Review Article

A New Look at Neurodevelopmental and Neuropsychological Outcome in Children with Congenital Heart Disease

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ABSTRACT

New surgical techniques and advances in intensive care and medical treatment have significantly decreased mortality rates for children and adolescents with complex congenital heart disease (CHD). Survivors are at risk for neurodevelopmental and neuropsychological morbidity caused by both genetic and environmental risk factors, which causes a distinctive pattern of developmental and neuropsychology impairment characterized by mild cognitive impairment, executive functions impaired social interaction, and impairments in core communication skills, including pragmatic language, as well as attention, impulsive behavior, and impaired executive functions among children affected with congenital heart disease. In view of this, the present study reviews the neurodevelopmental and neuropsychological impairment with an objective of insisting the importance in developing and implementing a neuropsychological intervention program for children with congenital heart defect to retrain neuropsychological and neuro-developmental functions. With increased survival rates, the focus of clinical research in the pediatric cardiac population has paralleled the population shift and transitioned from short term surgical survival to the assessment of long-term morbidity.

Keywords: Congenital Heart Defect, neuropsychological retraining, neurodevelopment, cognitive rehabilitation, behavioral and emotional retraining, temperament, early childhood.

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INTRODUCTION

Evidently, because of my disability, I need assistance. But I actually have continuously tried to overcome the restrictions of my condition and lead as full a life as potential."
Sir Stephen Hawking

In the past 20 years, it has become evident that children born with congenital heart disease are in greater risk of developing life-long neurologic deficits. Multi-factorial risk factors contributing to neurodevelopmental and neuropsychological abnormalities associated with congenital heart defect has been recognized. This leads to a dramatic shift in focus from newly acquired brain trauma related with corrective and palliative heart surgery to antenatal and preoperative factors leading altered brain development in Congenital heart defect (CHD) [1-4]. We are all aware of the 'viral hypothesis of Schizophrenia [4] and, an entity called Encephalitis Lethargica (EL) wherein hypersomnolence, psychosis, catatonia and Parkinsonism were attributed to an inflammatory disorder of the CNS as a result of the 'Spanish influenza' pandemic [5].

Congenital Heart Defect (CHD)

The Congenital Heart Disease (CHD) or Congenital Heart anomaly is defined as defect with the heart structures that are present at birth. The problem of congenital heart disease in India is probably vast, due high birth rate. This serious burden emphasizes the importance of this cluster of heart diseases. It affects new-born and account for a high proportion of infant mortality worldwide. The technology has improved that the diagnosis of CHD is made even before birth. With presently available treatment modalities, over 75% of infants born with CHD can survive beyond the first year of life and many can lead near normal lives thereafter [1]. However, this privilege of early identification and timely treatment is restricted only to children of developed countries. Unfortunately, majority of children born in developing countries are still on struggle to receive the basic line of treatment for CHD. Recent development in Medico surgical progression had led to decrease the mortality but increasing the risk of neurodevelopmental and neuropsychological problems in children affecting their wellbeing and quality of life. Congenital heart diseases (CHD) are comparatively common with a prevalence ranging from 3.7 to 17.5 per 1000 live births. Nearly 180,000 children are born with CHD every year in India. Early intervention is required for severe congenital heart defect survivors and the count ranges nearly 60,000 to 90,000. Around 10% of new-born deathrate in India may be accounted for CHD population alone.[2]

Causes of Congenital Heart Disease

The causes of congenital heart defect are usually multifactorial. The factors are usually both genetic and environmental. Chromosome abnormalities and congenital heart defect go hand in hand. Chromosomal problems that result in genetic syndromes, such as down syndrome, often result in a higher incidence of child heart malformations. Among children with chromosome abnormalities, around 30% will have a cardiac defect. Congenital heart defect is frequently associated with non-cardiac defects in malformation syndromes and are classified according to the causes, such as

1. Chromosome abnormalities
2. Single gene or gene pair abnormalities

Approximately 10% of children with congenital heart defect have identifiable genetic etiology, rest of the congenital heart defect are due to the interaction of genetics and environmental influence (multi-factorial). Genetics play a major role in identifying certain aspects of cardiac development, frequent occurrence of a chromosome abnormality in fetus with congenital heart defect have moderate to severe neurodevelopmental and neuropsychological abnormalities [3].

