Development and Behaviour phenotype of children with Nicolaides-Baraitser Syndrome (NCBRS)

Rudaina Banihani, MD
Neonatologist & Developmental Pediatrician
Newborn and Developmental Paediatric Department
Sunnybrook Health Sciences Centre

Disclosure

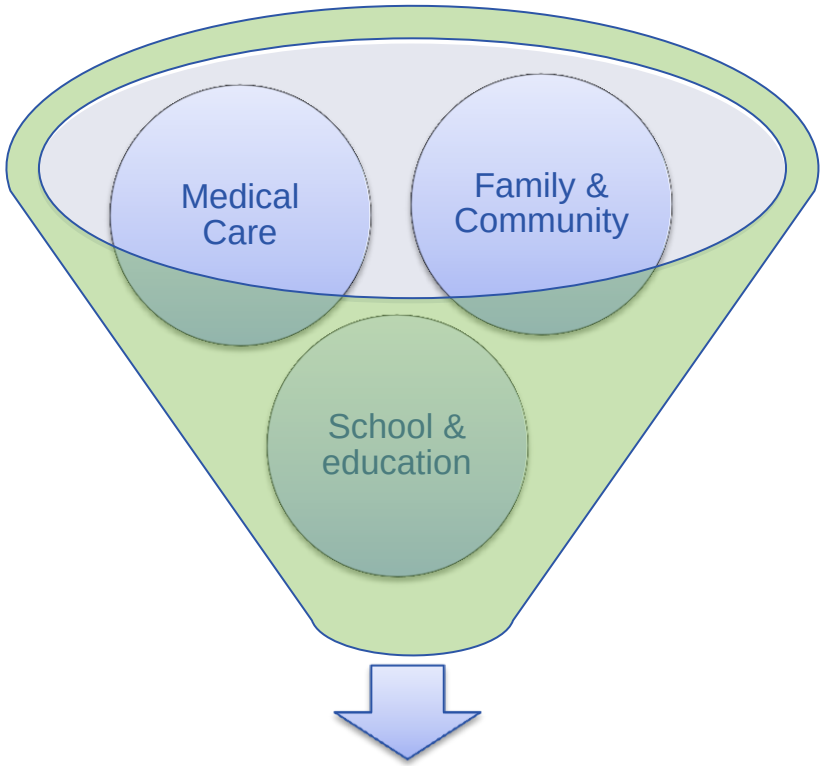
- I have no actual or potential conflict of interest in relation to this program
- I also assume responsibility for ensuring the scientific validity, objectivity, and completeness of the content of my presentation

This Talk will cover….

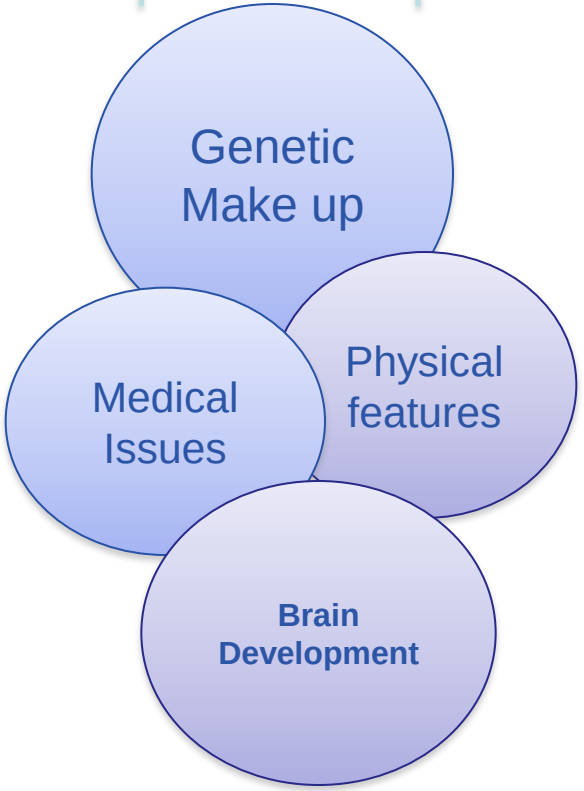
- “ Medical and physical Profile” of NCBRS
- “ Cognitive and Neurodevelopmental profile” of NCBRS
- Goals of known effective interventions
- Families Support

