Attention Deficit Hyperactivity Disorder

Dr Daryl Efron

The Royal Children's Hospital Melbourne

Attention Deficit Hyperactivity Disorder

- History
- Definition
- Neurobiology
- Causes
- Assessment
- Comorbidities
- Management
  - (non-pharm), meds
- Developmental trajectories

1798 Sir Alexander Crichton

AN INQUIRY

INTO THE

NATURE AND ORIGIN

OF

MENTAL DERANGEMENT.

COMPREHENDING

A CONCISE SYSTEM

OF THE

PHYSIOLOGY AND PATHOLOGY

OF THE

HUMAN MIND.

AND A

HISTORY OF THE PASSIONS AND THEIR EFFECTS.

By ALEXANDER CRICHTON, M.D.

PHYSICIAN TO THE WESTMINSTER HOSPITAL, AND PUBLIC LECTURER ON THE THEORY AND PRACTICE OF PHYSIC, AND ON CHEMISTRY.

VOLUME I.

LONDON:

PRINTED FOR T. CADELL, JUNIOR, AND W. DAVIES, IN THE STRAND.

1798.

"a history of the passions and their effects "

Mental restlessness:

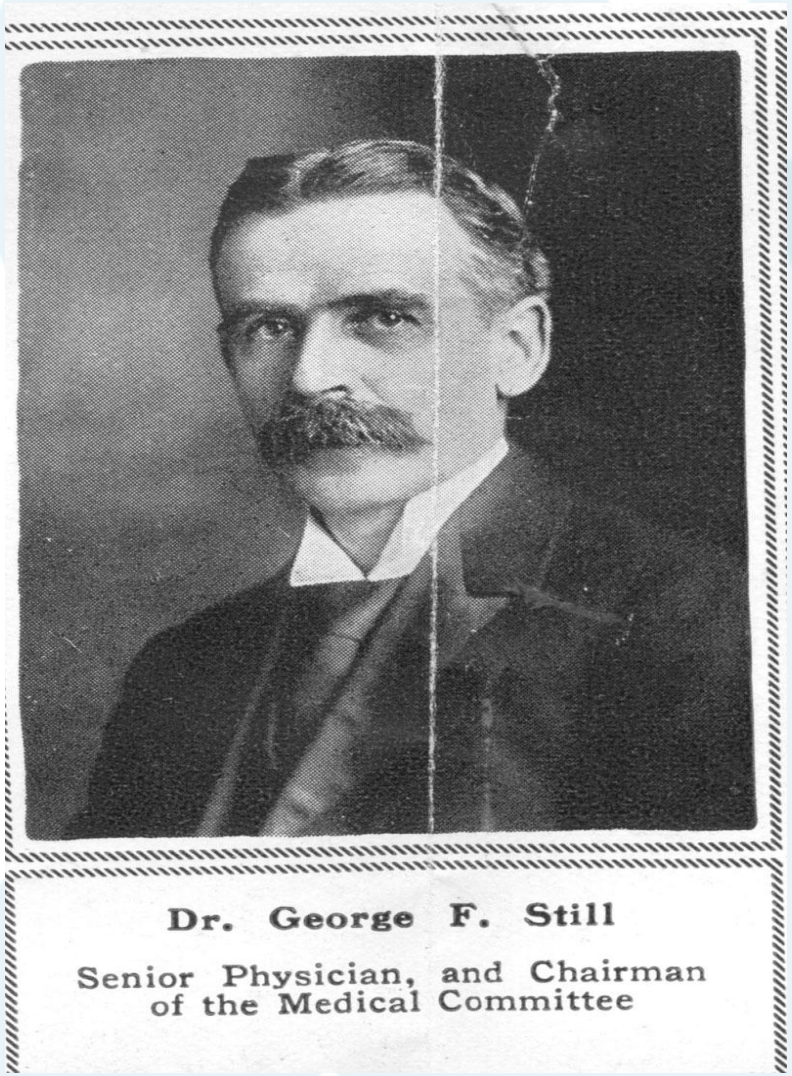
- Deficits in attention
- Occurring across situations (e.g. home & school)
- Begins early in life
- Causes impairment in learning

The Royal Children's Hospital Melbourne

1865
Dr Heinrich Hoffmann

Let me see if Philip can
Be a little gentleman;
Let me see if he is able
To sit still for once at table:"
Thus Papa bade Phil
behave;
And Mamma looked very
grave.
But fidgety Phil,
He won't sit still;
He wriggles,
And giggles,
And then, I declare,
Swings backwards and
forwards,
And tilts up his chair,
Just like any rocking-horse-
"Philip! I am getting cross!"

1902 Sir George Still



- RCP lectures
- 43 children
  - inattentive, impulsive, defiant and overly emotional
  - *“defective moral conduct”*

The Royal Children's Hospital Melbourne

History

1920's-30's	Post-encephalitic behaviour disorder (Spanish flu pandemic 1917-28)
1937	Charles Bradley - benzedrine
1950's	Minimal brain damage
1954	Ritalin (Ciba-Geigy) - Leandro Panizzon, wife Margeurite ("Rita")
1960's	Minimal brain dysfunction
1960's-70's	Hyperactivity
1980's	Attention deficit disorder (Douglas 1972) - 1980 DSM-III
1994	DSM-IV: ADHD

Definition

Developmentally inappropriate degrees of:

- impulsivity,
- inattention,
- and often hyperactivity

ADHD: DSM-IV criteria (1994)

Developmentally inappropriate degrees of:

- inattention,

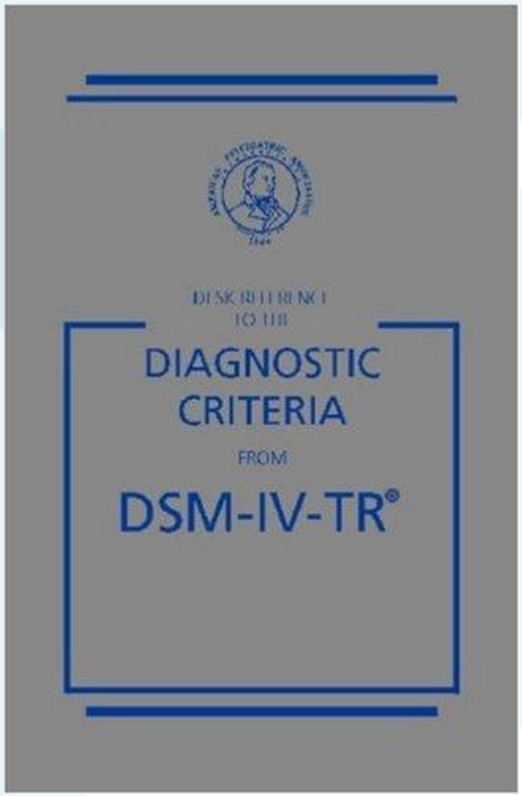
  Often has difficulty sustaining attention in tasks or play activities
  Often does not follow through on instructions and fails to finish schoolwork chores or duties in the workplace

- impulsivity,
- and often hyperactivity

  Often interrupts or intrudes on others
  Often leaves seat in classroom

ADHD - DSM-IV criteria (1994)

- Symptoms present > 6 months
- Onset before age 7
- Clear evidence impairment in ≥ 2 settings
  - in social, academic or occupational functioning
- Excl PDD, psychotic disorder, personality disorder



Subtypes

	Inattention (≥ 6/9)	Hyperactive / Impulsive (≥ 6/9)
Combined type (75%)	✓	✓
Predominantly Inattentive (25%)	✓	
Predominantly Hyperactive / Impulsive		✓

Inattentive type

Different to combined type

- symptoms (not disruptive)
- age of onset
- gender ratios
- assoc problems - language / learning, social skills deficits, anxiety
- response to stimulants less marked

Problems with DSM-IV

- Thresholds arbitrary (eg. >6 inatt, 4-5 H-I)
- Inattentives included in “Disruptive Behaviour Disorders”
- No variation by developmental stage
  - item content, thresholds
- Definition of impairment?
- How to combine reports from different informants?

