CONTINUITY AND DISCONTINUITY IN PSYCHOPATHOLOGY: ADHD

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www.ADHDynamisch.be

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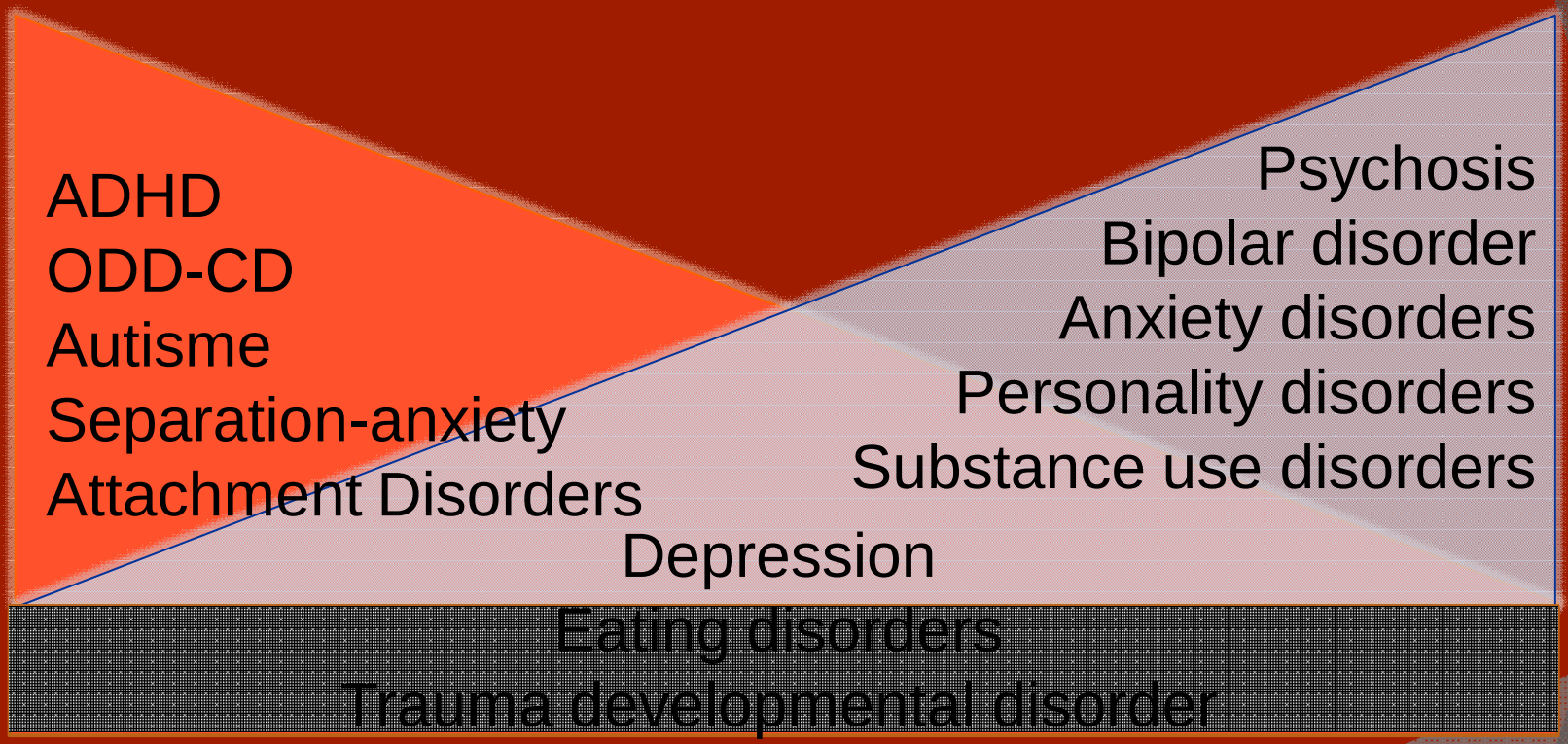
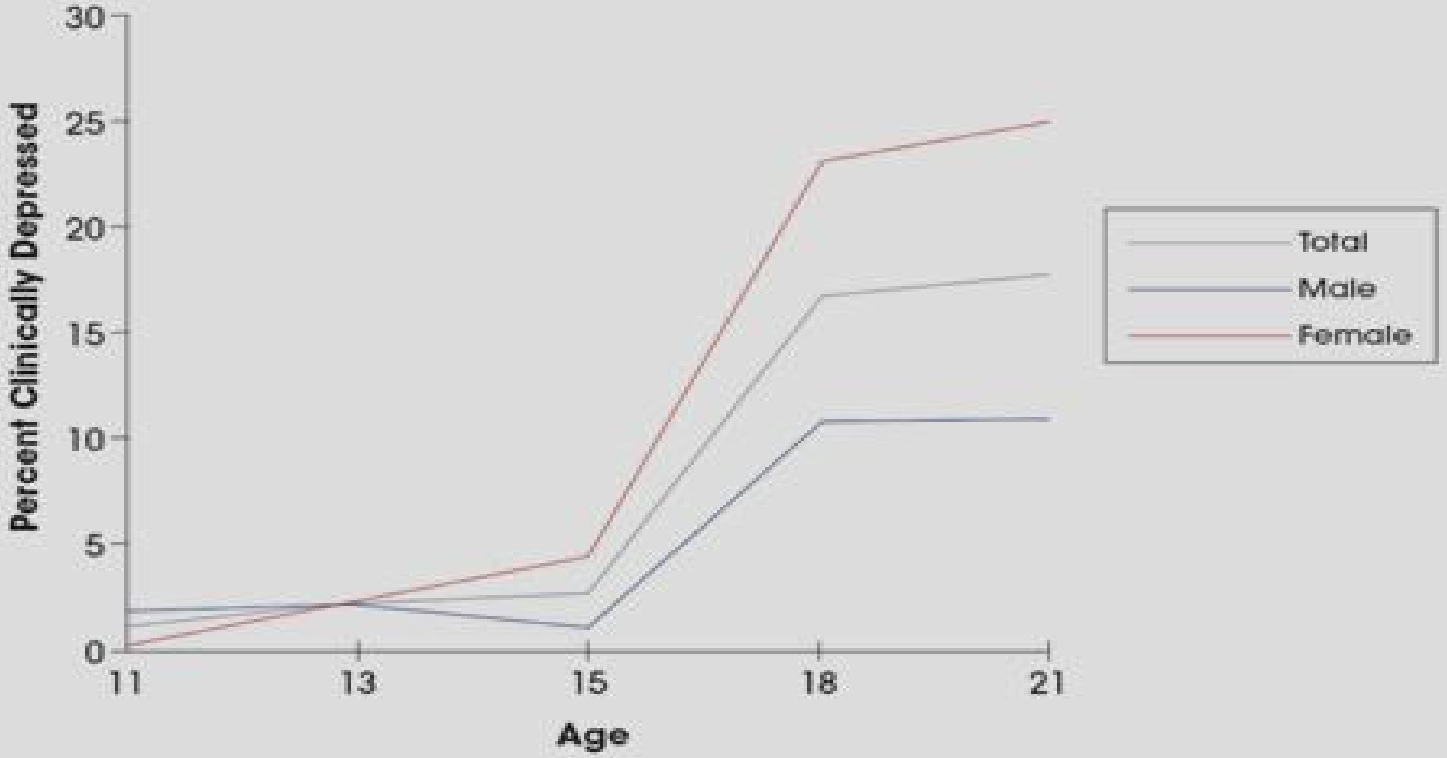
Age trends in psychopathology



