REVIEW ARTICLE

Developmental Brain Disorders in Children: Molecular Insights, Diagnosis, and Therapeutic Strategies

K. L. Varalakshmi[1], S. N. Umesh[2], Qudusia Sultana[3]*, Sowmya Srinivas[4], Sunita Pawar[5], Haritha S. Nath[6,7]

[1]Department of Anatomy, Ks Hegde Medical Academy, Mangaluru, Karnataka, India, [2]Department of Anatomy, Sri Chamundeshwari Medical College Hospital and Research Institute, Ramanagara, Karnataka, India, [3]Department of Anatomy, Yenepoya Medical College, Mangaluru, Karnataka, India, [4]Department of Prosthodontic and Crown and Bridge, JSS Dental College and Hospital, JSS Academy of Higher Education and Research, Mysuru, Karnataka, India, [5]Department of Pharmacy Practice, PES Modern College of Pharmacy, Pune, Maharashtra, India, [6]Department of Pharmacy Practice, Dr D Y Patil Unitech Society's, Dr D Y Patil Institute of Pharmaceutical Sciences and Research Centre, Pimpri-Chinchwad, Maharashtra, India, [7]Department of Pharmacy Practice, Dnyaan Prasad Global University, School of Pharmacy and Research, Pune, Maharashtra, India

Abstract

Brain disorders in children constitute a diverse group of neurological conditions that disrupt normal cognitive, motor, and emotional development. These disorders, often resulting from genetic abnormalities, environmental exposures, or perinatal injuries, include epilepsy, cerebral palsy, autism spectrum disorder, attention-deficit/hyperactivity disorder, and neurogenetic conditions such as Rett syndrome and Fragile X syndrome. This review aims to explore the molecular basis, clinical manifestations, diagnostic tools, and therapeutic strategies associated with pediatric brain disorders. A systematic review of contemporary research literature was conducted, with a focus on genetic studies, neuroimaging advancements, and the role of diagnostic tools such as electroencephalography and magnetic resonance imaging in early detection and management. The findings emphasize that early and accurate diagnosis, enabled by advances in neuroimaging and genetic testing, is critical for effective intervention and better outcomes. While current treatments are largely symptomatic and supportive, a deeper understanding of the molecular and genetic mechanisms has opened avenues for more precise and personalized therapies. These insights are transforming care approaches, aiming not only to manage symptoms but also to improve long-term quality of life for children and their families affected by developmental brain disorders.

Key words: Brain disorders, cerebral palsy, epilepsy

INTRODUCTION

Brain disorders in children encompass a wide spectrum of neurological conditions that can affect cognitive, motor, and emotional development. These disorders may be genetic, environmental, or acquired and can significantly impact a child's quality of life. Early diagnosis improves outcomes.[1-3] This review provides an overview of several major brain disorders in children, their molecular mechanisms, clinical manifestations, diagnostic approaches, and treatment options.[4-8]

Common symptoms of developmental brain disorders (DBDs)

DBDs are a group of conditions that arise from abnormal brain development occurring before, during, or shortly after birth. These disorders can significantly affect cognitive, motor, sensory, and emotional functions. A variety of symptoms are commonly observed in individuals with DBDs, which may vary in severity and combination depending on the specific disorder.

Table 1 summarizes the most frequently reported symptoms associated with DBDs, including structural abnormalities, sensory and motor impairments, cognitive deficits, and

Address for correspondence:
Qudusia Sultana, Department of Anatomy, Yenepoya Medical College, Deralakatte, Mangaluru - 575018, Karnataka, India. E-mail: qudsia.shariff@yahoo.co.in

Received: 12-02-2026
Revised: 19-03-2026
Accepted: 28-03-2026

Table 1: Common symptoms and characteristics of developmental brain disorders

S. No.	Symptom	Description	References
1	Corpus callosum malformation	Agenesis, hypogenesis, or dysgenesis of the corpus callosum causes developmental delays, poor coordination, and intellectual and social difficulties.	[9-11]
2	Language and reading difficulties	Delayed language development, phonological processing issues, and reading disorders such as dyslexia due to brain language area disruption.	[12]
3	Epilepsy	Seizures of varying severity often co-occur with intellectual disability or autism, frequently seen in neurodevelopmental conditions.	[13]
4	Visual and/or Hearing Impairment	Impaired sensory processing affects speech, language, and overall cognitive development.	[14]
5	Motor Impairment	Abnormal muscle tone, poor coordination, and delays in motor milestones are often linked to cerebral palsy and early brain injuries.	[15]
6	Intellectual delays	Below-average cognitive ability affecting reasoning, problem-solving, and adaptive behavior; may lead to a diagnosis of intellectual disability.	[16]
7	Learning difficulties	Problems in academic domains such as reading (dyslexia), writing (dysgraphia), and math (dyscalculia), often accompanied by attention-deficit/hyperactivity disorder or similar disorders.	[17]

learning difficulties. These manifestations not only hinder normal developmental progress but also require tailored therapeutic and educational interventions for optimal management.