ADHD: DSM-5 criteria (May 2013)

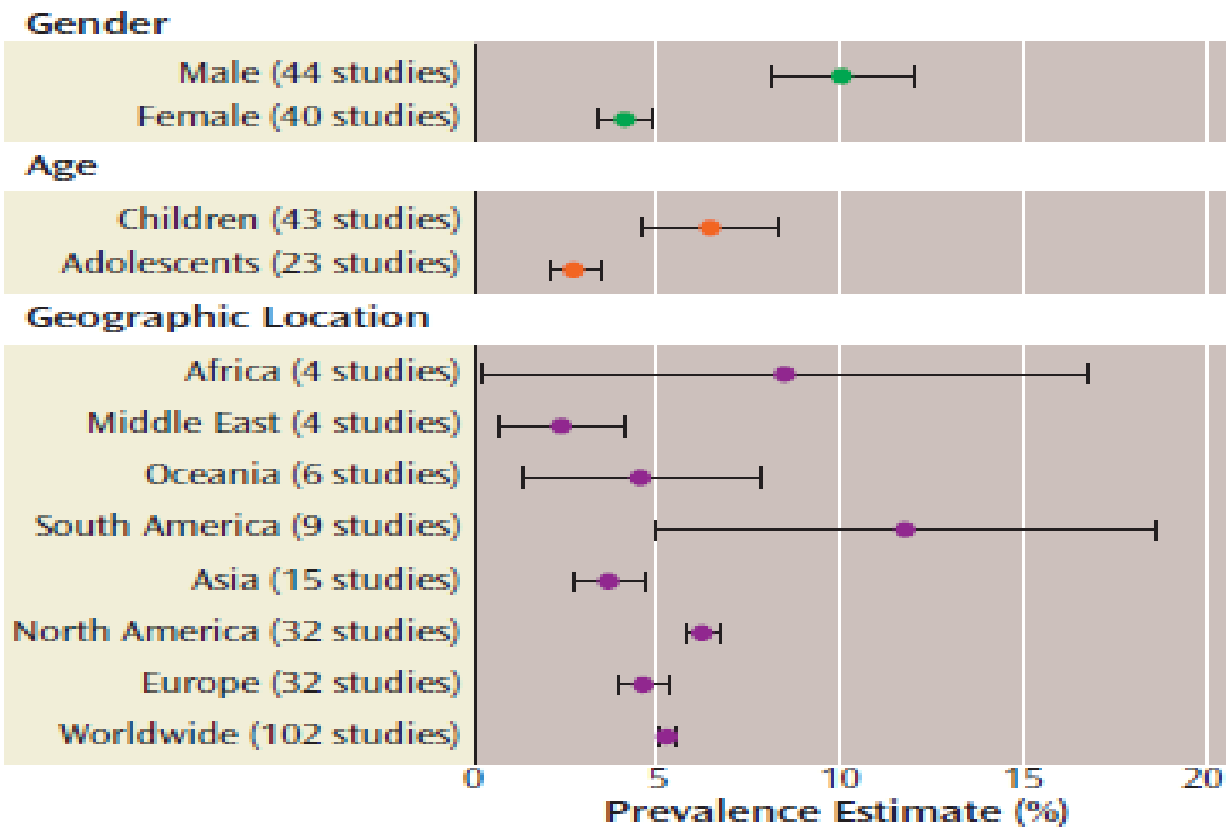
1. Onset before age 12 (during childhood)
2. Adults (age > 17 yrs)
   - fewer symptoms required
     - 5/9 from either / both lists
   - alternative item wording
     - feels restless
     - fails to meet deadlines, difficulty completing forms / paying bills
     - loses keys, mobile phone
     - makes important decisions on spur of moment
     - commits to relationship after brief acquaintance
3. PDD exclusion removed

DSM-5: descriptive text

- "Signs may be minimal or absent when the individual is …in a novel setting, is engaged in especially interesting activities, has consistent external stimulation (e.g. via electronic screens), or is interacting in one-on-one situations (e.g. the clinician's office)."
- Comorbidities
  - "Assoc features may include delayed language or social development, irritability / mood lability, learning disorders"
- Different informants
  - "Confirmation of substantial symptoms across settings requires consulting informants who have seen the individual in those settings"

Epidemiology

(Polanczyk et al. Am J Psychiatry 2007)



Aust 6.8% *(Graetz JAACAP 2001)*

The Royal Children's Hospital Melbourne

Prevalence

- Estimates vary: 2-18% (3-5%)
- All countries, all ethnic groups
- Uneven socio-economic distributions
- Males
  - 5-10X in clinic referrals
  - 2-3X in community settings
- Mean age at diagnosis 9 yrs (boys < girls)

Effects

Individual

- Reduced quality of life *(Klassen 2004, Sciberras 2011)*
- Underachievement *(Hinshaw 1992)*
- Social isolation *(Friedman 2003)*

Flow-on effects

- Family stress *(Johnston & Mash 2001, Cussen 2011)*
- Impact on schools, workplaces, broader community

Costs

$US31-52 billion / yr!

- health care, lost productivity, criminality etc

“A serious public health problem” CDC 2002

The Royal Children's Hospital Melbourne

Attention

Alerting

- Initial arousal to sensory stimuli (warning signal)

Orienting

- Attend quickly to source

* Executive

- Choices – shifting, switching
- Effortful control (non-habitual)
- Unique to humans

Neuropsychology

(Rappley NEJM 2005)

Response inhibition (self-regulation)

- Consciously inhibit immediately rewarding response
- Allocation of attention (will-power)

Working memory (temp file)

- auditory, visuo-spatial

Executive function deficits

(Douglas 1970; Schachar 2012)

- Planning, preparing, initiating (Tower of Hanoi)
- Holding (WM – verbal, visuoaspatial)
- Switching (mental flexibility eg. Wisconsin card sorting test)
- Error processing – identification, adjustment
- Inhibitory control
  - withholding (Go-no go, CPT)
  - cancelling (braking eg. Stop signal task)

Executive function deficits in ADHD

- Seen in all subtypes
- Variable between subjects
- Weak relationship with functional deficits
- Insufficient sensitivity and specificity for diagnostic purposes
- Lacks utility to predict course / outcomes

Neurophysiology

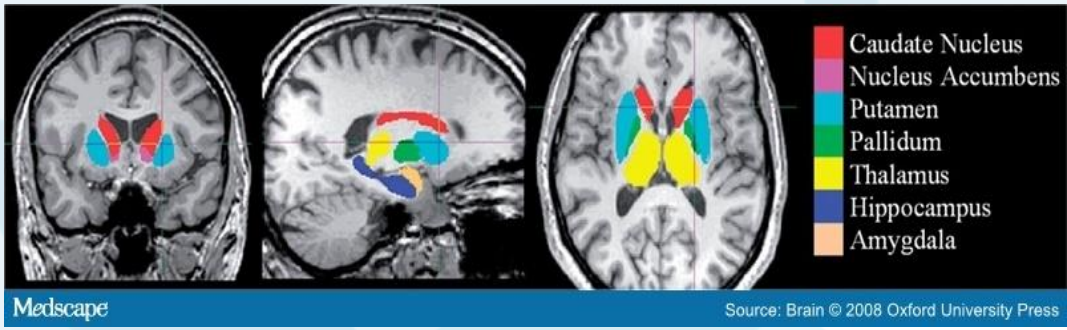
- Dopamine dysregulation (receptor / concentration) *(Sagvolden 2005)*
  - Mesolimbic – delay aversion, impulsivity, disinhibition
  - Mesocortical – inattention, poor planning
  - Nigrostriatal – neurological “soft signs”, clumsiness
- Disordered activation (fMRI)
  - under activation
  - activate more diffuse areas than controls during tasks
- Reduced “functional connectivity” (steady state) *(Sun 2012)*

Structural imaging

- MRI - total cerebral volume and cerebellar vol. 3% reduced cf controls *(Castellanos JAMA 2002)*
  - Reduced cortical thickness
  - Caudate vol smaller school-age, no diff older
  - Holds when control for med history
- Delayed cortical thickening, gyrification *(Shaw 2012)*
  - Normalization - remission / lack - persistence *(Halperin 2011)*
- Adults with ADHD – cortical thinning in DLPFC, R inf parietal lobe *(Makris 2007)*

