation on the researcher. This is supported by the magnitude of change between

the weighted score and total score. However the weighting system employed by the survey adds a degree of sensitivity and consequently the combined score which encompasses both of the former scores is recommended.

In addition to examining gross differences in the frequency of anomalies, patterns of anomalies were examined in each of the six groups. The Down syndrome group displayed the greatest frequency and variety of anomalies. Although many of these anomalies were found in the other groups certain features, were very useful in distinguishing this etiologically homogeneous group from the others. The anomalies upslanting palpebral fissures, furrowed tongue and short broad fingers though affecting only 25% to 50% of Down syndrome subjects constituted potent discriminators in that they occurred exclusively within this group. Decreased head circumference while rarely observed in other groups was typically present in these subjects. Clinodactyly of the fifth finger was highest in this group and proved a good discriminator although common in other groups. The anomalies prominent ears, epicanthus, single palmar crease, big gap between the first and second toes, deep crease on the sole of the foot between the first and second toes along with palatal anomalies were moderately frequent among Down syndrome subjects and effectively discriminated them from the other groups. These findings are consistent with those reported by Penrose and Smith (1966) who reviewed the literature regarding anomalies associated with Down syndrome.

In contrast to the Down syndrome group the Prenatal MR subjects constitute a more heterogenous group placing obvious restrictions on any discussion of anomaly patterns. Although some general observations can be made no conclusions can be drawn as this group is held together only by a very gross measure of the timing of the insult and may include a number of distinct syndromes or disorders. This group was best discriminated from the others using such anomalies as increased inner canthal distance, clinodactyly of the toes, big gap between the first and second toes, incomplete scapha helix, assymetrical ears, malformed ears, short great toe and partial syndactyly of the second and third toes. The Prenatal subjects shared in common with the other clinical groups a preponderance of increased head circumferences in contrast to the Down syndrome subjects whose measurements tended to be reduced.

The high frequency of anomalies in the Perinatal MR group suggests that this group is indistinguishable from the Prenatal MR group. The frequency of such anomalies as increased inner canthal distance, increased head circumference, assymetrical ears, malformed ears, prominent ears, short great toe, big gap between the first and second toes, clinodactyly of the toes, deep crease on sole between the first and second toes and partial syndactyly of the second and third toes observed in this group paralleled that of the Prenatal MR group in most respects and effectively discriminated these two groups from the lower anomaly Control, Postnatal MR and CP groups.

Of the lower anomaly groups consisting of the CP, Postnatal MR and Control groups only the CP and Control groups differed from each other to a statistically significant extent. While the CP group did not differ from Controls in the frequency of head measurements outside the normal range, Controls were equally likely to have increased or decreased measurements whereas CP's tended to have increased head circumferences. Increased inner canthal distance was quite prevalent in this group and was useful in discriminating it from other groups as was the anomaly asymmetrical length/size of the toes.

While the Postnatal MR group did not differ significantly from the Controls in terms of frequency or pattern of anomalies, there was a slightly higher frequency of anomalies among the Postnatal MR subjects previously described in connection with the Prenatal and Perinatal MR groups. As has been previously stated a degree of sampling error was expected in the selection of subjects and would account for this trend.

Those anomalies observed among Control subjects were largely those found to be prevalent throughout the study. Certain higher frequency anomalies served as general indicators of pathology in that they were absent or infrequent in the Controls relative to the clinical groups. These included increased inner canthal distance, high-steeped palate, clinodactyly of the toes, prominent ears, irregular spacing or abnormal shape of the teeth, deep crease on the sole between the first and second toes and epicanthus. A further 18 anomalies occurred only among the clinical subjects.

The analysis of verbal and spatial ability score and lateral dominance data involved the Control and MR groups. Level of intellectual functioning did not correlate with frequency of anomalies for the MR subjects. Some studies of hyperactive children have found that IQ diminishes with increased MPA score (Waldrop & Halverson, 1971; Waldrop, et al., 1976) while other reports have failed to find a relationship (Rapoport & Quinn, 1974; Steg & Rapoport, 1975). Intuitively one would expect there to be a relationship between IQ and anomalies however this clearly is not a simple one. Indeed many individuals with major congenital defects even those involving the CNS are of normal intelligence. This is certainly the case with Spina Bifida.