"Individuals with Intellectual disabilities *are people first, with the same rights and needs as everyone else. Their development is influenced by the quality of care, education and social experiences offered to them, just like all other people"*

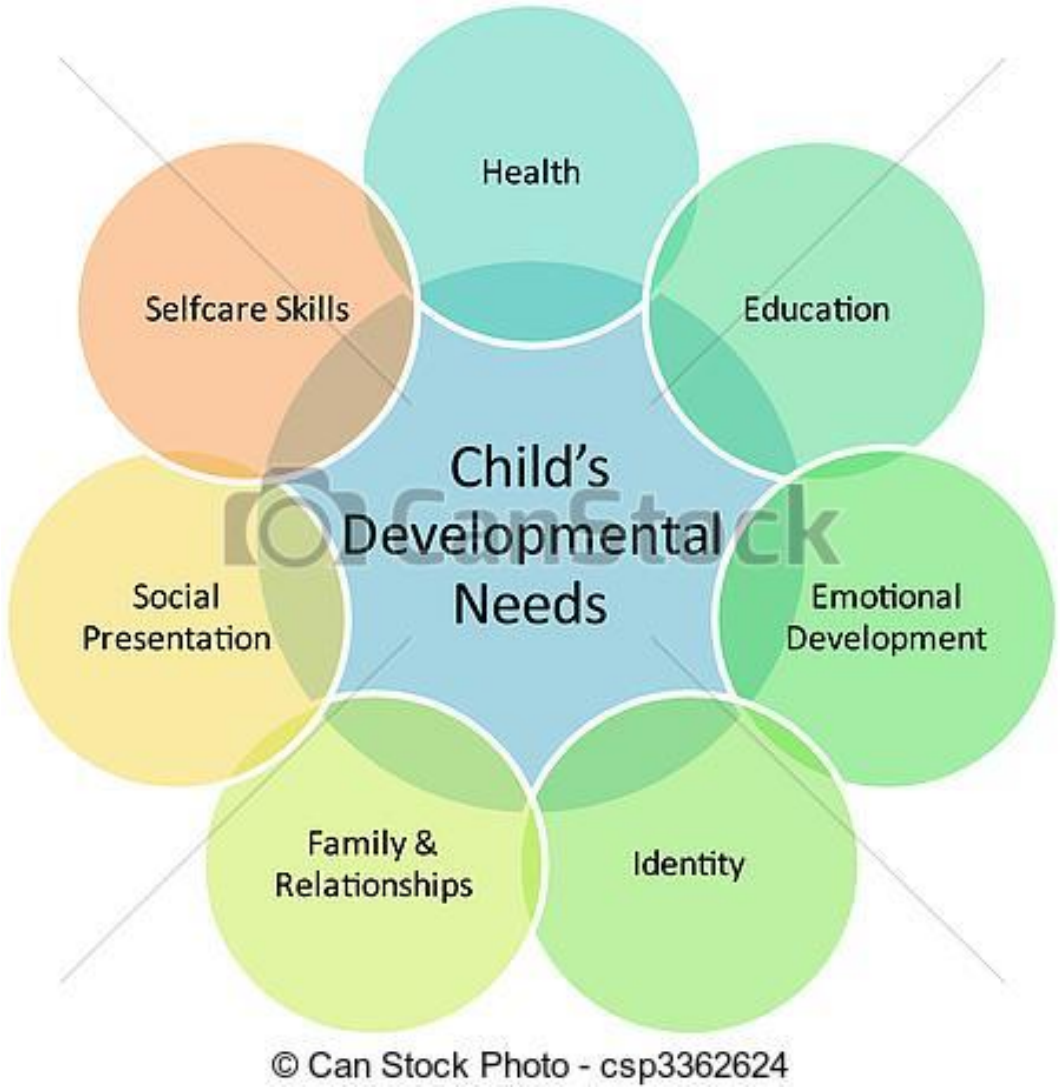
Environment



Individual



Development and Behaviour phenotype



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Basic Facts

- **Development is not fixed by genes at birth**
- **Development is a dynamic, social-interactive process**
- **Development is influenced by**
  - Social learning opportunities
  - Social Support for learning
  - Self-esteem , curiosity and motivation to learn
  - Biology and experience interact to influence brain development
- **Input and activity from brain influence the brain development**

What is NCBRS?

