ADHD in Special Populations
David Dossetor Child Psychiatrist with a special interest in Intellectual Disability and Autism.

Special Populations?
A Euphemism for those with an Intellectual Disability, or Non-mainstream populations from whom we can all learn

Special Populations: children and adolescent with
- Intellectual disability
- Autistic Spectrum Disorder
- Behavioural Phenotypes

Am I developmentally behind the mainstream or Do I have some special messages?

A Historical Context of ADHD
• 1902 George Still, described 20 children who were defiant, excessively emotional, passionate, lawless, spiteful, and had little inhibitory volition, three boys for every girl, troubling behaviors appeared before the age 8, raised in benign environments, with “good-enough” parenting. He speculated, there might be a biological basis to the unbounded behavior, a genetically inherited proneness toward moral corruption.
• 1917/18 Hyperkinetic Disorders was an outcome of Encephalitis Lythargica in children affected; adult more likely to develop parkinsonian symptoms
• 1934 Levin described “organic drive” from perinatal hypoxia to prefrontal cortex blood supply eg in measles;
• 1968 DSM added a new section for C&A in which included Hyperkinetic reaction of childhood or adolescence
• 1990s DSMIV/ICD10 By convention ADHD is not diagnosed in presence of autism, reflecting assumption it may be consequent to Autism or ID

Current Context of ADHD
A NSW judge has slammed doctors for creating a generation of Ritalin kids now committing violent crimes and coming before the courts.
Judge Paul Conlon said attention deficit hyperactivity disorder (ADHD) was the most over-diagnosed condition in the community, with "naughty kids whacked" on to drugs like the powerful stimulant Ritalin.

Definition
ADHD/Hyperkinetic Disorders are characterised by a developmentally inappropriate degree of inattention, impulsiveness and hyperactivity evident in home, school and social situations varying with the degree of demand on the child and external controls and reinforcers.

The context of normal development:
- Teachers view of hyperactivity
- Poor peer relationships: the best predictor of adult morbidity
Aetiology

- Associated with risk factors:
  - Genetic 80% of the variance (in mainstream cases)
  - Brain abnormality/damage
  - Intellectual delay, learning problems
  - Substance abuse in pregnancy
  - Early environmental/stress factors
  - Evidence of decreased activity of pre-frontal lobes on SPECT scan related to dopamine transporter genes (D4 receptor gene)
- Implication of multiple causal contributors

Nature/Nurture

Genetic studies of family behaviour shows that 30% of variance of parenting is influenced by the genetics of the child (Weiss et al)

How do parents attune to the needs of their special needs child?

ADHD category or dimension? (Levy et al)

Developmentally Supportive Treatments

- 1970s: In Autism, behavioural intervention works better than talking therapies: eg teaching a child to sit still as a prerequisite for concentration (Rutter & Bartak), precursor of Applied behaviour analysis.
- Practical Strategies: Teaching calmness, stillness, sense of time, self-monitoring, concentration, organization and planning:
  - What am I doing now?
  - Am I sitting in the right place?
  - Am I doing what the class is doing?
  - What do I need to work on?
  - What needs to be organised for the next event?
- 5 minute prompts
- Fading from external prompts (teacher/parent) to self-checking
- Using timers and visual charts

The Myths of Diagnostic Overshadowing in Developmental Neuropsychiatry

- Examples:
  - Because babies can’t tell you, therefore they don’t experience pain.
  - Because institutionalisation can lead to suboptimal care, then all emotional and behavioural problems will be relieved by community care
  - Autism was originally considered Childhood Schizophrenia
  - Depression doesn’t occur in those with intellectual disability
  - Autism doesn’t occur in those with an intellectual disability
  - One should only apply and single ICD diagnosis to explain psychiatric symptoms.
  - ADHD/Hyperkinetic Disorder shouldn’t be diagnosed in Autism/PDD