Relation between Brain and Heart in Fetal Development

The heart and brain develop simultaneously inside fetus. It is perhaps not surprising that disruption of organogenesis in one organ will impact the development of the other. A defect in the heart indicates to insufficient blood supply to the brain. Newborns with congenital heart condition show a high frequency of non- inheritable focal brain injury. Brain damage often leads to problems in domains of neurodevelopmental and neuropsychological dysfunction affecting cognition, behavior, thinking, and learning. Problems which felicitate heart with brain damage are decrease blood supply and blood flow, Genetic pathway, White mater maturation, Head circumference, Organogenesis, Transitional circulation

The last trimester of gestation is a critical period for development of the brain, and the presence of congenital heart defect contributes to later brain injury and difficulties in brain functioning. Blood flow mechanism are also found to affect the brain growth (e.g.: coarctation of aorta). The delayed postnatal brain development results from abnormal fetal cerebral blood flow suggesting two predictions [4]

1. Delayed brain development should begin during fetal life;
2. Different forms of congenital heart defect manifest different degrees of delayed development. These observations confirm that impaired brain development begins during fetal life are due to impaired fetal cerebral blood flow and oxygen supply.

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Genetic Pathway

Early morphogenetic programs in every organ share common genetic pathways. Early brain and heart development shares same genetic pathways. Brain development happens across prolonged time-course with setting brain growth and activity-dependent formation and refinement of connections within the trimester. This development is related to increased metabolic activity and also the brain relies upon the heart for nutrient delivery.

White Matter

Delayed development ends up in a mild vulnerability to cerebral white matter injury in newborns with congenital cardiovascular disease [5]. Delayed brain development and white matter injury affect the cognitive and executive functioning of the newborn.

Head Circumference

Despite established mechanisms that preserve brain oxygen and nutrient delivery, newborns with certain forms of congenital heart disease are born with smaller head circumferences possibly indicating impaired brain growth. Somatic and brain growth patterns vary by type of congenital heart disease. Newborns with hypoplastic left heart syndrome (HLHS) are smaller in all dimensions, but head volume is disproportionately decreased.

Organogenesis

Brain and heart development intersect at numerous levels. Early brain and heart organogenesis occur concurrently in the human fetus and invoke alike developmental programs including stem and progenitor cell proliferation, cell fate commitment, migration, left/right and dorsal/ventral patterning at later stages, after completion of gross morphological development in both organs, brain development remains with a dramatic increase in brain size due to expansion of neuronal microstructure (e.g. Dendrites, axons and synapses) and the onset of myelination. The formation and refinement of connections in the brain requires neuronal activity, leading to an increase in brain metabolism with dependence upon heart function for oxygen. Any defect in heart leads to developmental impairment of the brain structure leading to severe abnormalities after birth [6].

Transitional Circulation

The transition from fetal (placental) circulation to neonatal circulation is complex and necessitates preservation of cerebral blood flow during a period of a precipitous decline in pulmonary vascular resistance along with an increase in systemic vascular resistance. In neonates with complex congenital heart defect, the delayed maturation of the brain, in conjunction with lower-than-expected postnatal cerebral blood flow, may also lead to impaired autoregulation increasing the risk for brain injury during the pre-operative, intraoperative and post-operative period [7].

Epochs of Brain development and Neuropathology in Congenital heart defect

Development of the brain is considered to be a highly active process. It involves timing and orchestration of higher cellular events. Development of brain is a long process which begins at third week of gestation and development continues to life long. Children with congenital heart defect are at risk of altered brain development and pathological trauma which may result in poor neurological outcomes throughout their life. Developmental delay varies from motor delay and later on progression affects the language, social and finally the executive functioning. Some children have unaffected or undisturbed milestone till they reach the school age. As soon as they reach the school age, the child starts to exhibit deficits in neurodevelopment and neuropsychological domains which may vary from mild to severe. Children at highest risk for Neurodevelopmental and Neuropsychological Impairment are:

1. Neonates or infants requiring open heart surgery
2. Children with other cyanotic ("blue") heart lesions not requiring infant heart surgery

3. Congenital heart disease combined with any of the following such as Prematurity, Developmental delay, suspected genetic abnormality or syndrome associated with developmental delay, History of mechanical support (extracorporeal membranous oxygenation or ventricular assist device), Heart transplantation, Cardiopulmonary resuscitation, Hospital stay longer than two weeks after surgery, Perioperative seizures, Abnormal findings on brain imaging or small head circumference [8]

Neurodevelopmental and Neuropsychological spectrum in children with CHD

Children's brains have a remarkable capacity for recovery, these injuries may impact communication between different brain systems and directly damage regions of brain important for specific tasks. CHD affects neurodevelopment across the lifespan. Aspects of neurodevelopment most commonly impact the school-age children with CHD. Children with impairments struggle with cognitive skills, social skills, anxiety and depression. [9]. The spectrum of neurodevelopmental and Neuropsychological impairment is wide and leads to spectrum of multivariate developmental delay. Some children have minimal to no impairment, whereas others are severely affected. No practice guidelines for the evaluation and management of these impairments currently exist.

