

**Autism Spectrum Disorders –
Complex Cases and
Literature Update:
RACP 2007**

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Overview

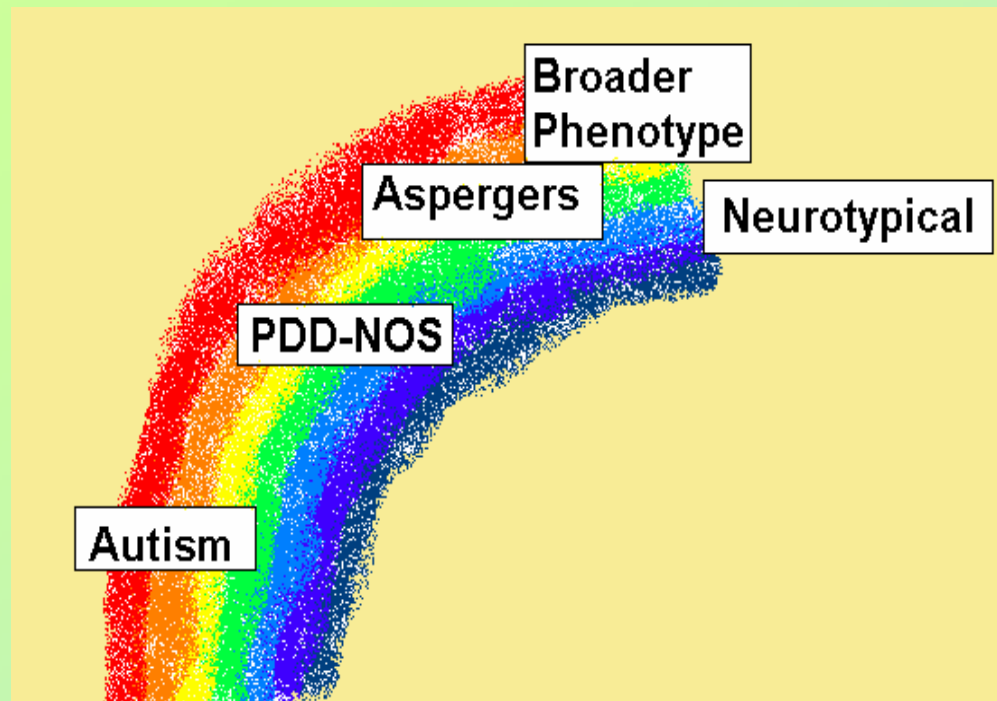
Part 1

- Diagnostic categorisations
- Cognitive profiles
- Psychiatric co-morbidities
- Aetiology
- Protocols for assessment
- Behavioural management
- Pharmacological management
- Questions

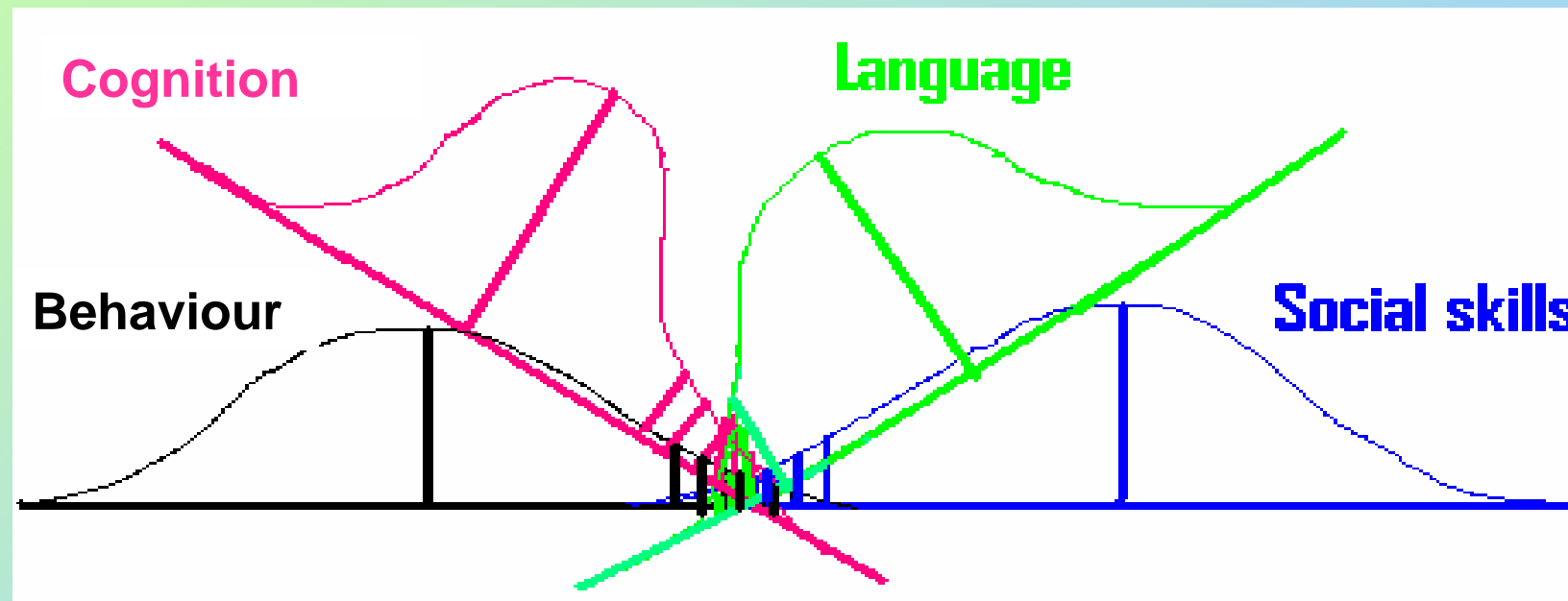
Part 2:

