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Cognitive Deficits and Behavioral Disorders in Children: A Comprehensive Multidisciplinary Approach to Managemente

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Abstract

Preservation of human cognition is an important objective of the health policies of both developed and developing countries in this era of rapid demographic transition. Threat to human cognition can occur at any age in either sex due to diverse causes. Cognitive impairments pose a major obstacle to the social and economic development of any nation. Therefore, it is essential to implement a policy of "Cognitive Watch" to prevent cognitive deficits and decline in children. Management of cognitive deficits in children is quite challenging since the plasticity of a growing brain is different from that of an adult brain in several aspects. The conditions leading to cognitive deficits in children are heterogeneous with respect to etiology, pathology and pathogenesis. This review addresses some of the important conditions leading to cognitive deficits in children and their optimal management. It focuses on diverse theories of cognitive development, diverse conditions leading to cognitive decline, the biological, genetic, metabolic and endocrine mechanisms leading to pathogenesis, and suitable intervention strategies, so that it is possible to approach cognitive deficits from their developmental perspective, leading to a comprehensive multidisciplinary management. There are several classifications for cognitive deficits and intellectual disability in children but most of them are distributed and fragmented, since there is no uniform pattern of classification. Etiology- and pathology-based classification is essential to promote disorder-specific treatment. We have made a proposal for such a classification incorporating the cognitive domains.

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Introduction

The term "Cognition" has its origin from the Latin word *cognosco* (*con* 'with'; *gnōscō* 'know), and means 'to conceptualize' or 'to recognize'. It refers to the mental processes (thinking, learning, remembering, abstraction, judgment, problem solving, language, imagination, perception, planning, execution) involved in acquiring knowledge and awareness about self and environment.

The evolution of the science of cognition has its beginning in Philosophy. Aristotle (BC 384-322) in his *Logic* and *Psychology and Philosophy of Mind* portrays cognitive domains pertaining to memory, perception, and mental imagery. Cognition had found a dominant place in Psychology since early 19th century. In Psychology, conventionally, the study of behavior has been divided into two broad categories, cognitive (pertaining to processes such as memory, association, concept formation, pattern recognition, language, attention, perception, motor programming, problem solving and mental imagery) and affective (pertaining to emotions that were not earlier considered as a cognitive process). This division is now considered largely artificial, and much research is currently being undertaken to examine the cognitive psychology of emotion, metacognition and metamemory.

Research into the neurobiological perspectives of cognitive functions began in the latter half of 20th century. Researchers in Cognitive Neuroscience, Clinical Neuropsychology and Cognitive Neuropsychology have explored cognitive processes as a function of the brain through the analysis of cognitive deficits in brain-damaged subjects, leading to the elucidation of neurobiological principles behind complex cognitive functions such as language and memory.

Cognitive Neuroscience, a term coined by George Miller and Michael Gazzaniga towards the end of 1970s, deals with the biological substrate underlying cognition with specific emphasis

on the neural substrate for mental processing. This discipline has imbibed the principles of Psychology and Neuroscience, articulating theories of Cognitive Science derived from Neuropsychology and computational models. The science of human cognition is multidisciplinary, involving Neurology, Psychiatry, Speech Language Pathology, Clinical Psychology, Linguistics, Computer Science, Philosophy and Mathematics.

"Preservation of Human cognition" is now an important objective of the health policies of all communities. Threat to human cognition, due to diverse causes, can occur at any age in either sex. The current phase of demographic transition in developed and developing countries has led to a rapid decline in birth rate and expansion of elderly population vulnerable to cognitive decline. The etiological agents include genetic causes, inborn errors of metabolism, endocrine dysfunction, demyelinating diseases, degenerative disorders, infections, vascular abnormalities, drugs, toxins, trauma, tumors, or simply, the process of aging as in the case of dementia of the elderly. The future of human development is dependent on the cognitive abilities of its child population. Children are the wealth of a nation, a wealth that guarantees a prosperous future. Cognitive impairments pose a major obstacle to the social and economic development of developed and underdeveloped countries. Therefore, it is essential to implement a policy of "Cognitive Watch" to prevent cognitive deficits and decline in children.

Management of cognitive deficits in children is quite challenging since the plasticity of a growing brain is different from that of an adult brain in several aspects. The conditions leading to cognitive deficits in children are heterogeneous with respect to the etiology, pathology and pathogenesis. Environmental factors have a significant impact on normal (Neuro-typical) or deviant (Neuro-atypical) development of the brain. The genomic project has unraveled the genetic basis of organogenesis and the temporal relation and evolution of structural and functional development. The concept of critical time for orchestration of genetic, epigenetic and environmental factors in neural ontogenesis is important in the understanding the etiology of neurodevelopmental disorders. The gene-, brain-, -behavioral associations or behavioral neurogentics is a relatively new concept that evolved in the latter half of 20th century providing predictivity to behavioral phenotypes based on specific genotypes; some examples include, Down syndrome, Fragile-X syndrome, Prader-Willi syndrome, Angelman syndrome and William's syndrome [1]. More than 1,000 inherited neurological disorders have been classified by Mendelian Principles and specific causative genes have been identified for several of these disorders. However, the genetic, epidemiological, environmental and etiological factors leading to cognitive deficits in children have been found to vary from population to population.

The question of how genes affect behavior has been a long-standing focus of research in social and behavioral science [2-4]. However, most of theories have been mainly speculative. Several theoretical models have been developed to explain the genetic mechanism underlying cognitive development [5].

Advanced neuroimaging techniques would be useful in delineating the structural and functional characteristics of the brain in several cognitive disorders that in turn would provide valuable information on the neurobiological basis of clinical symptoms, nature and extent of pathology, and gravity of problems, thereby leading to the formulation of effective intervention strategies.

Theories on cognitive development, previously concentrating on the influence of postnatal environment, have now shifted its focus to the importance of intrauterine environment and maternal physical, mental and spiritual health on cognitive development.

Scientific literature on cognitive deficits and cognitive disorders in children are vast, but scattered or clustered only on specific conditions, thereby providing little information on management and intervention. Syndromic or symptomatology-based diagnosis is often followed in several childhood disorders affecting cognition even when such disorders may be due to specific etiological or pathological agents. The diagnostic criteria have been revised several times with mere additions or deletions of symptoms. Thus, there is little information on the basic pathology of diseases at structural or functional level, posing a limitation on remedial intervention.

The present review intends to amalgamate the available information on cognitive development in terms of its successiveness and simultaneity with brain development to formulate an organized approach to cognitive disorders and deficits, thereby enabling researchers to incorporate genetic, structural, pathological and etiological factors, wherever possible. This approach will help to initiate preventive steps during appropriate period of development, to identify remediable conditions, and to invent comprehensive management strategies. It focuses on diverse theories of cognitive development, diverse conditions leading to cognitive decline, the biological, genetic, metabolic and endocrine mechanisms leading to pathogenesis, and suitable intervention strategies, so that it is possible to approach cognitive deficits from their developmental perspective, leading to a comprehensive multidisciplinary management. Clinicians and paramedical professionals involved in the management and cognitive rehabilitation of children with specific cognitive disorders and intellectual deficits can thus effectively adopt strategies for optimal intervention of individual conditions.

Definitions

Cognitive deficit: This is an inclusive term most often used to describe the deficits in intellectual functioning associated with global disorders (e.g. mental retardation, intellectual deficit). Less often, it is used to describe specific deficits in cognitive abilities (e.g. certain learning disabilities, autism, ADHD).

Intellectual disability: This term is now increasingly being used instead of mental retardation. It is characterized by significant limitation, both in intellectual functioning and adaptive behavior, as expressed in every day conceptual, social and practical adaptive skills.

Intellectual Functioning: Intellectual functioning, also called intelligence, refers to general mental capacity, such as learning, reasoning and problem solving. Intellectual functioning can be measured by an IQ test. Generally, an IQ score <70 indicates a limitation in intellectual functioning.