While Control subjects performed significantly better on the PPVT and CPM they did not differ from the MR groups on the measure of lateral dominance or the verbal spatial discrepancy score nor did the four MR groups differ from one another on any of these scores. Although the concept of "pathological left-handedness," that is the concept that a subset of left-handers have left cerebral hemisphere damage, has been demonstrated in MR subjects (Silva & Satz, 1979) the latter have been shown to parallel normals in frequency of handedness, degree of right hand usage and variance of dominant hand usage (Barry & James, 1978).

Individual anomalies were sometimes observed on only one body side but it was not uncommon to observe a second unilaterally expressed anomaly contralaterally in the same

individual. No relationship was ascertained between structural laterality and the lateral dominance of individuals or the discrepancy between verbal and spatial skill scores although some rather large discrepancies were evident in the MR subjects. It is not clear what if any significance can be attached to Smith's (1976) "intraindividual variance" in expression" of anomalies.

Wechsler (1941) reported a slight WAIS VQ greater than PQ discrepancy in MR subjects. He had expected MR individuals to perform relatively better on manipulative tasks thus producing a PQ greater than VQ discrepancy as had been observed with the Wechsler-Bellevue form I. Mathews (1974) in his review of neuropsychology and MR concluded that a discrepancy in favour of PQ was typical for MR individuals. However, Calvert and Crozier (1978) maintain that VQ-PQ discrepancies are a function of full scale IQ scores with lower IQ individuals having VQ greater than PQ, higher IQ individuals having PQ greater than VQ and little discrepancy in the intermediate range. Some support for this contention is forthcoming from the earlier works of Warren and Kraus (1961) and Brengelmann and Kenny (1961) although the latter authors found little discrepancy in the lower IQ range.

No differences in frequency of discrepancies favouring spatial versus verbal scores or any relationship between discrepancy score and level of retardation were observed in the present study. Thus no support can be provided either Mathews' (1974) contention that Wechsler PQ's exceed VQ's in MR individuals or Calvert and Crozier's (1978) findings that VQ-PQ discrepancies vary with full scale IQ score.

The Wechsler performance subtests rely upon adequate motor skills while the verbal tests require expressive language ability. Thus impairment of motor ability or expressive as opposed to receptive language skills constitute a potential confound when examining subjects for whom severe CNS pathology is assumed when verbal-spatial discrepancies are of interest. It is not surprising in view of the foregoing that reliable discrepancies were not observed in the present research despite the fact that large discrepancies did occur, as the tests employed relied neither on motor ability nor expressive language skills. It is reasonable to expect that with increasing CNS pathology motor impairments would be more prevalent and consequently that low-functioning MR subjects would obtain lower PQ's in comparison to VQ's. Wechsler VQ's may underestimate the verbal abilities of higher functioning individuals by sampling only the expressive component of language. Thus the nature of VQ-PQ discrepancies in the aforementioned reports may reflect more the method of measurement than any real verbal-spatial discrepancies.

It should be mentioned that the study by Brengelmann and Kenny (1961), utilized an additional performance measure, the Leiter International Performance scale, not dependent on motor ability. However this test taps both spatial and verbal ability though not requiring an expressive verbal response. The low scores observed on this measure relative to the other tests employed (Stanford-Binet and WAIS) in the lowest IQ subjects may

reflect the great difficulty experienced by low IQ individuals as compared to moderately or mildly retarded persons as observed by this author in grasping the fundamental matching concept required throughout the test.

The deleterious effects of institutionalization on intellectual development first demonstrated in the work of Skeels and coworkers (Skeels, Updgraff, Wellman & Williams, 1938; Skeels & Skodak, 1965; Skeels, 1966) were evident in the present study. Years of institutionalization and age exerted an equivalent negative effect on CPM score while in the case of PPVT score the effects of age were greatly exceeded by prolonged and early institutionalization. It would appear that the acquisition of language and its maintenance are particularly susceptible to the effects of institutionalization especially during the critical early years.