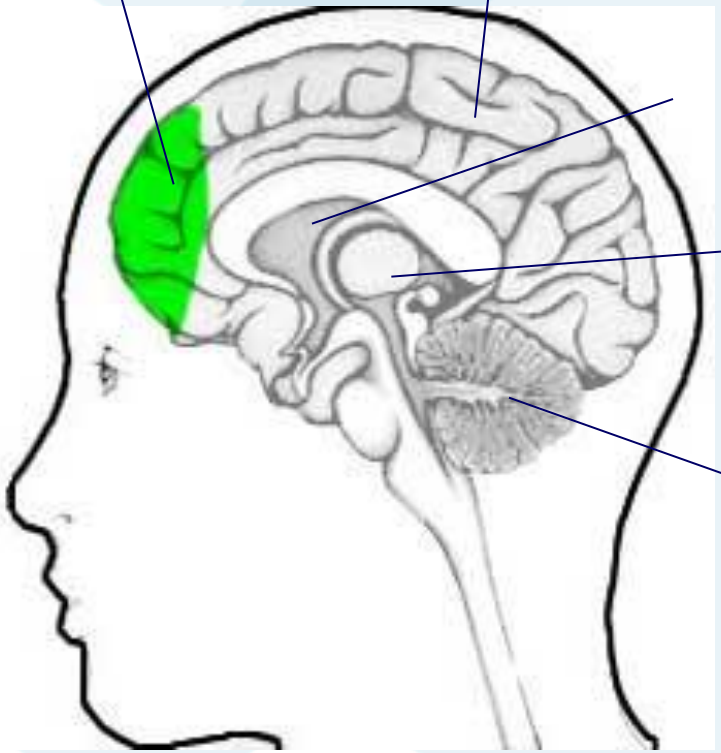
Brain structures involved

(Castellanos & Tannock Nature 2002)



Pre frontal cortex

Parietal cortex



Limbic System (amygdala, hippocampus, anterior cingulate)

Deep grey matter

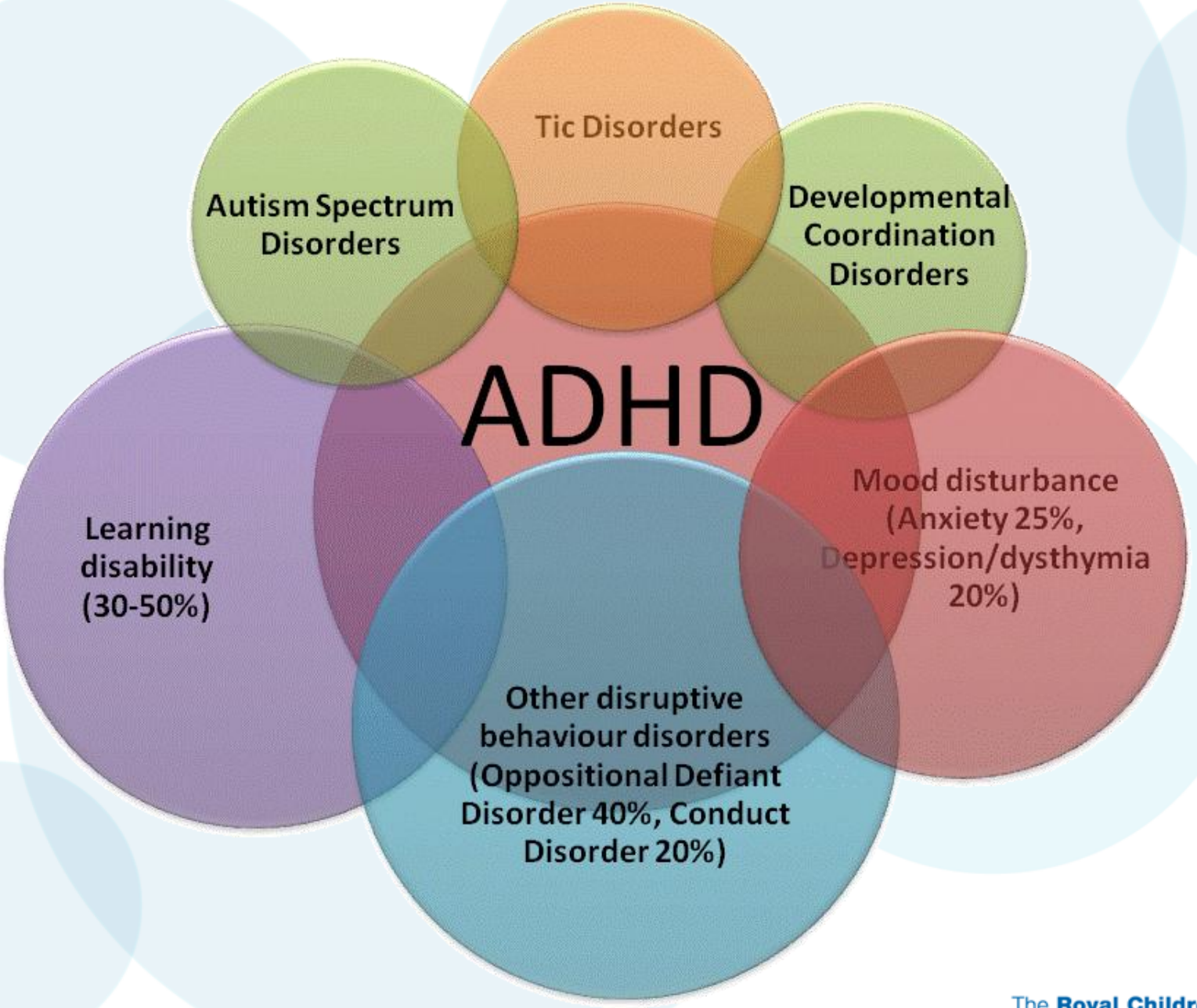
(caudate, putamen)