Costello ea 2011

Developmental course of depression

Developmental Course of Rates of Clinical Depression by Age and Gender From a Prospective Community Birth Cohort Study*

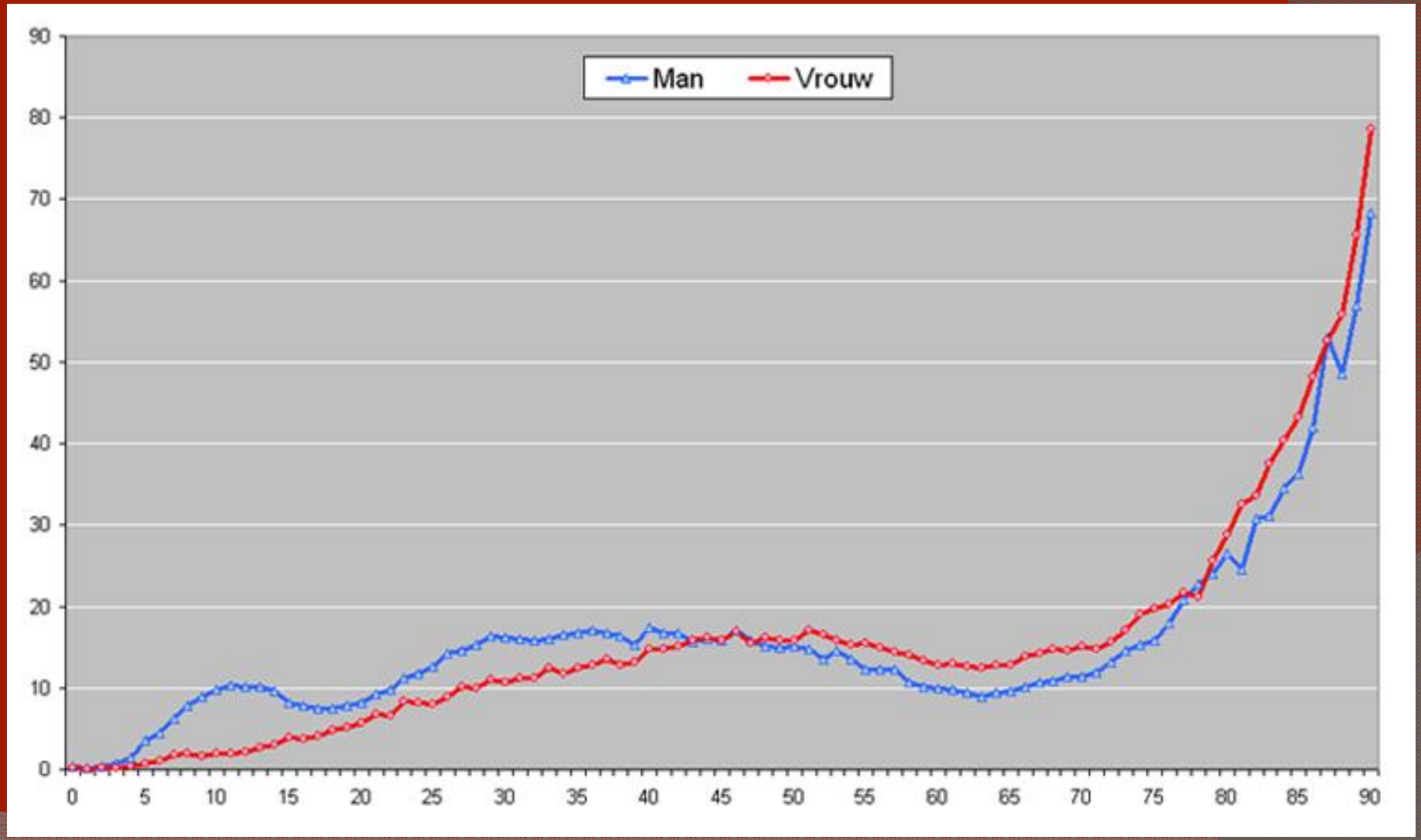


* More girls than boys begin to become depressed after age 13, and girls become substantially more depressed than boys during middle–late adolescence (ages 15–18).

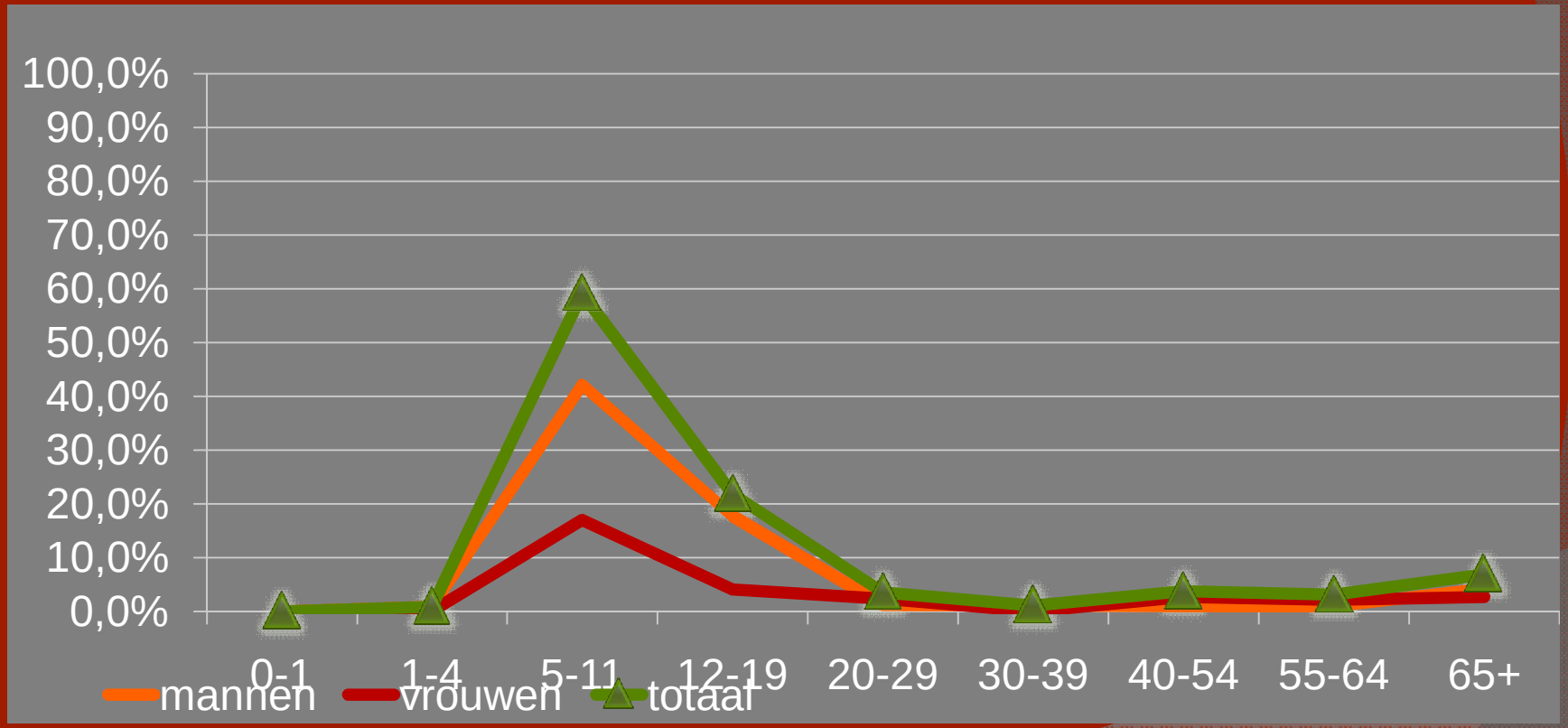
Source: Hankin BL, Abramson LY, Moffitt TE, McGee R, Silva PA, Angell KE. Development of depression from preadolescence to young adulthood: emerging gender differences in a 10-year longitudinal study. *J Abnorm Psychol*. 1998;107:128-140. Reprinted with permission. Copyright 1998, the American Psychological Association.