The present study once again verifies the value of the anomaly examination. This relatively simple noninvasive procedure provides an important contribution in the identification of etiology especially when information contained in the history is sparse or contradictory. A high incidence of anomalies directs attention to the first trimester of pregnancy a period of rapid cellular differentiation when the organ systems and overall morphology of the individual is established. The disruptive influence of teratogens and genetic precursors is manifested during the first trimester in a deviation from the course of normal embryogenesis producing anomalies. While the

presence of external anomalies is easily detected the presence of internal anomalies especially those affecting the CNS is assumed and supported by the observed link between anomalies and MR. The CNS is particularly vulnerable to noxious influences due to its prolonged and complex development. It is not possible to pinpoint the timing of the event which precipitates the development of anomalies from examining external physical anomalies alone. The appearance of external physical anomalies may be removed in time from their etiological source as is the case with the chromosomal error in Down syndrome, which may be present prior to conception. The examination of internal structural anomalies in areas such as the CNS and alimentary systems which begin to develop early in the first trimester, and biochemical anomalies may be more useful in this regard. The critical value of external anomalies is that they draw attention to the first trimester of prenatal development and stimulate investigation of individuals and disorders with respect to early developmental error in the search for etiologies.

The anomaly survey has potential as an early screening device facilitating early intervention for individuals at risk to developmental handicap and other childhood disabilities. The anomaly survey has already begun to prove itself in this regard (Burg et al., 1978; Waldrop et al., 1978). The recognition of anomalies has been of value in the selection of treatment in hyperactivity (Ferguson & Trites, 1980). The anomaly examination constitutes an important data base in providing the parents of MR

children with genetic counselling as they contemplate future pregnancies. Not the least of which it provides a valuable outcome measure in research that seeks to evaluate the genetic variable or the teratogenic potential of various substances and events to which the pregnant mother and embryo may be exposed.

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APPENDIX A

Norms for Selected Body Measurements

Head Circumference from Nellhaus (1968)

	Mean	SD
Male	56	1.35
Female	54.9	1.45

Inner Canthal Distance from Laestadius et al. (1969)

	Mean	SD
Male	3	.25
Females	3	.30

Outer Orbital Distance from Laestadius et al. (1969)

	Mean	SD
Male	11.3	.45
Female	10.8	.50

Interpupillary Distance from Pryor (1969)

	Mean	SD
Male	5.9	.38
Female	5.9	.34

Note. All measurements in cm.

APPENDIX B

Lateral Involvement Score (structural laterality)

<u>Score</u>	<u>Side of Body</u>	<u>Number of MPA's</u>
1	Left	10
2	"	9
3	"	8
4	"	7
5	"	6
6	"	5
7	"	4
8	"	3
9	"	2
10	"	1
11	Unlateralized	0
12	Right	1
13	"	2
14	"	3
15	"	4
16	"	5
17	"	6
18	"	7
19	"	8
20	"	9
21	"	10

APPENDIX C

Lateral Dominance Score
(functional laterality)

<u>Score</u>	<u>Items Left</u>	<u>Items Right</u>
1	11	0
2	10	1
3	9	2
4	8	3
5	7	4
6	6	5
7	5	6
8	4	7
9	3	8
10	2	9
11	1	10
12	0	11

Ministry of
Community and
Social Services

Rideau
Regional
Centre

P.O. Box 2090
Smiths Falls, Ontario
K7A 4T7
(613) 223-2590

APPENDIX D

Dear

We would like to have participate in a study of mentally retarded and cerebral palsied individuals. The study is to be conducted during the next few weeks at the Rideau Regional Centre in association with Carleton University.

The aim is to evaluate a diagnostic technique based on the presence of certain minor physical abnormalities and to compare these findings among various etiological groups. The information will be useful in establishing early diagnosis in the future. The routine screening of newborns for minor physical anomalies may be useful in identifying infants who are at risk to the development of problems. In this way help can be made available to families early, when it is likely to be most effective. However, it is necessary to standardize this procedure first with individuals with known problems before it can be used to predict outcomes in others.

The study will require about one half hour of the participant's time. It will involve a brief physical examination of the hands, feet and head, along with a picture recognition task and an evaluation of spatial ability. The physical examination involves no discomfort to the individual and most participants enjoy the required tasks which are not difficult.

If you are willing to consent, would you please sign the attached form and return it as soon as possible in the stamped envelope provided. If you have any additional questions, please contact Dr. W. Ghali at the Rideau Regional Centre.

Yours sincerely,

Marlene Rivier
Marlene Rivier.