Objectives

1. To examine the common types of pediatric brain disorders, including epilepsy, cerebral palsy (CP), autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), and neurogenetic syndromes such as Rett and Fragile X syndromes
2. To explore the molecular and genetic mechanisms underlying these conditions, including ion channel mutations, neuroinflammation, synaptic dysfunction, and gene-associated syndromes
3. To review the current diagnostic tools, such as electroencephalography (EEG), magnetic resonance imaging (MRI), and genetic testing, that aid in early and accurate diagnosis
4. To discuss the clinical presentation and symptomatology associated with various brain disorders in children
5. To evaluate existing treatment strategies and supportive therapies aimed at improving quality of life and functional outcomes
6. To highlight recent advances in personalized and targeted therapeutic interventions for DBDs.

TYPES OF BRAIN DISORDERS IN CHILDREN

Epilepsy

Epilepsy is one of the most common neurological disorders in children, characterized by recurrent seizures due to abnormal electrical activity in the brain. Seizures may range from generalized tonic-clonic seizures to focal seizures, depending on the brain area involved.

Molecular mechanisms

Epilepsy is often caused by abnormalities in the brain's electrical activity, which can result from a variety of genetic, developmental, and environmental factors. The molecular mechanisms underlying epilepsy can be categorized into several key pathways:

As shown in Figure 1, epilepsy arises through multiple molecular mechanisms, including ion channel mutations, synaptic dysfunction, genetic syndromes, and neuroinflammation. These pathways disrupt neuronal signaling and increase excitability, contributing to seizure development.

1. Ion channel mutations: A significant proportion of epilepsy cases are due to mutations in ion channel genes. For example:
   - *SCN1A* gene mutations lead to a dysfunctional sodium channel, resulting in a loss of inhibitory control over neuronal firing. This mutation is responsible for Dravet syndrome, a severe form of epilepsy
   - KCNQ2 mutations affect potassium channels, leading to defects in neuronal hyperpolarization, which is necessary for maintaining the resting potential and preventing excessive excitability.[18]
2. Synaptic dysfunction: Epileptic seizures can also arise from defects in synaptic function.
   - Synaptic vesicle protein 2a (SV2A): Mutations in genes encoding proteins such as SV2A or GABA receptors can disrupt neurotransmitter release or receptor activity, contributing to excitatory/inhibitory imbalance.

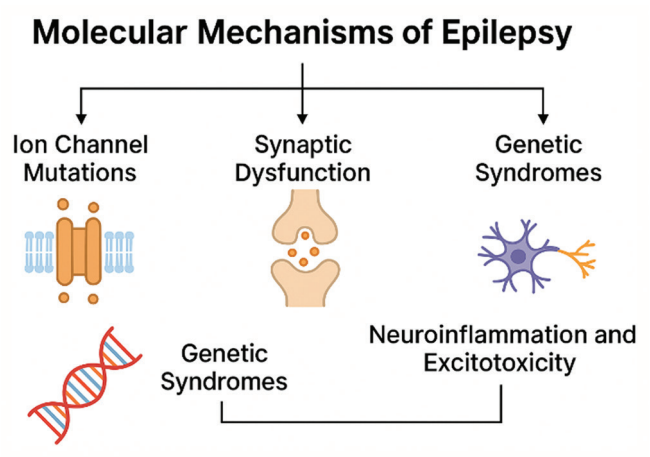

Figure 1: Molecular mechanisms underlying epilepsy

3. Genetic syndromes: Various epilepsy syndromes have distinct genetic causes, such as:
    - *TSC1*/*TSC2* gene mutations lead to tuberous sclerosis complex, which results in brain malformations and an increased risk of seizures.
4. Neuroinflammation and excitotoxicity: Chronic seizures can cause excitotoxic damage to neurons, a process where excessive glutamate release leads to neuronal death due to overactivation of NMDA receptors. This cycle of injury and inflammation can exacerbate epilepsy.[14]

Diagnosis of DBDs

The diagnosis of DBDs, particularly when epilepsy or other neurological symptoms are involved, requires a combination of clinical evaluation and advanced diagnostic tools. These tools help in identifying structural, electrical, and genetic abnormalities in the brain. Below are some key diagnostic methods:

EEG

EEG is a non-invasive procedure that records the brain's electrical activity using electrodes placed on the scalp. It is the primary diagnostic tool for epilepsy and helps detect abnormal electrical discharges or patterns that are indicative of seizures.