- Clinical case studies
- Summary
- Final questions & discussion





Diagnostic Categories



Diagnostic Criteria: Autism (DSM-IV)

- 1) Qualitative impairment in social interaction, *as manifested by at least two of the following*:
 - marked impairment in the use of multiple nonverbal behaviours such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction.
 - failure to develop peer relationships appropriate to developmental level.
 - a lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (eg, by a lack of showing, bringing or pointing out objects of interest).
 - Lack of social and emotional reciprocity

Diagnostic Criteria: Autism (DSM-IV)

- 2) Qualitative impairment in communication, *as manifested by at least one of the following*:
 - delay in, or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime).
 - in individuals with adequate speech, marked impairment in the ability to initiate or sustain conversation with others.
 - stereotyped and repetitive use of language or idiosyncratic language.
 - lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level.

Diagnostic Criteria: Autism (DSM-IV)

- 3) Restricted repetitive and stereotyped patterns of behaviour, interests, and activities, *as manifested by at least one of the following*:
 - encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus.
 - apparently inflexible adherence to specific, non-functional routines or rituals
 - stereotyped and repetitive motor mannerisms (eg, hand or finger flapping or twisting, or complex whole-body movements).
 - persistent preoccupation with parts of objects.

Diagnostic Criteria: Asperger Syndrome (Gillberg 1991)

A) Severe Impairment in Reciprocal Social Interaction

(2 out of 4)

- Inability to Interact with Peers
- Lack of Desire to Interact with Peers
- Lack of Social Cues
- Socially and Emotionally Inappropriate Behaviour

B) All-Absorbing Narrow Interests (1 out of 3)

- Exclusion of Other Interests
- Repetitive Adherence
- More Rote than Meaning

Diagnostic Criteria: Asperger Syndrome (Gillberg 1991)

C) Imposition of Routines and Rituals (1 of 2)

- Imposition on Self, in all aspects of life
- Imposition on others

D) Speech and Language Problems (3 out of 5)

- Delayed Development of Language
- Superficially Perfect Expressive Language
- Formal Pedantic Language
- Odd Prosody, Peculiar Language
- Impairment of Comprehension, including misinterpretation of literal and implied meanings

Diagnostic Criteria: Asperger Syndrome (Gillberg 1991)

E) Non-Verbal Communication Problems (1/5)

- Limited use of Gesture
- Clumsy/Gauche Body Language
- Limited Facial Expression
- Inappropriate Expression
- Peculiar, stiff gaze

F) Motor Clumsiness

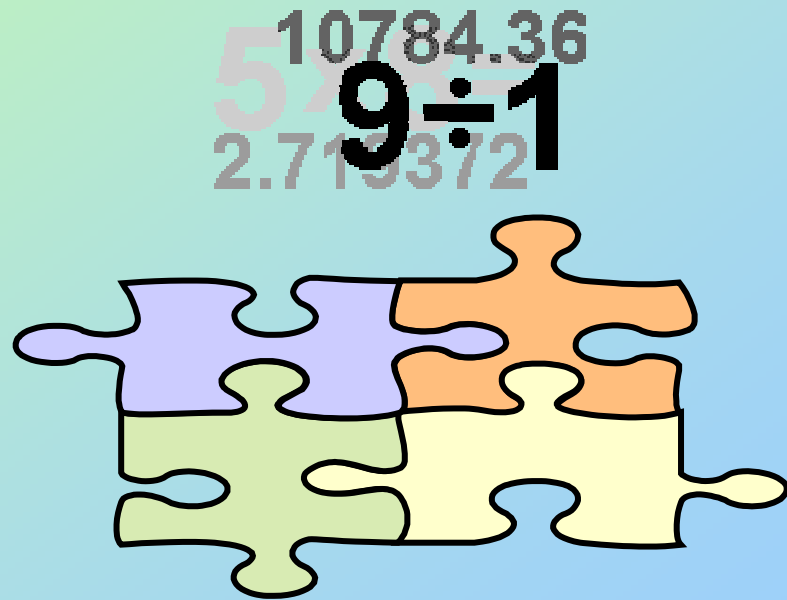
- Poor performance on Neurodevelopmental Assessment

Cognitive Profile

- Uneven pattern of skills
 - “deviant” not “delayed”
 - Significant difference between verbal and performance IQ
 - “visualisers” or “verbalisers”
 - Overall IQ usually meaningless and misleading

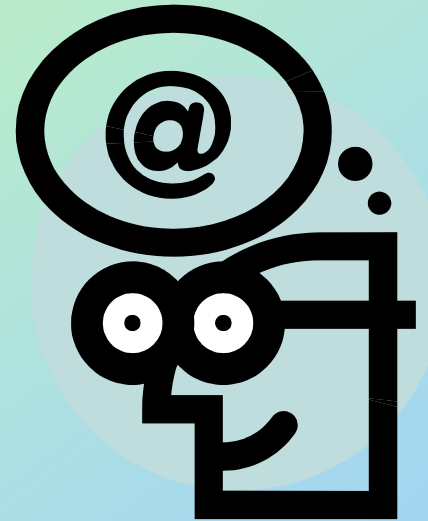
Cognitive Profile - Strengths

- Arithmetic
- Block design / Puzzles
- Memory
 - Factual information
 - Meaning of words