Adaptive Behavior: It refers to the collection of conceptual, social, and practical skills that are learned and performed by people in their everyday lives. Conceptual skills include language and literacy, money, time, number concepts and self-direction. Social skills involve interpersonal skills, social responsibility, self-esteem, gullibility, naïveté (i.e., wariness), social problem solving, and the ability to follow rules/obey laws, and to avoid being victimized. Practical skills include activities of daily living (personal care), occupational skills, healthcare, travel/transportation, schedules/routines, safety, use of money and use of telephone. There are standard tests to determine limitations in adaptive behavior.

Additional considerations: American Association on Intellectual and Developmental Disabilities (AAIDD) stresses those additional factors, such as the community environment typical of the individual's peers and culture, must be taken into account while defining and assessing intellectual disability. Professionals should also consider linguistic diversity and cultural differences in the way people communicate, move and behave.

Cognitive Development in Children

Different stages of cognitive development, along with influencing factors and cognitive defects are shown in **Figure 1**.

Genetic basis of cognitive development

Genetic basis of cognitive development have long been considered non-specific, considering the lack of convincing evidence. Even though genes can influence the structure and function of brain, it might have a limited influence on mind. The genetic basis of cognitive processing have been primarily derived from observations on variations in IQ (as much as 50% variation in IQ has been attributed to genetic variation) [6,7] and specific cognitive effect of genetic abnormalities in humans (e.g. dyslexia, syndromic mental retardation, autism). The prevailing hypothesis is that gene abnormalities result in structural abnormalities of the brain leading to cognitive, emotional or behavioral abnormalities [8]. Abnormalities of neurodevelopment, particularly that of the prefrontal cortex, have been observed in antisocial groups. Similarly, abnormalities of cortical thickness, especially in the brain regions related to social behavior, have been observed in autistic children [9,10].

At the cellular and molecular level, there is increasing evidence that genes modulate neuronal development and neural circuitry formation that are central to cognitive functions [11]. RhoGTPase and related molecules play an important role in various aspects of neuronal development including neurite outgrowth and differentiation, axon path finding, and dendritic spine formation

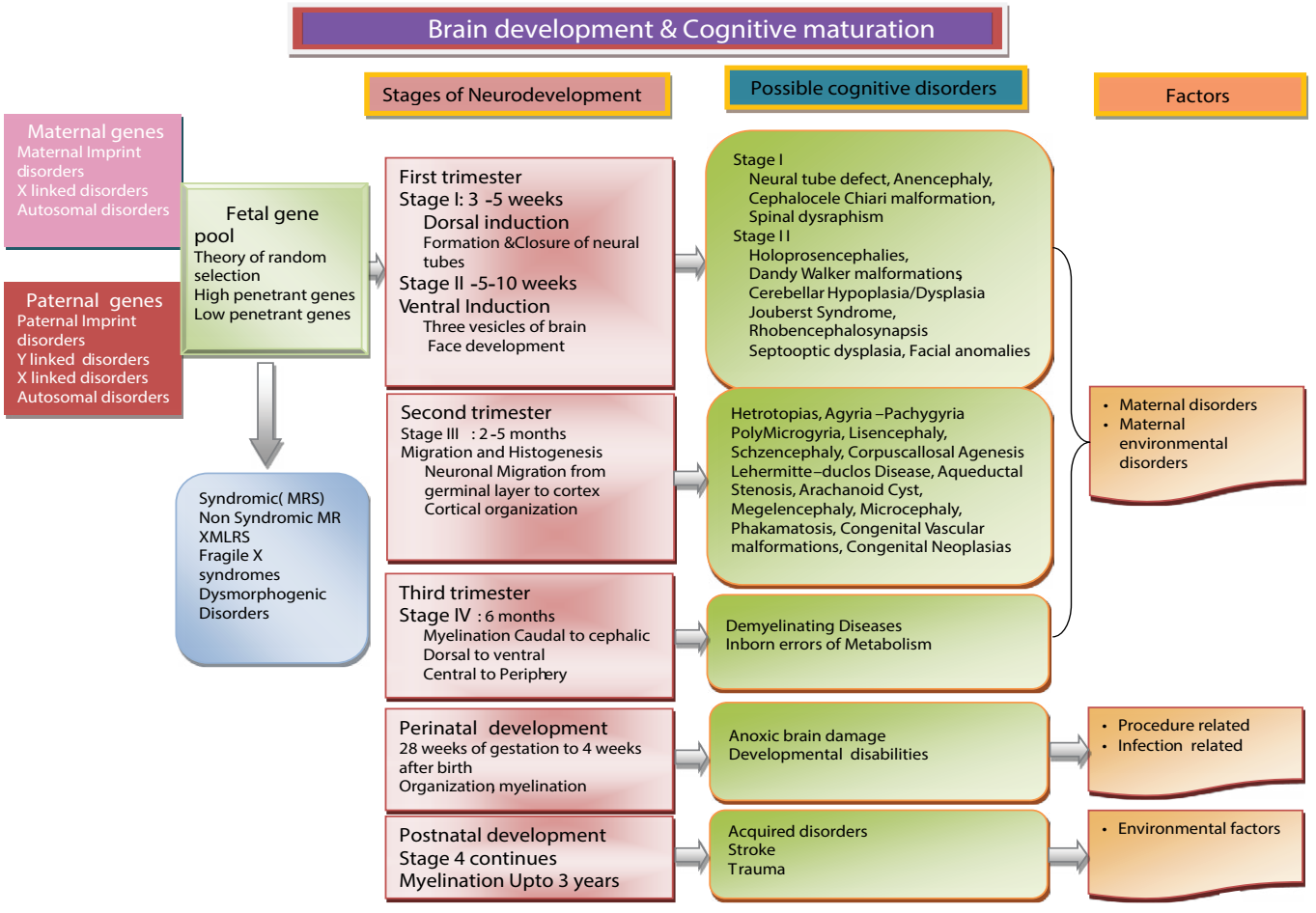

Figure 1 Brain development & Cognitive maturation.

and maintenance. Mutations in genes encoding the regulators and effectors of Rho GTPase may be associated with several neurological disorders involving cognitive deficits [11]. Rho-linked genes have been identified in various forms of mental retardation (MR), including syndromic and non-syndromic X-linked forms of MR (XLMR) as well as autosomal dominant MR [12,13]. About 30 genes associated with syndromic X-linked MR (MRXS) and 15 genes associated with Non-syndromic X-linked MR (MRX) have been identified.

Cognitive development during the intrauterine period

The concept of "infant intersubjectivity" was introduced in 2001 with potential application in clinical situations. According to this theory, there exists a specialized innate "human-environment-expectant" social regulatory and intersubjective function in the infant mind that constitutes the essential frame work for the regulation of all human cognitive development. There have been several studies on this innate anticipation of the infant to specific human cognitive functions including language, learning and responses to multimodal signals. While elaborating the studies on innate infant behavior on specific cognitive events, there has been a host of information on the influence of various external environmental factors including that of the maternal internal and external environment that influences the development of an infant.

Cognitive development in postnatal life

There are several theories on cognitive development, mostly empirical, that differ greatly across each other on how one should characterize the acquisition and nurture of conceptual representation that enriches the development of conceptual coherence and inference [14]. Jean Piaget (1896-1980) is probably one of the pioneers to carry out a systematic study of cognitive development in children, and forwarded one of the most significant theories in cognitive psychology "genetic epistemology" that gained wide acceptance in the 1960s and 1970s [15]. His views, often described as a constructivist view, were largely derived from his observations of how children approach problem solving. As per this theory, persons interpret their environment and experiences in the background of the knowledge and experience they already possess. According to Piaget, the essential building block for cognition is "Schema", an organized pattern of action or thought, used to understand and respond to the environment. As children grow, their experience widen, they interact more with the environment, and the individual schema gets modified, combined and reorganized to form more complex cognitive structures. Once they mature, these structures allow more complex and sophisticated ways of thinking and interacting with their environment. Intellectual growth occurs in terms of progressive changes in children's cognitive structures, which happens through four stages of development, sensory-motor, pre-operational, concrete-operational and formal-operational period.