Antipsychotica

Aantal verbruikers / 1000 in 2007 in **Nederland:**



Methylphenidate ~ Age



Development in real time…

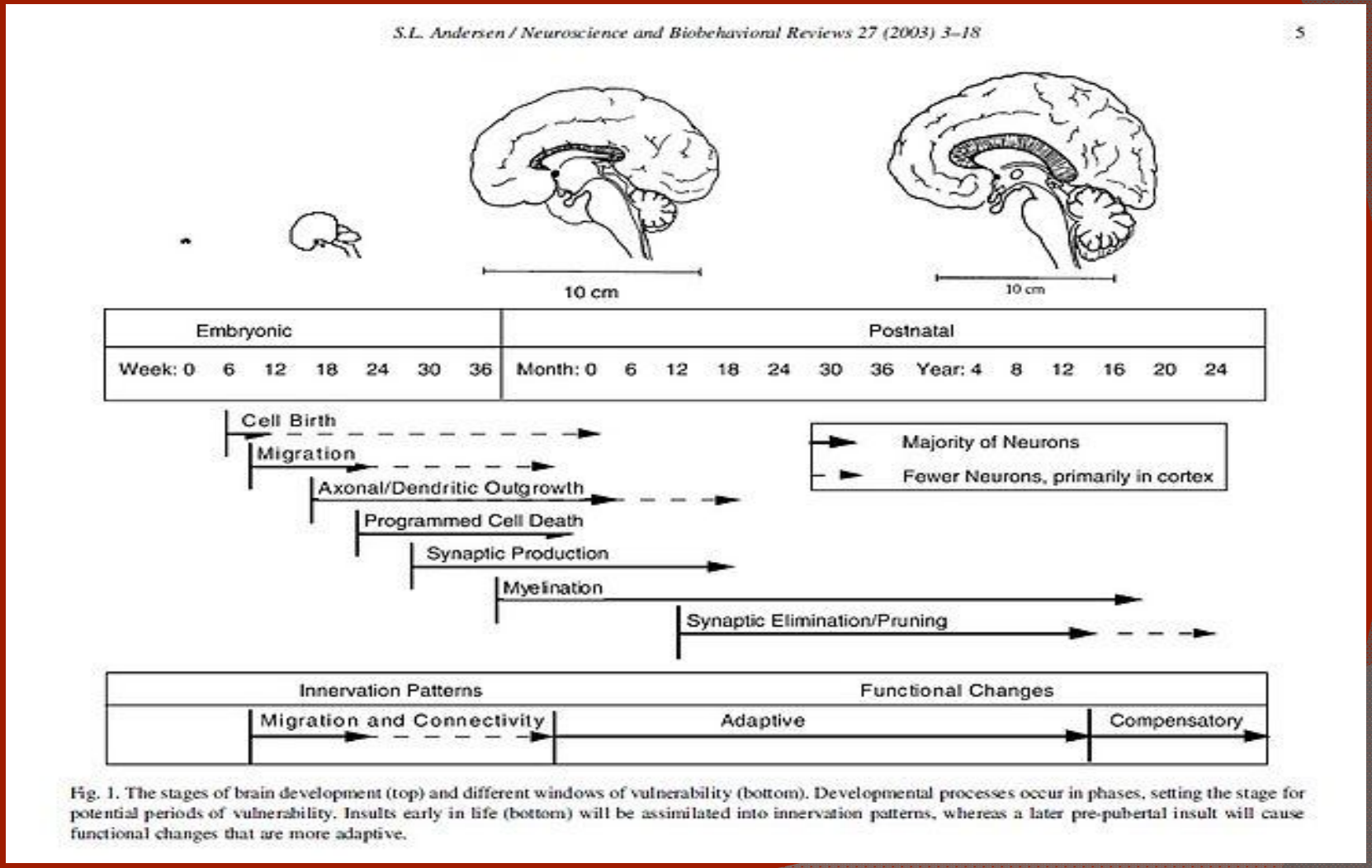
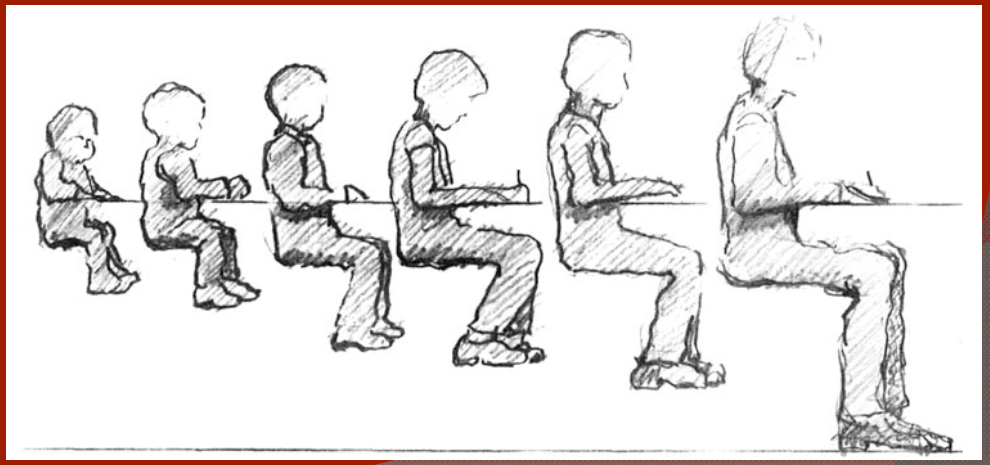


Fig. 1. The stages of brain development (top) and different windows of vulnerability (bottom). Developmental processes occur in phases, setting the stage for potential periods of vulnerability. Insults early in life (bottom) will be assimilated into innervation patterns, whereas a later pre-pubertal insult will cause functional changes that are more adaptive.

Continuity & Discontinuity in ADHD

- Developmental course ?
- Determinants of continuity ?
- Determinants of discontinuity
- Treatment effects?



Continuity & Discontinuity in ADHD

- Developmental outcome:
  - Is ADHD a childhood risk factor for negative developmental outcomes in young adulthood ?
- Developmental course
  - Does ADHD symptomatology persist into adulthood with its associated impairment ?