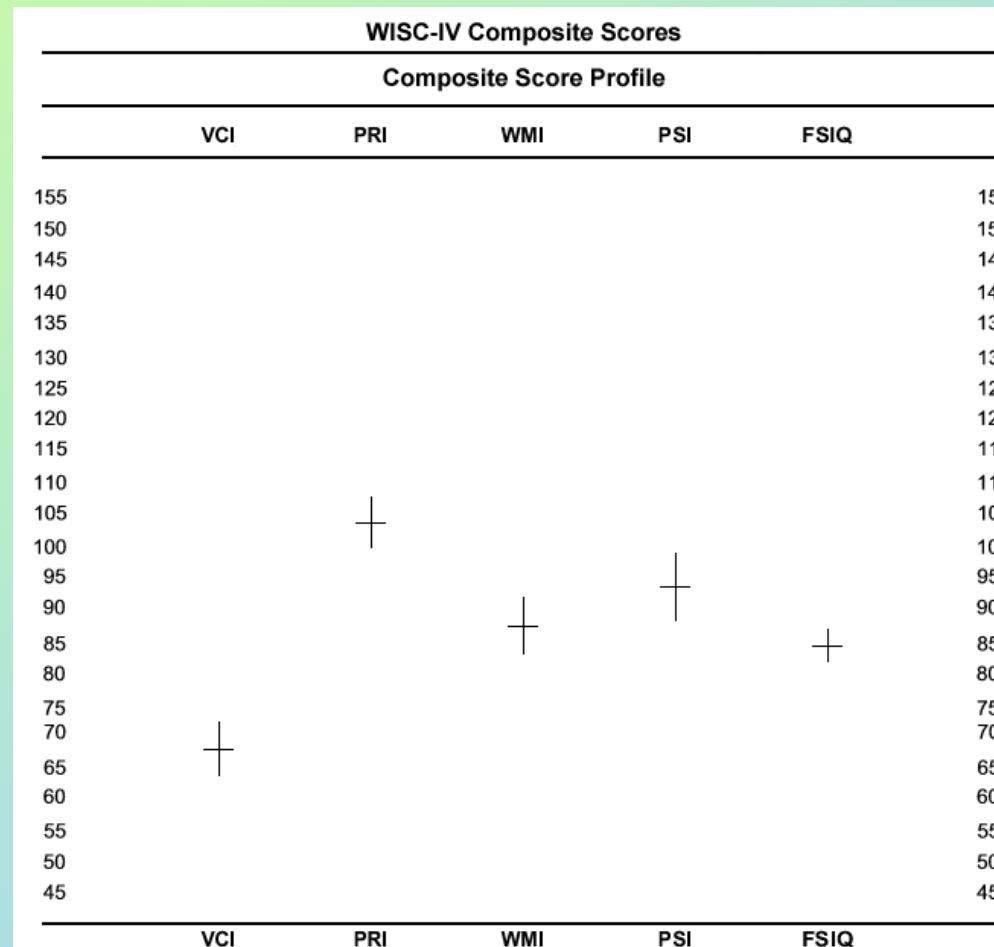
Cognitive Profile - Difficulties

- Executive functioning
 - ‘Monotropic’ attention
 - Central coherence
 - Cognitive flexibility
- Abstract / conceptual thinking
- Social skills
 - Theory of mind
 - Affective reciprocity



Cognitive Profile: Example

- 8 year old boy - Autism & ADHD

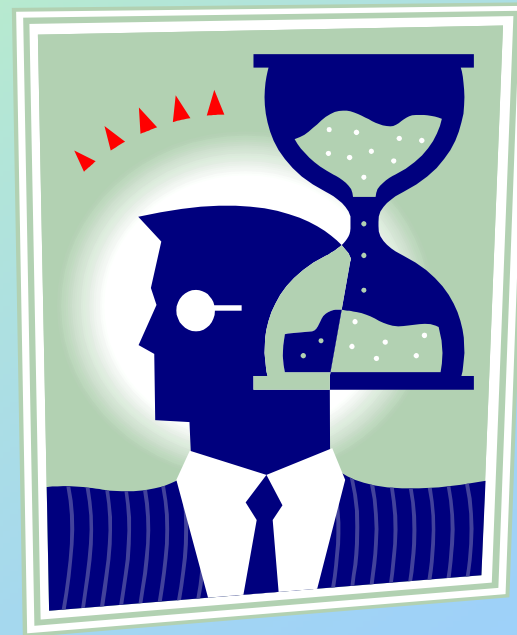


Cognitive Profile

- Autism
 - 75 - 80 % Intellectual Disability
 - Strength abstract visual-spatial skills
- Asperger
 - Overall higher level of intellectual functioning
 - Higher verbal reasoning/comprehension
 - Impaired spatial skills

Positive View of Cognitive Deficits of Asperger Syndrome

- Attention to detail
- Single mindedness
- Creativity
- Do not follow peers
- Honesty and directness
- Adherence to procedures
- Reliability
- Punctuality



Comorbidities

- ASD – expect comorbidity
- Autism – assoc. medical disorder
 - 10-25% metabolic/genetic disorder
 - 30% epilepsy
 - 10-20% hearing / visual impairment
- Aspergers
 - 72% 1 or more DSM-IV diagnoses
 - Strongest association with higher functioning

