Review

Cerebral Palsy and Patterns of Magnetic Resonance Imaging (MRI): a Review

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Cerebral Palsy is the most common chronic motor disorder of childhood, that affecting approximately 3 infants per 1000 live-births. The risk of brain injuries that potentially cause Cerebral Palsy has amplified with increasing in survival rates for preterm infants. In addition Cerebral Palsy has a huge economic impact, to immeasurable health, social, and psychological problems that affected children and their families suffer. Cerebral Palsy, among 18 common congenital disorders, has the highest lifetime costs per new case. Thus, efforts to prevent its occurrence, minimize the morbidity, and improve the patient outcomes are important at both the individual and societal levels. In each trimester, different patterns of brain damage or abnormal insults can represent times and etiology of injuries. Knowledge of the etiology and pathogenesis of abnormal brain growth during antenatal, perinatal and neonatal damages can be helping us for prevention. Also Magnetic Resonance Imaging (MRI) studies of subjects with multiple forms of cerebral palsy reported significantly more overall abnormalities, malformations, and white matter damage but in this review study we discuss in what extent MRI is useful in detecting cerebral palsy pathogenesis.

Keywords: Cerebral Palsy, Magnetic Resonance Imaging, MRI

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Introduction

Due to a defect or lesion of the immature brain, the term cerebral palsy (CP) describes a group of disorders of movement and posture (1,2), with various types and degrees of motor impairment (3) and is the commonest physical disability in childhood (4-8). In many cases the cause remains unknown (9-11). The definition is usually based on phenomenology; it only specifies that CP originates from an interference, lesion, or abnormality of the developing brain (12-14). CP may cause a range of associated problems including; hearing and visual deficits, nutritional and feeding problems, respiratory infections, epilepsy, pain, cognitive and communicative impairments in children (11). Due to prenatal or perinatal brain damage, CP is a permanent and non-progressive disorder become manifest early in life (12). Congenital hemiplegia is the most common form of cerebral palsy among children born at term, and second to diplegia among children born prematurely (8-11). The cerebral palsy that affecting approximately 3 in 1000 newborns (12), has not diminished in recent decades despite advances in obstetric and neonatal care . In fact, in the world, the risk of CP among term infants may have increased between the years 1975 and 1991, from 1.7 to 2.0 per 1000 live births. Approximately 8000 children with CP, based on these numbers, are born annually in the United States and approximately 10 to15% of very preterm children (born < 30 weeks gestational age) develop cerebral palsy, and 30 to 60% of them experience cognitive impairments (15). The decrease in perinatal mortality in very and extremely pre-term infants has led to an increasing prevalence of cerebral palsy (3-5,16).

Over the past 20 years, there have been radical changes in our understanding of etiology. Most cases of cerebral palsy, for over 100 years, were thought to be caused by asphyxia during either labor or the perinatal period. However there is a plethora of accepted medical and rehabilitative interventions, there is not often a complete understanding of the

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etiology, as well as the variability in treatment and outcomes (17). Remarkably, patients with similar etiology and clinical background can display different time courses (4). Also, in most cases, the etiology of CP remains unexplained (13). It is crucial that CP be recognized as a heterogeneous group of brain disorders with potentially different risk factors and causal pathways to devise rational and improved strategies for prevention (12). Despite term infants are at relatively low absolute risk, because term births constitute the large majority of all births, thus approximately half of all children with cerebral palsy have term births. Korzeniewski et al (12) believe that perinatal asphyxia, maternal age >35 years, and high risk pregnancy were the main factors associated with CP (12). In the study of Prasad et al, striking finding from the mothers' history was that 39.5% reported an infection during the pregnancy. Multiple pregnancies included 12% cases, more than half of the children (54.5%) were born at term and (70%) of children were admitted to the special care infant unit after birth (18). Other abnormalities in study of Korzeniewski et al were; microcephaly (60.5%), epilepsy (42%), visual abnormality (37%), and hearing abnormality (20%) (12,19).

Causes of CP are multiple and inflammation with excessive cytokine production, oxidative stress and excess release of glutamate stimulating the excito-toxic cascade are some of key factors.(19). Others are induced by hypoxic-ischemic and/or infectious mechanisms .Since asphyxia may be the result of other causes e.g., cerebral malformations or inborn errors of metabolism. The inflammation have addressed in some studies, as a more significant etiologic factor of brain damage in CP (20-23). On the other hand, the assessing of cortical folding during early brain development has provided insight into the underlying mechanisms of normal development of regional specialization and functional lateralization (24). Cortical neurogenesis predominantly is occurring in first and second trimester, characterized by proliferation, migration and organization of neuronal precursor cells, then neuronal cells. Brain pathology is characterized by mal-developments that can be genetic or acquired (13). The ‘gross architecture’ of the brain (neural cytogenesis and histogenesis), in late second and early third trimester, is established, growth and differentiation events are predominant and postnatal periods continues (axonal and dendrite growth, synapse formation and myelination). Also disruption of brain development during this period will often cause damages and lesions (25). Especially in early and mid-third trimester and in the child born prematurely, periventricular white matter is affected. Grey matter, either cortical or deep grey matter, e.g. basal ganglia and thalamus, appear to be more vulnerable in the end of the third trimester and in the term born child (13,26) and infarction in middle cerebral artery (MCA) that are reported mainly in children born at term or near term, may occur in the child born very pre-term maturely (13,26,27). Because different patterns of brain damage or abnormal growth in each trimester can represent times and etiology of injuries, the efforts to prevent its occurrence, minimize the morbidity, and improve the patient outcomes are important at both the individual and societal levels. Knowledge of the etiology and pathogenesis of abnormal growth during antenatal, perinatal and neonatal damages can be largely. Also magnetic resonance imaging (MRI) studies of subjects with multiple forms of cerebral palsy reported significantly more overall abnormalities, malformations, and white matter damage but the question is, what extent MRI is useful in detecting cerebral palsy pathogenesis?