- Types of EEG:
    - Routine EEG: Conducted while the patient is awake or asleep to detect interictal epileptiform discharges
    - Video EEG monitoring: Combines EEG with continuous video recording to correlate seizure activity with electrical changes
    - Ambulatory EEG: Allows for long-term recording in the patient's home to capture infrequent events.[19]

EEG helps to

- Confirm the diagnosis of epilepsy
- Classify the type of seizures (focal or generalized)
- Localize the origin of epileptic activity in the brain
- Assess the effectiveness of treatment.

Treatment

Antiepileptic drugs (AEDs) are the first-line treatment for epilepsy. In cases of drug-resistant epilepsy, surgical options such as resective surgery or the implantation of a vagus nerve stimulator may be considered to reduce seizure frequency and improve quality of life.

CP

CP is a group of disorders affecting movement and posture due to abnormal brain development or damage to the developing brain. It is commonly diagnosed in infancy or early childhood.

Molecular mechanisms

CP is primarily caused by injury or abnormal development of the brain's motor areas, which disrupts the control of movement, as shown in Figure 2. The molecular mechanisms include:

1. Hypoxic-ischemic injury: The most common cause of CP, particularly in preterm infants, involves brain damage due to a lack of oxygen (hypoxia) or restricted blood flow (ischemia) during critical periods of brain development.
    - This injury leads to cell death and inflammation, primarily in the periventricular white matter, resulting in periventricular leukomalacia (PVL), which is often observed in premature infants.
2. Genetic factors: Although CP is primarily acquired, some forms have genetic predispositions. For example:
    - Mutations in the *KIF1A* gene, involved in axonal transport, have been associated with a hereditary form of CP
    - Genetic mutations affecting neuronal migration and synaptic plasticity may also contribute to the development of CP
3. Neuroinflammation: Immune system activation during brain injury leads to the release of pro-inflammatory cytokines, which exacerbate neuronal injury and hinder normal brain development.
4. Glial cell activation: In CP, activation of glial cells, especially astrocytes and microglia, may cause the release of pro-inflammatory signals that worsen neuronal injury. This neuroinflammatory response can contribute to developing spasticity and motor deficits.[20,21]

Neurological examination

A comprehensive neurological examination is a foundational diagnostic step in evaluating a child suspected of having a DBD. This examination is typically performed by a pediatric neurologist and includes:

- Assessment of motor development: Evaluation of muscle tone (hypotonia or hypertonia), strength, coordination, and reflexes
- Developmental milestones: Monitoring of age-appropriate milestones such as sitting, crawling, walking,

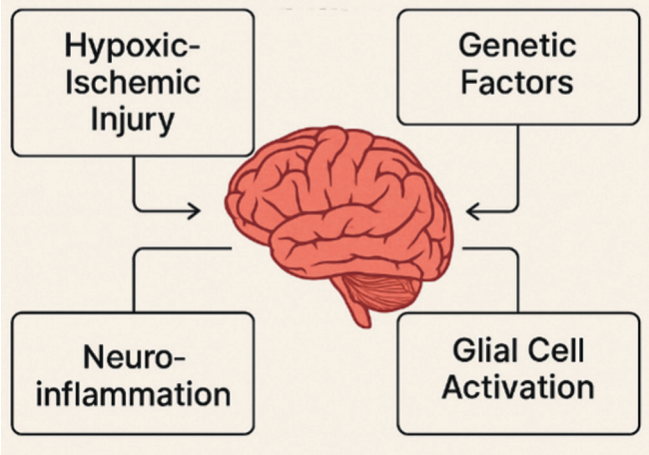

Figure 2: Molecular mechanisms of cerebral palsy

and speech
- Observation of movement patterns: Identifying abnormalities such as spasticity, dystonia, or ataxia
- Sensory function testing: Evaluation of vision, hearing, and proprioception.