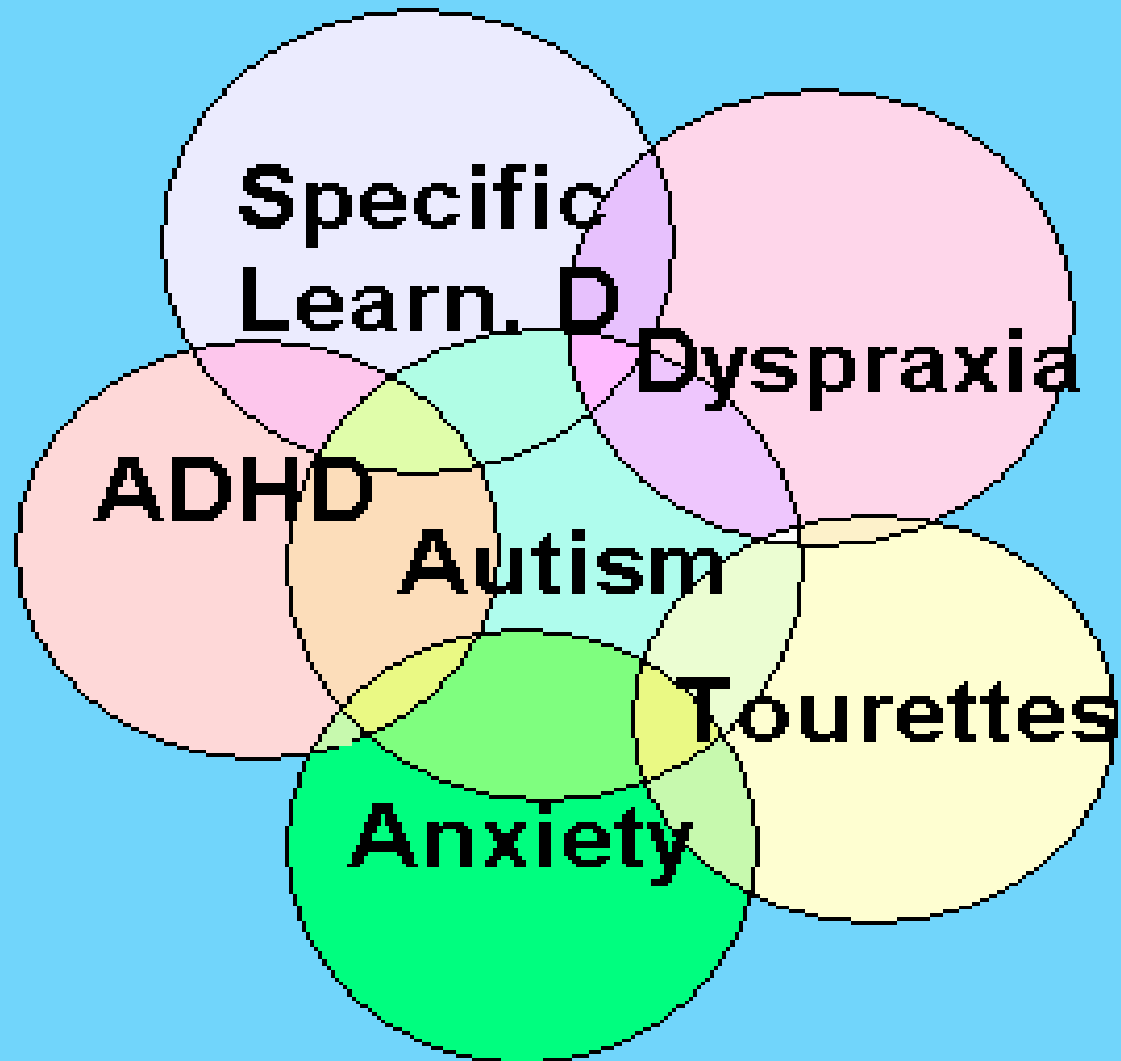
Comorbidities

- ADHD – >30%
 - Both frontal lobe
 - Needs to be developmentally inappropriate
- Tourettes syndrome – 8-20%
 - Verbal and motor stereotypies

