An Approach to Evaluation of Developmental Delay

Michael Shevell MD, CM, FRCP
Division of Pediatric Neurology
Montreal Children’s Hospital-McGill University Health Centre
Case #1-Jeremy

- 2 ½ year old boy
- Second child of his parents
- Mother’s brother “slow”
  - Special school attendance
  - Group home
  - Sheltered workshop
- Pregnancy/labour/delivery uneventful
- PMHx uneventful/No current medications
Case #1-Jeremy

- First birthday initial parental concern-not yet sitting or babbling
- Sat @ 15 mths, crawled @ 18 mths, walked @ 2 yrs
- Two specific words currently, points & gestures
- Does not follow commands, inconsistent eye contact, restless, inattentive
- No loss or regression of skills
Case #1-Jeremy

- No obvious dysmorphic features
- No focal findings
- Developmental
  - Unable to go up/down stairs
  - Unable to scribble, use a spoon
  - No distinct words/comprehension demonstrated
  - Poor eye contact
  - Could not identify body parts
Case #2-Susan

- 1 ½ year old only child
- No FHx of neurological problems
- Mother had 3 first and second trimester miscarriages prior to her birth
- Pregnancy itself uneventful
- Labour spontaneous @ term with uneventful delivery
- No neonatal difficulties aside from mild jaundice
- No PMHx/current medications
Case #2-Susan

- First concern @ 6 mths - not reaching with right hand
- Sat @ 1 yr - Now pulling to stand & cruising but not walking
- First words @ 1 yr - Now multi-word vocabulary, two word phrases, good comprehension
- Sociable, jovial, playful child
Case #2-Susan

Examination

- No facial asymmetry
- No obvious field cuts
- Left hand preference
- No dyskinesias
- Palmar grasp on right, pincer on left
- Right thumb slightly smaller than the left
- Heel cord tight on right
- Stretch reflexes brisker on right with upgoing plantar response
Case # 3-Robert

- 3 year old boy-middle of three children
- Father had a learning disability when younger
- Uneventful pregnancy/labour/delivery
- No neonatal complications
- No significant PMHx/current medications
Case #3 - Robert

- First concerned @ 2 yrs - not speaking
- Good comprehension - follows commands, identifies body parts/colours
- Little spontaneous speech - first words @ 2 ½, 20 word vocabulary, no two word phrases
- Gestures/points
- Plays with toys and others
- Makes eye contact, no repetitive behaviours
- Normal general & neurological examination
Neurodevelopmental Disabilities

- Chronic disorders
- Etiologically heterogeneous
- Essential feature a recognized disturbance or delay in one or more recognized developmental domains
- Significant & continuing impact on a child’s developmental/functional progress
- Common pediatric problem affecting 5-10% of the pediatric population
Developmental Domains

- **Motor**
  - Gross
  - Fine
- **Speech/Language**
  - Receptive/Expressive elements
  - Phonology/Syntax/Semantics/Fluency skills
- **Social**
- **Cognitive**
  - Concrete & Abstract reasoning
  - Problem solving/Number concept
- **Activities of Daily Living**
  - Feeding, dressing, toileting, self-hygiene
Neurodevelopmental Disabilities

- Global Developmental Delay
- Mental Retardation/Intellectual Disability
- Developmental Language Disorders (Specific Language Impairment)
- Gross Motor Delay
  - +/- Cerebral Palsy
- Autistic Spectrum Disorders
- Primary Sensory Impairments
  - Visual
  - Auditory
- School Related
  - ADHD
  - Learning Disability
Global Developmental Delay

- Significant delay in two or more developmental domains
  - Usually all domains affected
- Significant = performance two or more standard deviations below the mean on age appropriate standardized norm referenced tests

- Term usually applied to children less than 5 years of age
- Later diagnosis of mental retardation/intellectual disability frequent
Mental Retardation/Intellectual Disability

- Significant sub-average general intellectual functioning existing concurrently with deficits in adaptive behaviour
- Limitations in at least two areas of adaptive behaviour that reflect the degree to which an individual functions effectively within society
- Systems of support required across the lifespan
  - Individual
  - Educational
  - Vocational
  - Recreational

- IQ scores < 70 (IQ normally distributed-mean =100, SD=15)
- Term usually applied to children older than 5
Global Developmental Delay & Mental Retardation/Intellectual Disability