- A rare genetic condition that is present at birth
- Usually recognized during childhood
- Can affect anyone
- No difference in occurrence in males/females
- There are < 100 confirmed cases worldwide
- The physical features and medical problems associated with NCBRS can vary widely from child to child

What Causes NCBRS?

- Mutations in the SMARCA2 gene, part of BAF chromatin remodeling complex
- It's located on chromosome 9p24.3
- No familial cases are known except the present (molecularly proven) monozygotic twins
- Parental consanguinity has not been reported
- Recurrence risk seems to be (very) low
- Chromosome analysis has shown a normal karyotype in all patients

Major Features of NCBRS

Major Features of NCBRS	
Mild prenatal growth retardation	**Presenting Features**
Mild postnatal growth retardation	
Severe developmental delay	
Severely impaired speech	
Seizures	
Microcephaly	**Physical Features**
Sparse hair	
Progressive skin wrinkling	
Thick, anteverted alae nasi	
Long and broad philtrum	
Large mouth	
Thin upper and thick lower vermilion	
Progressive prominence of distal phalanges	
Progressive prominence of inter-phalangeal joints	
Short metacarpals–metatarsals	

Typical Features of NCBRS

- **Face –** It is usually triangular in shape, dense eyelashes, prominent nose with thick nostrils, thin upper lip, full lower lip and wide mouth
  - The facial characteristics become much more pronounced with age→ the subcutaneous fat in the cheeks decreases, making the skin sag and wrinkle

http://www.ncbrs.com/our-stories/callum

Typical Features of NCBRS

- **Teeth -** are widely spaced
  - Delayed eruption of the baby and adult teeth
- **Hair -** sparse scalp hair is a key sign of NCBRS.
  - all diagnosed cases
  - The growth and texture is normal
  - Overtime the sparseness of the hair increases, while in others it decreases with time
  - Pubic hair develops normally.
  - Facial hair is limited in adult Male
- **Skin -** Eczema and skin sensitivity 1/3

Typical Features of NCBRS

- **Hands -** as the child ages, the finger tips become broad and the joints become more prominent
- **Feet -** sandal gaps
  - Progressive thickening of the distal toe tissues especially at the 5th toe

American Journal of Medical Genetics Part C: Seminars in Medical Genetics
Volume 166, Issue 3, pages 302-314, 28 AUG 2014 DOI: 10.1002/ajmg.c.31409
http://onlinelibrary.wiley.com/doi/10.1002/ajmg.c.31409/full#ajmgc31409-fig-0005

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Infrequent Findings of NCBRS

- **Hernias** - groin and umbilical hernias are more common in individuals with NCBRS than the general population
- **Undescended testes** - about 60% of boys, often requiring surgery
- **Scoliosis** - < 1/3 of children and It ranges from mild to severe
- **Cardiac problems -** (double aortic arch; mitral valve regurgitation; thick ventricular septum; small persistent foramen)
- **Vesico-ureteric reflux**, **mild dyslipidemia**, **abnormal carnitine profile**

Growth

- 45% had low birth weight at birth
- 56% have short stature
- 100% growth less than the 50th→ no evident disproportion
- Microcephaly of variable degree
  - 35% at birth
  - 82% later

How NCBRS Can Affect the Kids Health

- **1/3 Low muscle tone** (called **hypotonia**)→ Babies in particular may seem especially "floppy"
  - For infants:
    - Poor Sucking and feeding problems 46.9 %
    - Constipation and other digestive issues
    - Choking
  - Toddlers and older kids :
    - Motor Skill Delay
    - Adaptive/self care Skill Delay : like feeding, dressing, and toilet teaching
    - Speech Skill Delay
    - Constipation and other digestive issues