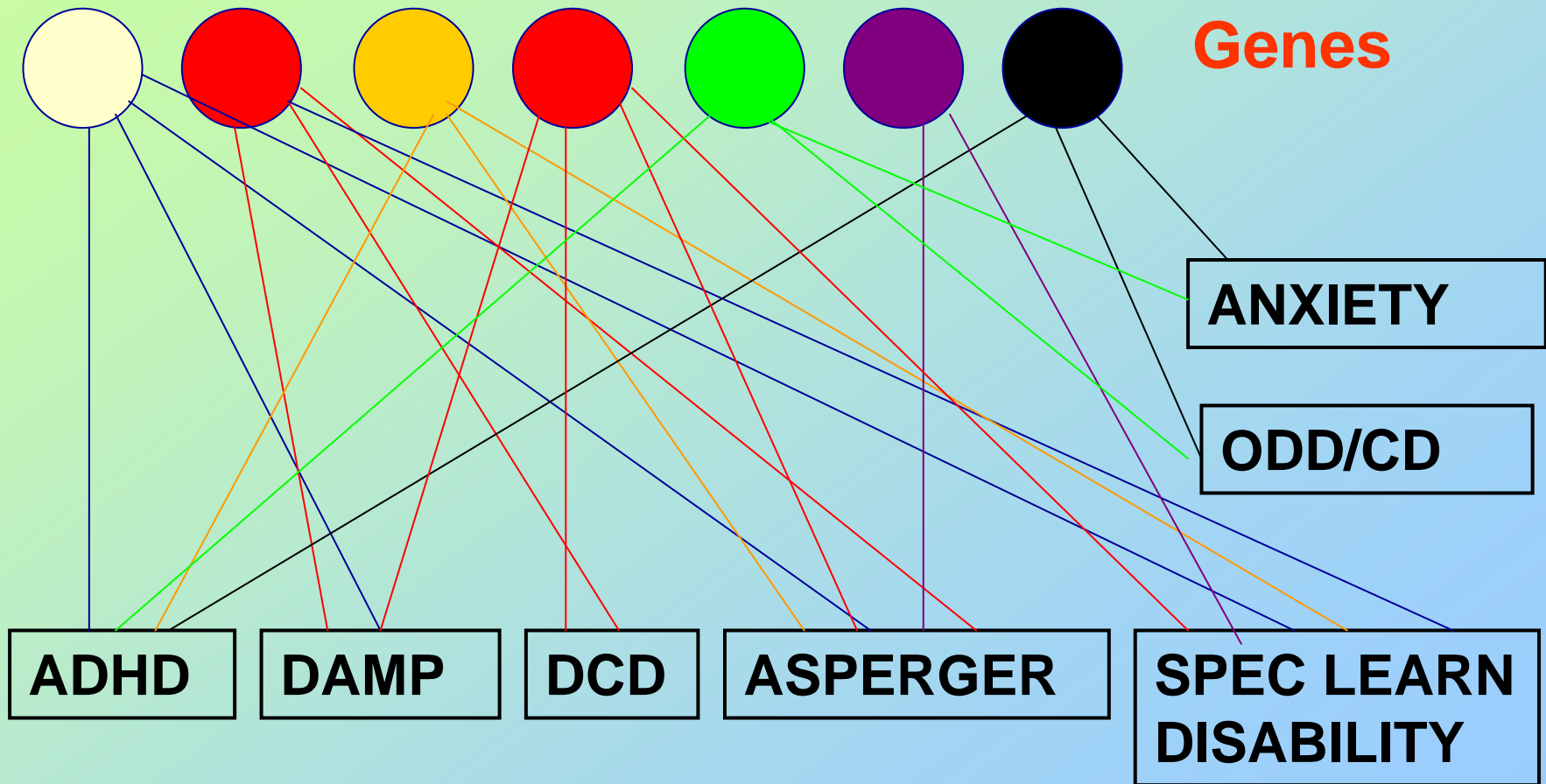
Comorbidities

- Anxiety disorders 17-84%
 - Specific phobia – 44%
 - OCD – 37%
 - Separation disorder – 12%
 - Anorexia
- Mood disorders
 - Depression - 10%
 - Bipolar – low rates
 - Schizophrenia – no more at risk

Overlapping Neuromaturational Delays



Interacting Genes

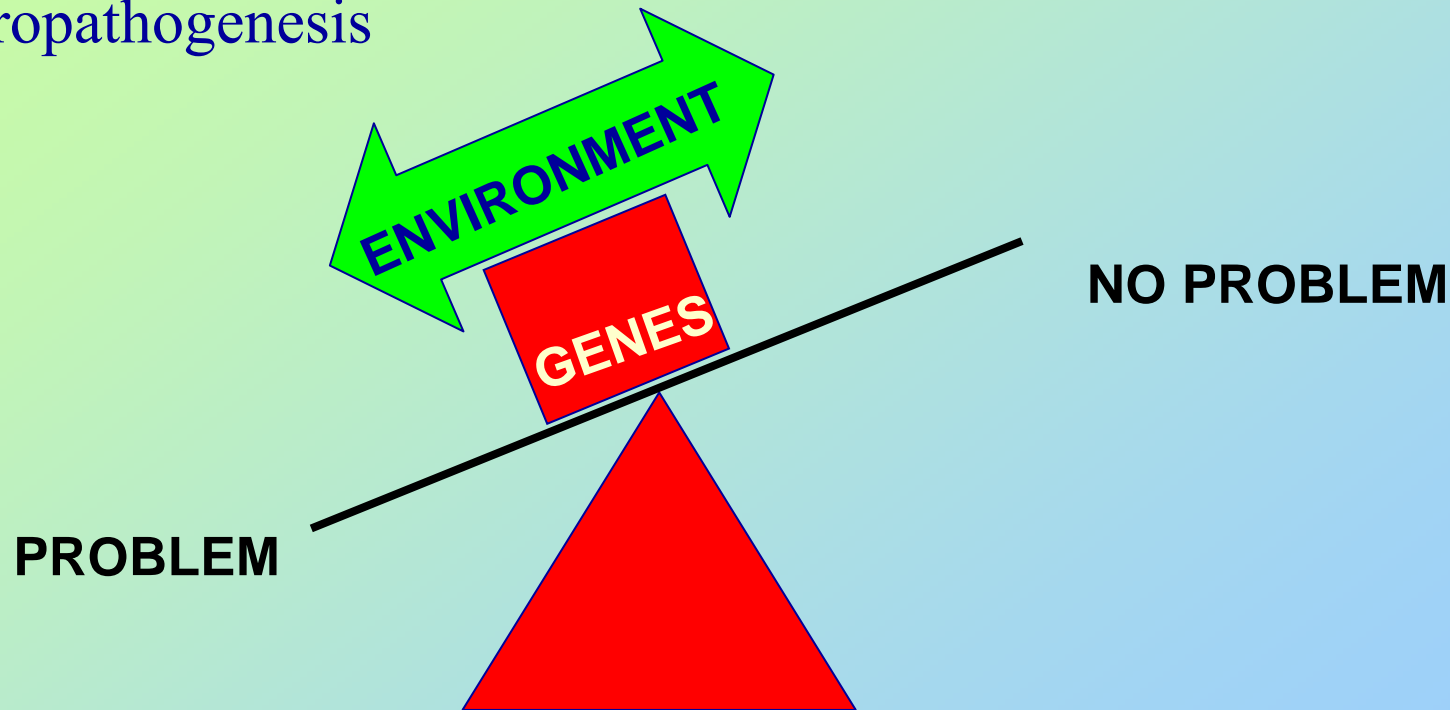


Aetiology

- Evidence Genes involved:
 - **Twin Studies**
 - 50% monozygotic concordance
 - 5% dyzygotic concordance
 - Siblings 35-fold ↑ risk cf population
 - = Genetic factors play 70-90% role, assuming multi-factorial threshold model
 - **Associated single gene disorders:**
 - Tuberous Sclerosis
 - Fragile X
 - Retts
- Evidence Environment involved:
 - **Higher than expected incidence of Autism in:**
 - Antenatal Thalidomide
 - Antenatal anticonvulsant use (Carbamazepine/Valproate)
 - Congenital Measles/Rubella
 - Metabolic conditions: untreated PKU
 - **Evidence Autism not caused by:**
 - MMR
 - Allergies