The Challenge of Differential Diagnosis

1. Hyperactivity with features of emotional and conduct disorder; (Child Psychiatric Model)
2. Manic Depressive Disorder; (Adult Psychiatric Model)
3. Lennox Gastaut Syndrome; (Neuropsychiatric Model)
4. Adolescent Turmoil; (Chronological Age Model)
5. Difficulties of developmental toddlerhood; (Developmental Age Model)
6. Atypical psychosis of Chronic Organic Personality; (DSM-III-R Organic “dustbin” Labels)
7. Overactivity with stereotyped movements in severely retarded children; (New ICD-10 category)

The Working Diagnosis

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Multi-modal approach to treatment

1. Behavioural treatment and limit setting
2. Marital counselling and work on parental feelings
3. Night sedation and Thioridazine
4. A two week inpatient assessment including a trial of Lithium (also treated with Carbamazepine or Valporate for Epilepsy)

Outcome:
Admitted to a Social Services Care Hostel

Process for Improvement

1. Clear communication and strict limit setting.
2. Space in which to express his energy and activity.
3. A peer group culture of adolescents with developmental disability.

Psychiatric Diagnosis

Diagnostic classifications: - A purposeful system with limitations
- Multi-aetiological

Formulation: a weaving together of medical concepts of general medicine, neurology, developmental phenomenology and life stress / social factors.

Psychiatric phenomenology may not be reliable - depending on developmental age of <7 years or IQ of <50
Problems of atypical symptoms such as stereotypies and SIB and atypical population.
The correlation between behaviour and subjective mental phenomenon.
Do psychiatric disorders have validity in a non mainstream population?
What is the difference between a developmental disorder and a psychiatric disorder?

Psychiatric Diagnosis

Other heuristic concepts for understanding behaviour:
- Neuroanatomical models eg. Frontal lobe syndrome
- Neuropsychological models
  - Parallel processing of memory vs hysterical variability
- Neurobiological models
  - Serotonin
  - Endorphins
- Animal models
  - eg. strial frontal pathways in SIB and Dopa type 1 receptor blockade
  - territoriality, pecking orders and deprivational models of aggression
- Behavioural Phenotypes

The Truths of Psychiatry of Intellectual Disability/Developmental Psychiatry

- Treating situations of extreme disturbance in a community setting of hardship, isolation, poorly coordinated services: poverty and paralysis of “caring systems”
  - Size of the mental health problem in ID is equivalent to that of Schizophrenia (Einfeld & Tonge)
  - in Australia there is no recognised MH service for ID
- the main difference is the burden of care on families (ave 7/24, 7/7), who are special in their love, dedication, commitment and would rather see their child and themselves die than hand them over for institutionalisation.
  - Cost is $15-150,000/per year a young person
  - Recent lifetime costs for Autism 2.4 Million UK pounds
- In this context medication is a necessity that frequently enables survival, despite constrained quality of life of young person with ID and family

Developmental Psychiatry

- Methodological problems of research
- Problems of academia and research for minority populations and a minority subspecialty
- Rely on gold standard of clinical experience and expertise and peer review
- Personal View: Concept of ADHD is helpful as it provides a hypothesis for treatment in a situation otherwise considered of poor prognosis; treatment often gives families a second chance to love their child.
- Basic rules of Development: taught by mentors, experience and research
  - Assess developmental profile: motor, self-help, receptive & expressive communication, social development, educational and other community skills
  - Behaviour should first be considered from a developmental context
  - If development is delayed, then it is likely to be unevenly delayed.
  - If one domain is delayed, then there is an increased expectation of another domain being delayed
- Examples
  - if specific language is delayed is more likely to have ID or probs of social reciprocity
  - If you have coordination disorder then you are more likely to have enuresis
  - If you have delayed development you are more likely to have ADHD
  - Autism is more likely in ID (now confirmed by genetic linkage studies)
- Implication:
  Developmental processes (and impairments) are genetically linked to each other
Is ADHD a valid disorder in Children with intellectual delays.