This examination helps assess motor and neurological impairments and can guide the need for further diagnostic testing.[22]

MRI

MRI is a non-invasive imaging tool that provides detailed views of the brain's anatomy. It is commonly utilized in children with developmental delays, abnormal neurological examinations, or seizures.

- Uses in DBDs:
  - Detecting structural abnormalities such as cortical dysplasia, ventriculomegaly, or agenesis of the corpus callosum
  - Identifying white matter injury, particularly PVL – a common finding in preterm infants associated with CP
  - Assessing brain growth and myelination patterns is important for diagnosing conditions such as leukodystrophies.

MRI can help differentiate between congenital and acquired causes of developmental delays and support a definitive diagnosis.[23]

Genetic testing

Genetic testing has become increasingly valuable in diagnosing DBDs, especially in children with unexplained developmental delays, congenital anomalies, or a family history of neurological disorders.
- When to consider genetic testing:
  - No clear etiology is found on clinical or imaging studies
  - Presence of dysmorphic features or multiple congenital anomalies
  - Strong family history or consanguinity
- Common techniques:
  - Chromosomal microarray (CMA): First-line test for detecting deletions/duplications
  - Whole exome sequencing (WES): Explores all coding genes and is useful in complex or undiagnosed cases
  - Targeted gene panels: For known disorders such as Rett syndrome or tuberous sclerosis.

Identifying a genetic cause can:
- Aid in prognosis and personalized treatment
- Inform family planning and genetic counseling
- Sometimes predict the risk of progression or associated complications.[24]

Treatment

There is no cure for CP, but therapies such as physical therapy, occupational therapy, and speech therapy are essential. Medications such as baclofen and botulinum toxin can help manage spasticity. In severe cases, surgical interventions may be needed.[18]

ASD

ASD is a neurodevelopmental disorder characterized by impairments in social interaction, communication, and repetitive behaviors. It is estimated that 1 in 54 children are diagnosed with ASD.

Molecular mechanisms

ASD is a complex neurodevelopmental disorder influenced by both genetic and environmental factors. Molecular mechanisms include:
1. Synaptic dysfunction: Many ASD-related genes are involved in synaptic function. For example:
   - SHANK3 mutations, which affect synaptic signaling and receptor clustering, are associated with Phelan–McDermid Syndrome, a form of ASD
   - Mutations in the *MECP2* gene (also implicated in Rett syndrome) can affect synaptic plasticity and neural connectivity.
2. Neuroinflammation: Research suggests that an inflammatory response in the brain, potentially due to maternal immune activation during pregnancy, plays a role in the development of ASD. Elevated levels of pro-inflammatory cytokines can interfere with normal neurodevelopment, contributing to ASD symptoms.
3. Neuronal connectivity: Abnormalities in the formation and maintenance of neuronal connections, especially in the prefrontal cortex and amygdala, which regulate social behavior and emotion processing, have been observed in ASD.
4. Dysregulated protein synthesis: The mechanistic target

of rapamycin (mTOR) pathway, which regulates protein synthesis, has been implicated in ASD. Mutations affecting mTOR signaling may cause abnormal protein production and neuronal growth, contributing to developmental delays and cognitive impairments.[14]

Autism diagnostic observation schedule (ADOS)

The ADOS is considered the gold standard for observational assessment in the diagnosis of ASD. It is a semi-structured, standardized tool used by trained clinicians to evaluate social interaction, communication, play, and imaginative use of materials.

- Modules: ADOS includes multiple modules designed for individuals of different language abilities and developmental levels, from toddlers to adults
- Procedure: The assessment typically takes 30–60 min and involves activities that elicit social and communicative behaviors relevant to autism
- Purpose: Helps clinicians observe and rate behaviors commonly associated with ASD in a controlled setting.

ADOS is often used in conjunction with developmental history and clinical judgment to confirm or rule out a diagnosis.[19]

Autism diagnostic interview-revised (ADI-R)

The ADI-R is a structured, comprehensive, caregiver-based interview designed to assess behaviors related to autism. It provides a historical view of the child's development and symptomatology.

- Format: Conducted with a parent or primary caregiver, typically over 1.5–2.5 h
- Content: Covers three core domains – language/communication, reciprocal social interactions, and restricted/repetitive behaviors
- Value: Particularly useful for evaluating symptoms that may have been present in early childhood but are no longer overtly observable

ADI-R complements the ADOS and contributes to a more thorough and accurate diagnosis by capturing early developmental milestones and patterns.[20]

Genetic testing

While not routinely performed for all individuals with ASD, genetic testing is recommended when there is a suspicion of an underlying genetic syndrome, intellectual disability, or dysmorphic features.