The meta-cognitive theory was put forward by Flavell [16], who was also influenced by Piaget. Metacognition, by definition, is the knowledge of one's own cognitive and affective processes and states as well as the ability to consciously and deliberately monitor and regulate these processes and states [17]. According to Flavell's formal model, metacognitive monitoring has four classes of phenomena, meta-cognitive knowledge, meta-cognitive experiences, tasks/goals, and strategies/ activities [18].

Yet another celebrated theory of cognitive development is that of Lev Vygotsky's socio-cultural theory that focuses on the role of social and cultural influences. While each child is born with an innate set of abilities (elementary mental functions) it will get molded into higher-order cognitive functions (higher mental functions) only with inputs from the social world in the form of social interactions with peers and more capable adults. Vygotsky believed that adults in the society foster the cognitive development of children in an intentional systematic way by engaging them in challenging and meaningful activities. Language learning which occurs through social interaction is an important component of a child's intellectual development. Vygotsky's concept of "zone of proximal development", the difference between the actual developmental level as determined by independent problem-solving and the level of potential development that might be reached through problem solving under adult guidance, is important in the context of learning and instruction. This also explains why children with similar mental development differ in the capability to learn from guidance.

The information processing theory of cognitive development evolved out of the American experimental tradition in Psychology. The theory is anchored on the concept that human beings process the information they receive, the perspective that equates the mind to a computer/system that processes information through the application of logical rules and strategies. According to this theory, the components of the mind include, the attention system to bring in information, working memory for actively manipulating the information, and long term memory for passively holding the information for future application. The basic structures of information processing system do not change with development, but development occurs through changes in the efficiency of the processes (encoding and representation, strategies, automatization and generalization) one applies to the information [19].

The neo-Pigetian theories, are those strongly grounded in Piaget's theory but re-interprets Piaget's concepts in an information-processing context. A popular neo-Piagetian theorist is Robbie Case, who proposed that developmental change is characterized by increasing sophistication of children's underlying cognitive structures. Again, the stage-like development of children's abilities is based on increase in memory capacity and on child's formation of executive control structures, which is a mental blue-print for solving a class of problems. He also replaced Piaget's assimilation and accommodation with cognitive skills of ability to set goals, solve problems and the need to explore [20].

Learning and Cognitive Development

The exact mechanisms behind cognitive development of children, especially in the domains of learning, thinking, reasoning and socio-emotional influences on learning, are still intriguing, overhauled by multiplicity of theories, mostly empirical **(Table 1)**.

intellectual disability in children but most of them are distributed and fragmented, mostly because there are no uniform patterns of classification. While some of them relied on symptomatology, others anchored on severity. Etiological classifications are often

Table 1 Theories of cognitive development.

Theory	What it means?	Implication
1. Cognitive Dissonance (Festinger, 1957)	Fundamentally motivational in nature. Perception of an inconsistency among an individual's cognition generates a negative intrapersonal state (dissonance), which motivates the individual to seek and implement strategies to alleviate this aversive state	Appropriate attitude formation to a particular task/situation/behavior Decision making Problem solving
2. Constructivist Theory (Piaget 1980; Vigotsky and Burner)	Constructivism is a psychological theory. It is a post-structuralist psychological theory that construes learning as an interpretive, recursive, on-linear building process by active learners interacting with their surrounding physical and social world. The theory is based on complexity models of evolution and thought	Self perception of information and development of knowledge from experiences/real life situations and through social interaction Creative thinking/experiments by learner
3. Social Learning theory (Bandura)	Most human behavior is learned observationally through modeling: by observing others, one forms an idea, and on later occasions this coded information serves as a guide for action. Social learning theory explains human behavior in terms of continuous reciprocal interaction between cognitive, behavioral and environmental influences	Observation through modeled behavior (therapy technique) Appropriate attitude and emotional reaction (behavioral modification)
4. Social Development theory (Vigotsky, 1978)	Explains social influence on cognitive development. Learning is a universal aspect of the process of developing culturally organized, specific human psychological function.	Social interaction (natural situation)
5. Conversation theory (CT) (Pask, 1970)	Conservation theory regards social system as a symbolic language oriented system where responses depend on an individual's interpretation of another individual's behavior, and where meanings are agreed through conversation. The theory portrays multilevel agreement oriented conversation among participants supported by modeling facilities, suitable communication and action interface, and hence, applied epistemology.	Conversation exchange and discussion (general, educational)
6. Operant conditioning (Skinner)	This theory explains learning as a function of change/modification in overt behavior. This is achieved through the presentation of reinforcements: positive, negative, or punishments. According to the theory of operant conditioning, learning is controlled by an association between a particular behavior and its consequences.	Appropriate reinforcement and punishment to a particular behavior
7. Conditions of Learning (Gagne)	There are different types and levels of learning of which, the major categories are verbal information, intellectual skills, cognitive strategies, motor skills and attitudes. The theory is mainly focused on intellectual skills which can be organized in a hierarchy based on its complexity.	Delivering apt instructions for each activity Sequential learning
8. Andragogy (Knowles, 1980; 1984)	Knowles used the term andragogy for explaining the theory of adult learning. He expounded adult learning based on 6 assumptions, 1) the need to know, 2) self-concept, 3) adult learner experience, 4) the readiness to learn, 5) orientation to learning, and 6) motivation. The core part of adult learning is from their experience.	Adult learning through instructions Problem-oriented activities
9. Situated Learning (Lave and Wenger, 1990)	This theory states that learning is ensued through social relationships, cultural background and by connecting prior knowledge with a new context.	Contextual learning Social interaction Community-based
10. Genetic Epistemology (Piaget)	Piaget tried to illustrate knowledge development with respect to different cognitive structures. He believed that cognitive structural changes in children transpire as a result of adaptation to the environment, which eventuates through assimilation and accommodation.	Age appropriate/stage appropriate activities
11. Subsumption theory (Ausbel, 1962)	Ausbel's illustration about this theory is confined to different processes (superordinate, representational, and combinatorial) for learning that occur during reception of information. Subsumption is the primary process in learning, in which new material is integrated with previously presented information in the existing cognitive structure on a substantive, non-verbatim basis.	Organized material-based learning
12. Component Display theory (Merrill)	Merrill portrays learning in two dimensions: content and performance. The theory describes four primary presentations (rules, examples, recall, and practice) and five secondary presentations (prerequisites, objectives, helps, mnemonics, and feedback). The significance of this theory is learner control.	Education and learning
13. Experiential Learning (Rogers)	Rogers referred two types of learning: 1) cognitive learning which involves academic knowledge, 2) experiential learning which denotes applied knowledge. Experiential learning is the most significant and long lasting learning which includes motivation, personal interests, self evaluation and self direction of a learner	Applied learning