ADHD: DEVELOPMENTAL OUTCOME

Developmental outcome

Review of 351 outcome studies (1980-2010)

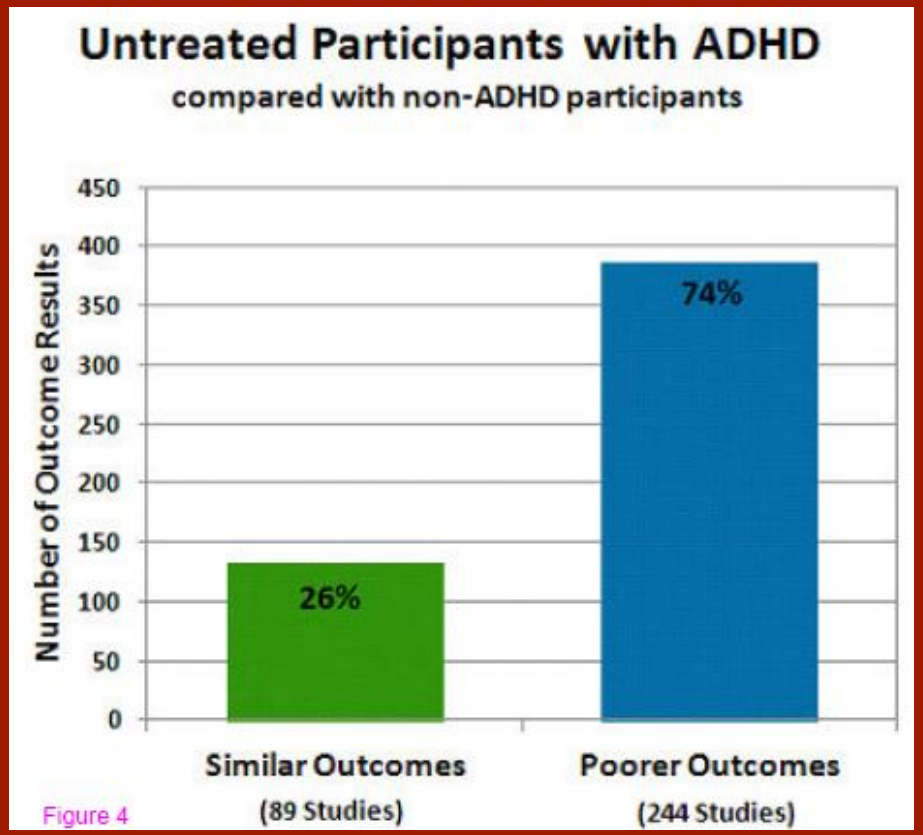


Figure 4

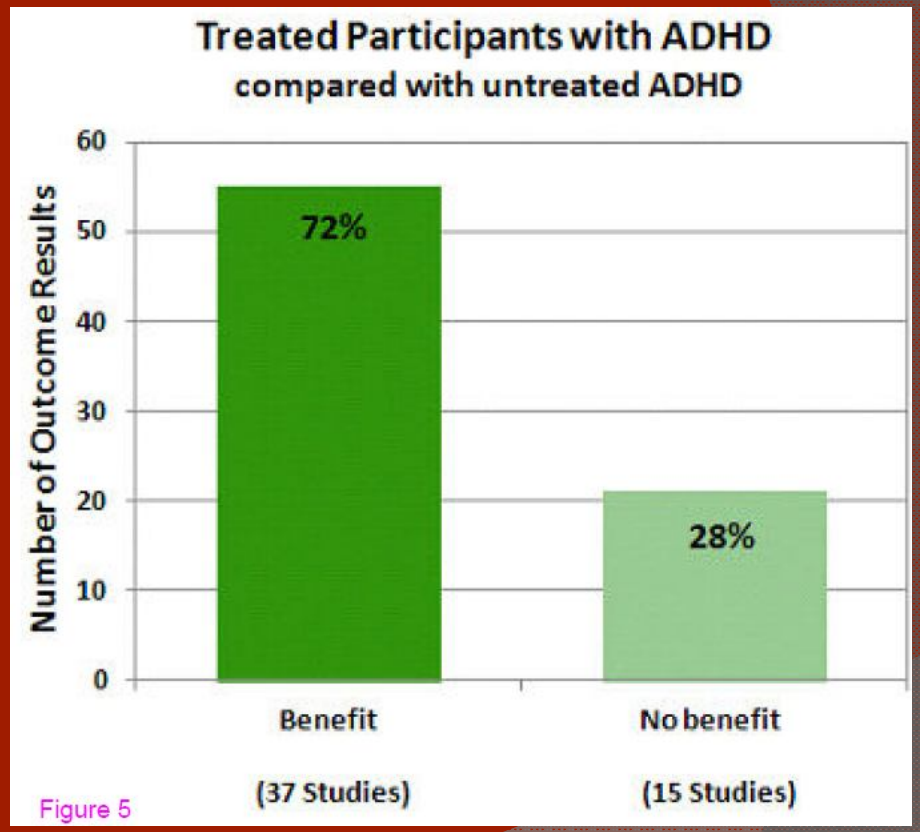


Figure 5

Note: 6 studies report a better outcome in ADHD

Shaw ea 2012, Biomed Central

Psychiatric outcome ?

- Cumulative risk by age 21, controlled for baseline psychopathology
  - ODD: 78 % vs 20 % controls
  - CD: 46 % vs 16 % controls
  - MDD: 46 % vs 7 % controls
  - Tics 43 % vs 7 % controls
  - ASPD: 29 % vs 9 % controls
  - BPD: 29 % vs 3 % controls

Biederman ea 2006

Substance use disorders: meta-analysis Nicotine dependence

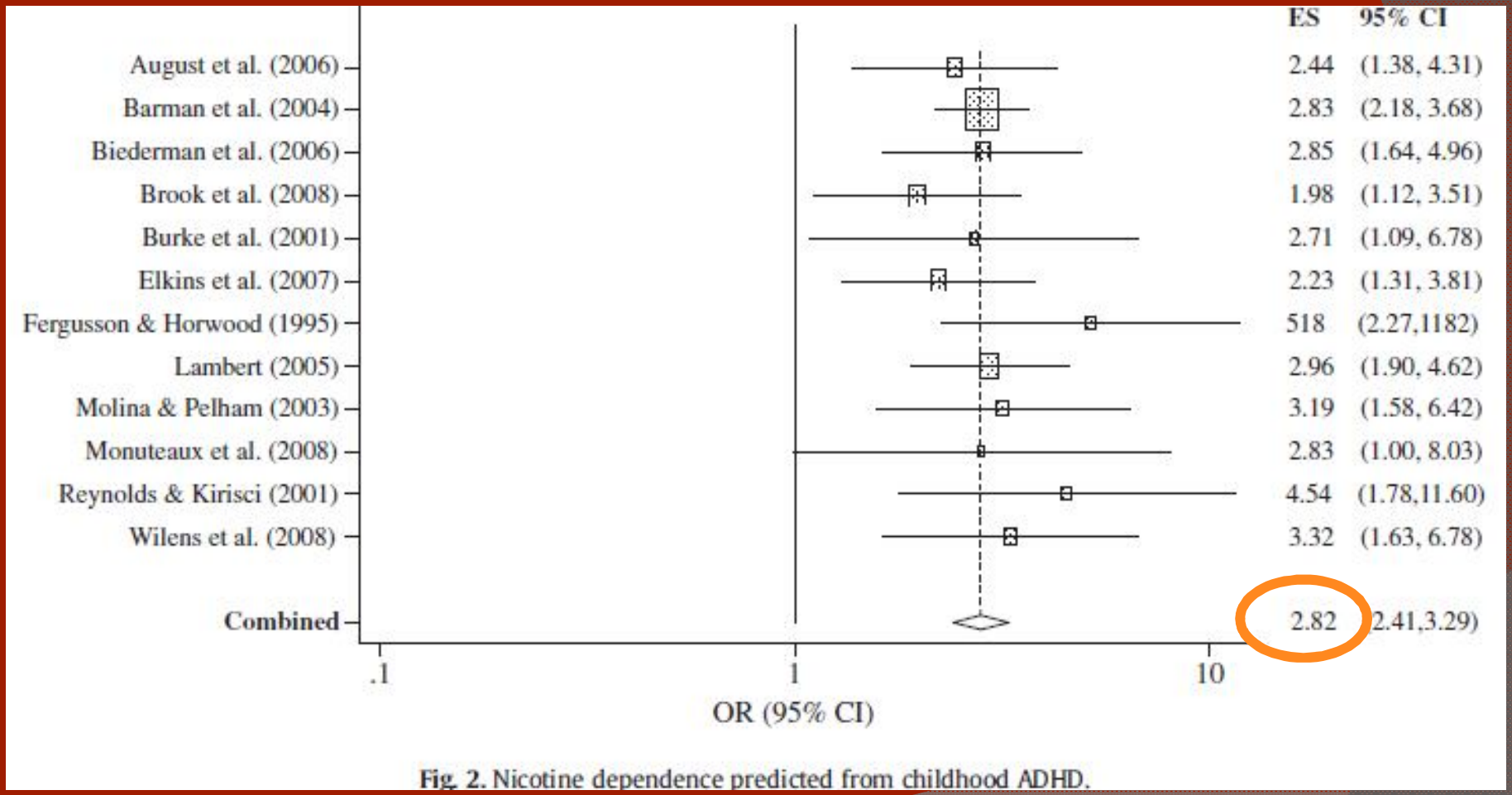


Fig. 2. Nicotine dependence predicted from childhood ADHD.

