Disorder	Stream of Development*				Clinical Manifestations/ Associated Features/ Diagnosis	Etiology
	M	C-NV	L	S/A		
Developmental disabilities						
Developmental delay		√	√		- Observational diagnosis – degree of delay in specific streams of development (>2 SD below the mean of functioning) - Non-specific diagnosis (usually in preschoolers), usually replaced as get older with other more specific diagnosis (e.g., ID, LD, others)	- May be none identified; more severe delays more likely to be associated with organic etiology (exposure, genetic, other) - Chromosomal abnormalties seen 4-34%
Intellectual disability (ID)		√	√		- Clinical diagnosis using standardized assessment tools (e.g., IQ tests for verbal and non-verbal skills) - Score is > 2 SD below mean (score under 70) - Prevalence 1-10% of population (depends on severity)	- May be none identified; more severe delays more likely to be associated with organic etiology (exposure, genetic, other)
ADHD		√			- Clinical diagnosis – standardized rating scales (from multiple settings – including home, school, community) and cognitive - May be associated with behavioral disorders (such as oppositional defiant disorder, conduct disorder) and/or learning disorders (see LD)	- Genetics of ADHD well studied
Autism Spectrum Disorders (ASD)			√	√	- Clinical diagnosis – using caregiver interview, standardized questionnaire, standardized observation tools - Core features – social/communication and behavioral impairment (DSM5) - High frequency of associated comorbid conditions (e.g., behavior difficulties, affective/ psychiatric; ADHD; language	- Genetics under investigation – many studies; highly genetic/ familial - Presence of associated disorders/ features may “drive” the genetics (e.g., seizures/ epilepsy

Disorder	Stream of Development*				Clinical Manifestations/ Associated Features/ Diagnosis	Etiology
	M	C-NV	L	S/A		
					based learning problems, other) - Broader autism phenotype common – subthreshold symptoms in relatives (supports genetics)	
Learning disorders (LD)		√	√		- Clinical diagnosis – using standardized language tools (questionnaires, direct testing) - Frequent overlap with other disorders (e.g., ASD; co-occurs with ADHD; delays and impairment with	Some studies of genetics Highly familial
Hearing loss			√		- Clinical suspicion - Confirmation by audiologic examination - Physical manifestations (e.g., ear anomalies, others) - Ophthalmologic evaluation - May have an impact on streams of development (e.g. , language) with resulting/ associated developmental disorder	- Organic/ congenital - May be PART OF other genetic syndrome or disorder - Acquired (e.g., injury, trauma)
Vision impairment		√			- Clinical suspicion - Physical manifestations (e.g., cataract, anomalies, others) - Ophthalmologic evaluation - May have an impact on streams of development with resulting/ associated developmental disorder (such as problem solving)	- Organic/ congenital - May be PART OF other genetic syndrome or disorder - Acquired (e.g., injury, trauma)
Communication disorders (Language impairment/ disorder)			√		- May be identified early by milestone delay(s) in language or later with processing or other language impairment	- Genetics has been studied - May be PART OF other genetic syndrome or disorder

Disorder	Stream of Development*				Clinical Manifestations/ Associated Features/ Diagnosis	Etiology
	M	C-NV	L	S/A		
					- Note: language delay common in preschoolers (5-10%) and may "catch up" later and not be significant. - Clinical evaluation using standardized questionnaires, speech/language evaluation, cognitive evaluation - May be part of other broader developmental disorder (such as LD or ID)	
Cerebral Palsy	√				- May be identified early by gross motor (and/or fine motor) milestone delay(s) - Clinical diagnosis based on – ongoing delays and abnormal quality of movement and posture	- Metabolic and/or Genetic disorders - Acquired – perinatal injury or anoxia - Work-up may include neuroimaging, metabolic studies, genetic studies

<u>Developmental disabilities</u>

- Descriptive/ category of disorder
- diagnosed using clinical evaluation
- may be associated with different etiologies
- *Core "streams" of development (1 or more involved)
    - Motor (M)
    - Cognitive (C)
        - Problem solving/ non-verbal (NV)
        - Language (L)
    - Social/ adaptive (S/A)
- May have associated/comorbid

"There is no … limit to the potential number of gene defects and organic brain syndromes thast could contribute to neurodevelopmental disabilities…"

Genetic Disorders associated with specific genetic syndromes or diagnoses

- High association between genetic variation(s) and clinical manifestations of developmental disorder
- Specific genetic findings do not always result in the same clinical manifestations (or severity) of developmental disorders
    - Example – Fragile X – not all individuals will have ASD; some individuals will have milder cognitive impairment
- These diagnoses might be made based on clinical manifestations – including dysmorphic features, associated problems (e.g., neuroimaging abnormalities), characteristic clinical features (e.g., regression and hand wringing in Rett's syndrome) AND/OR referral to genetics service A AND/OR laboratory studies.

Commonly found syndromes associated with developmental disorders

1. Angelman's Syndrome
2. Fragile X (FMR-1 related disorders) [most common cause of inherited ID)
3. Prader-Willi Syndrome
4. Rett's Syndrome
5. Rubinstein-Taybe Syndrome
6. Smith-Magenis
7. Velocardiofacial Syndrome
8. Williams Syndrome
9. OTHERS (not included in Technical Report)
    a. Tuberous Sclerosis Complex
    b. Neurofibromatosis
    c. Cytogenetic abnormalities (for example)
        i. Trisomy 21
        ii. Turner syndrome
    d. Duplications – IDIC15, others
    e. PTEN gene mutations (e.g., with macrocephaly
    f. Muscular