14. Structure of Intellect (Guilford)	Guilford introduced three important components of intelligence: operations, contents and products. Each component comprised of different operations. Each of these components are independent and combine freely in order to construct 150 different components of intelligence	Using combinations of multiple intelligent level operations
15. Connectionism (Thorndike)	This interprets the association between stimulus and response and its strength or weakness is determined by the nature and frequency of S-R (stimulus – response) pairings. The theory construed through three primary laws, 1) law of effect, 2) law of readiness, and 3) law of exercise. Practice and reward plays an important role in learning. Intelligence varies with respect to the number of connections learned.	Repeated practice Reward-based learning
16. Information Processing theory (Miller, 1956)	This theory describes how sensory information is systematically processed, transformed and stored by different processing systems. Miller annotated that environmental information will pass from sensory storage to working memory, and later into long term memory in a hierarchical order	Short term memory activities Meaningful chunking of information
17. Cognitive load theory (Sweller, 1988)	Cognitive load theory evolved out of the problem solving study done by Sweller. He postulated that learning and problem solving difficulties can be manipulated by using an effective instructional design. According to this theory, cognitive load can be of 3 types, intrinsic, extraneous and germane. Cognitive load can be explained in terms of element interaction and learning pattern. Simultaneous learning of elements and its high interaction will leads to high cognitive load, whereas successive learning and low element interaction leads to low cognitive load	Designing of learning materials with minimum cognitive load
18. Multiple intelligence (Gardner)	There are at least 7 distinct forms of intelligence by which people gather knowledge from the world and these forms are presented in varying degrees with respect to person or culture. The proposed multiple forms of intelligence are verbal-linguistic, logical-mathematical, visual-spatial, body-kinesthetic, musical-rhythmic, interpersonal and intrapersonal. An individual should be encouraged to use the preferred intelligence to augment learning	Strengthening of favored intelligence in learning
19. Drive Reduction theory (Hull, 1943)	This is a theory of motivation where reinforcement plays an important role for successful learning. A behavior emerges in response to primary drives (e.g. hunger, thirst) or secondary drives (e.g. money) in order to fulfill physiological needs. This drive will reduce when the goal is fulfilled, and this reduction will act as a reinforcer for learning. Reinforced training sections can improve learning by increasing stimulus response strength	Need-based learning. Appropriate reinforcement
20. Dual Coding Theory (Paivio, 1971)	Human cognition/recalling occurs by the simultaneous interaction between verbal representations/language and mental images of objects or events	Learning based on verbal and non-verbal interaction
21. Criterion Referenced Instruction (Mager)	This includes a comprehensive set of methods for training programs in a variety of media. Students should be self motivated for the successful process of learning. In this training, students get repeated practice sessions.	Learner motivation Competence- and performance-based Practice
22. Gestalt theory (Wertheimer, 1923-24)	Human perception occurs as a whole, rather than studying each component, since it is complex. Grouping of elements is determined by four primary factors: proximity, similarity, closure and simplicity. Organization of these factors helps in perception and problem solving	Organized grouping of information Problem solving activities
23. Triarchic Theory (Sternberg)	Sternberg has given a broader definition to intelligence by formulating triarchic theory. He explained intelligence in three aspects: componential, experiential and contextual intelligence. This comprises of knowledge acquisition, dealing with novel situations and applying, modifying and changing the environment respectively. According to him intelligence performance is highly related to the socio-cultural environment of an individual	Reality-based learning Skill learning
24. Minimalism (Carroll)	Carroll developed this theory as a framework for designing training materials. He stated that each person should use their own experience as a motive for their learning, rather than using passive techniques. Learning tasks should be meaningful, realistic, self contained, self directed and error recognized, so that we can minimize the usage of reading and other passive learning strategies. This is primarily useful in computer-assisted activities	Learner-directed meaningful and realistic activities
25. Elaboration Theory (Reigeluth)	Reigeluth theorized an easy method of learning by chunking down the concepts. Information can be presented sequentially by arranging it in an increasing order of complexity which would be helpful in understanding the meaning of a learning context. Finally, the elaboration approach results in the advancement of cognitive structures.	Hierarchical order of complexity based

26. Script Theory (Schank, 1975)	Schank proposed this theory to interpret language understanding and higher thinking processes. He introduced the word 'script' which is a mental construct consisting of a sequence of activities and events. He also postulated that all memories are constructed on the basis of personal experiences, and stored as scripts. Script is a basic concept which helps an individual to make inferences from situations and discourses	Theme-based learning
27. Cognitive Flexibility Theory (Spiro, et al)	Cognitive flexibility theory explains the process of learning in complex and ill structured domains. The ability of a person to restructure his knowledge through his adaptive responses to radically changing situation is termed as cognitive flexibility. An effective learning is focused on context, and hence learning activities should be presented specifically from multiple representations of the content. This theory also emphasizes on the importance of knowledge construction, rather than its transformation by an individual itself	Context-dependent activities
28. Sign Learning (Tolman, 1930)	Tolman's theory of sign learning created a bridge between behaviorism and cognitivism. He illustrated that knowledge can be acquired through a meaningful behavior, and thus learning can be perceived as goal-directed and purposive. In order to achieve a goal, an individual will use the easiest way of learning. He also introduced five types of learning: approach learning, escape learning, avoidance learning, choice-point learning and latent learning	Purpose-directed activities

Infant brain shows tremendous potentials for learning even during intrauterine life. DeCasper and Fifer [21] have demonstrated that human responsiveness to sound begins in the third trimester of life, and by birth reaches sophisticated levels. Fetus also learns to recognize specific bits of music [22]. These responses are presumed to be mediated by brain stem development that occurs at the 6th-7th week of gestation, and maturing in a caudal to rostral fashion forming the medulla, pons, and midbrain. Spontaneous and stimulus-induced behavior of human fetus, particularly changes in heart rate, respiration and body movements, has been used to examine sensory and cognitive development. This has provided crucial information for the identification of processes, mechanisms and experiential factors underlying development [23]. Majority of the neurons constituting the mature brain are formed before birth, by 7th month of gestation [24]. This indicates that environment within the womb can affect later cognitive development. Certain drugs and toxins, therefore, have specific effect on cognitive development as exemplified by the adverse effect of prenatal alcohol exposure in a variety of cognitive skills [25].

Statistical learning theory is the frame work for machine learning derived from the principles of statistics and functional analysis. Statistical learning theory deals with the problem of finding a predictive function based on data. It has successful applications in the field of computer vision, speech recognition, and bioinformatics. The goal of learning is prediction, and falls into several categories such as, supervised learning, unsupervised learning, online learning and reinforcement learning, of which, supervised learning is the one best understood. This theory has been applied in the biological model of learning through sensory systems. Research on visual and auditory learning has revealed that neural sensory statistical learning plays a crucial step in cognitive development after birth [26]. Statistical learning is unconscious, continues throughout life and is one of the basis for developing stereotypes.

Neuroconstructivism is a theoretical framework for cognitive development that has emerged from research in Cognitive Neuroscience, and is anchored on the biological constraints of pattern of brain activity that comprises mental representation [27]. The theory is built on the basic mechanisms involved in gene–gene interaction, gene–environment interaction and, crucially, ontogeny. These factors are considered to play a vital role in how the brain progressively sculpts itself, and how it gradually becomes specialized during development. The proponents of the theory debate against the conventional innate modularity of mind, which implies that a brain is composed of innate neural structures or modules which have distinct evolutionarily developed functions. Neuroconstructivism can be seen as a bridge between Jerry Fodor's psychological nativism and Jean Piaget's theory of cognitive development. Neuroconstructivism is important in understanding cognitive disorders as these are explained by altered constraints on brain development that in turn alter a child's developmental trajectory [28].

Cognitive Deficits in Children

In this review, we attempt to provide a bird's eye view of cognitive development, from theoretical to structural and functional development, so that it is possible to approach cognitive deficits from its developmental perspective, thereby leading to a comprehensive multidisciplinary management.

Cognitive deficits in children may be global as in the case of mental retardation, or specific as in learning disabilities, autism, developmental language disorders, anoxic brain damage, stroke, post infectious syndrome, and post traumatic and post demyelinating conditions. Cognitive deficits have also been observed in psychiatric and psychological disorders such as childhood schizophrenia and behavioral disorders. While majority of these disorders are developmental in nature with a strong genetic basis, there are several acquired causes for these disorders, with gene-environment interactions playing a key role in the etiopathogenesis and clinical severity of such conditions. Identification of these causative factors is of primary importance in the prevention and management of the aforementioned conditions, which are generally thought to be non-curable.

Causes for Cognitive Deficits in Children

There are several classifications for cognitive deficits and

difficult and elaborate because of the heterogeneous nature of the disorders. Symptomatology-based classification often lack precision as they are based on the narrative ability of the individual or relative. There is not yet a single test that closely establishes the diagnosis in majority of the cases. Most of the disorders are believed to have a genetic basis and several candidate genes have been identified. Nevertheless, how exactly the genes lead to individual symptoms or combination of symptoms is not yet fully elucidated. In order to promote disorder-specific treatment, an etiology- and pathology-based classification is essential. We have made a proposal for such a classification **(Table 2)** incorporating the "Cognitive domains".