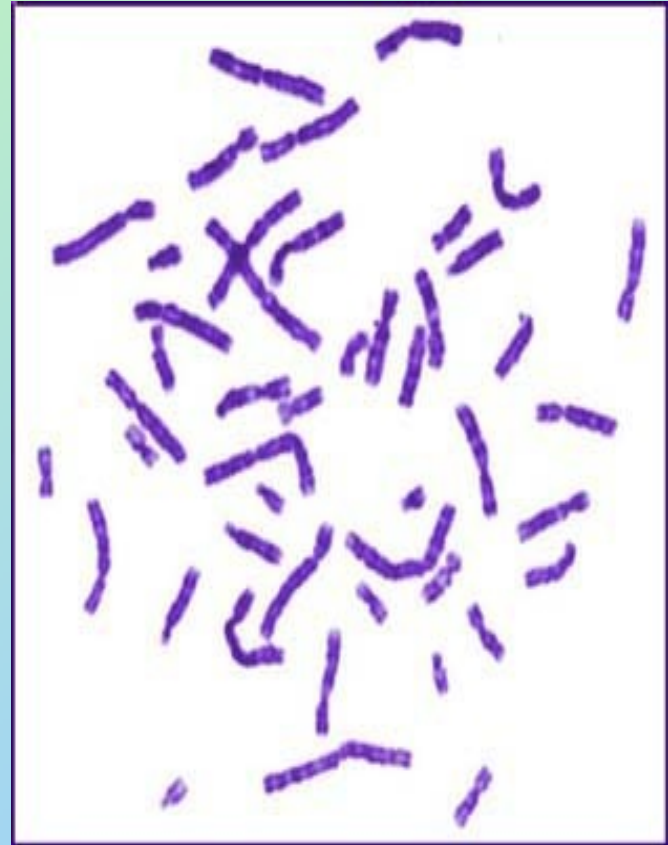
Environment/Gene Interaction

Dysfunction of widely distributed neural networks, caused by polygenic and environmental influences, converging on a common neuropathogenesis



Aetiology

- Half human genome codes brain development and function
- Multiple interacting genes
- Structural brain changes
- Neurotransmitter abnormalities
- Family history invariably present
- Genetic linkage studies:
 - Biological markers
 - Specific behavioural phenotypes
 - Whole genome scans