How NCBRS Can Affect the Kids Health

- **Hearing loss** not common → if present conductive type
- **Vision**: Myopia in 16% and astigmatism 6.5%

http://www.ncbrs.com

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Epilepsy

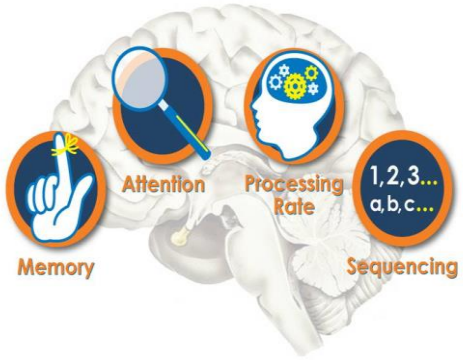
- 2/3 of patients
- The type of seizure is variable
- Start in average around 1.6 years, not uncommonly progressively get worse
- Increasing Seizures frequency in some patients despite multiple anti-epileptic drugs
- Sodium valproate is the medication of first choice
- It’s noticed a co-occurrence of decreasing mental abilities with the onset of seizures.
- EEGs are usually not significantly abnormal

- Cognitive Skills
- Communication and Language
- Adaptive Skills
- Social & Behaviour
- Motor Skills

Cognitive and learning skills

Intellectual Disability (ID)in NCBRS

- One of the main Features
- Deficits in IQ and adaptive functioning
  - IQ less than 70
  - Effective coping with common life demands
  - Ability to meet standards of independence
  - Difficulties adapting to new environments
  - Difficulties with safety awareness, self-care and communication skills
- Wide rang:
  - 45.9% sever (IQ 20 to 34)
  - 36.1% moderate (IQ 35 to 49)
  - 18% mild (IQ 50 to 70)



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Intellectual Disability (ID)in NCBRS

- Which result in …
  - Develop more slowly than their peers and the degree of delay varies
  - Arriving at each stage of development at a later age and staying there for longer
  - The gap between them and their peers will widen with age
- 11/1161 patients in an Italian cohort with ID where found to have NCBRS

Mari F, Marozza A, Mencarelli MA, et al. Coffin-Siris and Nicolaides-Baraitser syndromes are a common well recognizable cause of intellectual disability. *Brain & development*. 2015;37(5): 527-36

Intellectual Disability (ID)Consequences

- Avoidance strategies when faced with cognitive challenges
- Their use of existing problem solving skills →Less-than-efficient
- Difficulties to consolidate newly acquired cognitive skills into their repertoire
- Increasing reluctance to take the initiative in learning
- Respond to encouragement on a task vary

Wishart (1995)

One of the reasons for the decline in IQ scores

- Uncontrolled Epilepsy (Specific in NCBRS)
- The very slow development of speech and language
  - Some early intervention programs have reported success in slowing or stopping the IQ decline

"Speech and language therapy"

Early Intervention

- Monitor health
- Speech and Language Therapy
- Occupational /Physical Therapy
- School
- Parent Education→ help them to became effective advocate “ Expert “ on their child
- Spiker and Hopmann (1997)
  - The intensity of EI not predictive of mental development
  - Stressed family – intense EI → less improvement and increased maternal anxiety