Global developmental delay (GDD) and intellectual disability (previously known as mental retardation)

Cognitive deficits in children may affect all domains of cognitive functions including motor and executive functions. Global developmental delay is a subset of developmental disability defined as a significant delay in two or more domains of development (Gross/fine motor, speech/language, cognition, social/ personal, and daily living activities) (AAN guideline summary for Clinicians; www.aan.com/professionals/practice/index.cfm). The prevalence of GDD is estimated to be 1-3% in children <5 years [29]. The causes of GDD are diverse, and usually an underlying causative pathology is identifiable in most cases [30-33]. The term “global developmental delay’ is generally used for children under 5 years, while the term “intellectual disability” is used for older children, as the Intelligence Quotient (IQ) testing is not valid and reliable before 5 years. Intellectual disability is also heterogonous group of disorders where the cognitive deficit is global. Intellectual disability is defined as the significant limitation in intellectual functioning and adaptive behavior which covers every day social and practical skills. The disability commences before the age of 18 years. The prevalence of intellectual disability is estimated to be 2-3% of the population [34,35]. Intellectual disability has a diverse etiology and varying severity. Therefore, an etiological diagnosis is possible only in 50-70% of cases [36].

Causes of global development delay and intellectual disability include genetic disorders, inborn errors of metabolism, endocrine disorders, developmental and degenerative disorders of the central nervous system, demyelinating disorders, intrauterine infections, hypoxic ischemic insults, prematurity, birth trauma and exposure to drugs and toxins. There is a genetic cause in >50% of the cases. [37] Numerical abnormalities of chromosomes include autosomal abnormalities (live born polyploidies), trisomy13 (Patau syndrome), trisomy 18 (Edward syndrome) and trisomy 21 (Down syndrome). Numerical abnormalities of sex chromosomes (e.g. XXX) are sometimes associated with cognitive impairment. Structural chromosomal abnormalities include deletions, insertions, inversions and translocatios. Cytogenetically invisible deletions like interstitial microdeletions and subtelomeric deletions can also produce psychomotor retardation and behavioral problems. Subtelomeric deletions are associated with 5-10% of all idiopathic intellectual disabilities [38]. X-linked retardation causes 10-20% of all inherited cases of intellectual disability. At least 209 different X-linked intellectual disabilities have been reported [39], of which Fragile X syndrome is the most common (1/4,000-6,000) [40].

Cognitive deficit affecting single/specific domain cognitive functions

Cognitive deficits may be confined to single/specific domain of cognitive function such as speech and language functions or very specifically to sub domains or module of a specific cognitive function.

Specific language Impairment (SLI) is defined as an unexpected persistent impairment in language ability despite adequate opportunity and intelligence, in the absence of explanatory medical conditions.

SLI is further classified according to the sub domain or modality of impairment into development articulation disorder, specific speech articulation disorders, developmental expressive language disorder, developmental receptive language disorder, developmental mixed receptive expressive disorder and acquired aphasia with epilepsy (ICD-10, DSM-IV-TR).

The exact etiology of SLI is not fully sorted out and attributed to heterogeneous causes. There is a significant contribution of genetic factors. SLI is highly heritable and affects 5-8% of preschool children. Over the past few years there have been several investigations to unravel the genetic factors associated with language impairment. So far variants in four specific genes have been found to be associated with spoken language disorders, forkhead box P2 (FOXP2), contactin associated protein-like2 (CNTNAP2), calcium-transporting ATPase2C2 (ATP2C2), and c-MAF inducing protein (CMIP) [41].

Specific disorders of scholastic skills are best examples of cognitive deficits affecting specific domains. These include specific disorders of reading (Dyslexia), writing (Dysgraphia), arithmetic ability (Dyscalculia), non-verbal learning disability and Gerstman syndrome.

Dyslexia has a prevalence of 5-12% and is linked with chromosome regions 1p34-p36, 6p21-p22, 15q21 and 18q11. Four candidate genes in 6p21-p22 region have recently been identified, with the results indicating that a disturbance in neuronal migration could lead to the symptoms associated with dyslexia [42].

Cognitive deficit affecting multiple domains cognitive functions

Autism Spectrum Disorder (ASD), also known as Pervasive Developmental Disorder (PDD), is a complex neurodevelopmental disorder characterized by impairments in social interaction and communication, restricted repertoire of interests and stereotyped activities [43-45]. It is often diagnosed before the age of four, and is at least four times more frequent in males than females. One of the salient features of ASD is the striking etiological, clinical and genetic heterogeneity.

The current prevalence of ASD in world population is estimated to be ~1% (CDC, 2014). The prevalence is ~1.5% in USA (CDC, 2014), 1% in UK (Brugha, 2011), and slightly higher in Asian countries,

Table 2. A Thematic Approach to Cognitive Deficits in Children in Children and its Causes.

COGNITIVE DOMAINS AFFECTED	B. ETIOLOGY AND PATHOLOGY (CAUSES)
GLOBAL DEFICITS A.1. AGE (<5 YEARS) A.1.a. Global developmental delay (GDD) A. 2. AGE (>5YEARS) A.2.a. Intellectual Disability (MR) A.3. SEVERITY A.3.a. Mild IQ 50-69 A.3.b. Moderate IQ 35- 49 A.3.c. Severe IQ 20-34 A.3.d. Profound IQ Below20 A.4. DOMAIN-SPECIFIC *A.4.a. Single Domain* *A.4.a.1. Specific Disorders of language Development (SLI)* A.4.a.1.1. Specific Speech articulation disorders A.4.a.1.2. Developmental .Expressive Language Disorder A.4.a.1.3. Developmental Receptive Language Disorder A.4.a.1.4. Developmental Mixed Receptive Expressive Disorder A.4.a.1.5. Acquired Aphasia with Epilepsy (Landau-Kleffner syndrome) A.4.a.1.6. Other disorders of Speech and Language functions A.4.a.1.7. Developmental Speech and Language Disorder ,unspecified *A.4.a.2. Specific Disorders of Learning (Scholastic skills)* A.4.a.2.1. Specific Reading Disorder (Dyslexia) A.4.a.2.2. Specific Disorder of Writing (Dysgraphia) A.4.a.2.3. Specific spelling Disorder A.4.a.2.4. Arithemetical Disorder (Dyscalculia) A.4.a.2.5. Mixed disorder of Scholastic Skills A.4.a.2.6. Non-Verbal Learning Disability A.4.a.2.7. Developmental Gerstman syndrome A.4.a.2.8. Learning Disabilities associated with Specific syndromes A.4.a.2.9. Learning Disabilities associated with Specific Medical or Surgical Conditions A.4.a.2.10. Learning Disabilities Unclassified. *A.4.b. Multiple Domains* *A.4.b.1. Pervasive Developmental disorders* A.4.b.1.1. Childhood Autism A.4.b.1.2. Asperger's Syndrome A.4.b.1.3. Childhood Disintegrative Disorders A.4.b.1.4. Pervasive Developmental Disorders Not otherwise specified A.4.b.1.5 .Pervasive Disorders associated with specific Genetic or Metabolic Disorders A.4.b.1.6. Pervasive Developmental Disorders Post Infectious or Post traumatic A.4.b.1.7. Pervasive developmental Disorders associated with specific neurological disorders *A.4.b.2. Rett's Syndrome* *A.4.b.3. ADHD* A.4.b.3.1. ADD A.4.b.3.2. ADHD A.4.b.3.3. Combined	CONGENITAL DEFICITS B. 1. Temporal relation of expression of symptoms B.1.a. During the period of embryogenesis *B.1.a.1. Structural abnormalities of the Developing Brain* *B.1.a.1.1. Disorders of Dorsal induction (3-5 weeks)* B.1.a.1.1.1. Neural tube Defects (NTDS) B.1.a.1.1.2. Anencephaly B.1.a.1.1.3. Cephalocele B.1.a.1.1.4. Chiari malformations B.1.a.1.1.5. Spinal dysraphic disorders *B.1.a.1.2. Disorders of Ventral Induction (5-10 weeks)* B.1.a.1.2.1. Holoprozencephalies B.1.a.1.2. 2. Dandy Walker malformation B.1.a.1.2. 3. Cerebellar hypoplasia /dysplasia B.1.a.1.2. 4. Jubert syndrome B.1.a.1.2.5. Rhombencephalosynapsis B.1.a.1.2.6. Septooptic Dysplasia B.1.a.1.2.7. Facial anomalies *B.1.a.1.3. Disorders of Migration (2-5 months of gestation)* B.1.a.1.3.1. HetrotopiasB.3.a.1.2.Agyria- Pachy gyria B.1.a.1.3.2. Polymicrogyria B.1.a.1.3.3. Lissencephaly B.1.a.1.3.4. Sczencephaly B.1.a.1.3.5. Corpus callosal agenesis B.1.a.1.3.6. Lhermitte –Duclos disease *B.1.a.1.4. Disorders of Histogenesis (2-5months of gestation)* B.1.a.1.4.1. Acqueductal Stenosis B.1.a.1.4.2. Arachanoid Cyst B.1.a.1.4.3. Megalencephaly B.1.a.1.4.4. Microcephaly B.1.a.1.4.5. Neurocutaneous Syndromes (Phakomatosis) B.1.a.1.4.6. Congenital Vascular malformations B.1.a.1.4.7. Congenital Neoplasia *B.1.a.1.5. Disorders of Myelination (6 months to 3 years postnatal)* B.1.a.1.5.1. Dysmyelinating Disorders (Leukodystrophies) B.1.a.1.5.2.Metabolic Disorders B.1.b. Intra uterine infection (First Trimester 0-3 months) B.1.b.1.1. Toxoplasma B.1.b.1.2. Other Infections