- Common syndromes associated with ASD:
  - Fragile X syndrome: The most common inherited cause of intellectual disability
  - Rett syndrome: Primarily affects girls and includes regression of motor and language skills
  - Tuberous Sclerosis Complex: Characterized by benign tumors and neurological symptoms.
- Types of genetic tests:
  - Chromosomal microarray analysis (CMA): Detects copy number variations
  - Fragile X DNA testing: Specifically identifies *FMR1* gene mutations
  - WES: Used in complex or undiagnosed cases.

Genetic findings can help guide clinical management, offer prognostic insights, and provide genetic counseling to families.[21]

Treatment

There is no cure, but early intervention with behavioral therapies (e.g., applied behavior analysis) can significantly improve outcomes.[22,23] Medications may help manage specific symptoms such as anxiety or irritability, but no medication addresses the core symptoms of ASD.

ADHD

ADHD is characterized by symptoms of inattention, hyperactivity, and impulsivity. It affects approximately 5–7% of school-aged children and can persist into adulthood.

Molecular mechanisms

ADHD is characterized by inattention, hyperactivity, and impulsivity. The molecular mechanisms underlying ADHD primarily involve neurotransmitter imbalances:

1. Dopaminergic dysfunction: Abnormalities in the dopamine system are central to ADHD. Studies show reduced dopamine receptor (D2) availability and dopamine transporter (DAT1) dysfunction in key brain regions such as the prefrontal cortex and striatum, which are involved in attention and impulse control.
2. Genetic factors: Several genetic loci have been linked to ADHD, including:
   - Dopamine receptor D4 and DAT1 polymorphisms, both of which affect dopamine signaling
   - Alpha-2A adrenergic receptor mutations can influence the regulation of norepinephrine, which is crucial for attention.
3. Neuroanatomical changes: Structural differences in brain regions, particularly the prefrontal cortex, basal ganglia, and cerebellum, have been identified in ADHD. These regions are involved in regulating attention, motor control, and executive function.
4. Glutamatergic system: Abnormalities in glutamate signaling have been implicated in ADHD, affecting synaptic plasticity and neurotransmission in the

prefrontal cortex, which may contribute to cognitive dysfunction.[24,25]

Conners rating scales

The Conners rating scales are among the most widely used standardized tools for evaluating ADHD symptoms and related behavioral issues. These scales are completed by parents, teachers, and sometimes the child (age-dependent) and provide valuable insight into behavior across settings.

- Versions: Includes Conners 3 (for children aged 6–18) and Conners Early Childhood (for ages 2–6).
- Scales covered:
  - Inattention
  - Hyperactivity/impulsivity
  - Executive functioning
  - Learning problems
  - Peer relations and aggression.
- Scoring: Yields T-scores that help clinicians assess symptom severity in comparison to age-matched peers.

The Conners scales are frequently used in conjunction with clinical interviews and observational data to confirm an ADHD diagnosis.[26]

Behavioral assessment

Behavioral assessments are crucial in diagnosing ADHD, especially because the disorder must manifest across multiple settings (e.g., home and school) and cause functional impairment.

- Direct observation: Clinicians may observe a child in structured and unstructured settings to evaluate attention span, impulsivity, and motor activity
- Behavior logs: Parents and teachers often maintain daily logs of behaviors to help detect patterns or triggers
- Structured interviews: Clinical interviews with caregivers and teachers provide additional context about the duration, onset, and impact of behaviors.

This approach aligns with DSM-5 criteria, emphasizing the persistence and pervasiveness of symptoms to differentiate ADHD from situational or environmental influences.[27]

Neuroimaging

While not routinely used for clinical diagnosis, neuroimaging techniques have provided valuable insights into the neurobiological underpinnings of ADHD.

- Functional MRI (fMRI): Studies using fMRI have shown altered activity in brain areas associated with attention and executive function, like the prefrontal cortex, anterior cingulate cortex, and basal ganglia
- Positron emission tomography (PET): PET scans reveal abnormal dopamine transporter activity, particularly in the striatum and prefrontal regions, suggesting dysregulation of neurotransmitter systems
- Structural imaging: Some studies indicate reduced total brain volume or delayed cortical maturation in children with ADHD.