Benefits of Early Intervention

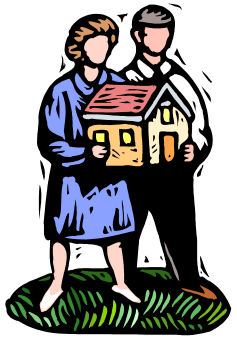
Helps children with disabilities

Gains in cognitive, physical, language, and social skills

Benefits families

Helps families manage the child

Reduces stress



Benefits society

Reduces need for institutional placement

Reduces need for special education

Saves money

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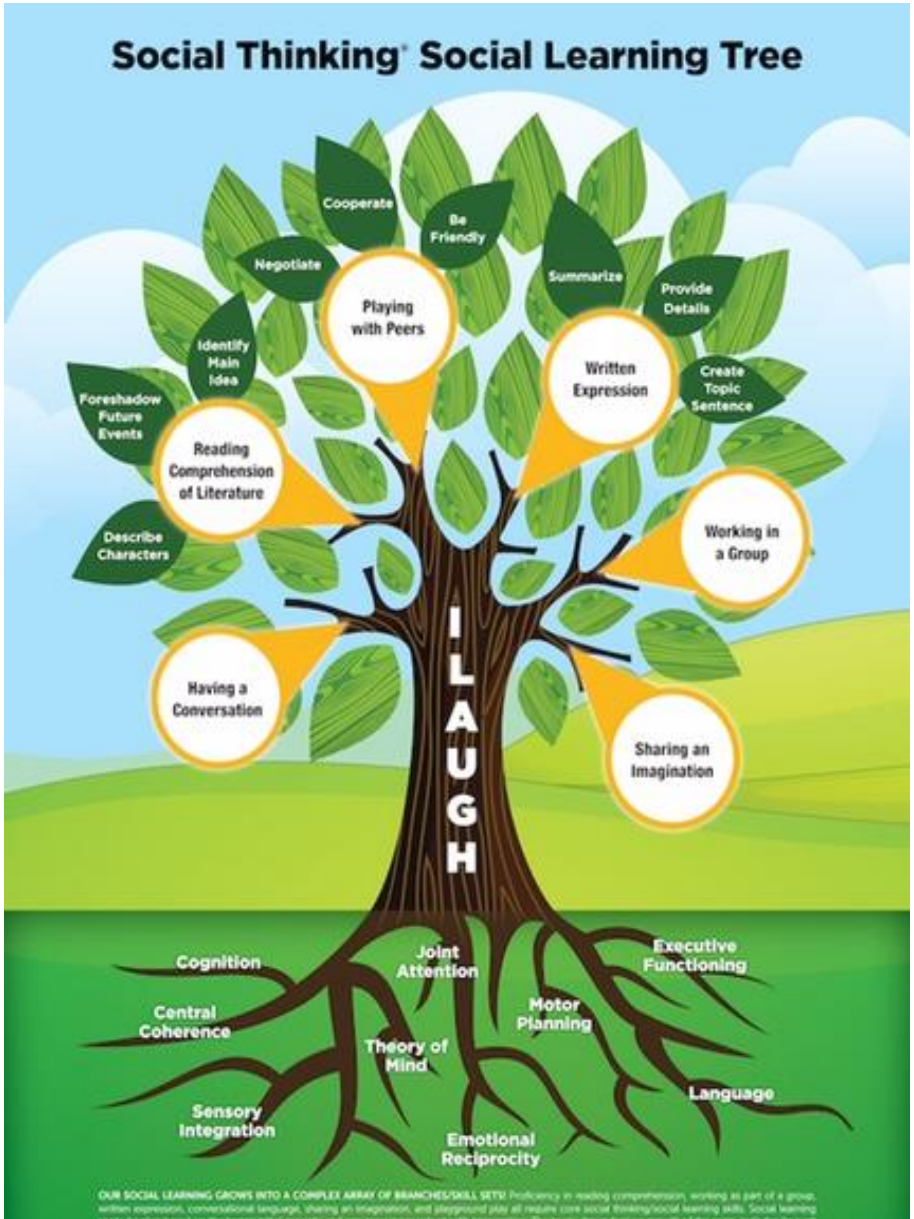
Speech and Language



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Language development IN NCBRS

- It is particularly limited
- At least 30% of kids never develop speech
- Speech Delay first Words ~ 18 months
- Mostly use Single words
- Lots of repetition and word approximation
- 15% their initial words were lost or significantly reduced later in life
  - In some patients the loss of speech coincided with their first seizure
  - Regression due to Autism spectrum disorders (ASD) !

Social Development

- Differ widely→ Happy and Friendly
  - Temperament
  - How they are treated by others
  - Experiences in the family, school and community
- Sever ID are likely to have more difficulty
- Language development plays a big role
- Joint attention develop later in 2nd year
  - Delay in learning to understand words
  - The earlier development of joint attention, the faster the expressive language develops

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What Are Important Skills to Teach Young Children with ID and Language delay ?

- Communication skills
  - Allow the child to get their needs met
  - Replace maladaptive behaviors and engage in social interactions
- Non-verbal communication
  - Teaches that people's faces/bodies carry important information
- Interactive Play Skills
  - Teaches flexibility
  - Improves relationships
  - Replaces self-stimulatory behaviors

Behaviour

- No more behaviour difficulties than children of the same developmental ability
- Typically no major behaviour difficulties
  - Temper Tantrums and period of Aggression -- ? Language Level
  - Short attention Span
  - Sensitive to loud noise
  - High threshold for pain
  - Oral Sensitivity → like Salty and Spicy foods
  - Eating difficulties were much less common
  - Sleeping and night-waking difficulties
  - Few has persistent behaviour difficulties that Is consistent with Autism Spectrum Disorders (ASD)