COGNITIVE DOMAINS AFFECTED	B. ETIOLOGY AND PATHOLOGY (CAUSES)
A.4.b.4. ADD/ADHD associated with other specific genetic or developmental disorders *A.4.b.5. Overlapping Syndrome* *A.4.b.6. Unclassified*	B.1.b.1.3. Rubella B.1.b.1.4. Cytomegalovirus, B.1.b.1.5. Herpes Infections B.1.b.1.6. Anoxia or Hypoxemia B.1.c. Exposure to Drug and Toxins B.1.c.1. Maternal Alcohol B.1.c 2. Teratogenic Drugs B.1.c.3. Anti-Epileptic Drugs B.1.c.4. Foetal Valproic acid syndrome B.1.c.5. Phenytoin B.1.c.6. Others. Anti TB. Steriods, Hormones B.1. d. Influence of genetic disorders B.1.e Inborn errors of metabolism B.1.f. Related to blood group incompatibilities B.1.g. Intra uterine growth retardation related to Malnutrition B.1.h. Effect Endocrine Disorders B.1 .i. Foetal malpositions, ,Cord around the neck, B.1.j. Abnormalities related to Placenta, or Uterine environment or amniotic fluid B.1.k. Systemic diseases of the mother , Diabetes,Hypertension,hear diseases, anemia ,specific malnutrition,Specific infections including HIV B.2. Trauma B.2.a. Birth Related B.2.a.1. Obstructed labour B.2.a.2. Birth Trauma B.2. a.3. Anoxia B.2.a.4. Instrumentaion B.2.a.5. Ceaserian section B.2.b. Neonatal Period B.2.b.1. Neonatal infections/septicemia B.2.b.2. Neonatal Hypoglycemia; Hypokalemia. Hypomagnesaemia, Hyaocalcemia B.2.b.3. Neonatal Seizures B.2.c. Congenital cardiac, respiratory disorders, gastrointestinal disorders that interfere with circulation, respiration or acute feeding problems B.2.d. Infancy <2 years B.2.d.1. Epilepsy &epileptic syndrome B.2.d.2. Neurodegenerative Disorders of Childhood B.2.d.3. Infections of CNS.Meningitis,Encephalitis B.2.d.4. Demyelinating Dysmylenating diseases B.2.d.5. Hypothyroidism,Hyperthyroidism B.2.d.6. Inborn Errors of Metabolism B.2.d.7. Mitochondrial cytopathies B.2.d.8. Lyzosomal Disorders B.2.d.9. Peroxisomal disorders B.2.d.10. Others B.2.e. Early Childhood (2-7 years) B.2.e.1. Epilepsy &epileptic syndrome B.2.e.2. Neurodegenerative Disorders of Childhood B.2.e.3. Infections of CNS.Meningitis,Encephalitis B.2.e.4. Demyelinating Dysmylenating diseases B.2.e.5. Hypothyroidism,Hyperthyroidism B.2.e.6. Inborn Errors of Metabolism B.2.e.7. Mitochondrial cytopathies B.2.e.8. Lyzosomal Disorders B.2.e.9. Peroxisomal disorders B.2.e.10. Others B.2 .f. Late childhood (8-14 years) B.2.f.1. Progressive Myoclonic Epilepsy B.2.g. Pre adolescence & Adolescence (14-18 years) *B.2.h. OTHERS*

Source: ICD-10, DSM-IV-TR

ranging from 1.81% to 2.6% [38,39]. In the past few decades, an alarming increase in the prevalence of ASD has been observed in different countries worldwide.

***Genetic basis of ASD*:** Multiple domains of cognitive functions are affected in ASD. The triad symptoms of ASD include qualitative impairment in verbal communication (language), lack of reciprocal social interaction and stereotypic motor activities (ICD_10, DSM V).

Using modern genetic tools as many as 235 genes have been found to be associated with autism, with supportive evidence from ≥4 independent studies (Autism database-AutDB; http://autism.mindspec.org/autdb/Welcome.do). These genes were identified through single nucleotide polymorphism (SNP) association studies and/or sequencing and/or gene expression analyses. SNPs, which are single base alterations in a DNA sequence, are responsible for much of the genetic variation in the human genome. Genetic association studies can be used to examine whether a particular genetic variant is associated with the disorder. Since most of the associated SNPs are located in the non-translated portions of the genome, their functional impact cannot be determined. However, several functional SNPs, leading to a defective protein, have also been identified in the exonic regions of autistic individuals.

Despite the diversity, ASD patients exhibit similar behavioral and neuronal conditions, although differing in severities and co-morbidities. This commonality of neurological phenotypes suggests that the susceptible genes may act through a limited set of pathways [46]. Several studies have suggested a role for the genes involved in synaptic assembly, such as the synaptic cell adhesion molecules (CAMs), ion channels, neurotransmitter receptors, and the scaffolding and cytoskeletal proteins that work harmoniously to provide synaptic structural integrity and functionality [47].

The concept of copy number variations (CNVs) as a possible genetic contributor to the development of ASD emerged ever since the publication of first CNV based study on autism families [48]. Since then, multiple large studies have been performed using different platforms to examine different cohorts. Several novel or rare CNVs, both de novo and inherited, were identified, especially affecting regions like 1q21, 5p15.2, 7q11-13, 15q13.3, 16p11.2, 17p11.2 and 22q11.2 [48-50]. De novo events were often more deleterious than inherited variations . The reported CNVs in autism are often enriched in genes with important functions in the nervous system like post synaptic translational regulation, neuronal cell adhesion, neuronal activity modulation and excitatory and inhibitory function imbalance [51]. Functional impact of CNVs were recently been investigated by studying the expression profile of genes within the rare de novo CNVs [52]. Genes which are involved in neural-related pathways were found to be mis-expressed.

Over the past three years, several independent groups have conducted whole exome sequencing using non-overlapping ASD samples [53-59], using 189 trio families, showed that de novo point mutations are overwhelmingly paternal in origin. Such a paternal bias in de novo point mutations has also been reported by Battaglia et al., [53], during the same period. Several novel genes were identified through these studies as playing a role in liability for ASD. These results further highlight the extreme genetic heterogeneity of ASD, while pointing towards a relatively small number of implicated biological pathways. Many of these de novo mutations identified disrupted genes in neural development and plasticity, chromatin related proteins involved in transcriptional regulation, especially during prenatal brain development [60].