- Related, complementary, non-synonymous terms
- Chronologically framed by what can be reliably observed and measured
  - Many children with GDD will later be diagnosed as MR
  - Many children with MR originally diagnosed as GDD

- Diagnostic labels
  - Clinically recognizable entities
  - Mandates a particular evaluation, management & intervention approach
Developmental Language Disorders

- Inadequate acquisition of language comprehension and/or expression
- Preservation of normal cognitive function
  - Accurate objective assessment may be problematic
  - Language as marker for cognition
- Substantial discrepancy between language and non-verbal skills
  - Language: 2 SD < mean & 1SD < non-verbal skills

- Language delay especially evident - careful evaluation may suggest more subtle problems in other domains
- Absence of neurological disease, global developmental delay/mental retardation, autistic features or hearing loss
Cerebral Palsy

- Static non-progressive motor impairment of early onset that is cerebral in origin
  - Core essential feature is motor impairment
- May or may not have associated co-existing cognitive difficulty or epilepsy or sensory impairment
- Objective abnormalities in strength, bulk, tone, reflexes (stretch, plantar or primitive), resistance to passive stretch on neurological examination
- Pyramidal and/or extrapyramidal findings
Cerebral Palsy-Static & Non-progressive

- Process responsible for cerebral palsy cannot be on-going
- No infliction of additional injury or damage to the CNS over time
- Clinical manifestations may change against the backdrop of a maturing nervous system
- Excludes neoplastic, neurodegenerative or metabolic processes from definition of CP
Cerebral Palsy

Early onset

- Symptomatic presentation prior to 12 months of age
  - Early handedness
  - Motor delay
  - Stiffness
Cerebral Palsy

Cerebral origin

- Excludes neural tube defects, neuromuscular disorders
- Long list of syndromes traditionally excluded from CP “diagnostic” label
  - e.g. Angelmann’s Syndrome
Gross Motor Delay

- Single domain
- Normal cognitive/language/social skills
- Significant restricted delay in motor skills
  - Fine/gross motor both typically involved
- May or may not occur within context of a cerebral palsy syndrome
Autistic Spectrum Disorder (Autism/Pervasive Developmental Disorder)

- Qualitative and quantitative distortion (i.e. deviancy & delay) in the acquisition of developmental skills
- Particularly with reference to social and language domains
- Associated, often prominent behavioural disturbances
  - e.g. stereotypies, obsessions, desire for sameness
- Onset under 30 months of age
Evaluation of Childhood Developmental Delay

Aims & Objectives
1. Confirm the existence of a delay
2. Categorize and classify precisely the neurodevelopmental disability
3. Search for a possible underlying responsible etiology
4. Referral to appropriate rehabilitation services
5. Inform & counsel family
6. Manage associated medical/behavioural conditions
   - Spasticity, epilepsy, inattention, feeding, sleep disturbances
   - Aggression, stereotypies, obsessions, opposition
   - Actualization of full developmental potential
Developmental Delay- Etiologic Determination

- Etiology = specific diagnosis that can be translated into useful clinical information for the family, including providing information about prognosis, recurrence risks and preferred modes of available therapy
- Usually a question asked and answered only by neurologic assessment
Developmental Delay-Etiologic Determination

Importance

• Recurrence risks estimation
• Prevention
• Specific therapy
• Modify management (associated conditions, programmatic approach)
• Prognostication
• Family empowerment
• Limitation of unnecessary testing
Elements of Evaluation

- History
- Physical Examination
  - General
  - Neurological
  - Developmental
- Laboratory Investigation
- Referral
  - Consultations
  - Rehabilitation services
History

Comprehensive Family History

- Developmental, health, school attainment status of siblings, parents and other relatives
- Significant neurological impairments
  - CP/GDD/ASD/MR/DLI
  - Epilepsy (convulsive disorders)
  - Mental illness
  - Neuromuscular disorders
- Parental consanguinity
- Ethnicity
History

Mother’s pregnancy/prenatal care

- PV bleeding
- Gestational diabetes
- Premature labour
- Medical conditions/medications
- Toxin exposure-alcohol, illicit drugs
- Intrauterine infections
- IUGR/Antenatal anomalies
- Foreign birth
**History**

Labour/Delivery
- **Timing**
  - Premature/Term
- **Mode**
  - Vaginal/Forceps/C-S (indication)
  - Vertex/Breech presentation
- Meconium /FHR changes/APGAR scores (1/5 minutes & beyond)
- Birthweight