Cerebellum

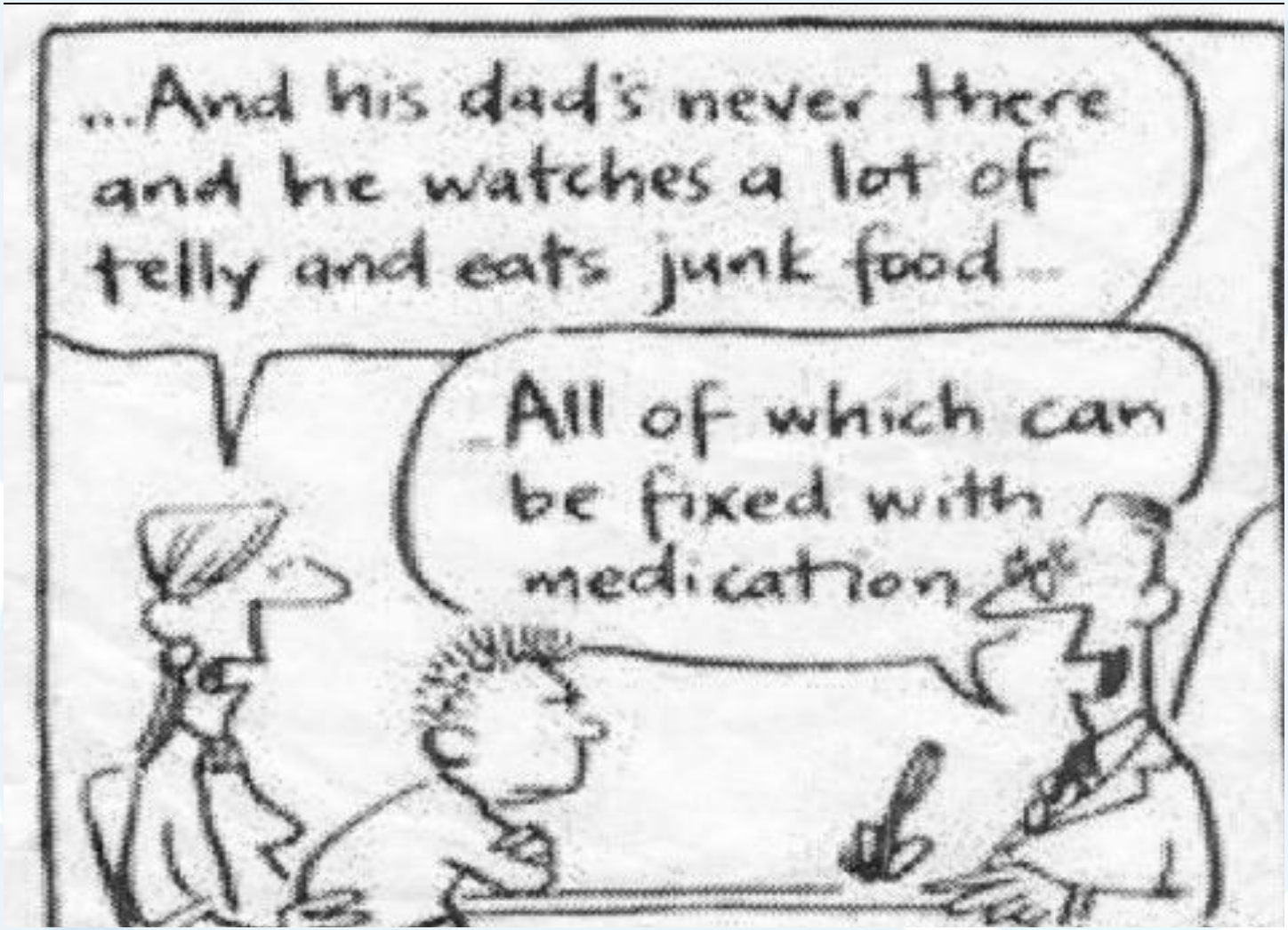
The Royal Children's Hospital Melbourne

Co-morbidities

- 80% have one or more
- Often dictate priority interventions
- Assoc with different trajectories
  - Aggression – conduct disorder, antisocial PD
  - Anxiety - depression



The Royal Children's Hospital Melbourne


...And his dad's never there and he watches a lot of telly and eats junk food...
All of which can be fixed with medication

Aetiology - Genetics

(Hay & Levy 2002, Faraone 2005; ADHD Molecular Genetics Network)

- Heritability > 70%
  - 1st degree relatives - 4-8 X increased risk
  - MZ twins >50% concordance; sibs 33%
- Linkage studies
  - Neurotransmitters with candidate polymorphisms: dopamine (DRD4, DAT1), NA, MAO, GABA, serotonin – inconsistent / unreplicated findings
- Genome-wide scan (GWAS)
  - Hypothesis-free – need v large samples (cross-disorder now)
  - No genome wide associations (Neale et al meta-analysis JAACAP 2010)

Many genes of small effect (OR for any one ~ 1.2)

Aetiology - Genetics

(*Williams et al, Lancet 2010)*

Rare chromosomal deletions and duplications in attention-deficit hyperactivity disorder: a genome-wide analysis

Nigel M Williams, Irina Zaharieva, Andrew Martin, Kate Langley, Kiran Mantripragada, Ragnheidur Fossdal, Hreinn Stefansson, Kari Stefansson, Pall Magnusson, Olafur O Gudmundsson, Omar Gustafsson, Peter Holmans, Michael J Owen, Michael O'Donovan, Anita Thapar

Summary

Background Large, rare chromosomal deletions and duplications known as copy number variants (CNVs) have been implicated in neurodevelopmental disorders similar to attention-deficit hyperactivity disorder (ADHD). We aimed to establish whether burden of CNVs was increased in ADHD, and to investigate whether identified CNVs were enriched for loci previously identified in autism and schizophrenia.

Lancet 2010; 376: 1401–08
Published Online
September 30, 2010
DOI:10.1016/S0140-6736(10)61109-9

SNP microarray (n=410 cases, controls 1156)

- copy no. variants (deletions, duplications) burden incr. 2.1
- **loci signals overlap with autism, ID, SCZ, epilepsy (multifinality)**

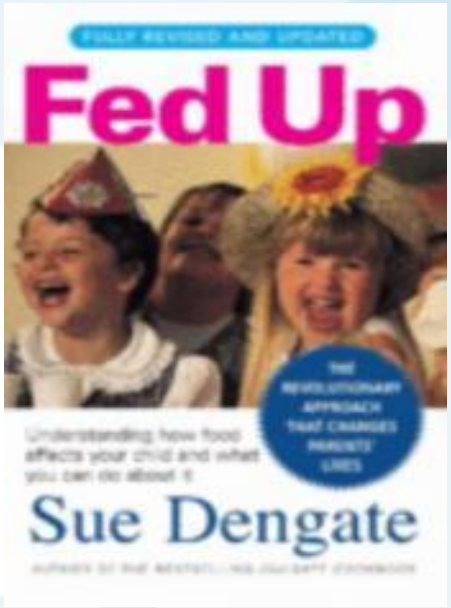
Aetiology - Environmental exposures

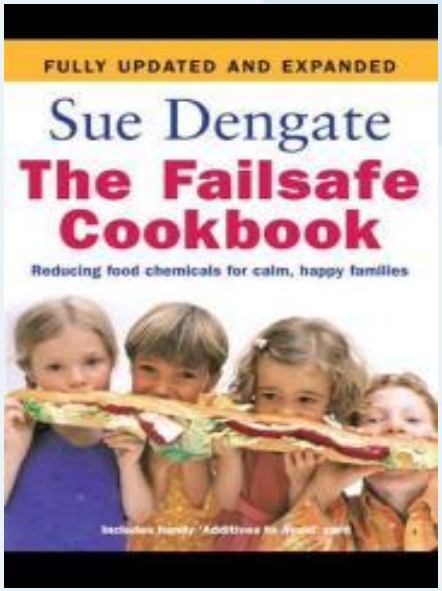
Toxins

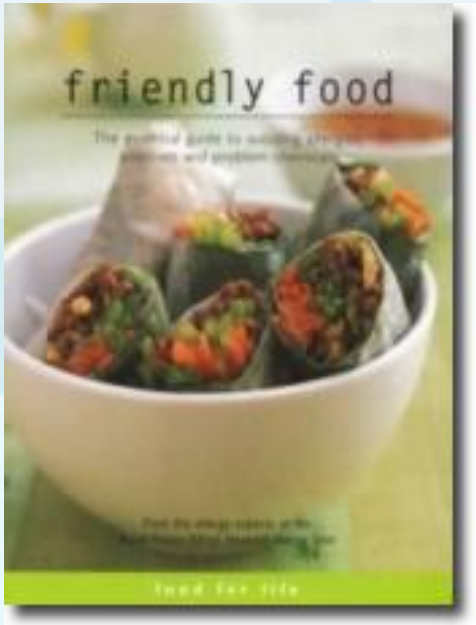
- embryopathic
  - tobacco *(Thapar 2003)*
  - alcohol (FASD) *(Talge 2007, Peadon 2010)*
- Childhood neurotoxins
  - lead *(Goodlad 2013)*

Diet (food sensitivities)