Attention deficit hyperactivity disorders (ADHD) (Hyperkinetic Disorder in ICD-10) is another group of neurobehavioral disorders where the cognitive deficit extends into more than one cognitive domain-attention, executive function, language and learning. The prevalence of the disorder is 3-5% in children [61,62], with a high male-female ratio [61]. Though considered as a childhood disorder, ADHD can extend into adulthood, and can cause life-long effects on cognitive and social functioning [63,64]. There are certain structured assessment tools with internationally accepted diagnostic criteria (DSM IV) that can make accurate diagnosis to reliable level. The etiology and pathology of ADHD is poorly understood. ADHD is a complex disorder influenced by genetic and environmental factors. Genetic epidemiological studies have consistently reported a heritability of 75-91%. It is a highly heritable disorder. Meta-analysis of pooled data have shown association between ADHD and polymorphisms in DRD4, DRD5 and SLC6A3 that encode dopamine D4 and D5 receptors and dopamine transporter, respectively. ADHD is often reported along with several genetic syndromes such as tuberous sclerosis, Tourette's syndrome, inborn errors of metabolism such as phenylketonuria, mitochondrial cytopathies, epilepsy and epileptic syndromes. ADHD is described as a comorbid condition in ASD and various types of LD.

Global Prevalence of Cognitive Impairment

The number of children with cognitive deficits is escalating. Cognitive deficits may be developmental or acquired, occurring in all ages and in both sexes due to heterogeneous causes. The causes include prenatal and perinatal insults, malnutrition, genetic disorders, infectious diseases (e.g. meningitis, parasites, cerebral malaria), in utero drug and alcohol exposure, newborn birth asphyxia, low birth weight, head injuries, and endocrine disorders. Given a world population of approximately 6.5 billion, of whom 5.3 billion live in developing countries, where half the population is aged less than 15 years, the estimated number of children with cognitive limitations is ~780 million. This includes 130 million children with impairments resulting from severe malnutrition in the first year of life (5% of all children living in developing countries), 260 million with iron-deficiency anemia in the first 2 years of life (10% of all children living in developing countries), 260 million with severe parasitic infections (10% of all children living in developing countries), and 130 million with other conditions causing brain impairment, including genetic and metabolic disorders. Individuals with cognitive deficits experience significant limitations in both intellectual functioning and in adaptive behavior, which adversely affects daily social and practical skills.

Even though many of these cognitive disorders have a genetic basis there are preventable measures at various levels from conception to early period of development. The scientific basis of carrier state and temporal relation of disease manifestation provide us themes to develop working models for prevention or amelioration of the severity of the disease. The theory of developmental origin of Health and disease (DOHaD) can be used as building block for developing treatment strategies for several genetically determined diseases. As development is a continuum,

supplementation of growth factors can be remedial to many disabling conditions.

Approach to Children with Cognitive Deficits

Children with intellectual disability or Global developmental delay should have a comprehensive evaluation to establish the etiology of the disability. This is illustrated in **Figure 2**. A specific etiological diagnosis offers the opportunity to discuss treatment, prognosis and advise against genetic recurrence. A diagnosis can also avoid unnecessary testing and evaluation and costly repeated investigations and can lead to opportunities for improved health and functional outcome. The key elements of diagnostic evaluation are: Medical and developmental history, antenatal, natal and perinatal history 3-generation family history and Pedigree charting, Dysmorphologic examination, Neurologic evaluation and judicious use of laboratory and neuroimaging technique.

A multidisciplinary team approach is the one globally advocated for the management of children or adults with cognitive deficits. In the case of children special emphasis is on planning of educational intervention. The proposed Multidisciplinary team includes,

- Members of the multidisciplinary team
- Neurologists
- Pediatricians
- ENT Specialist
- Psychiatrists
- Physiatrist
- Clinical Psychologists
- Speech Language pathologists
- Physiotherapists
- Occupational therapists
- Clinical linguists
- Special educators/educational experts
- Geneticists
- Biochemists
- Neuroradiologist
- Electro- physiologist
- Computer experts

Early Identification is the Gold Standard Rule for All Developmental Disabilities

Specific guidelines and protocols are utilized to detect infant hearing impairment, visual impairment and global developmental delay. Specific screening for inborn errors of metabolism, endocrine dysfunction, and genetic tests are also being carried out.

Conditions that should be screened in newborn

- 3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)
- 3-OH 3-CH3 glutaric aciduria (HMG)
- Argininosuccinic academia (ASA)
- Beta-ketothiolase deficiency (BKT)
- Biotinidase deficiency (BIOT)
- Carnitine uptake defect (CUD)
- Citrullinemia (CIT)
- Congenital adrenal hyperphasia (CAH)
- Congenital hypothyroidism (HYPOTH)
- Cystic fibrosis (CF)
- Galactosemia (GALT)
- Glutaric academia type 1 (GA1)
- Hb S/beta-thalassemia (Hb S/Th)
- Hb S/C disease (HB S/C)
- Hearing deficiency
- Homocystinuria (HCY)
- Isovaleric academia (IVA)
- Long-chain L-3-OH acyl-CoA dehydrogenase deficiency (LCHAD)
- Maple syrup urine disease (MSUD)
- Medium chain acyl-CoA dehydrogenase deficiency (MCAD)
- Methylmalonic academia (Cbl A,B)
- Methylmalonic academia (mutase deficiency) (MUT)
- Multiple carboxylase deficiency (MCD)
- Phenylketonuria (PKU)
- Propiionic academia (PROP)
- Sickle cell anemia (SCA)
- Trifunctional protein deficiency (TFP)
- Tyrosinemia type 1 (TYR 1)
- Very-long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

Delineation of deficits and identification of the nature of deficits and its extent

- Detailed clinical history, systematic clinical and neurological evaluation with specific emphasis to look for congenital anomalies and dysmorphogenesis
- Detailed family history and pedigree charting
- Biochemical, metabolic and endocrine evaluation for