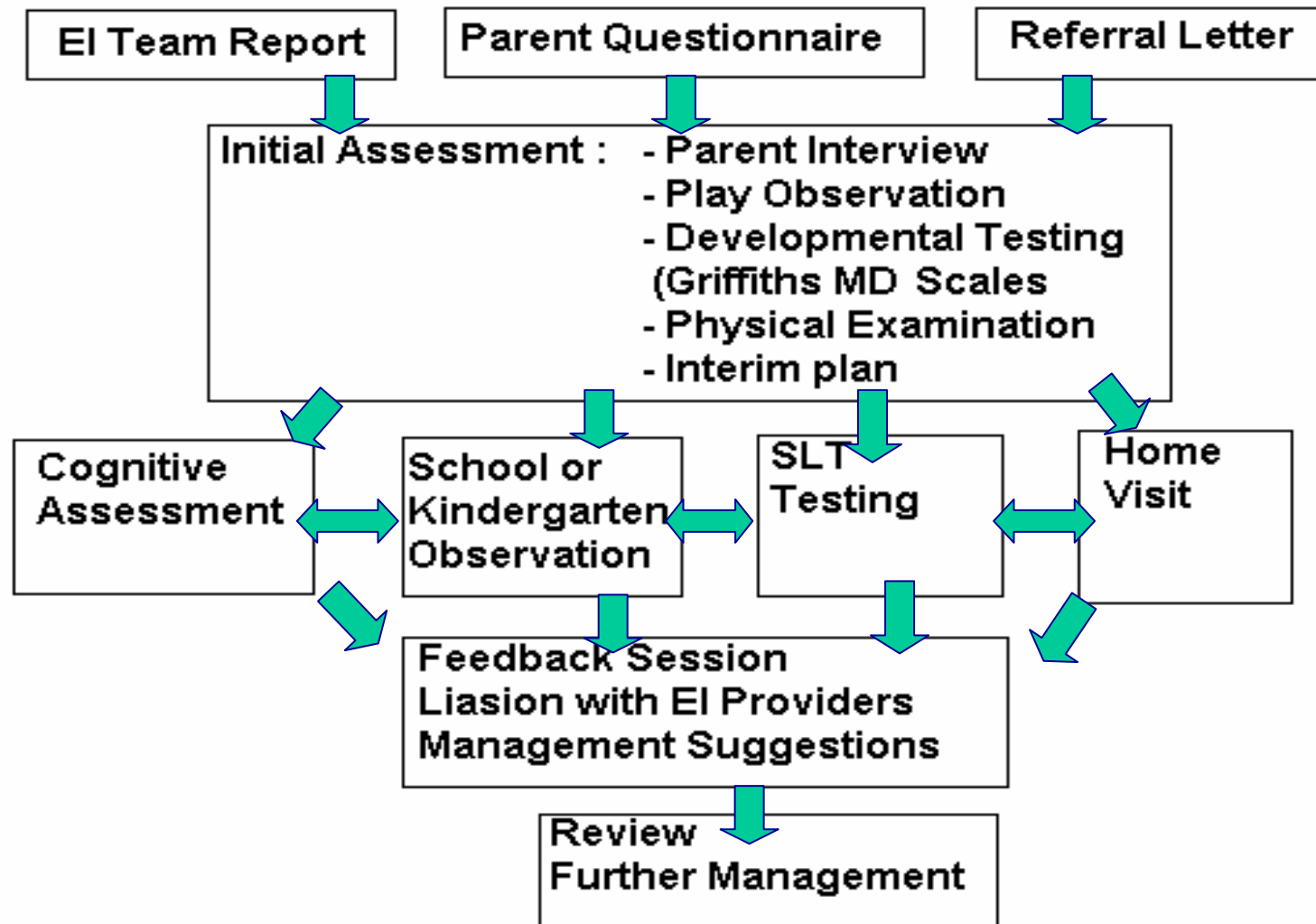
Aetiology

- 12 Genome-wide scans and multiple follow-up studies and meta-analyses
 - no significant linkage but some regions of interest: 2q 7q, 16p, 17q 19p
- Mechanisms:
 - Neurotransmitter/receptor genes
 - Chromosomal breakpoints
 - Genes for language impairment or dyslexia associated with balanced translocations
 - Epigenetics (DNA methylation and Histone acetylation) “Master Switches”
 - MET receptor kinase gene (common polymorphism → ↑ risk of family recurrence)
 - MECP2 (Retts)
 - Multiple spontaneous mutations (7% vs 1%)

Aetiology

- Candidate genes:
 - 2q24-33 • mitochondrial aspartate/glutamate carrier
 - 7p15 • HOX A and B (affect transcription of other genes in early development)
 - 7q22 • Reelin (neuronal migration)
 - 7q31 • WNT2 (influences development)
 - FOXP2 (mutation there found in a family with speech disorder and/or ASD)
 - IMMP2L (mitochondrial membrane)
 - Ray1/ST7 (tumour suppressor)
 - 11p • Neurexin 1 (nerve cell communication)
 - 15q11-13 (same region as in Prader-Willi/Angelman) • UBE3A
 - GABA receptor gene
 - 17q11 • Serotonin transporter gene (40% ASD kids ↑ levels in platelets but poor correlation blood vs CSF levels. Parents of these kids have same familial trait)
 - 19p13 • ?
 - 22q13.3 • (NB: Subtelomeric regions = gene-rich areas)
 - Xq • Neuroligins (post-synaptic cell adhesion molecules)

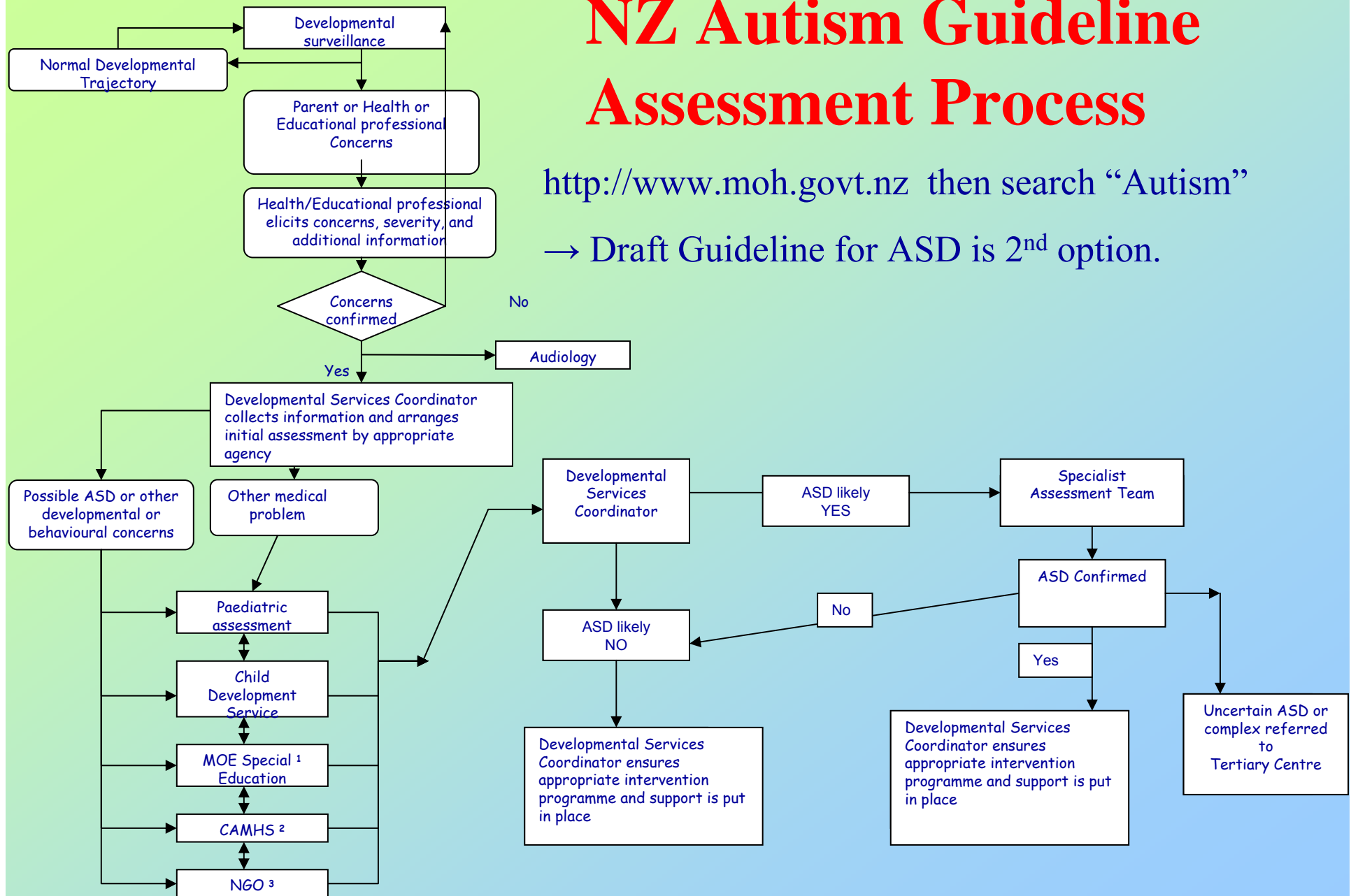
Assessment Process



NZ Autism Guideline Assessment Process

<http://www.moh.govt.nz> then search “Autism”