Key Findings

- Rochester Birth Cohort n=5718, found 70 children with borderline/mild ID of whom 30% had ADHD vs 6.4% of N RJ, IQ=51 excluded. Odds ratio = 6.3 (Lee & Ousley 2006)
- Compared w/ w/o ADHD, Lachar found ID w/ ADHD had more disruptive beh incl hyperactivity, disorganization, poorer family relations and also increased depression, anxiety and weaker social skills, in the same way as pops ADHD w/o ID. He also found increased errors of omission (inattention) & commission (impulsivity) on CPT, no diff between groups**** (Lachar et al 1993)
- Sex ratio in MR & ADHD are equal
- Trajectory of symps are equivalent in Mild ID w/ PDD & ADHD (eg Yoshida & Uhlenhaut 2004)
- Teachers rate ADHD symptoms similarly w/ or w/o ID
- ID & ADHD show similar co-morbidity studies eg ODD 30-50%, CD 25% Generalised anxiety 25%, and depression 13% Tic Disorder. 50% have 2 co-morbid conditions; LDisability 15-40% & language impairment 15-75%. Reading disability; Mild mentally delayed cases (IQ 51-80) accounted for 34% of population cases (Ishii et al 2003)
- Diagnostic Criteria for Learning Disabilities/MR (UK) recognises the validity of ADHD in adults 15-55%
  - The lower the IQ the higher the prevalence and
  - Lower IQ is likely to have more extreme symptoms (Seager & O’Brien 2003)
- Family studies not done with MR

Is ADHD a valid disorder in Children with intellectual delays.


Laboratory Studies

- Molecular genetics: MEZIO studies (in normal IQ), found stronger cross twin correlations for IQ & ADHD in MZ, suggesting a shared genetid aetiology and phenotypic correlation between the traits accounting for 86% of cross phenotype correlation and 100% cross research diagnosis. (Kamali et al 2003)
- Differences in length of Taq I polymorphism of the dopamine beta hydroxylase were assoc w/ signif differences in symptoms H& I, and neuroc testing; yet also had an effect on IQ (Barkley et al)
- Neuroimaging: Syndromal ID & ADHD assoc w corpus callosum abn esp linking temporal and parietal cortices. In VCFS, those with and without ADHD showed differences in posterior Corpus Callosums (Antshel et al 2003)
- Neuropsychology: research slow, although profiles in mild ID are now described

Course/outcome

- ADHD w mean IQ 101 score 73 on Vineland, indicating impairment equivalent to mild ID
- ADHD w ID: more functional impairment is expected though not researched
- Prog of ADHD is affected by IQ eg affecting progression into adulthood.
- ID & ADHD FU for 4 yrs into adolescence: 50% continued to have ADHD, as well as higher rates of co-morbidity: anx 50%, tics 40%, elimination Disorders 40%; best predictor of ADHD at T2 was ABC inappropriate speech scale score. (Aman et al 2003)

Is ADHD a valid disorder in Children with intellectual delays.


Treatment response:
- chart review of 10 adults improved on either stim (Lee, Handen & Handen 2004)
- Methylphenidate Rs: 44% showed 30% reduction; Lower functional level may be assoc w/ less favourable response (Hassan et al)
- with increasing effects with increasing dose of stimulants, both beh & neuroc testing: yet continue to have pros, 1-5yrs later 68% still had pros (Santos & other studies)
- Also clomipramine has dose related effect (Aggarw et al 2001)
- Comparison of Risperidone and Methylphenidate for ADHD in Children and adolescents with moderate mental retardation.
  - N=45, single blind, randomised parallel group trial
  - Both reduced ADHD symps but More pronounced effect for risperidone;
  - Slms reduce wt, risperidone increases wt.
  - Choice might be influenced by side effects and co-morbidity.
  - Prudden to trial starts (By-A, et al 2001)
- BT developed in ID: DRO, TO, response cost, overcorrection are now used in ADHD (eg Barkley 2005)
- meta analysis indicated response contingent procedures were more effective than others (Didden et al 97)

Is ADHD a valid disorder in Children with intellectual delays.