**Neonatal**
- Encephalopathy
  - Invariably occurs if intrapartum difficulties are of neurologic relevance
- Seizures
- Feeding difficulties
- Associated conditions
History

Medical
  • Chronic conditions, hospital admissions, surgery, medications, vaccination status

Social
  • SES, marital/custodial status, child care arrangements

Special services
  • Rehabilitation
  • Social supports

Family Centered Care
  • What are the family’s major challenges?
  • What should “we” focus on to provide greatest benefit?
History

Developmental

- Age of initial concern
- Domain(s) of concern
- Progression in each domain
- Current capability in each domain
- Activities of daily living
- Play skills
- Any loss or regression of skills?
  - Possibility of a neurodegenerative condition
<table>
<thead>
<tr>
<th></th>
<th>Motor</th>
<th>Language</th>
<th>Social/play</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td>Head up in prone</td>
<td></td>
<td>Smiles, fixes, and follows</td>
</tr>
<tr>
<td>3 months</td>
<td>Head/chest up in prone, grasp placed object</td>
<td>Coos</td>
<td>Laughs</td>
</tr>
<tr>
<td>4 months</td>
<td>Rolls, reaches</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Sits with support, transfers</td>
<td>Babbles, turns to sound</td>
<td>Mouthing objects</td>
</tr>
<tr>
<td>8 months</td>
<td>Sits without support, weight bears</td>
<td>Turns to name</td>
<td></td>
</tr>
<tr>
<td>10 months</td>
<td>Pincer grasp, starting to cruise, crawling</td>
<td>“Bye-bye” wave</td>
<td>Drinks from cup</td>
</tr>
<tr>
<td>12 months</td>
<td>Walks but falls easily</td>
<td>First words</td>
<td>Finger feeds, objects in and out of containers</td>
</tr>
<tr>
<td>15 months</td>
<td>Walks steadily, scribbling</td>
<td>Pointing, multiple single words</td>
<td>Spoon use, assists in dressing</td>
</tr>
<tr>
<td>18 months</td>
<td>Up/down stairs with assistance, climbing, throws ball</td>
<td>Two-word phrases, pointing to body parts</td>
<td>Build towers, play with others</td>
</tr>
<tr>
<td>24 months</td>
<td>Up/down stairs, 1 step @ time, kicks ball</td>
<td>Three-word phrases, pronoun</td>
<td></td>
</tr>
</tbody>
</table>
Box 34-3 Normal Language Milestones

Receptive
Some words understood by 9 months of age
Follows one-step commands by 12 months without being cued by a gesture

Expressive
Cooing: 2 months
Babbling: 6 months
Variable babble: 8 months
One word other than dada and mama: 12 months
10 to 50 words used meaningfully: 16 to 20 months
Two-word phrases: 20 to 24 months
Points to at least one body part and to named objects and people on command: 20 months
Vocabulary of more than 200 words: 2 years
Two-word combinations: 2 years
Follows two-part commands: 2 years
Sentences of three or four words: 3 years
Compound and complex sentences: 4 years
Passive voice: 6 years
Box 38-4 Red Flags for Language Development

Prompt referral should be made for any of the following:

- No vocalizations by 6 months
- No polysyllabic babbling by 12 months
- No spontaneous (not echoed) single words by 18 months
- No spontaneous phrases by 24 months
- No spontaneous sentences by 36 months
- Any loss of babbling, single words or phrases, at any age
- Any loss of comprehension, including responding to name, at any age
Physical Examination

- Fluid & adaptable
- Maintain child’s proximity to caregiver
- Tell child what to expect even if non-verbal
- Leave intrusive (ie hands-on) aspects to end

General

- Height/Weight
- Dysmorphic features (look at parents!)
- Hepatosplenomegaly
- Cutaneous markers of phakomatosis
- Spine
Physical Examination

Neurological

- Head circumference-OF
  - Percentile
  - Measure parents if <3rd or > 98th
- Visual/auditory apparatus integrity
- Bulbar findings

Motor
- Focal findings
- Dyskinesias
- Dexterity/co-ordination/planning
- Strength (Gower sign/up & down stairs)
- Gait-walking & running
- Balance
Physical Examination

Developmental

- In the preschool child developmental assessment is the bulk of the neurologic examination
- Non-invasive & non-intrusive
- Observational, detached, non-threatening
- Appropriate playthings
  - Blocks, crayon & paper, balls, simple puzzles, stuffed animals/dolls etc