Contact Person:
Dr. W. Ghali,
Acting Supervisor,
Medical Staff,
Rideau Regional Centre.

Dr. R. M. Knights
Dr. R. M. Knights,
Carleton University.

APPENDIX E

CONSENT FORM FOR RESEARCH

Ms. M. Rivier,
c/o Dr. W. Ghali,
Health Services,
Rideau Regional Centre.

I hereby consent to the participation of
_____ in a study of minor physi-
cal anomalies in mentally retarded and cerebral pal-
sied persons.

I have been informed in writing of the
procedures to be employed and I understand that there
is no reason to suppose that the above named person
is at any risk. I also understand that, if I re-
quest it, the findings of the study will be made
available to me.

(Witness)

(Parent or Guardian)

(Date)

(Address)

APPENDIX F

Complete List of Chi Squares

	x ²	df	p
HEAD			
Head circumference inc/dec	49.19	20	.0008
HAIR			
Fine hair	4.11	5	NS
Multiple/unusual hair whorls	7.31	5	NS
Abnormal eyebrows (e.g., synophrys)	6.49	5	NS
Low posterior hair line	4.11	5	NS
Body hirsutism	3.13	5	NS
EYES			
Epicanthus	15.17	10	NS
Increased inner canthal distance	23.94	10	.008
Upslanting palpebral fissures	32.73	5	.00001
Downslanting palpebral fissures	5.30	5	NS
Microphthalmia	11.65	5	.04
EARS			
Low-set ears	3.30	5	NS
Adherent ear lobes	9.82	10	NS
Malformed ears	10.29	5	NS
Assymetrical ears	8.76	5	NS
Prominent ears	18.80	5	.002
Scapha helix incomplete	10.68	5	NS
MOUTH			
High-steepled palate	15.20	10	NS
Other palatal anomalies	8.39	5	NS
Furrowed tongue	26.87	5	.00006
Other tongue anomalies	7.30	5	NS
Large lower lip	7.30	5	NS
Irregular spacing of teeth	6.00	5	NS
Abnormal shape of teeth	7.90	5	NS

APPENDIX F continued

	χ^2	df	p
HANDS			
Clinodactyly of 5th finger	18.91	10	.04
Single palmar crease	17.88	5	.003
Single crease on 5th finger	5.29	5	NS
Short broad fingers	15.65	5	.008
FEET			
Assymetrical length/size of the toes	13.46	10	NS
Partial syndactyly of the 2nd and 3rd toes	7.30	5	NS
Big gap between 2nd and 3rd toes	16.74	5	.005
Clinodactyly of toes	11.45	10	NS
Abnormally short great toe	9.55	5	NS
Malformed toenails	6.55	5	NS
Deep crease on sole between 1st and 2nd toes	28.80	5	.00003

Note. Includes only those anomalies affecting more than one individual.

APPENDIX G

Discriminant Function Analysis with Seven Most Frequent Anomalies

	Discriminant Functions		
	1	2	3
Eigen Value	1.19	.59	.30
Relative %	.55	.27	.14
Canonical Correlation	.74	.61	.48
Wilks' Lambda	.20	.44	.70
Chi Square	104.56(30)	53.60(20)	23.62(12)
	p<.001	p<.001	p<.03
Standardized Discriminant Function Coefficients			
Head circumference inc/dec	.82	-.17	-.35
Increased inner canthal distance	-.33	-.58	.82
High-steepled palate	-.32	-.18	-.25
Clinodactyly of 5th finger	-.36	.25	-.10
Clinodactyly of toes	.10	-.48	-.23
Big gap between 1st and 2nd toes	-.31	-.40	-.57
Centroids of Groups			
Control	.66	.80	-.59
Down Syndrome	-1.47	-.23	-.38
Prenatal MR	.42	-.75	-.19
Perinatal MR	.64	-.70	.12
Postnatal MR	-.08	.60	.16
Cerebral Palsy	-.18	.27	.88

Note. The anomaly adherent ear lobes did not meet the entry criterion for inclusion in the analysis.