S.S. Lee et al. / Clinical Psychology Review 31 (2011)

Other Substance use disorders (abuse or dependence)

- Alcohol: OR 1.74
- Marijuana: OR 1.58
- Cocaine: OR 2.05
- General illicit drugs: OR 2.64

Conclusion: Childhood ADHD predictive of substance use disorders

This relationship may be partially or fully explained by comorbid conduct problems.

S.S. Lee et al. / Clinical Psychology Review 31 (2011)

Academic risk

- Behavioural:

%	Controls	ADHD
Held back	13	42
Suspended	19	60
Expelled	6	14
High school dropout	5	35

- Academic:

	ADHD *N*=264 %	Comparison *N*=185 %
Post-high school education		
No School	26.9	4.9
Vocational	18.6	5.9
Junior/Community	25.0	12.4
Four-Year	29.5	76.8

Controlled for IQ and parental education

Barkley ea 2002, Kuriyan ea 2012

Occupational outcome

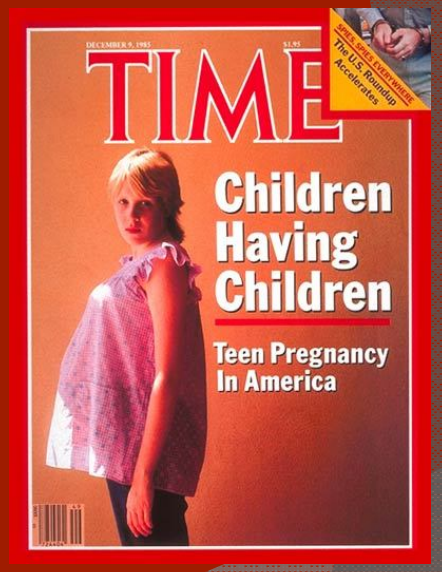
%	ADHD	Controls
Ever been fired	**61**	**43**
Ever been laid off	**33**	**13**
Quit due to dislike	**53**	**36**
Salary per hour ($)	**14,2**	**16,5**

	ADHD *N*=142 %	Comparison *N*=75 %
Hollingshead Level		
Group 1 (Unskilled)	72.5	36
Group 2 (Clerical)	21.8	44
Group 3 (Professional)	5.6	20

Kuriyan ea 2013

Developmental outcome

- Sexual & reproductive outcomes
  - Earlier intercourse
  - More sexual partners
  - Less use of contraception
  - Higher rates of
    - Teenage pregancy (OR: 42)
      - Less than half have custody
    - Sexually transmitted diseases (OR: 4)

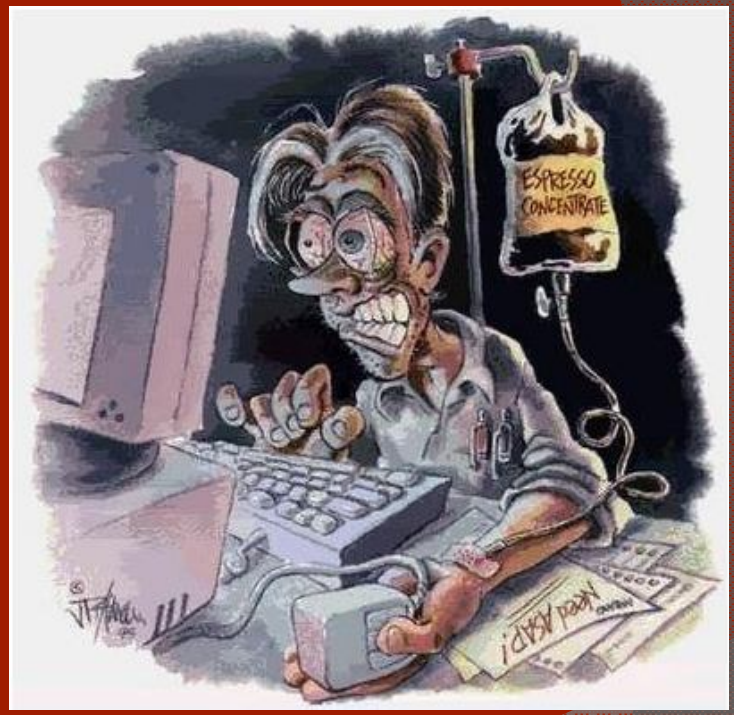


Barkley ea 2002, Hazell 2007

Developmental outcome

Screen addiction:

- Addiction = preoccupation, urge, withdrawal symptoms, causing impairment



	ADHD	No ADHD
Problematic Internet use	33 %	1.5 – 8%

- Males = females

Yoo ea 2004, Ko ea 2008, Han ea 2009, Aboujaoude 2010, Weinstein & Lejoyeux 2010

Developmental outcome

Driving-related risks:

- driving without licence (37 vs 11%)
- licence revocations (23 vs 0%)
- at fault for crashes (49 vs 11%)
- citations for traffic violations (77 vs 47%)
  - Speeding
  - Failure to stop

Cox ea 2004 a,b

Delinquency

- Mordre et al. BMC Psychiatry 2011:
  - 541 Child Psychiatric inpatients
  - FU 19-41 after hospitalization
  - **24% had been convicted:**
  - Predictors:
    - Conduct Disorder: RR 2
    - Hyperkinetic ConductDisorder: RR 2.7
    - Male gender: RR 3.6
    - Chronic Family problems RR 1.3
    - ADHD = emotional dis = attachment dis
    - PDD , MR: RR < 1