Autism and NCBRS

- Some reported kids presented with autistic features
- Although in none of these kids was the diagnosis of ASD formally made
- Gana S. 2011 describe two unrelated kids with clinical features suggesting Nicolaides-Baraitser syndrome and ASD
- Mutations in nBAF subunit genes have so far been linked to Coffin-Siris syndrome (CSS), Nicolaides-Baraitser syndrome (NBS), schizophrenia, and Autism Spectrum Disorder (ASD)

Lopez AJ and Wood MA. Role of nucleosome remodeling in neurodevelopmental and intellectual disability disorders. *Front Behav Neurosci*. 2015;9: 100

Putting it all together

- Addressing Behavior
  - When does ***IT*** happen?
  - Consider the reason
    - Too much, too soon?
    - Boring, repetitious?
    - Child's communication skills?
    - Emotion
      - Sad, mad, scared
    - How have you reinforced the behavior?

ABC-Behaviour

A → B → C

(Antecedent) (Behaviour) (Consequence)

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Putting it all together

- Using visual supports
  - Helps with transitions and behavior
  - Use support strategies:
    - www.Usevisualschedules.com
    - Social Stories: www.thegraycenter.org
- Teach the language of emotion: Cognitive Affective Training (CAT) : Dr. Tony Attwood
    - visual, interactive, and customizable communication elements
    - Helps kids become aware of how their thoughts, feelings and actions all interact

Teaching Signs

- Make sure the signs you teach can be immediately reinforced
- Choose iconic signs to begin teaching (look like the object)
- Make sure all those in the child's environment know the child's signs so they can be reinforced
- Early signs to avoid frustration: more, yes/no, potty, open

Other ways to Enhance Communication

- Picture Exchange Communication System
- Assistive and augmentative technology
- Communication Boards
- Reinforce All Vocal Attempts
- Use Imitation
- Use Music
- Use Books
- Use iPad
- Follow the Child's Lead
- Use the child's interests

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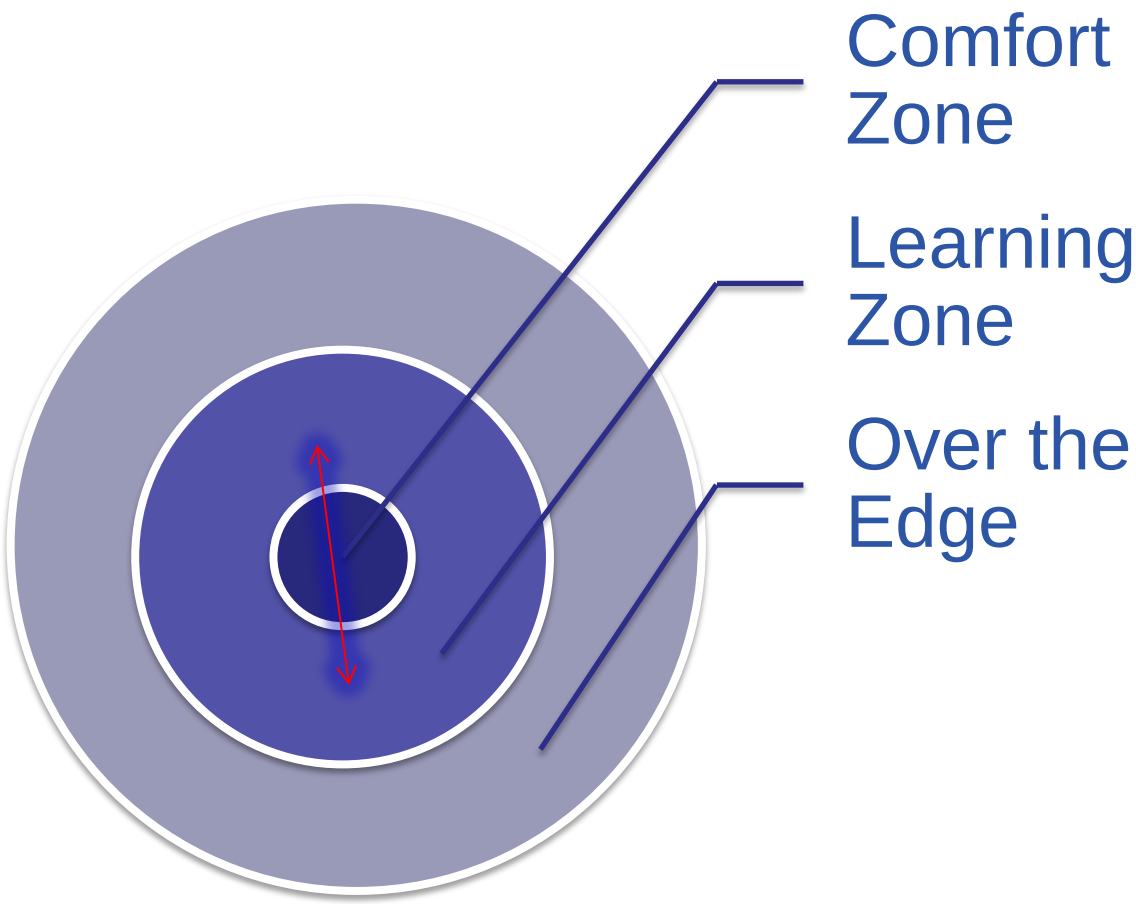
Move In and Out of the Comfort Zone