- colourings, preservatives
- salicylates, amines







The Royal Children's Hospital Melbourne

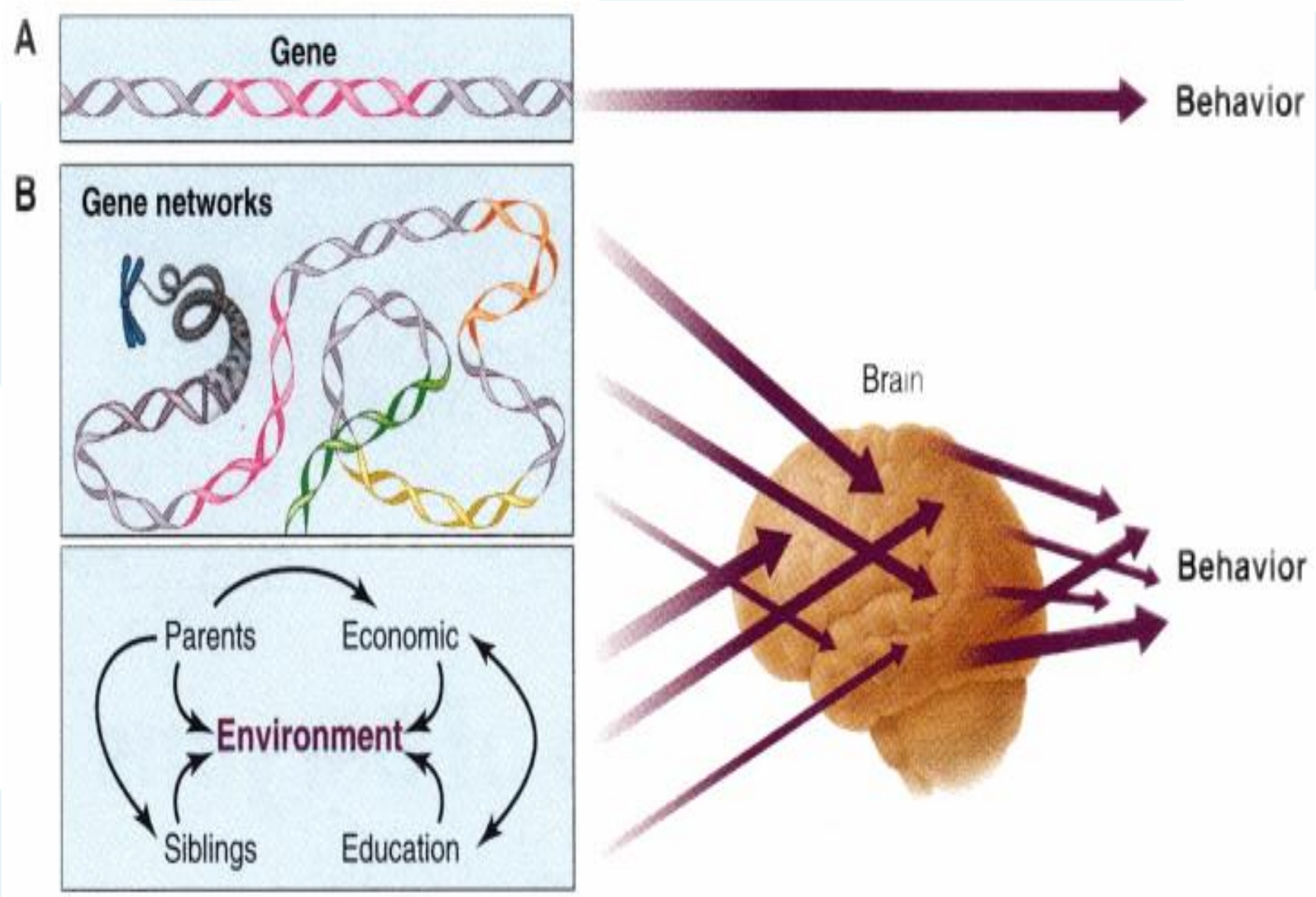
Biological risk factors

- Premature birth *(van Baar 2009, Lindstrom 2011),*

  low birth weight (OR 2- 2.5) *(Galera 2011)*
  - decr grey matter, white matter injuries
  - disruption of cortical development / connectivity
  - contribution of sensory stress, sleep deprivation, repetitive pain, disrupted parent-child interaction?
- Brain injury
  - traumatic *(Herskivitz 1999),* CVA - putamen *(Max 2002),* infective

Parenting / family

- Family dysfunction, parental stress
  - common in ADHD *(Johnson & Mash 2001)*
- Parental psychopathology, family conflict more strongly assoc with ODD / CD than ADHD *(Deault 2010)*
- ADHD predicted by
  - Post-natal depression *(Sciberras 2011)*
  - Early deprivation *(Kreppner 2001)*
  - Psychosocial disadvantage *(Biederman 1995)*
  - Harsh / coercive parenting of young children *(Hughes & Ensor 2007)*
- Early maternal "scaffolding behaviour" (supportive, assisting risk-taking / growth) protects against ADHD in children with dev delays *(Baker 2010)*



Hamer Science, 2002

Genetics – environment

(Wilcutt et al 2010)

Critical periods

- Brain vulnerability / expression varies depending on developmental stage of insult

  eg. embryotoxins, attachment, binocular vision / amblyopia

Interaction effects

- polymorphism plus exposure $\rightarrow \uparrow$ risk

  eg. DAT-3 / smoking in utero *(Kahn 2003)*

Epigenetics

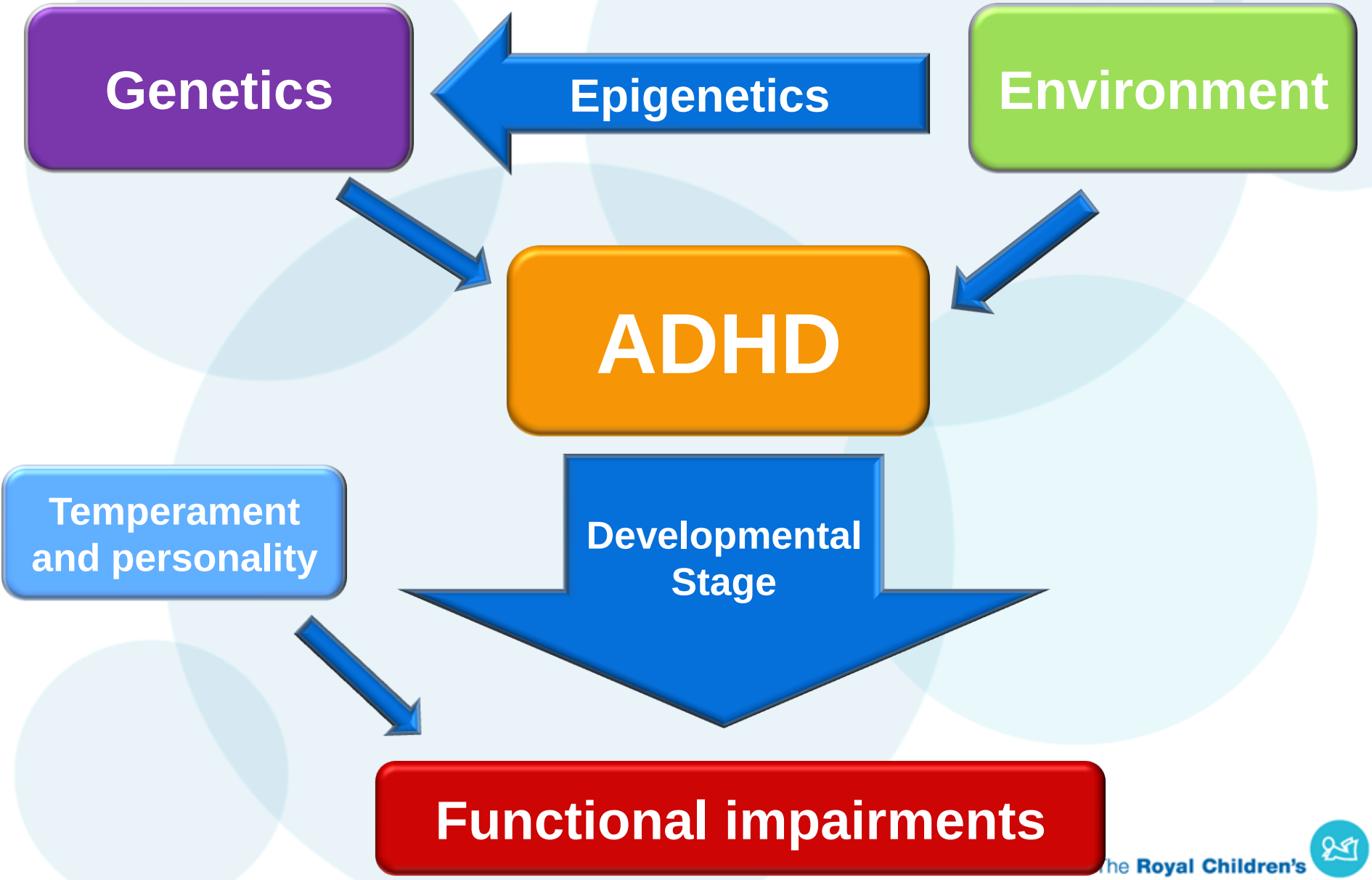
- inherited changes in phenotype caused by variation in gene expression (chromatin remodelling, DNA methylation)

Polygenic disorders – pathway analysis *(Neale 2009)*

PHENOTYPE	behavioural traits
PHYSIOLOGY	functional connectivity, activation
STRUCTURE	
EPIGENETICS	Environmental influences
GENETICS	SNPs, microdeletions / microduplications,

Polygenic disorders – pathway analysis *(Neale 2009)*

PHENOTYPE	behavioural traits
COGNITIVE ENDO-PHENOTYPE	**executive functions (developmental skills)**
PHYSIOLOGY	functional connectivity, activation
STRUCTURE	
EPIGENETICS	Environmental influences
GENETICS	SNPs, microdeletions / microduplications,