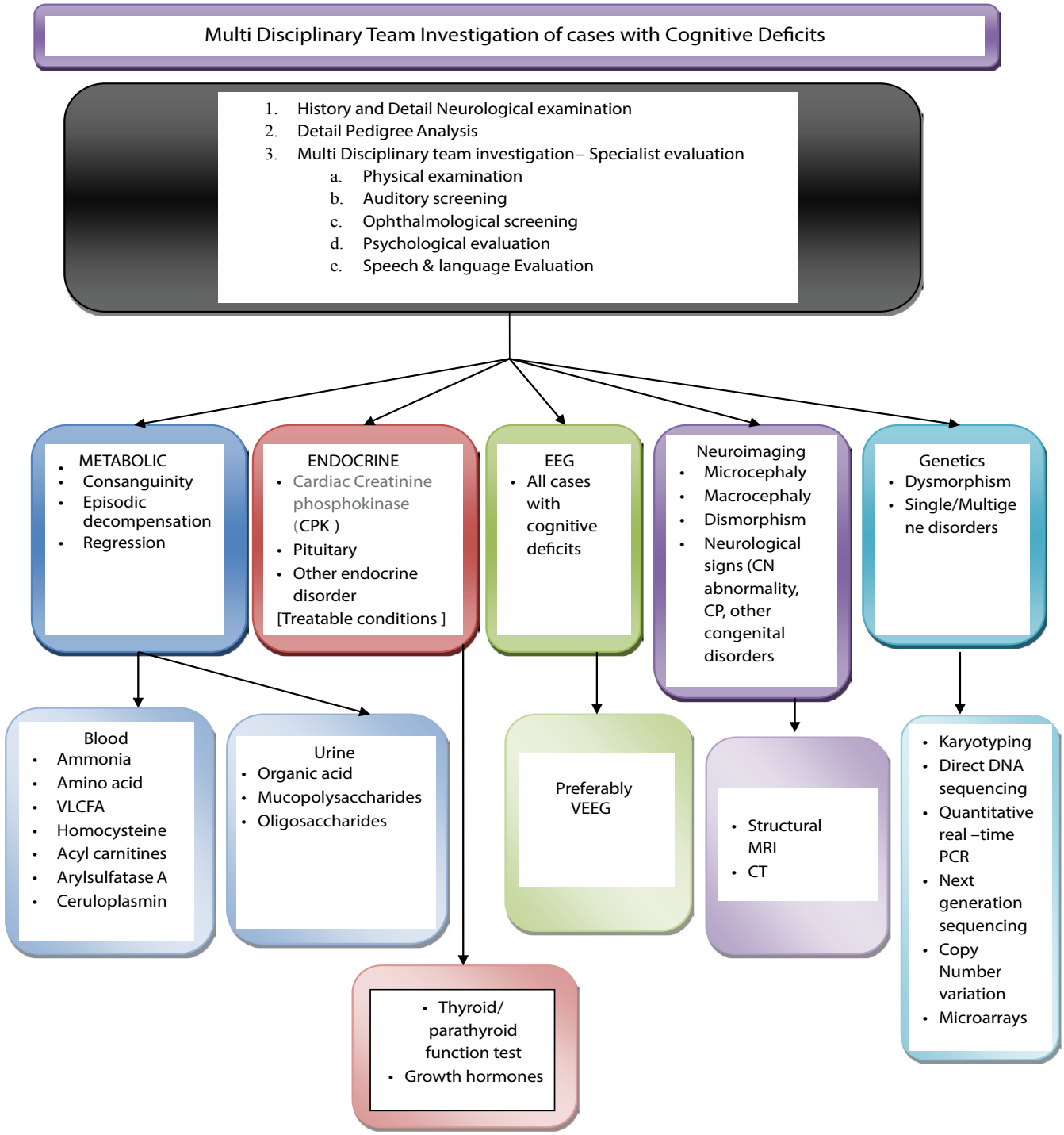

Figure 2 Multi-Disciplinary Team Investigation of cases with Cognitive Deficits.

identifying treatable conditions

- Genetic investigation based on clinical observations
- EEG preferably VEEG
- Neuroradiological assessment (MRI, CT scan) based on biological markers and clinical judgment
- Audiological evaluation BERA
- Assessment of cognitive deficits: Psychometric evaluation
- Assessment for language functions: Speech language pathologist
- Assessment by Physiotherapists/Physiatrists for motor kinesthetic disability

Measurement of Cognitive Function

Descriptions of numerous screening tests appropriate for pediatric office use are available at the Developmental-Behavioral Pediatrics Online Community. Instruments include the following child development inventories,

- Three age-specific forms for screening in children aged 3-72 months
- Bayley Scales of Infant Development II (BSID-II): Comprises mental, motor, and behavior rating scales
- Stanford-Binet Intelligence Scale, 4th edition
- Wechsler Intelligence Scale for Children, 3rd edition
- Wechsler Preschool and Primary Scale of Intelligence-Revised
- Other less commonly used measuring techniques include the following:
- Differential Abilities Scale: Appropriate for children and adolescents aged 2.5-18 years
- Wide Range Intelligence Test: Possibly the preferred test to determine IQ in those aged 4-85 years
- Columbia Mental Maturity Scale (CMMS): Appropriate for children aged 4-10 years
- Detroit Tests of Learning Aptitude–P: Appropriate for children aged 3-9 years
- Good enough-Harris Drawing test (Draw-a-man): Used for children aged 3-16 years
- Kaufman Assessment Battery for Children (K-ABC): Appropriate for children aged 2.5-12.5 years

Genetic Evaluation of Intellectual Disabilities

A comprehensive evaluation is required to establish the etiology of intellectual disability or global developmental delay. The key elements of evaluation includes medical and developmental history, antenatal, natal and perinatal history, pedigree charting, dysmorphologic examination, neurologic evaluation, and genetic test. Since the use of karyotyping to first identify trisomy 21 in 1959, genetic testing has evolved tremendously. Fragile-X testing still continues to be recommended for the initial evaluation of intellectual disability or global developmental delay. Chromosome microarray, which has replaced the standard karyotyping and fluorescent in situ hybridization subtelomere tests, has now become a first line test for the evaluation of intellectual disability. Advances in genetic research now permit genome-wide discovery of chromosomal copy-number changes and single-nucleotide changes in patients with intellectual disabilities using technological advances such as microarray-based comparative genomic hybridization (array CGH), single nucleotide polymorphism (SNP) genotyping arrays, and massive parallel sequencing (also called next generation sequencing). This has opened up new possibilities for the evaluation of individuals with intellectual disabilities or global developmental delays who have previously eluded a genetic diagnosis [37,50,65-67]. Recent guidelines of American Academy of Pediatrics (AAP) on genetic testing in children warrant pediatrician's awareness of the newest genetic screening modalities.

Compilation of Observation and Planning

Assimilation and integration of data by specialists in a conference setting offers the most specific and accurate diagnosis.

Differential diagnoses are lengthy for children with cognitive deficits and include the following,

- Metabolic derangements
- Adrenal disease
- Ingestions of toxic substances (e.g. lead)
- Seizure disorders
- Subictal and infectious disorders (e.g. chronic Lyme disease)
- Physical causes (e.g. visual and hearing defects) that may impair cognitive development
- Genetic causes
- Congenital causes

Hurdles in the Management of Cognitive Deficits in Children

The scientific awareness and resources for prevention are limited in majority of the developing countries. Therefore, the challenge for this century is to encourage community leaders and government officials to take upon prevention of cognitive impairment as the highest priority for society. There are suggestions that specialists in child behavior and development work with United Nations agencies to develop a "World Cognitive Impairment Watch" to assess and assist each country annually in terms of risk factors, prevention programs, and early intervention programs.

Availability of technically trained manpower

In the United States, the number of child behavior and development specialists, including child psychologists, behavioral-developmental pediatricians, and child psychiatrists, is approximately 8,000. This amounts to one specialist for every 8,500 children aged <18 years. Compare this with Uganda, where, in 2002, there were two child psychologists, no child psychiatrists, and no behavioral-developmental pediatricians for a population of 10 million children. In Saudi Arabia, there is just one behavioral pediatrician. In Laos and Afghanistan, there are no child psychologists, child psychiatrists, or behavioral pediatricians, and no special education programs. This is the norm in several developing countries where there is little recognition that some diseases, which affect children in the early years of life, may have long-term negative impacts in terms of brain function. Thus, while number of children with cognitive limitations is increasing, they have little access to professional expertise.

Futuristic Plans for Children with Cognitive Deficits

All possible measures should be taken through judicious planning of the investigations so that the best possible etiology and pathology can be arrived at. Each member of the team should view the case as a whole and generate a constructive approach for remediation and rehabilitation.Cooperation with schools and other agencies involved

Obtaining signed releases of information and regularly scheduled (perhaps annually or more often if needed) routine conferences

Identification and management of concurrent illness, seizure disorders, or physical etiology of cognitive impairment in a medical setting

In the case of mental retardation, a combination of appropriate school placement with a high level of slow-paced appropriate material working towards specific goals, good behavioral management, and strategies at home is the most helpful intervention. Parents should be able to access educational and social service resources within the school setting.

Common behavioral problems, including oppositional behavior or social skills deficits, may be referred to a mental health professional skilled in working with such patients.

Children who have speech and language delays and other learning disabilities require an educational plan that not only sets goals each year, but also meets these goals. If the fully implemented and supportive academic approach turns out to be problematic by middle school, serious consideration should be given to prevocational and vocational training in high school.

Future Research

Theories on cognitive processing, based on neurobiological experimental paradigms on adult lesion model, may not be fully applicable to the developing cognitive functions of a child. The current concepts of Neuropsychology or Neurodevelopment may be further expanded and explored on the basis of psychological models of cognitive development such as that of Piaget's. Knowledge of the neurobiological basis of cognitive processing is influenced greatly by advances in contemporary sciences including, Computer Science, Genetics, Developmental Neurobiology, Neurochemistry, Neurophysics, Neuroradiology, and Nanotechnology. Therefore, a multidisciplinary team approach consisting of Neurologists, Pediatricians, Clinical Psychologists, Speech Language Pathologists, Physiotherapists, Occupational Therapists, Clinical Linguists, Special Educators, Geneticists, Biochemists, Neuroradiologists, and Computer experts is essential to develop a multisectoral protocol for the comprehensive management of cognitive impairments in children.

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