Although these methods are primarily used in research settings, they support the neurodevelopmental basis of ADHD and may, in the future, contribute to biomarkers for diagnosis.[28]

Treatment

The primary treatment for ADHD is the use of stimulant medications such as methylphenidate and amphetamines. Non-stimulants such as atomoxetine may also be used. Behavioral therapy and environmental modifications are often integrated into treatment.[29]

Neurogenetic disorders

Neurogenetic disorders, including Rett syndrome, Fragile X syndrome, and mitochondrial disorders, are characterized by cognitive and developmental delays, as well as neurological impairments. These disorders typically have a genetic basis.

Molecular mechanisms

Neurogenetic disorders in children, including Rett syndrome, Fragile X syndrome, and mitochondrial disorders, are caused by mutations in specific genes that disrupt normal brain development and function:

1. Rett syndrome
   - *MECP2* gene mutations cause abnormal DNA methylation and histone modifications, leading to impaired neuronal differentiation, synaptic function, and plasticity. This leads to a loss of previously acquired skills and progressive neurological decline in affected children.
2. Fragile X syndrome
   - Caused by a CGG trinucleotide repeat expansion in the *FMR1* gene, leading to silencing of the gene and a lack of fragile X mental retardation protein (FMRP), which plays a crucial role in synaptic plasticity and dendritic spine maturation. The absence of FMRP leads to an overabundance of protein synthesis at synapses, disrupting normal synaptic function and contributing to cognitive deficits.
3. Mitochondrial disorders
   - Mitochondrial disorders involve mutations in mitochondrial DNA or nuclear genes encoding mitochondrial proteins. These mutations impair mitochondrial function, leading to a lack of energy production in neurons. This can result in developmental delays, motor deficits, and seizures due to insufficient ATP for neuronal activity.[30]

Genetic and metabolic brain disorders such as Rett syndrome, Fragile X syndrome, and mitochondrial disorders often

present with developmental delays, cognitive impairments, and neurologic symptoms. Accurate diagnosis is essential for early intervention, personalized care, and family counseling. Below are key diagnostic modalities used in clinical practice:

Genetic testing

Genetic testing is a cornerstone in diagnosing neurogenetic disorders, especially when clinical features suggest a specific syndrome or when a family history is present.

- Rett syndrome
  - Caused by mutations in the *MECP2* gene on the X chromosome
  - Affects mainly females and is characterized by normal early growth followed by a regression in motor and language skills
  - Genetic testing confirms the diagnosis in over 95% of classical cases.
- Fragile X syndrome
  - Results from a CGG trinucleotide repeat expansion in the *FMR1* gene
  - It is the most common inherited cause of intellectual disability and is often associated with autism-like behaviors
  - DNA testing determines the number of CGG repeats, identifying full mutations, premutations, or normal alleles.
- Utility
  - Facilitates early diagnosis and intervention
  - Informs genetic counseling for families regarding inheritance patterns and recurrence risks.[31]

MRI

MRI plays a critical role in diagnosing mitochondrial and metabolic disorders, where structural and functional brain abnormalities are often present.

- Mitochondrial disorders:
  - These disorders affect cellular energy production and may cause progressive neurodegeneration.
  - MRI may reveal:
    - Basal ganglia lesions
    - Cerebral atrophy
    - Symmetrical signal abnormalities, particularly in the brainstem or thalamus
  - MRI findings are often suggestive, prompting further biochemical testing or muscle biopsy.
- Other applications:
  - In Rett syndrome, MRI may show non-specific findings such as cerebral atrophy
  - In Fragile X, enlarged ventricles and increased caudate volume have been noted in some individuals.[32]

Neurological examination

A thorough neurological and developmental assessment is essential to identify clinical signs suggestive of genetic or metabolic disorders.

- Developmental milestones: Careful evaluation of motor, language, cognitive, and social milestones helps detect delays or regressions.
  - Example: Children with Rett syndrome may show normal development initially, followed by loss of hand skills and speech
  - In Fragile X, signs may include developmental delay, poor eye contact, and social anxiety.

- Cognitive functioning
  - Evaluations often reveal intellectual disability, impaired executive functioning, or speech/language difficulties
  - Behavioral characteristics such as hand-wringing (Rett) or hyperactivity (Fragile X) provide important diagnostic clues.
- Motor examination
  - In mitochondrial disorders, muscle weakness, ataxia, or movement disorders may be observed.[33]

These clinical insights guide further genetic or neuroimaging studies and help distinguish between overlapping syndromes.