• Review that tests Robin & Guze criteria of reliability and predictive validity:
  - clinical correlates.
  - family history.
  - treatment response.
  - lab studies.
  - course, outcome.

Background

• IQ of ADHD is 9 pts lower; correlation = -.3 in general population
• Most research in ADHD excludes people with ID, and the interview/psychometric instruments aren’t validated in ID eg DISC. are in >80IQ
• How do you determine if symps are excessive for mental age?
• Measures of impairment: In PDD impairment ratings are similar with or without ADHD: is it does matter?
• Rutter IOWP study showed rates of ID 4-5x greater in ID
• The answer is to review the literature on those with IQ between 50 and 80

ADHD in Autism and PDD

- ADHD was reported in 78% of clinic population of PDD. Hyperactivity more in Autism vs other ASDs (Lee & Ousley 2006)
- ADHD symptom subtypes in children with PDD. Subtypes readily identifiable w & w/o PDD (Gadow K, et al; 2006)
  - Control study of Inattention, Hyperactivity and Impulsivity in teenagers with ID w/kw/autism: Tot N=72, 4 groups; used ADI-R and DSM clinical diagMild-mod, ave age 16; (Bradley E. 2006)
  - One in 2 teens with ID & Autism had HII,
  - compared with 1/7 of ID alone.

Drug Therapy for ADHD-like symptoms in Autistic Disorder. (Hazel P, 2006)

- By convention ADHD is not diagnosed in presence of aut, reflecting assumption it may be consequent to Aut or ID
- Inattention affects 60% and hyperactivity 40%; an important cause of impairment
- Are their qualitative differences?
  - May have restricted attention;
  - overactivity may arise from stereotypes, tics, anxiety, agitated depression, or mania.
- Aggression is common in Autism & may be incorrectly attrib to ADHD
- Care in history and observation before prescribing
- There is no specific drug treatment for Autism; yet medications have been used for discrete problem areas
  - Inattention
  - Tics
  - Stereotypic rituals
  - Hyperactivity
  - Sleep problems
- Self injurious behaviour
- Paper reviews efficacy & tolerability of medications for hyperactivity and inattention in Au from medline search where there was systematic outcome measure of symptoms H & I, mostly Conners Scale and Aberrant Behaviour Checklist
Drug Therapy for ADHD-like symptoms in Autistic Disorder.

- Increase in meds for Autism by 50% from 1993-2001 to 30%
- Antidepressants most common,
- Stimulants, antihypertensives have doubled (alpha agonists)
- mood increase in antipsychotics,
- not in anxiolytics (Aman et al 05)

Psychostimulant medication
- Dopaminergic pathways implicated in ADHD & Autism
- Retrospective chart unstandardised study of 195 improved 25% but 60% had adverse events, esp agitation (Stigler et al 2004)

- RCTs more encouraging
  - Quintana n=10, found improvement on Aberrant Behaviour Checklist, but parental reports of Hyperactivity showed no shift from placebo
  - Handen n=13 compared with two doses of MPH: 8/13 were responders of >50% reduction of Hyperactivity
  - Research Units on Pediatric Psychopharmacology Autistic Disorder Network study (RUPP): n=72 at 3 diff doses of MPH 49% responded with effect size of 0.54; teachers ratings indicated greatest effect with greatest dose

Selective Noradrenergic Reuptake Inhibitors (SNRI)
- No RCTs
  - Atomoxetine Chart review n=20 (not nec ADHD)
    - Signal reduction of Hyperactivity and Inattention
    - adverse events common: decreased appetite, irritability, mandibular and salivation