Continuity and discontinuity

- Developmental outcome DATA

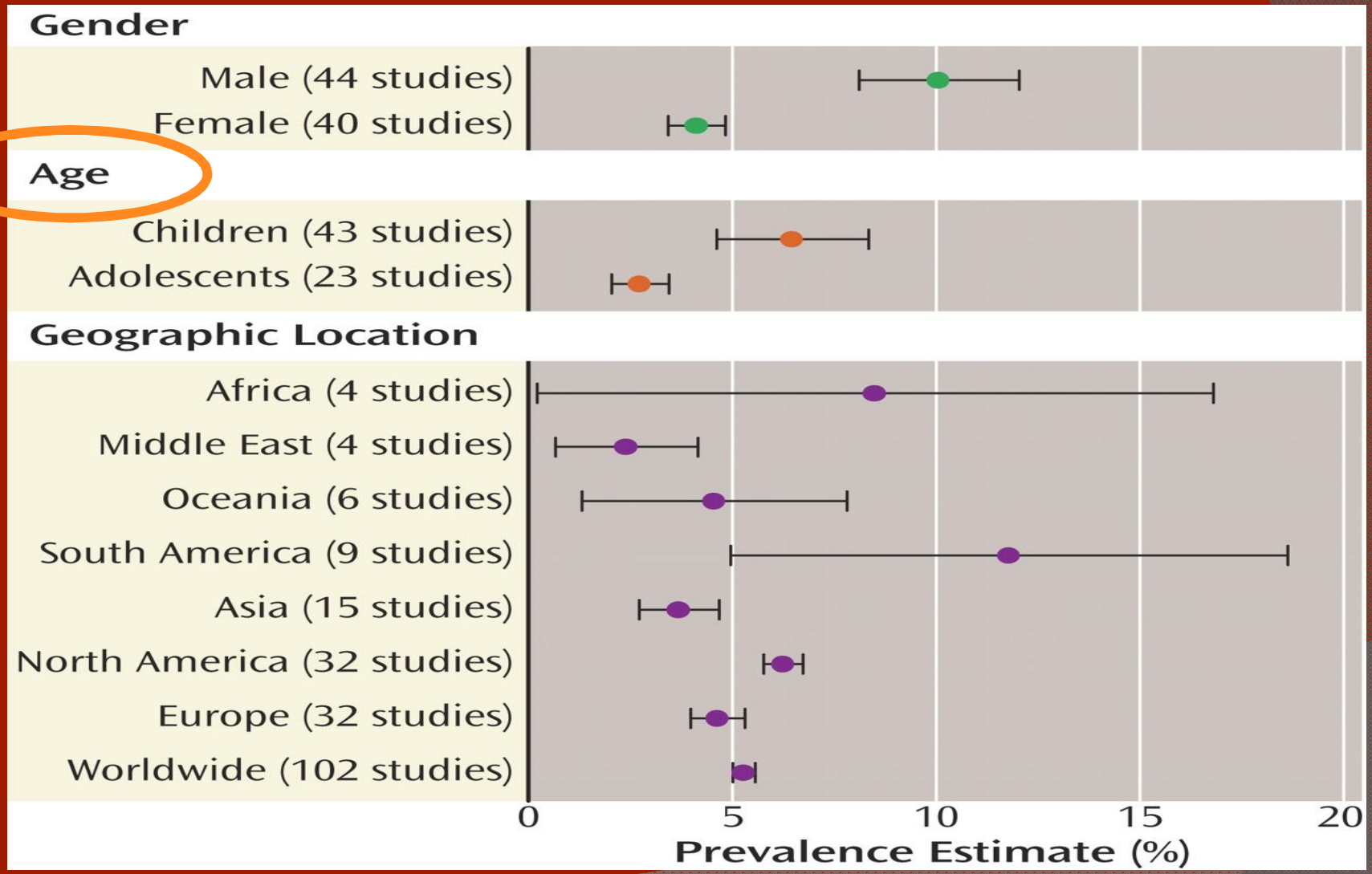
+

- Diagnosis of ADHD in adults: demonstrated to be valid and associated with impairment

≠ ADHD is a chronic disorder

ADHD: DEVELOPMENTAL COURSE

ADHD prevalence worldwide



Polanczyk ea 2007

Developmental Course

Epidemiological follow-up studies

Study		Method	Sources	Age range	%
Verhulst ea 1985 Verhulst ea 1997	NL	Ratings Interview	Teacher Parents	8 & 11 13-18	9.5 1.8
Esser ea 1990	D	Ratings Interview	Parents	8 13	4 2
Gomez ea 1994	E	Interview	Teacher Parents	8 11 15	14.4 5.3 3

Developmental Course

Clinical follow-up studies:

	Follow-up	Age-range	persistence
Barkley ea 1990	8y	12-20y	71.5%
Biederman ea 1996	4y	9-22y	85%
August ea 1998	5y	12-15y	69%
Steinhausen ea 2003	2.6y	10-16y	46%

Developmental course

- Meta-analysis of persistence in FU-studies:
  - Adolescence: 50-60 %
  - Adults at 25y: 10-66%
    - 15% full syndrome
    - 65% partial syndrome
- Predictors of persistence
  - Familiality of ADHD
  - Psychiatric comorbidity
  - Psychosocial adversity

Faraone ea, Psychological Medicine, 2006, 36, 159–165

Symptom decline & gender

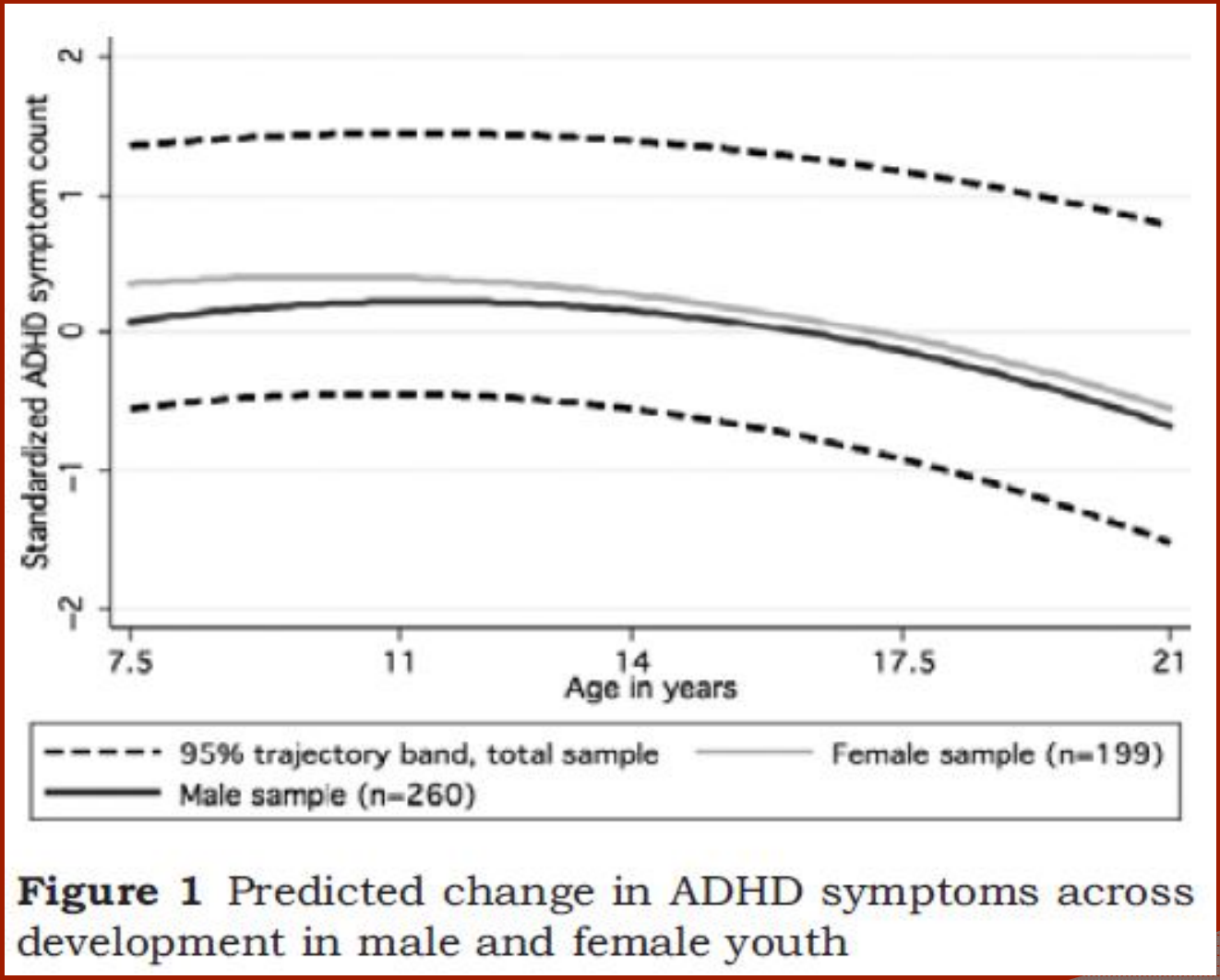


Figure 1 Predicted change in ADHD symptoms across development in male and female youth