- Supplemented by formal developmental assessment
  - Office based
  - OT/PT/SLP/Psychology assessments
Physical Examination

Developmental

- Fine Motor
  - Blocks
  - Pencil/Paper skills-scribbling, copying
  - Eating skills (report)

- Gross Motor
  - Rolling, sitting, crawling, standing, cruising, walking (gait), running
  - Ball playing
  - Stairs
  - Tricycle, bicycle (report)
Physical Examination

Language
- Identification of body parts, pictures, colours, shapes
- Spontaneous/story telling
- Plurals, pronouns, sentence structure
- Following commands

Cognition
- Puzzles, concepts (numbers, big/small, on/under, long/short, open/close)
- Analogies
- Categories
Activities of Daily Living
• Feeding
• Dressing
• Toileting

Social
• Play-Key discriminator between GDD/DLI/ASD
  • Self
  • Other children
• Interaction
  • Parents
  • Examiner
History & Physical Examination: Status

1. Static vs Progressive encephalopathy
2. Type of developmental delay (NDD subtype)
   - Frames etiologic assessment & rehabilitation referrals
3. Current developmental level (functional skills)
4. Possible suspected underlying etiology
   - Directs targeted evaluation
5. Suspected timing (prenatal vs perinatal vs postnatal)
6. Current rehabilitation and social service provision
   - Identification of needs
Laboratory Investigation

- Selective and rational
- Determined by history & physical examination & type of neurodevelopmental disability
- Not determined by severity of delay
- Controversy regarding extent
- Recent advances
  - Genetics
  - Molecular biology
  - Neuroimaging
Laboratory Investigation

CK (muscle weakness)

Toxins
- Thyroid (absent neonatal screening)
- Lead (psychosocial impoverishment/CDC guidelines)

Metabolic Screening
- CBG/lactate/pyruvate/ammonia/LFTs/amino acids/organic acids/VLCFA
- Absent neonatal screening, consanguinity, episodic decompensation, prior affected child, multiple non-ectodermal organs affected, imaging changes

Radiologic
- Bone age (macrosomia)
- Skeletal survey (dysmorphology/storage)
Laboratory Investigation

Genetic

- Karyotype (high resolution)
- FISH (e.g. PWS/Angelman 15q-)
- Sub-telomeric probes
- Array Comparative Genomic Hybridization*
- Molecular (e.g. Fragile X-Triplet repeat expansion FMR1, Rett syndrome-MECP2)
- Specific enzymatic analysis (decreasing importance)
Laboratory Investigation

Electrophysiologic
- EEG
- EMG/NCS
- Evoked Potentials

Neuroimaging
- CT
- MRI
  - Newer techniques
    - Volumetric
    - DWI
    - fMRI
    - MRS
Referral

Consultations
- Genetics-syndromic diagnosis, testing
- Ophthalmology-visual integrity
- Audiology-hearing screen
- Psychiatry-behavioural issues
- Nursing-specific care needs, feeding, family support
- Social services-financial, respite

Rehabilitation Services/Community Resources
- Occupational therapy-fine motor, ADL, feeding
- Physiotherapy-gross motor
- Speech-language pathology-language
- Psychology-cognition, behaviour
Recommended Testing
American Academy of Neurology/Child Neurology Society

- Practice Parameters
  - Guidelines for diagnostic evaluations based on available evidence
  - Best practice given a particular situation
    - Global Developmental Delay
    - Cerebral Palsy
    - Autism
  - Algorithms developed yet individual latitude given clinical situation
Recommended Testing
Global Developmental Delay

- Lead
  - Targeted to those with identifiable risk factors
- Thyroid
  - Targeted to those without newborn screening or specific systemic features of hypothroidism
- Metabolic
  - Indicated if no newborn universal screening
  - Historical or physical examination findings suggestive of possible metabolic etiology
    - Parental consanguinity
    - Prior loss
    - Episodic decompensation
    - Regression
    - Dysmorphic features/hepatosplenomegaly
Recommended Testing

Global Developmental Delay-Parameter Recommendations

- Genetic
  - Karyotype routinely even if no dysmorphic features
  - FMR1 molecular genotyping
  - FISH if delay unexplained or specific syndrome suggested

- EEG
  - Only if suggestion of seizures or an epilepsy syndrome

- Neuroimaging
  - Routine with MRI preferable to CT especially in the context of physical findings