Selective Serotonin Reuptake Inhibitors (SSRI)
- Fluoxetine n=5 chart review (not nec ADHD)
  - Found 14% increase in Hyperactivity (ns); 2 had SE of agitation
- Clomipramine RCT n=12 (not nec ADHD)
  - Signal reduction of Hyperactivity
- Clomipramine vs haloperidol vs placebo (not nec ADHD) n=57
  - Clomipramine NS vs placebo
  - One case had severe agitation and aggressive onset needing hospitalisation and withdrawal of clomipramine
- Mitotane (SNASSRI) n=20 open label (not nec ADHD)
  - No reduction in Hyperactivity/ Anxiety
  - SE of increased appetite
  - One case had severe agitation and aggressive onset needing hospitalisation and withdrawal of clomipramine

Antipsychotics
- Valproate open label n=14 4-46yrs (not nec ADHD)
  - 75% became less impulsive
  - SEs w/gain and salivation
- Topiramate n=15 chart review (not nec ADHD)
  - 30% more reduction of Inattention & 30% of Hyperactivity
  - SEs cognitive slowing, rash
- Lamotrigine RCT n=26 (not nec ADHD)
  - no differences and increased SEs

Antidepressants
- Naltrexone in ADHD associated with self preoccupied SIB
- Propranolol in episodic dyscontrol, anxiety and PTSD
- I consider clonidine where I suspect Hyperactivity is associated with Anxiety
- Carbamazepine can be useful
- Tricyclics esp Amitriptyline is effective, as second line medication
- Atypicals are effective but limited by their SEs
- No evidence on sustained release
- Haloperidol
  - 24% reduction of Hyperactivity
  - SEs nausea and vomiting (1) & mild irritability (1)
  - No evidence on sustained release
  - Clonidine effects equivocal
  - RCT shows Stimulants are effective; Some benefit may have been underestimated if used in absence of Hyperactivity
  - Donezepil
  - Cholinergic
  - Guanafacine (NA in Aus/NZ)
  - 26% were much improved
  - Transient sedation in 31%
  - 24% reduction of Hyperactivity
  - 4/5 lost wt (although attributed to the discontinuation of previous antipsychotic)
  - 50% and ASD 25%
  - 75%
  - 65%;
  - 38% & Others incl Schizophrenia, Anstel K et al & Shprintzen R. 2006
  - 80% Psych Disorder; 95% Hyperacusis; Leyfer et al, 2006
  - 50% and ASD 25%
  - 43%
  - 40%;
  - Smith Magenis Syndrome 90%
  - ID, Aggression, autism, self injurious behaviour, inattention cycle, obsessions, anxiety, specific learning probs etc
  - Fragile X 75% but hyperactivity declines after puberty
  - Soto’s Syndrome/Cerebral Gigantism 38%
  - Tuberose Sclerosis 35%
  - Williams Syndrome (microdeletion of 7q 11.23) 65%;
  - 80% Psych Disorder; 95% Hyperacusis; Leyfer et al, 2006
  - Turners Syndrome girls 45XO:
  - 80% Psych Disorder; 95% Hyperacusis; Leyfer et al, 2006
  - CHARGE Syndrome: ADHD approx 45%;
  - Cornelia de Lange’s Syndrome
  - Soto’s Syndrome/Cerebral Gigantism 40%;
  - ID, Aggression, autism, self injurious behaviour, inattention cycle, obsessions, anxiety, specific learning probs etc
  - Fragile X 75% but hyperactivity declines after puberty
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  - Neurofibromatosis NF1 Aut dom
  - 50% Philip & Turk 2006.
  - Velo Cardio Facial Syndrome 43%
  - Simple Phobia 22.6% Anxiety Disorders 17% Enuresis 14% Major Depression 12% & Others incl Schizophrenia, Autism et al & Depression R. 2006

- Chart review of 2231 youths referred to a Fetal Alcohol Syndrome Clinic: mean age 8.7yrs; across 4 US states; from 4 clinics that routinely evaluate and diagnose FAS.
- Estimate 25 kids/week are born with FAS; half were native Americans.
- Categorised according to levels of risk for gestational alcohol exposure: 4= weekly binge drinking in preg, 3= exposure but level unclear, 2= unknown exposure, 1= no exposure; Diagnosis only if in medical record.
- First ranking disorder in was rates in gp 4:
  - ADHD 41(49)%;
  - Learning disorder 17(45)%;
  - ODD/CD 16(41)%;
  - Anger control probs , unspec mood disorder & sleep disorder 10(50)%;
  - Mental Retardation 7.5(55)%