Treatment

Treatment is supportive and focuses on managing symptoms. In Rett syndrome, therapies target motor skills and communication. Fragile X syndrome may benefit from medications for anxiety and hyperactivity, while mitochondrial disorders require treatment to improve mitochondrial function.[34]

Summary

DBDs in children encompass a wide range of conditions caused by genetic, environmental, or acquired factors, significantly affecting cognitive, motor, and emotional development. Early recognition and diagnosis are essential for improving outcomes. This review focused on the common symptoms, major types, molecular mechanisms, diagnostic tools, and treatment strategies for two prominent disorders: epilepsy and CP.

Common symptoms of DBDs include malformations of the corpus callosum, language and reading difficulties, epilepsy, visual and hearing impairments, motor delays, intellectual disabilities, and learning disorders. Epilepsy, a prevalent neurological condition, is linked to mutations in ion channel genes, synaptic dysfunction, and neuroinflammation. Diagnosis relies heavily on EEG, with AEDs and surgical interventions being the mainstays of treatment.

CP results primarily from hypoxic-ischemic injury to the developing brain, with contributions from genetic factors, neuroinflammation, and glial cell activation.

A comprehensive neurological exam, MRI, and genetic testing are vital in the diagnostic process. Treatments for CP focus on supportive therapies, addressing motor deficits, and managing associated conditions.

CONCLUSION

DBDs pose significant challenges to affected children and their families. Understanding the diverse presentations and underlying molecular mechanisms is crucial for accurate diagnosis and effective intervention. Advances in diagnostic tools – like EEG, MRI, and genetic sequencing – have greatly enhanced our ability to identify and treat these disorders early. Continued research into the molecular basis of DBDs will pave the way for more personalized and targeted therapies, ultimately improving quality of life and developmental outcomes for children with these complex neurological conditions.