Diagnostic journey of the vulnerable child

Stage	Diagnosis
Infancy	Infant distress / sleep dysregulation
Toddlerhood	Language delay
Pre-school	Aggression / social-emotional delay
Start of school	ADHD / ODD
Mid-primary school	Learning disorder
Mid-primary school	Autism spectrum disorder

Transitions

- Anticipated
  - Commence school, high school
- Random
  - birth sibling, family rearrangements (parental separation / re-partner), parental illness, grief,
  - mismatch with new teacher

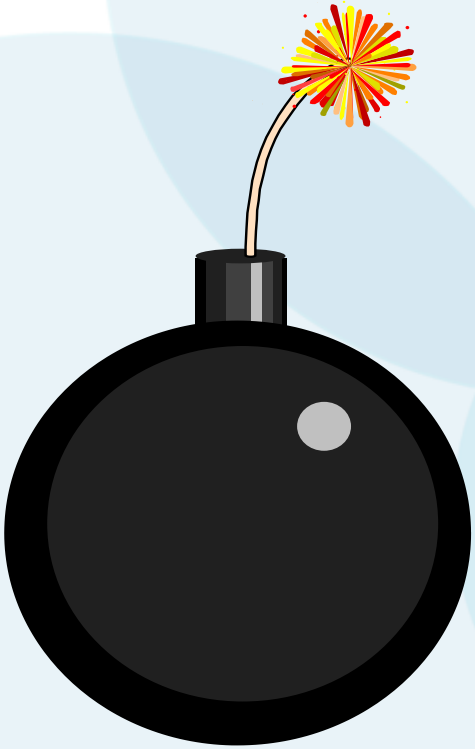
ADHD and adolescence

Poor impulse control

disorganised

lack social judgement

easily frustrated



hormones

emotional reactivity

disregard for safety

defiance of authority

The Royal Children's Hospital Melbourne

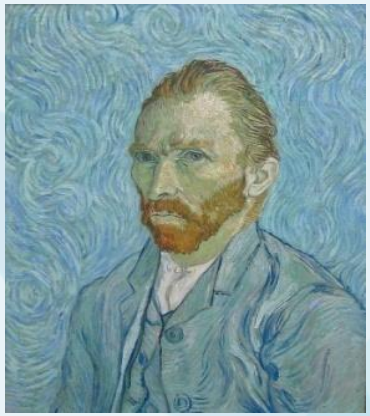
Long-term outcome

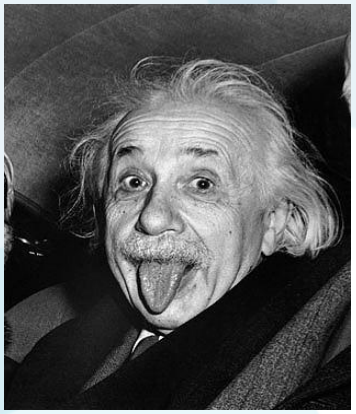
Increased risk

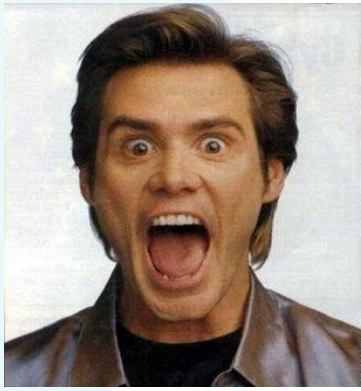
- ADHD - persistence / partial remission ~65% *(Greydanus 2007)*
- Academic failure / school drop-out *(Barbaresi 2007, Barkley 2006)*
- Smoking, alcohol, substance abuse
- Mental health problems eg. mood, ASPD
- *(Biederman, 1997; Elkins 2007; Farone, 2006; Secnik,, 2005)*
- Unemployment / low occupational status / job retention *(Barkley 2006; Manuzza, 1993)*
- Injuries eg MCA *(Barkley 1996)*
- Delinquency / crime & incarceration
- Relationship difficulties
- Early parenthood / problems with parenting

Famous People with ADHD

- Albert Einstein
- Jim Carrey
- Vincent Van Gogh
- Stevie Wonder
- Michael Phelps







The Royal Children's Hospital Melbourne

Assessment

- **History**
- Examination
- **Behaviour rating scales** (parent & **teacher**)
  - broad band eg Achenbach
  - ADHD specific eg Conners
- Other professional assessments
  - Psychology
    - cognitive, academic achievement
  - Speech pathology, occupational therapy, special education etc

Laboratory measures

- Neuropsychological tests
  - attention, memory, problem-solving, planning, processing speed
  - computerized tests of attention eg. TOVA, CPT
- Surface EEG - inc theta-beta ratio
- Quantitative EEG (brain mapping)
- fMRI
- PET, SPECT scanning

Differences in *group mean data*

Insufficient sensitivity and specificity for diagnosis

Differential diagnosis

- Normal
- Specific learning disorder
- Intellectual disability
- Emotional disturbance
  - adjustment reaction
  - attachment disorder / PTSD
  - anxiety/depression
- Personality disorders (adolescents / adults)
  - Borderline, narcissistic (disorganised, dysregulated)

Management

ALWAYS

- Behaviour modification
- Educational strategies
- **“Housekeeping”**

OFTEN

- **Medication**
- Talking therapies
  - individual
  - group
  - family

Housekeeping

- Comorbidities
  - learning disorders, anxiety, ASD
- Sleep
- Nutrition
  - macro, micro
- School
  - fit, bullying
- Seizures, general health

Professional services

- Paediatricians
  - make diagnosis in 73% *(Concannon et al JPCH 2005)*
  - prescribers of stimulants for 91% *(WA Dept Health 2007)*
- Psychology, child psychiatry, allied health, complementary practitioners
- Education – no extra support *(Efron et al Aust J Spec Ed 2008)*
- Adults – few services

Non-pharmacological interventions

(Sonuga-Barke Am J Psychiatery 2013)

	Effect size (ADHD symptoms)
Elimination diet	0.5
Exclude artificial colourings	0.3
FFA supplements	0.2
Cognitive training	0
Behavioural interventions / parent training	0
Neurofeedback	0

Behaviour modification

- Calmness
- Consistency
- Anticipate & avoid

- Lack internal locus of control
  - Praise and reward good behaviour
  - Ignore minor irritating behaviour
  - Immediate consequences for unacceptable behaviour eg. time out, removal of privileges

Classroom adaptations

- Position in classroom
- Instructions
- Allow time, help pacing
- Breaks
- Frequent positive reinforcement
- Clear graded consequences

Medications in ADHD

- Stimulants
  - methylphenidate (Ritalin)
  - dexamphetamine
- Atomoxetine (Strattera)
- Clonidine (Catapres)

(Tricyclic antidepressants)

Psychostimulants

- dextroamphetamine - Bradley 1937 (post-LP headache)
- methylphenidate *(Ritalin)* 1956

- sympathomimetic
  - block re-uptake, ↑ pre-synaptic release, inhib MAO
  - ↑ DA and NA in synaptic cleft
- ↑ arousal & alertness

Stimulants: effects

- Improved vigilance / sustained attention
- Reduced impulsivity
- Reduced motor activity

- Increased compliance
- Improved parenting style
- Improved peer interactions / social standing