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Imitation: Allows the child to learn from the environment

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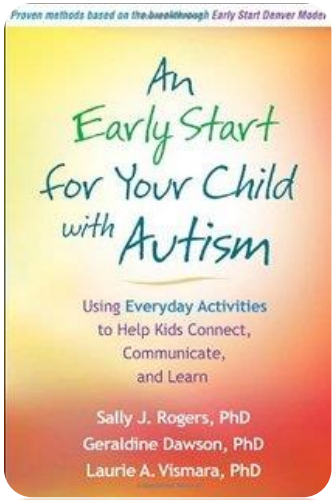
Most Common Approaches Used

- Behavioral Approaches- ABA- Applied Behavior Analysis
- Applied Verbal Behavior, TEACCH
- Developmental Approaches- SCERTS, Floortime/DIR, RDI
- Early start Denver Model**



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Hanen Method

- Teaching communication and play skills through adult- child interactions.
- Parents/therapists are to:
  - Observe, Wait and Listen (OWL)
  - The child leads and teaching is conducted based on the interests of the child

Motor Skill Development

Motor Skill in Kids with NCBRS

- The majority achieve all the basic skills “ Sitting /Walking”
- Same sequence as in typical children but later
- They improve with practice
- There is considerable individual variation in rates of progress

- Recreational skills vary
- Balance seems to be a particular difficulty relative to progress in general coordination and muscle strength
- In Older Individual slowing down movement has been reported*

Motor Skills Not Always Delayed

Learning specific movements

- Slower to react & initiate a movement
- Slower to complete a movement
- More accurate - make fewer errors
- Reaction times improve with practice

Health and physical issues affect movement

- Visual impairments
- Hearing impairments
- Uncontrolled Epilepsy
- FTT
- Physical characteristic – recreational choices

Physiotherapy

- Will not make them walk earlier
- Avoid negative compensatory postures from developing
  - Turned out legs
  - Lordotic gait
  - Sitting with rounded back
  - Work on Balance and Coordination

Consider Groups as they get older !

Occupational Therapy

- Promote Independence
  - Self care skills (feeding, dressing, grooming etc.)
  - Skills related to school performance
  - Play and leisure skills

OT's work in conjunction with speech therapists and physiotherapists as there is overlap in their fields

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What do parents and teachers want for a child with ID ?

The Dance of Partnership (Why do my feet hurt?)

- http://www.danceofpartnership.com

Do You Hear What I Hear? Parents and Professionals Working Together for Children with Special Needs

by Janice Fialka and Karen C. Mikus

- “I want him to say my name”
- “I wish she could tell me her thoughts and wishes”
- “I want him to play like other kids and have friends”
- “I want her to read”
- “I want him to be successful at whatever he wants to do in life”
- “I want him pay attention and learn in school”

Use Whatever Works to Teach the Most Important Skills to each Individual child at the Given Time

Social –
Communication Skills
and Civil Behavior are the foundation to future social, emotional, cognitive, and academic success