ADHD symptom decline accelerates with age

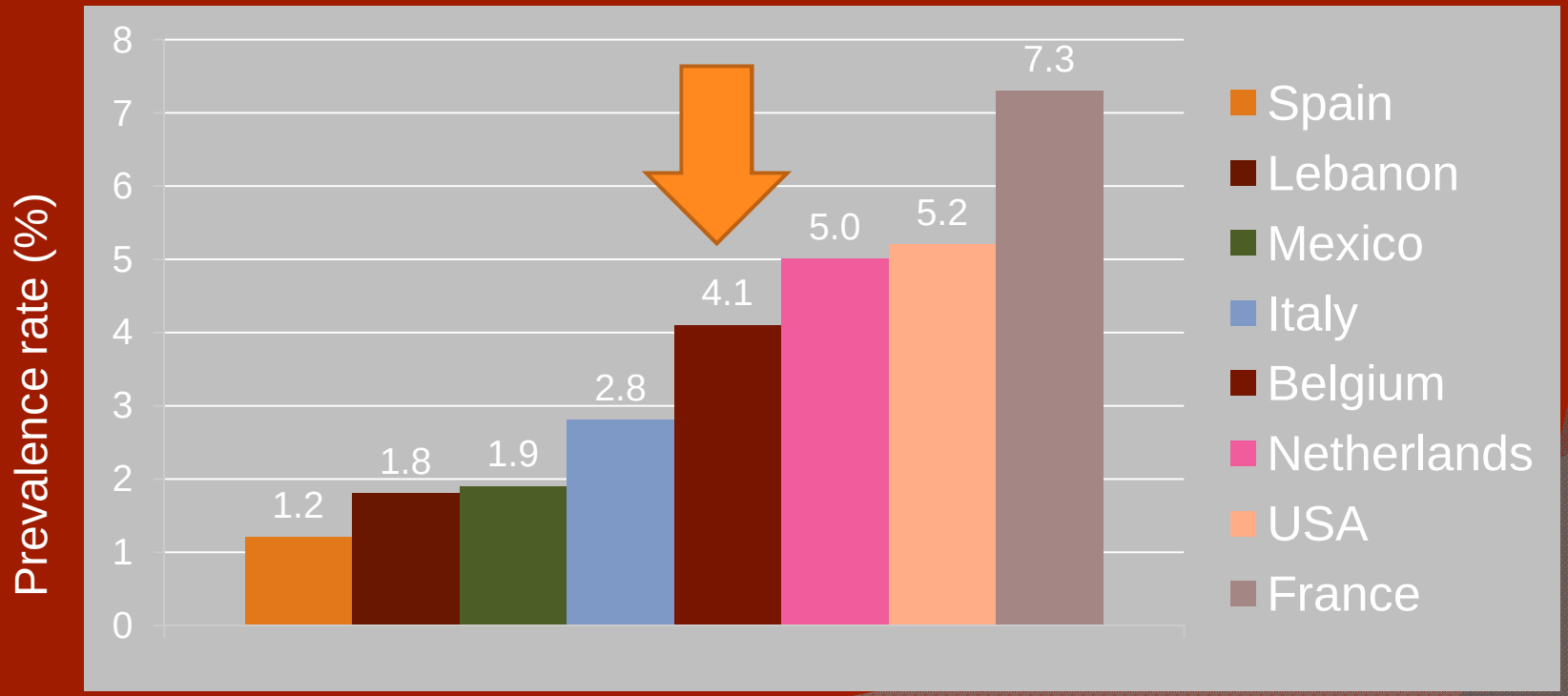
Is the same in both sexes

Stability of comorbid psychopathology is greater in females

Monutaux ea *Journal of Child Psychology and Psychiatry* 51:3 (2010)

Adult ADHD prevalence

- Worldwide estimates: 1.2 – 7.3 %
- Prevalence Belgium: 4.1 %



Kessler et al. 2006; Fayyad et al. 2007; Lara et al. 2008

Problem: Continuity /discontinuity

- Prospective FU from childhood:
  - Low persistence rates of full syndrome 1%
- Prevalence in adults:
  - Higher prevalence 4%

- Explanation ?
  - Changing fenotype of same genotype ?
  - Partial Syndromes ? Disfunction with less symptoms ?
  - New genotype ?
  - Different rater (self versus parent/teacher) – different perception ?

Do symptoms of hyperactivity manifest differently in adults ? US perspective:

Aimless restlessness often migrates to purposeful restlessness

DSM IV Symptom Domain	Common Adult Manifestation
• Squirms and fidgets • Can't stay seated • Runs/climbs excessively • Can't play/work quietly • "On the go" / "Driven by motor" • Talks excessively	• Adaptive behavior — Work two jobs/long hours — Select very active job • Constant activity leading to family tension • Often felt rather than manifested

American Psychiatric Association. 1994. 83-85., ADHD in Adulthood 1999, Weiss, Hechtman and Weiss

Do symptoms of impulsivity manifest differently in adults ?

Impulsivity in adulthood often carries more serious consequences

DSM IV Symptom Domain	Common Adult Manifestation
• Blurts out answers	• Low frustration tolerance
• Can't wait turn	— Quitting a job
• Intrudes/interrupts others	— Ending a relationship
	— Losing temper
	— Driving too fast

American Psychiatric Association. 1994. 83-85., ADHD in Adulthood 1999, Weiss, Hechtman and Weiss

Do symptoms of inattention manifest differently in adults ?

Many adults do not complain of attentional problems because they have compensated to some extent

DSM IV Symptom Domain	Common Adult Manifestation
• Difficulty sustaining attention • Doesn't listen • No follow through • Can't organize • Loses important items • Easily distractible, forgetful	• Poor time management • Difficulty — Initiating/completing tasks — Changing to another task when required • Adaptive behavior — Self select lifestyle — Support staff

American Psychiatric Association. 1994. 83-85., ADHD in Adulthood 1999, Weiss, Hechtman and Weiss

DSM-5 : ADHD adaptations

Examples of dev. adaptations

New impulsiveness items

DSM-IV	DSM-5
Difficulty sustaining attention in tasks or play activities	Idem (eg. during lectures, conversation or during lengthy readings)
Is forgetful	For adolesc. & adults:returning calls, paying bills, keeping appointments
	Tends to act without thinking
	Often impatient
	Uncomfortable doing things slowly and systematic
	Difficult to resist temptations or opportunities

DSM-5: ADHD adaptations

- New subtype: restrictive inattentive type
- Age of onset: before 12 years (>< 7 jaar)
- From 17y: 4/9 symptoms (>< 6/9)
- Sources: parents and teachers or other "third party" whenever possible
- Impact: "clear proof of disfunction socially, school- or job functioning
- Exclusion: ASS no exclusiecriterion