Stimulants effects

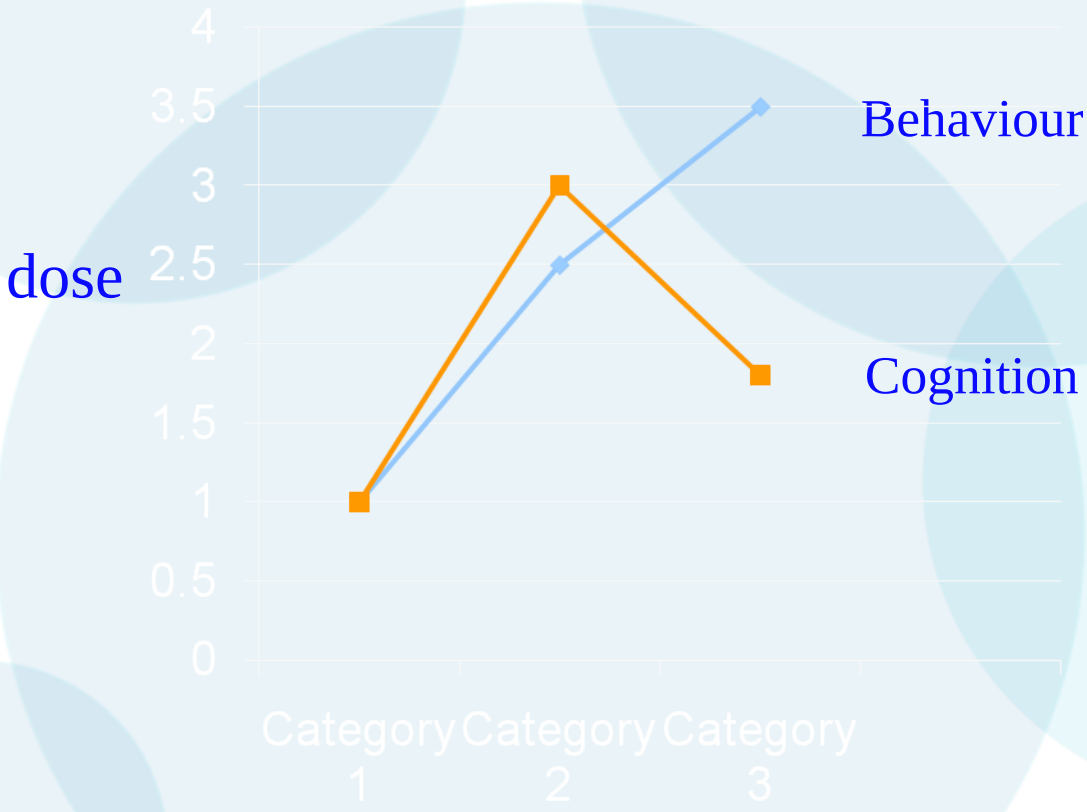
Cognitive

- Working memory / task planning
- Attention span / task completion

Academic

- Mental arithmetic
- Reading comprehension
- Handwriting
- Retention of new material

Stimulants – dose-response curve



Stimulants: side-effects

- **Anorexia → poor weight gains**
- **Emotional blunting (lose spark) – 5-10%?**
  - genotypic risk marker - COMT Met-Met?
- Anxiety
- Tics

- (Initial insomnia)
- Mild mean inc. HR, BP

Stimulants – risk sudden death?

- 2006 - alarm sans data *(Nissen NEJM)*
- Epidemiology – no incr. over background rate sudden unexplained death
- FDA recommendations:
  - History
    - child: syncope, dizziness, palpitations, SOB, chest pain
    - family: CVS disease, premature sudden death
  - Examination
  - If H +/or E raise concern, or child develops symptoms
    - ECG, ECHO +/- cardiol consult

Stimulant side-effects - long-term

- growth suppression
  - Possible small effect in sub-group
    - av 2cm less growth over 3 yrs

    (MTA: Swanson JAACAP 2007)
- substance abuse

  - protective ?

  - Wilens Pediatr 2003 meta-analysis

  - Groenman et al BJPsychiatry 2013. 388 pts w ADHD, 327 treated with stimulants, 61 not. Mean age 16, retrospective f/up after 4 yrs, controlled for ODD, CD. Stimulant med reduced risk SUD by approx 2 (HR 1.1-3.4). No effect on nicotine use

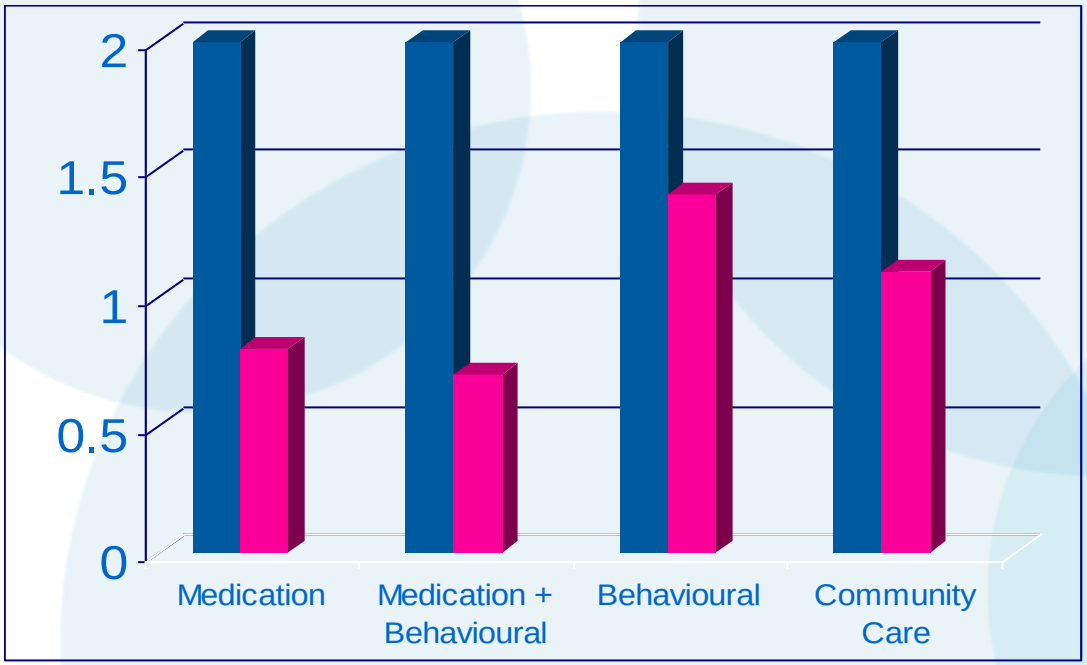
Stimulants: long-term effects

- growth suppression
  - Possible small effect in sub-group
    - av 2cm less growth over 3 yrs

    (MTA: Swanson JAACAP 2007)
- substance abuse
  - no increase
  - protective ? (*Wilens 2003, Groenman 2013)*

Stimulant medication

(MTA Arch Gen Psychiatry 1999. n = 579)



- Longer term benefits uncertain – MTA 8 year follow-up *(Molina JAACAP 2009)* (messy data - assignment contaminated after 14 months etc)
  - no diff in symptoms or function
  - 60% initially assigned meds no longer taking – no diff in function

Methylphenidate

		Duration
Ritalin 10	tablets	3-4 hrs
Ritalin LA	capsules	6-8 hrs
Concerta	long tablets	10-12 hrs