The patterns of Magnetic Resonance Imaging (MRI)

MRI, which often used for reveals anatomic abnormalities, could offer a unique, non-invasive opportunity to predict neurological deficits, even as early as the newborn stage (4). It seems that MRI is a useful tool for diagnosing of the etiology and pathogenesis of abnormal growth during antenatal, perinatal and neonatal damages. Recently MR imaging has been used to detect fetal brain damage (28). Also it can be used for determination of the anatomical pattern and likely timing of the brain lesion.(29) Because the human brain undergoes complex organizational changes during development, internal and external uterus (30), MRI has also been used to detect antenatal, perinatal and neonatal abnormalities and timing on the basis of standardized assessment of brain maturation (31).

MR imaging provide information which has the potential to improve current NICU clinical practice and by identifying practices correlated with altered structure and poor outcome, we can develop early intervention strategies for therapy services by providing the means of identifying those infants who would most benefit from intervention, and can promote the development of neuro-protective agents targeted in time and cerebral region. Also MRI has considerably

higher sensitivity than cranial ultrasound (US) (32). Its higher sensitivity is important to detect early damage occurring before reliable US imaging. In addition of hypoxia-ischemia, MRI can also show other patterns of injury, such as central cortico-subcortical damage, diffuse cortical involvement, bilateral parasagittal lesions, as well as brainstem, cerebella and hippocampus lesions. Compared to investigations using computed tomography (CT) (86% vs. 70%) , MRI studies of subjects with multiple forms of CP reported significantly more overall abnormalities, malformations, and white matter damage (12).

About brain development, MRI also provides information on changes occurring during brain development, like that myelination of white matter, glial cell migration and development of complex gyral patterns (33). The natural history of acquired fetal brain lesions in relation to stage of development can be illustrated by MRI (15). In the developing fetus, the detection of a single type of damage is evidence of acute or chronic lesions, which can be seen alone or in combination. Patterns can indicate infection or hypoxia-ischemia at various stages of intrauterine life. Abnormality in MRI finding is present in most (77%-89%) children with CP (34,35). Of course, 17% of subjects did not exhibit an image abnormality. Thus, normal neuroanatomy is also a common finding among subjects with CP (12). Obstetricians and neonatologists need knowledge of the timing of asphyxia, infections and circulatory abnormalities to improve prevention in pre-term and full-term neonates.

Neuroimaging contributes to the assessment of brain insult timing primarily by providing information concerning either neuronal migration or glial reaction. The process of neuronal migration is thought to be complete by the 20th week of gestation; therefore, migration disorders are thought to be indicative of insults occurring during the first half of pregnancy. The timing of brain insults is also accessed via the brains ability to mount a glial response. This ability is thought to begin somewhere around the 2nd to 3rd trimester; its absence, commonly concomitant with malformations, indicates an insult occurring around the first half of gestation. When a glial response is present, the degree, best seen on MRI, is used to assess the timing of the insult. Studies report that insults deriving CP occur during the prenatal, perinatal, and postnatal periods in 32%, 44%, and 6% of subjects respectively. On average, the timing of insult was unable to be estimated in 18% of the subjects (36).

The occurrence of severe birth asphyxia, which is rarely seen in developed countries, continues to be a major problem in developing countries and accounted (62%) of the patients (18). History of birth asphyxia is present in 41.9% of CP, (77.5% in quadriplegic CP, 11.5% in hemiplegic and 10.5% in diplegia (31). MRI of the brain demonstrated hypoxic-ischemic findings in all neonates born with perinatal asphyxia who later progressed to cerebral palsy. These results support the hypothesis that MRI performed in the neonatal period plays an essential role in predicting cerebral palsy in both term and preterm neonates, regardless of their gestational age (13).