- Hearing/Vision
  - Obligatory
Recommended Testing

Cerebral Palsy

• Neuroimaging
  • If not done previously
  • MRI preferable to CT
    • If dysgenesis consider genetics evaluation-LIS1, DCX
    • If CVA found detailed work up for coagulopathy-PT(INR)/PTT, MTHFR, homocysteine, Protein C & S, Anti-thrombin III, Factor V Leiden, Prothrombin G20210A, lipoprotein screen
    • If basal ganglia involvement without prior asphyxia consider metabolic testing (?mitochondrial, organic aciduria)

• Screening
  • Developmental Delay
  • Hearing/vision
  • Speech-language
  • Feeding
  • EEG if seizures suspected
Recommended Testing

Autism

- Genetic
  - Karyotype
  - FMR1 especially if co-existing MR, FHx or suggestive dysmorphic features

- Metabolic
  - Suggestive clinical or physical examination features

- EEG
  - Landau-Kleffner syndrome, ESES
  - Not routinely undertaken
  - If seizures suspected or regression apparent (significant loss of social and communication function)

- Neuroimaging
  - Not indicated
Suggested Testing

Developmental Language Disorders

- Screen for possible autism
- Screen for hearing deficit
- EEG if loss of language skills documented

Gross Motor Delay (no cerebral palsy-no pyramidal/extra-pyramidal findings)

- Suspected central etiology
  - Neuroimaging
  - Karyotype/FISH (i.e. PWS)

- Suspected peripheral etiology
  - CK
  - EMG/NCS
  - Specific genetic testing as directed by EMG/NCS findings-DMD, PMP22
  - Biopsy if negative genetic results
Etiologic Yields - Neurodevelopmental Disabilities

- Cerebral palsy - 80%
- Global Developmental Delay/Mental Retardation - 50-60%
- Gross Motor Delay - 50-60%
- Autistic Spectrum Disorder - <5%
- Developmental Language Disorders - <5%
Case #1-Jeremy

Delay Diagnosis?
- Global Developmental Delay

Testing?
- Karyotype versus CGH
- FMR1 Molecular Genotype
- MRI Scan

Results
- FMR1 Triplet Repeat Expansion

Etiologic Diagnosis
- Fragile X Syndrome
Case #2-Susan

Delay Diagnosis?
- Hemiplegic Cerebral Palsy

♦ Testing?
  - CT/MRI

♦ Further Testing?
  - Coagulopathy work up

♦ Results
  - L hemisphere porencephalic cyst

♦ Further Results
  - Factor V Leiden mutation

♦ Etiologic Diagnosis
  - L MCA CVA (prenatal) secondary to Factor V Leiden mutation
Case #3 - Robert

Delay Diagnosis?
- Developmental language disorder (specific language impairment)

♦ Testing?
- Hearing screen (audiometry)
- Autism screen

♦ Results
- Normal hearing
- No Autistic Spectrum Disorder

♦ Etiologic Diagnosis
- None evident
Co-Morbid Conditions

- Occur with increased frequency across spectrum of neurodevelopmental disabilities
- May be major burden on child & family limiting actualization of full potential
- Potentially modifiable from both intrinsic & extrinsic perspectives
Co-Morbid Conditions

- Identify **AND** manage
- Medical, rehabilitation and behavioural treatment options
- Effective treatment of co-morbid conditions requires linkages with various disciplines & resources
  - Spasticity, epilepsy, inattention, feeding, sleep disturbances
  - Aggression, stereotypies, obsessions, opposition
Second (Follow-Up) Visit

- Value often overlooked
- Six to nine months after initial assessment
- Developmental trajectories not necessarily smooth or predictable
- Validates & perhaps corrects initial diagnostic impressions & formulations

- Refutes or discovers a possible neurodegenerative process
- Review & integration of evaluations requested
- Review results of laboratory investigations
  - Etiologic diagnosis ?
  - Additional testing ?
Second (Follow-Up) Visit

- Reviews and assures provision of relevant rehabilitation services
  - Long term community resources
- Forum to solicit concerns about possible co-morbid conditions & their effect on child & family
- Forum to answer questions regarding:
  - Present diagnosis & implications (if etiology found)
  - Prognosis
  - Realistic expectations
Key Points

- Recognition of sub-types of neurodevelopmental disabilities-classification & definitions
- Overview of comprehensive neurodevelopmental assessment
- Aspects of specialty evaluation & management
- Importance of etiologic determination
- Co-morbid conditions as a source of burden of care
- Value of second visit