The Royal Children's Hospital Melbourne

Ritalin LA

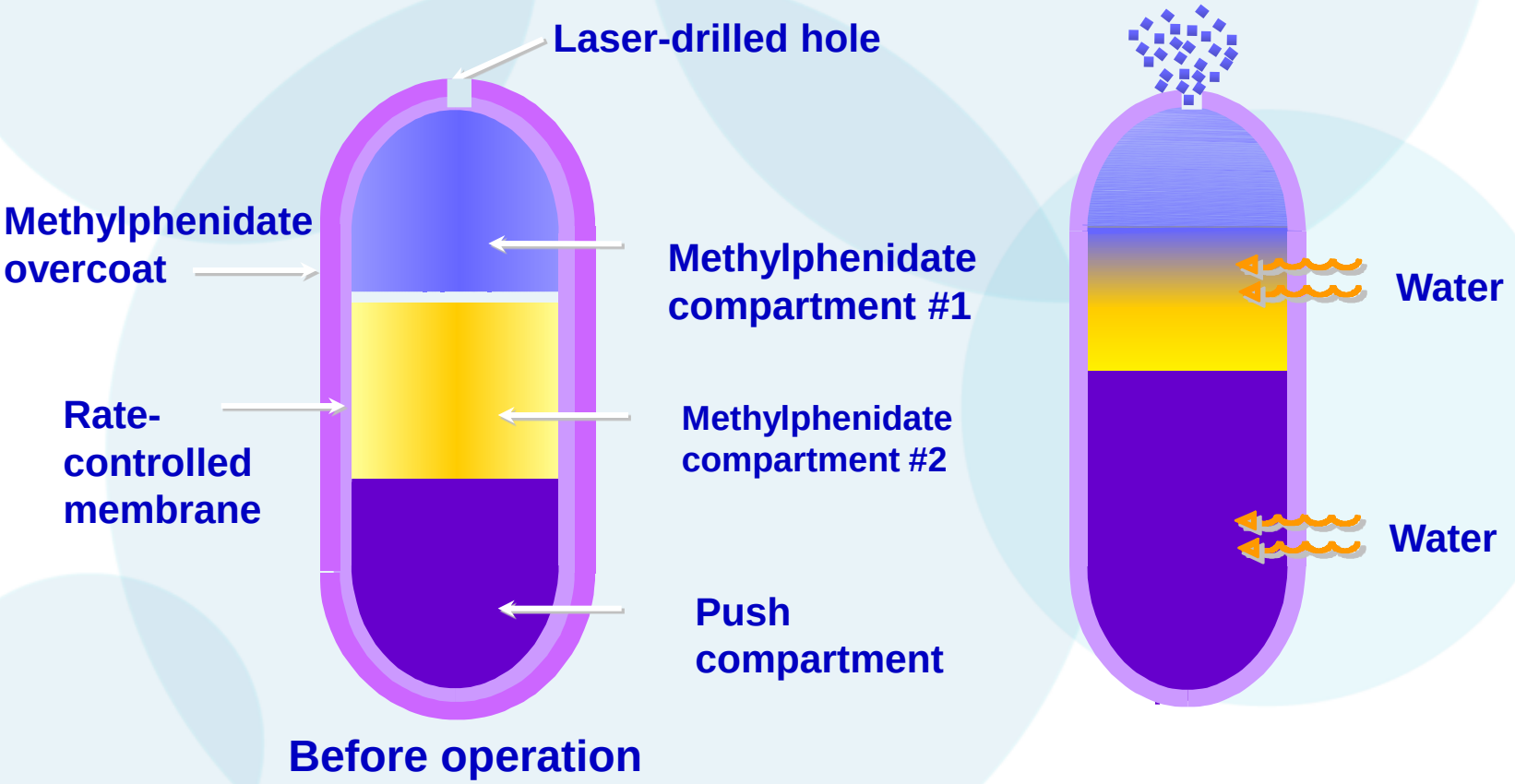
- caps with 50:50 immed:delayed- release MPH beads
- don’t crush or chew; can open into soft food
- 10 / 20 / 30 /40 mg caps

Ritalin LA – in practice

- some delayed onset
- usually no dip
- usually as effective as IR MPH BD
- often wears off after 5-6 hours

CONCERTA

OROS Delivery System



The Royal Children's Hospital Melbourne

Concerta (2003)

- Ascending profile (“acute tolerance”); 10-12 hrs
- 18 mg (5/5/5), 27mg (7.5), 36 mg (10), 54mg (15) (USA have 72mg)
- = MPH IR TDS > placebo by teacher and parent ratings (Pelham et al Pediatrics 2001)

Stimulants: Troubleshooting

- Early emotional lability - perservere
- Rebound - 3.30 dose
- Wearing off early - extra dose
- Weight loss - post-meals, w/e “holidays”
- Insomnia - earlier, ↓ dose, pm dose, clonidine
- Dysphoria - alt. stimulant, ATX
- Tics
- Seizures

Practical tips

- Start 7 days
- Don’t over-attribute
- Always assume non-compliance
- Document scripts written
  - calculate time tabs will last

Stimulant use in Australia

- Nationally: 1% boys, 0.5% girls *(Salmelainen 2002; Hollingworth ANZ J Psychiatry 2011)*
- Rates vary by state, region
- 81% children with ADHD *(Efron 2013)*
  - Predicted by age (peak adolescence); not SES, gender, comorbidity

Atomoxetine (Strattera)

- selective noradrenaline reuptake inhibitor
- once/d - steady state effect
- **takes up to 8 weeks for full effect**
- smaller effect size than stimulants
- few SEs - can be sedating
- some anti-anxiety and anti-tic effects

Clonidine

- α_2 adrenergic agonist
  - widely distributed in brain
  - implicated in pathophysiology of disruptive behaviour disorders
- psychoactive properties via NA, 5-HT and DA systems ∴ interest in application to many psych syndromes (Tourette, BAD, SCZ, PTSD, social phobias, panic disorder, BZD w/d)

Clonidine in ADHD

- moderate positive effect size (variable)

  *(*Meta-analysis: *Connor JAACAP 1999)*
  - recommend 2nd line
- Added to stimulants - reduces ODD / CD symptoms

  (Hazell JAACAP 2003)
- some decr. tics
- AEs: sedation, irritability

Safe use of clonidine

- **Store safely**
- HR, BP (incl postural drop)
  - baseline and monitor
- lowest possible dose - < 200mcg/d
- use BD in combination with MPH
- taper slowly (rebound hypertension)

Antidepressants

- **SSRIs**
  - for comorbid anxiety
- **Tricyclics** (amitriptyline**,** imipramine, desipramine)
  - if comorbid anxiety, depression
  - baseline ECG if > 2mg/kg/day
  - anticholinergics AEs
- **Moclobemide, SNRIs**

Predictors of outcome - intuition

- Age of onset / Severity
- Subtype
- Comorbidities
- Age of diagnosis / intervention
- Type / quality of intervention
- Parental psychopathology

PATHWAYS / TRAJECTORIES

The Royal Children's Hospital Melbourne

Longitudinal studies in ADHD: Problems

- Clinical samples
- Poorly characterised samples (especially comorbidities)
- Wide age-range at recruitment
- Infrequent measurement
- Few included inattentives
- Most Nth American

Research gaps

- Continuity of EF deficits (attention, WM)
- Stability of caseness
- Gender comparisons
- Predictors of better / worse outcomes
  - **modifiable risk factors**
  - Influence of interventions on long-term outcomes

Developmental trajectories:
Diagnostic journey of the vulnerable child

- Infant distress / sleep / feeding disorder
- Language delay
- Pre-school aggression
- Social-emotional delay
- ADHD-Combined type
- Learning disability
- Oppositional defiant disorder
- High functioning autism
- Generalised anxiety disorder
- Depression
- Substance use disorder

Developmental trajectories

- " Emergence"
  - transition of degree rather than kind
  - precipitated by envir challenges
  - early (temperamental / dev delay in emotional regulation & impulse control)

    vs late
    - prognostic significance unknown
    - most identified in middle childhood
- Persistence
- "Remission" (partial)
- "Relapse"

Causal pathways: Principles Of Developmental (Psycho)pathology

Aetiological heterogeneity

- Multiple risk-factors
  - some fixed, some modifiable
  - a continuum of neurobiological risk in population
- Individual effect sizes small
- Dynamic interactions
  - incl. with individual child (non-ADHD) factors
  - moderating factors can alter trajectories
- Critical windows

Clinical phenotype is dynamic

- fluctuation in symptom expression, & assoc impairment, day-day, year-year (real?)

Causal pathways: Principles Of Developmental (Psycho)pathology (cont.)

- Different subgroups follow different pathways
- Equifinality - diff risks → same outcomes
- Multifinality – same pattern RFs → diff outcomes
- Dimensionality
  - "casesness" is arbitrary
- Neuroplasticity *(eg. prevention of autism Dawson 2008)*

Causal pathways

(*Nigg 2006, Sonuga-Barke 2010)*

VISION

Identify:

- Early developmental phenotypes
- Mediating processes (dynamic)
  - targets for early intervention

Goals:

- reduce likelihood emergence
- limit persistence
- increase likelihood remission
- reduce long-term burdens

The Royal Children's Hospital Melbourne

Early intervention

- Primary (prevention) - not feasible; predictive power of risk markers not strong enough
- **Secondary** (early phenotypic indicators eg. family Hx / RFs / hyperactivity / dysregulation) – potential
- Tertiary (early tx of disorder) – pharmacol, non-pharmacol
  - no evidence of alteration to dev trajectories

Interventions which might alter developmental trajectories

- Parent support & training *(Shaw 2008)*
  - Eg. Triple P *(Sanders)*, Incredible Years (*Webster-Stratton)*
    - Evidence red. levels oppositionality / conduct problems
- Neuropsychological (speed rate of dev)
  - Attention training *(Sohlberh & Mateer 2001)*
  - Working memory training *(Klingberg et al 2005)*
    - Improvements in lab performance demonstrated - ? transferrable to classroom / playground / home; sustained?
- Operant conditioning
- Combination
  - homework exercises to improve self-regulation
    - Games: conc, turn-taking, delay gratification
    - “Teachable moments”
  - parents agents of change