The patterns of MRI in children with cerebral palsy are:

1. White matter damage

According to the studies of pathological observations with patient phenotypes, white matter injury (WMI) is often observed in spastic diplegia and quadriplegia. The abnormalities of white matter are particularly frequent in children with CP born premature. The term periventricular leukomalacia (PVL), damage to the white matter, often is diagnosed in patients who have ventriculomegaly with irregular outlines of the trigone and body of the lateral ventricle, a reduced quantity of periventricular white matter, deep prominent cerebral sulci, and periventricular single abnormalities of low intensity on T1-weighted images and high intensity on T2-weighted images. Despite conventional thinking, PVL is common among full term infants. Incidence of white matter damage, across all studies, was reported in nearly 30%-40% of all subjects (37,38) and (30). Also myelin abnormalities are quite common in CP.

2. Grey matter damage

The grey matter damage is defined as injuries to the basal ganglia, cortical defects, thalamic abnormalities, and diencephalic lesions. The hallmark of acute perinatal hypoxia-ischemia in term infants, central grey matter damage, is an important cause of death and cerebral palsy.

3. White and Grey matter damage

The white and grey matter damage, most commonly among hemiplegics, infarcts are commonly found in both white and grey matter surrounding the middle cerebral artery among subjects with CP.

4. Ventriculomegaly, atrophy, and cerebrospinal fluid abnormalities

The ventriculomegaly, common subjects with CP, includes enlarged, dilated, or reduced ventricles (unilateral or bilateral), abnormalities of the atria

and ventricular or occipital horns, and posterior fossa abnormalities (39,40).
Although the white matter damages are the most common abnormality (13,41) but combined grey and white matter abnormalities are more common among children with hemiplegia. Isolated white matter abnormalities are more common with bilateral spasticity or athetosis, and with ataxia. Isolated grey matter damage is the least common finding. In preterm-born, periventricular white matter lesions occurred more often than in term-born children (90% vs 20%) (13).

Discussion

MRI in comparison with cranial ultrasound is more accurate and sensitive for detecting the early brain damage. Of course in all of the reviewed studies, MRI was reported with high percentage in detecting the cerebral palsy (42) and there is reasonable evidence that sensitivity of MRI in term infants increased up to 97–100% (40). From abnormality reported by MRI, the most common patterns in children with CP were periventricular white matter lesions (PWM) (83%) (20), with preference in preterm children and mainly in bilateral spasticity or athetoid type. PWM lesions have been reported at 20% of term-born infants, especially as mild bilateral spastic type (diplegia) and mainly with PVL pattern, but also are found in unilateral spastic type with focal periventricular gliosis. PWM in term children with CP may have a prenatal origin and these children have no significant perinatal or newborn history (13). In many studies, higher incidence of periventricular changes in preterm-born infants and grey matter abnormalities in term infants is reported (13,27). Contrary to conventional thinking, PVL is not uncommon among full term infants. Kwong's study of 122 subjects with spastic CP reported one third of term infants exhibited signs of PWM damage (38).
Although in Ingeborgs study, isolated gray matter damage is one of the most common findings (13). But in other finding these lesions are the least common. They were the typical lesions of the term-born children with athetoid CP or severe BS-CP (12). Originally; the basal ganglia/ thalamus or bilateral cortico-subcortical lesions suggest a peri or neonatal Origin. Among children with hemiplegia, the combined grey and white matter abnormalities are more common. Brain malformations are less common cause of CP in the preterm children (3% vs. 16% in term-born infants) (38). Almost 10 percent of cerebral palsy can be attributable to brain malformations (22). Abnormality reported by MRI, indicate that about 20% of very low birth weight infants have cystic and/or diffuse white-matter injury (periventricular leukomalacia) (25), and it is seem that there have been an increasing number of reports of the past 6 years that show its prevalence in children with a birth weight of less than 1500g is declining in many countries (13).
In the most circumstances, cerebral damage in the preterm infant has a pattern that corresponds to the period of birth of children with CP, but does not tell us when exactly the injury is acquired (shortly before, during, or after birth) (13). However, the reports indicated that originally the most cases of CP result around the time of birth (40%), and the most white matter lesions had occurred in perinatal period (44%) and their greatest risk is between 23 and 32 weeks of pregnancy, although these lesions are common in term infants with CP (12). Also a prenatal- or neonatal origin suggested for gray matter damage (13). It is also noted that neuronal migration disorders, as indicating the insults of the first half of pregnancy, and also the presence of a glial response, as indicating the insults of the second half of pregnancy can be used to detect brain insult timing (38) .
Although the timing of brain insults is extremely unclear and unreliable**,** but the findings from abnormality reported by MRI, suggest that MRI, may be a useful tool for diagnosing of the etiology and pathogenesis of abnormal growth during antenatal, perinatal and neonatal damages. Korzeniewski et al (2008) believe that methods of timing brain insult based on CT/MRI findings should be clarified and standardized to avoid further confusion (12).

Conclusion

According to the reviewed studies, most children with cerebral palsy have abnormal neuro-radiological findings. MRI plays a significant and valuable role in revealing the pathologic basis of CP and had strong correlations with clinical findings in term- and preterm- born children. Also it has high potential to detect the type, extent, and possible time of brain damage in children with CP.

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