The range of neurodevelopmental impairment is wide. Some have minimal to no impairment whereas others are severely affected. Critical moments in children affected with congenital heart disease occur in four steps of life they are

1. **Infancy:** Cardiac surgery/frequent hospital admission can cause interruption and/or modification of the relationship between child and parents
2. **Onset of preschool:** Physical activity limitations, childhood onset of school, learning deficits
3. **Adolescence crisis:** Corporeal image and sexuality
4. Adult age Pregnancy

Neurodevelopment and Neuropsychology

Neurodevelopment is a term referring to the brain development of neurological pathways that influence performance and functioning. (Intellectual, social and emotional skills). Neuropsychology is the learning of the structure and function of the brain and the relation to certain specific psychological behavior and process. Assessment of neuropsychology is a performance-based technique to evaluate intellectual and behavioral functioning. The purpose of neuropsychological evaluation helps to illustrate interprets about the structural and functional uniqueness of a person's brain by evaluating an individual's cognitive functions [10]. Neuropsychological rehabilitation is based on neuroplasticity involving the principles of re-organizing and re-establishing the loss of functions of brain. Neuropsychological retraining act as substitute assistance for the deficit when deficient purpose can neither be restructured nor restored.

Importance of neuropsychological retraining in pediatric cardiology is essential because early the children with heart defect are screened and treated the most effective the outcome. Incorporation of a new stratification method and scientific procedure may result in increased investigation, screening, assessment, analysis, and management of developmental disorders or disabilities (DDs) in the complex CHD population and consequential improvement in neurodevelopment and neuropsychological outcomes in this population to be high-risk in nature. With early acknowledgment of developmental delays, children have the best chance to reach their full potential. Many school-aged survivors of infant cardiac surgery require multidisciplinary treatment which include equal contribution by the medical and neurodevelopmental facilitative services. The neurodevelopmental and psychosocial morbidity related to CHD and its treatment often limit educational achievements, employability, lifelong earnings, insurability, and quality of life (QOL) for many patients. With early identification of DDs this population have the simplest likelihood to achieve their full potential. Early Intervention is usually based on Formal Developmental and Medical Evaluation which includes individualized approach, genetic evaluation and structural brain imaging is mandatory to be followed by Neurodevelopmental and Neuropsychological Evaluation [11].

Importance of age-Specific Neurodevelopmental and Neuropsychological Evaluation: Domains and Instruments:

The use of age-specific standardized measures for evaluation is recommended. These measures provide the practitioner with information about the child's functioning and enable the identification of deficits with known prevalence in the CHD population. Structured follow-up programs that focus on children who are at high risk for DD or exclusively on those with heart defects may be considered to optimize neurodevelopmental and neuropsychological outcome,

Formal evaluation during infancy and early childhood (birth to 1 year of age, 1–3.5 years of age, and 3.5–5 years of age) may enhance early recognition of DD or developmental delays. Standardized measures for formal evaluation of infants, toddlers, and preschoolers are available and may be beneficial when used in conjunction with medical assessment of neurodevelopmental status. Inclusion of a developmental pediatrician, pediatric neurologist, and/or pediatric psychologist on the evaluation team is recommended.

There are several developmental domains to monitor in toddlers (1 to 5 Years of Age). For they are Cognitive, gross motor, fine motor, communication (including speech, expressive language, receptive language, and pragmatics), adaptive skills, and social and behavioral interactions. Evaluation at this time optimizes identification and planning of additional educational supports and services before the child's entry into the educational system [12].

For school-aged children and adolescents, DDs may become more apparent during times of transition when the complexity and types of developmental tasks required of the child increase. Difficulties arise as the complexity of the educational curriculum progressively increases, and it can be useful and beneficial to monitor the transitions between the following developmental and educational stages

Adolescence is a critical time for identification of any preexisting or emerging impairments so that appropriate structure and supports may be implemented to maximize their potential through transition to adulthood.

CONCLUSIONS

The importance of early detection and intervention plays a major role to provide a complete treatment module to the children with congenital heart defect. This paves a futuristic pathway in treatment of congenital heart disease where treatment becomes multidisciplinary where Physicians and Psychologist work together to deliver the treatment as a whole.

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