→ Draft Guideline for ASD is 2nd option.



Behavioural Interventions

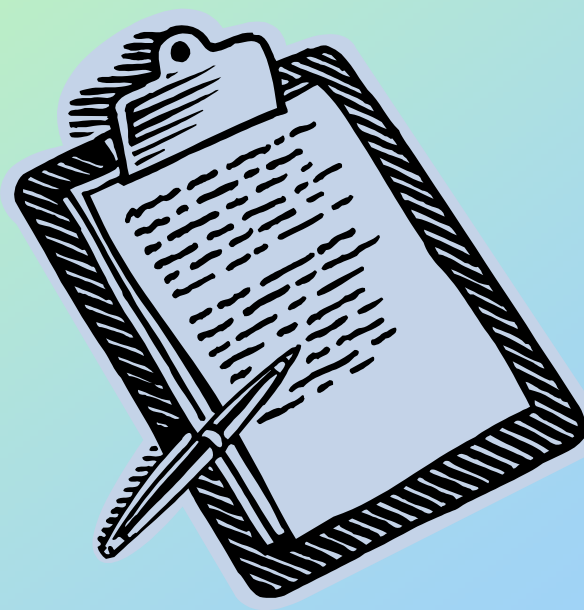
- Research outcomes
 - Few good studies
- Most effective
 - Start young
 - Intensive (20hrs p.w.)



Functional Analysis of Behaviour

- Look for ABC's
 - Antecedents
 - Behaviour (specific)
 - Consequences

- FIDO
 - Frequency
 - Intensity
 - Duration
 - Outcome



ABC Chart Example

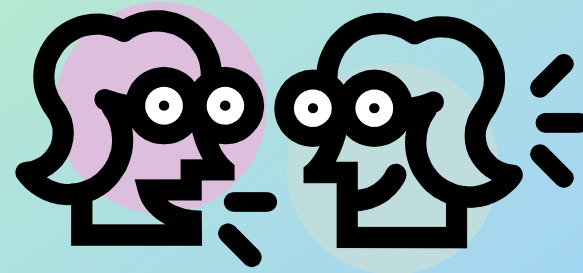
Day Date / Time	Place Where are you?	People Who is there?	Situation What's happening? (Antecedent)	Target Behaviour	Consequence What happened next?

Using the ABC chart

- Can you see any patterns?
- What is the effect on the behaviour of consistently changing the antecedent or consequence?
- With ASD often respond better to change in antecedent not consequence

Verbal Behaviour Strategies

- Instructions
 - Brief, concise, concrete, direct
 - Break things down into small steps
- Make it a discovery not advice
 - “what happens if...”
- Prepare for changes
 - “First.... Then...”
- Be specific when rewarding a child
 - “doing.... was the right thing to do”
- Social stories
 - www.thegrayscale.org



Other Behaviour Techniques

- Environment
 - Predictable / Consistent / Calm
- Visual communication
 - Visual timer
 - Pictures “First... Then...”
 - Comic strip conversations
 - Signs
- Desensitisation
- Token systems
 - need to ensure reward is reinforcing



Behavioural Strategies for “Tantrums”

- View outburst as being anxiety/stress not anger
- Calm & redirect not negotiate
- Physical exercise
 - trampoline, vacuuming, star jumps,
 - bouncing ball, running on the spot
- Relaxation
 - Blowing bubbles
 - Box of calming activities
- Decrease sensory stimulation
 - taped stories, music, earplugs, sunglasses, hat



Special Interests / Repetitive Behaviours

- 90% ASD have special interest
 - useful when developing interventions
- Repetitive behaviours, routines, questions
 - achieve predictability
 - facilitate/avoid social interaction

Strategies for Special Interests / Repetitive Behaviours

- Only change behaviour if dangerous / unacceptable
- Changing a behaviour easier than eliminating a behaviour
- Controlled access
 - “Special times/places” for “special interest”
- Write down answers to repetitive questions

Pharmacological Management

- Risperidone (aggressive, disturbed, anxious behaviour)
- SSRI (obsessive compulsive, anxious behaviour)
- Stimulants (hyperactive, short attention span)
- Atomoxetine/Clonidine (mixed profile)
- Melatonin (sleep)
- Omega 3 (general brain enhancement?)

Conclusions from Case Studies

- An ideal ASD assessment includes:
 - MDT approach
 - Observation other than in clinic
 - Information from multiple informants
 - Considering
 - other diagnoses
 - context the child is in
 - Okay to delay giving definite diagnosis!

Conclusions from Case Studies

- Complex case management includes:
 - Coordinated team of professionals and parents
 - Structured consistent multi-strategy approach
 - Visuals/behavioural analysis/positive reinforcement
 - Sensory modulation
 - Medications
 - Services and supports: financial, social, emotional and housing
 - Recognizing physical and mental illness in parents or inappropriate school placement as key determiners for lack of success in behavioural management