REFERENCES

1. Berg AT, Rychlik K, Levy SR, Testa FM. Complete remission of childhood-onset epilepsy: Stability and prediction over two decades. Brain 2014;137:3213-22.
2. Cunha-Reis D, Caulino-Rocha A. VIP modulation of hippocampal synaptic plasticity: A role for VIP receptors as therapeutic targets in cognitive decline and mesial temporal lobe epilepsy. Front Cell Neurosci 2020;14:153.
3. Allen J, Zareen Z, Doyle S, Whitla L, Afzal Z, Stack M, *et al*. Multi-organ dysfunction in cerebral palsy. Front Pediatr 2021;9:668544.
4. Gong C, Zeng P, Lian B, Li J, Liu J, Liu Y, *et al*. Associations of risk factors and the number of risk factors with the classification, GMFCS level and comorbidities with cerebral palsy: a retrospective study. BMC pediatrics. 2024;24(1):822.
5. Lord C, Elsabbagh M, Baird G, Veenstra-Vanderweele J. Autism spectrum disorder. Lancet 2018;392:508-20.
6. Geschwind DH. Genetics of autism spectrum disorders. Trends Cogn Sci 2011;15:409-16.
7. Polanczyk G, De Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: A systematic review and metaregression analysis. Am J Psychiatry 2007;164:942-8.
8. Alves PN, Foulon C, Karolis V, Bzdok D, Margulies DS, Volle E, *et al*. Subcortical Anatomy of the Default Mode Network: A Functional and Structural Connectivity Study. [BioRxiv Preprint]; 2019.
9. Neul JL, Kaufmann WE, Glaze DG, Christodoulou J, Clarke AJ, Bahi-Buisson N, *et al*. Rett syndrome: Revised diagnostic criteria and nomenclature. Ann Neurol 2010;68:944-50.
10. D'Oosterlinck F, Goethals I, Boekaert E, Schuyten G. Child and adolescent psychiatry. Soc Psychiatry PsychiatrEpidemiol 2008;43:635-41.
11. Paul LK. Developmental malformation of the corpus callosum: A review of typical callosal development and examples of developmental disorders. J Neurodev Disord 2011;3:3-27.
12. Bishop DV. Genes, cognition, and communication: Insights from neurodevelopmental disorders. Ann N Y Acad Sci 2009;1156:1-18.
13. Berg AT, Scheffer IE. New concepts in classification of the epilepsies: Entering the 21st century. Epilepsia 2011;52:1058-62.
14. Papatheodoropoulos C. Compensatory regulation of excitation/inhibition balance in the ventral hippocampus: Insights from fragile X syndrome. Biology (Basel) 2025;14:363.
15. Novak I, Morgan C, Adde L, Blackman J, Boyd RN, Brunstrom-Hernandez J, *et al*. Early, accurate diagnosis and early intervention in cerebral palsy: Advances in diagnosis and treatment. JAMA Pediatrics 2017;171:897-907.
16. Schalock RL, Borthwick-Duffy SA, Bradley VJ, Buntinx WH, Coulter DL, Craig EM, *et al*. Intellectual Disability: Definition, Classification, and Systems of Supports. 11th ed. Washington, DC: American Association on Intellectual and Developmental Disabilities; 2010.
17. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.
18. Zavala-Tecuapetla C, Cuellar-Herrera M, Luna-Munguia H. Insights into potential targets for therapeutic intervention in epilepsy. Int J Mol Sci 2020;21:8573.
19. Smith SJ. EEG in the diagnosis, classification, and management of patients with epilepsy. J Neurol Neurosurg Psychiatry 2005;76:ii2-7.
20. Amador A, Bostick CD, Olson H, Peters J, Camp CR, Krizay D, *et al*. Modelling and treating GRIN2A developmental and epileptic encephalopathy in mice. Brain 2020;143:2039-57.
21. Greco P, Nencini G, Piva I, Scioscia M, Volta CA, Spadaro S, *et al*. Pathophysiology of hypoxic-ischemic encephalopathy: A review of the past and a view on the future. Acta Neurol Belgica 2020;120:277-88.
22. Shevell MI, Ashwal S, Donley D, Flint J, Gingold M, Hirtz D, *et al*. Practice parameter: Evaluation of the child with global developmental delay [RETIRED] report of the quality standards subcommittee of the American academy of neurology and the practice committee of the child neurology society. Neurology 2003;60:367-80.
23. Siva A. Common clinical and imaging conditions misdiagnosed as multiple sclerosis: A current approach to the differential diagnosis of multiple sclerosis. Neurol Clin 2018;36:69-117.
24. Srivastava S, Love-Nichols JA, Dies KA, Ledbetter DH, Martin CL, Chung WK, *et al*. Meta-analysis and multidisciplinary consensus statement: Exome sequencing is a first-tier clinical diagnostic test for individuals with neurodevelopmental disorders. Gen Med 2019;21:2413-21.
25. Mahajan R, Mostofsky SH. Neuroimaging

endophenotypes in autism spectrum disorder. CNS Spectrums 2015;20:412-26.
26. Chahrour M, Jung SY, Shaw C, Zhou X, Wong ST, Qin J, *et al*. MeCP2, a key contributor to neurological disease, activates and represses transcription. Science 2008;320:1224-9.
27. Lord C, Risi S, Lambrecht L, Cook EH Jr., Leventhal BL, DiLavore PC, *et al*. The autism diagnostic observation schedule-generic: A standard measure of social and communication deficits associated with the spectrum of autism. J Autism Dev Disord 2000;30:205-23.
28. Rutter M, Le Couteur A, Lord C. Autism Diagnostic Interview-Revised. Vol. 29. Los Angeles, CA: Western Psychological Services; 2003. p. 30.
29. Schaefer GB, Mendelsohn NJ, Professional Practice and Guidelines Committee. Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. Genet Med 2013;15:399-407.
30. Cortese S, Kelly C, Chabernaud C, Proal E, Di Martino A, Milham MP, *et al*. Toward systems neuroscience of ADHD: A meta-analysis of 55 fMRI studies. Am J Psychiatry 2012;169:1038-55.
31. Marriage BJ, Clandinin MT, Macdonald IM, Glerum DM. Cofactor treatment improves ATP synthetic capacity in patients with oxidative phosphorylation disorders. Mol Genet Metabol 2004;81:263-72.
32. Percy AK. Rett syndrome: Exploring the autism link. Arch Neurol 2011;68:985-9.
33. Hagerman RJ, Hagerman PJ. The fragile X premutation: Into the phenotypic fold. Curr Opin Genet Dev 2002;12:278-83.
34. Sulaiman SA, Rani ZM, Radin FZ, Murad NA. Advancement in the diagnosis of mitochondrial diseases. J Transl Genet Genom 2020;4:159-87.

Source of Support: Nil. **Conflicts of Interest:** None declared.