APPENDIX H

Discriminant Function Analysis with Eye Anomalies

	Discriminant Functions	
	1	2
Eigen Value	2.18	.36
Relative %	84.80	13.89
Canonical Correlation	.83	.51
Wilks' Lambda	.22	.71
Chi Square	98.80 (20)	22.37 (12)
	p<.001	p<.04

Standardized Discriminant Function Coefficients

Epicanthus	-.26	-.03
Increased inner canthal distance	-.00	.99
Uplanting palpebral fissures	-.77	-.07
Microphthalmia	-.51	.01

Centroids of Groups

Control	.45	-.97
Down Syndrome	-1.83	-.05
Prenatal MR	.45	.46
Perinatal MR	.21	.46
Postnatal MR	.34	-.27
Cerebral Palsy	.39	.36

APPENDIX I

Discriminant Function Analysis with Ear Anomalies

	Discriminant Functions	
	1	2
Eigen Value	.38	.18
Relative %	50.24	23.53
Canonical Correlation	.53	.39
Wilks' Lambda	.51	.70
Chi Square	44.77(20)	23.33(12)
	p<.001	p<.03

Standardized Discriminant Function Coefficients

Assymetrical ears	-.23	.45
Prominent ears	.93	-.13
Scapha helix incomplete	.12	.57
Malformed ears	.22	.20

Centroids of Groups

Control	-.43	-.13
Down Syndrome	.96	-.39
Prenatal MR	.19	.82
Perinatal	.19	.05
Postnatal	-.60	-.17
Cerebral Palsy	-.32	-.18

APPENDIX J

Discriminant Function Analysis with Oral Anomalies

	Discriminant Function
<hr/>	
Eigen Value	1.04
Relative %	79.78
Canonical Correlation	.72
Wilks's Lambda	.38
Chi Square	63.05 (25)
	$p < .001$
Standardized Discriminant Function Coefficients	
High-steeped palate	-.41
Other palatal anomalies	-.43
Furrowed tongue	-.69
Other tongue anomalies	.25
Large lower lip	-.29
Centroids of Groups	
Control	.53
Down Syndrome	-1.54
Prenatal MR	-.03
Perinatal MR	.29
Postnatal MR	.31
Cerebral Palsy	.44

APPENDIX K

Discriminant Function Analysis with Hand Anomalies

Discriminant Function

Eigen Value	.75
Relative %	88.41
Canonical Correlation	.65
Wilks' Lambda	.52
Chi Square	43.22(15)
	$p < .001$

Standardized Discriminant Function Coefficients

Clinodactyly of 5th finger	-.54
Short broad fingers	-.57
Single transverse palmar crease	-.44

Centroids of Groups

Control	.27
Down Syndrome	-1.44
Prenatal MR	.25
Perinatal MR	.49
Postnatal MR	.18
Cerebral Palsy	.25

APPENDIX L

Discriminant Function Analysis with Foot Anomalies

	Discriminant Functions	
	1	2
Eigen Value	1.04	.30
Relative %	62.79	17.90
Canonical Correlation	.72	.48
Wilks' Lambda	.28	.57
Chi Square	82.81(30)	36.37(20)
	p<.001	p<.02

Standardized Discriminant Function Coefficients

Partial syndactyly of 2nd and 3rd toes	.04	.40
Big gap between 1st and 2nd toes	-.48	.01
Deep crease on sole between 1st and 2nd toes	-.79	-.31
Short great toe	-.09	.50
Clinodactyly of toes	.01	-.03
Assymetrical length/size of toes	.01	-.80

Centroids of Groups

Control	.37	-.21
Down Syndrome	-1.43	-.17
Prenatal MR	.24	.60
Perinatal MR	-.33	.10
Postnatal MR	.50	.50
Cerebral Palsy	.65	-.82

APPENDIX M

Discriminant Function Analysis with PPVT, CPM and Lateral Dominance Scores

Discriminant Function	
Eigen Value	2.57
Relative %	98.07
Canonical Correlation	.85
Wilks' Lambda	.27
Chi Square	73.37 (8)
	p<.001
Standardized Discriminant Function Coefficients	
PPVT Score	.75
CPM	.28
Centroids of Groups	
Control	1.65
Down Syndrome	-.75
Prenatal MR	-.37
Perinatal MR	-.27
Postnatal MR	-.26

Note. Lateral dominance variable did not meet the entry criterion and was not entered into the analysis.

END

0 3 H 0 9 H 8 2

FIN