- Mechanisms:
  - Genes for ADHD predispose to maternal drinking as well as ADHD in child
  - Gestational alcohol causes ADHD via damage to developing dopa neuro systems
  - ADHD in FAS is a distinct subtype of ADHD syndrome
  - Prenatal Etoh is a measure of post natal mothering causing psych probs

ASD & ADHD in boys w Fragile X premutation; Facchin F et al. & Hageman R. 2006.

- Premutation: 55-200 CGG are considered unaffected
- SCQ/ADI-R and Conners N=14 probands and 13 control brothers
- 93% had ADHD symptoms, 79% had ASD vs 38% & 8%


- Developmental Coordination Disorder & ADHD each 7% prevalence
- Twin study 1285 pairs 5-15
- Rate of co-morbidity is 50% (Barkeley)

- Strengths and Weaknesses of ADHD symptoms and normal behaviour scale (SWAN), Developmental Coordination Disorder Questionnaire (DCDQ)
- Structural equation modelling
- Show a strong shared additive genetic component between most subtypes of ADHD and DCD

Case scenario

- “Martin” 12yo: Complex developmental disorder of presumed genetic origin and major disruptive problems
- Presentation: Small for age, skinny, red hair, minimal eye contact, restless and fidgety
- Expressive dysarthria particularly for Rs and Ss which sounded possibly palatal and due to problems of muscle tone and coordination
- Talking of sad events: death of GMGM (6/12ago), the cat that ran away 2 yrs ago, a friend who drowned 3 yrs ago.
- “used to get bashed at school”, didn’t like school, did like soccer; has a few friends but none in his class.
- When anxious get aggressive and self injurious

Diagnosis:

- Mild Intellectual Disability
- Developmental motor dyspraxia disorder,
- Eneuresis, Soiling
- Complex language disorder with specific receptive, expressive and semantic pragmatic problems; (”put a sock in it”)
- PDD nos (ASD) (serious deficits in social relating skills and understanding, is ignored by peers, stereotypic interests in cars and space, sensory sensitivities)
- ADHD
- Depression
- Various anxiety disorders: separation, phobic, panic & general
- Selective eating disorder
- Problems with father, PTSD, couldn’t eat for 4 days, school refused for 10 days
- Inadequate support from education system to support special needs
Treatment

Multiple problems needs multi-component treatment

- Skilled mothering
- Court protection from F
- Paediatrician called Case Conference to coordinate and value different agencies contribution
- OT Sensory assessment for sound and tactile sensitivity; splints for writing
- Advocacy in school: integration funding, made library monitor for recess
- Medications:
  - Ritalin 15, 10, 10 helps developmental and educational perf and emotional reg
  - Amitriptyline 25mg. helps ADHD, enuresis, writing, emotional regulation including anxiety such he could access anxiety management skills better, increased appetite
  - Risperidone 0.5 lam & 3pm helps aggression, anx and appetite
  - Clonidine 100mcg at night
  - Epile withdrawn
- Orthopaedics: Serial plaster to ankles for his shortened achilles secondary to toe walking

Note that brother has been on every medication and particularly benefited from Lamotragine and Propranolol.

Went to Gold Coast by plane for week’s holiday with Mother!

Conclusion

- ADHD is a predominantly biologically-based process of inefficient mental processing of consciousness
- Special populations are likely to help us understand multiple different ways in which this inefficient processing occurs
- We have such limited understanding of the early biological development of the mind.
- As we make strides in our understanding of mental development, we shall learn more about helping troubled disabled children
- The complacent and ill informed will continue to complain that we have caused the problems of hardship and disability in children