Problem: Continuity /discontinuity

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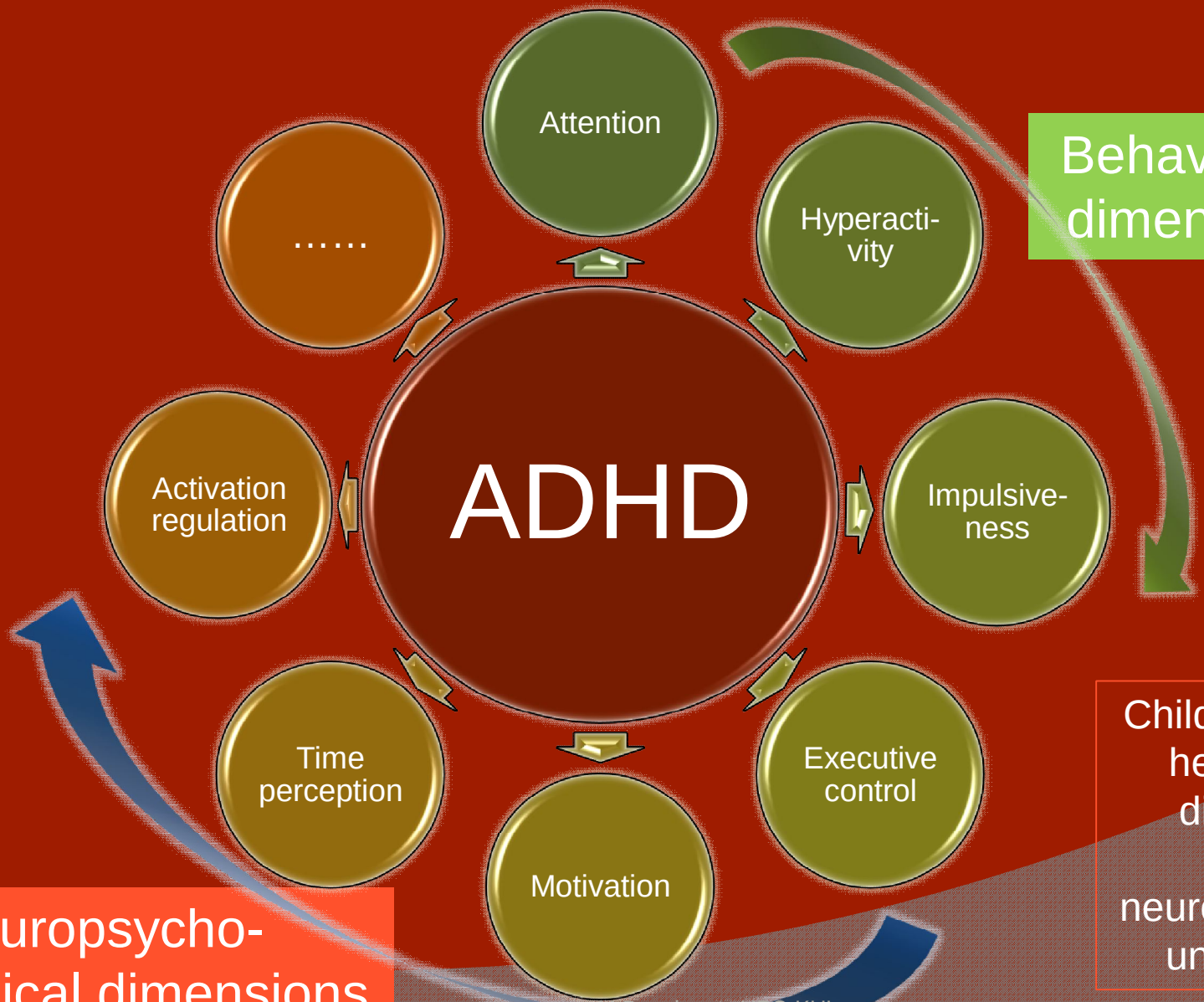
Neuropsychological profiles



Behavioural dimensions

Neuropsycho-logical dimensions

Childhood ADHD = heterogenous disorder with multiple neuropsychological underpinnings

Developmental neuropsychological profiles:

	Childhood	Adolescence / Young adulthood	
		PERSISTERS	**REMITTERS**
Working Memory	**XXX**	**X**	
Word processing	**XXX**	**X**	
CPT errors	**XXX**	**X**	
CPT variability & state regulation	**XXX**	**X**	**X**
actigraph	**XX**	**X**	**X**

- Primary deficits:
  - perceptual sensitivity (prepotent stimuli)
  - State regulation (hypo-activation) / hypo-arousal
- Epiphenomena:
  - Effortful control / executive functioning

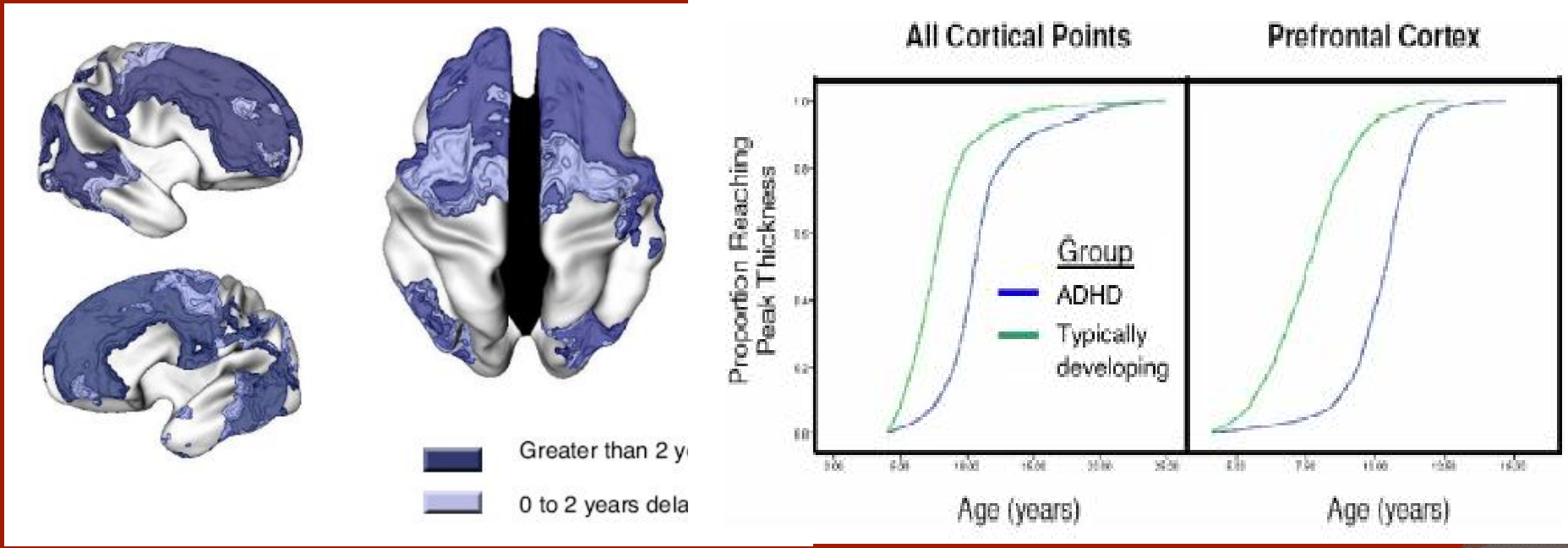
Halperin ea 2008, JCPP

Developmental hypothesis ?

- Adult subcortical disfunction remains stable regardless of adult symptom persistence
- Adult cortical disfunction is associated with persistence / remittance of symptoms

OR: persistence of symptomatology will depend on whether prefrontally mediated EF (developing during childhood & adolescence) can compensatie for the more primary subcortical deficits

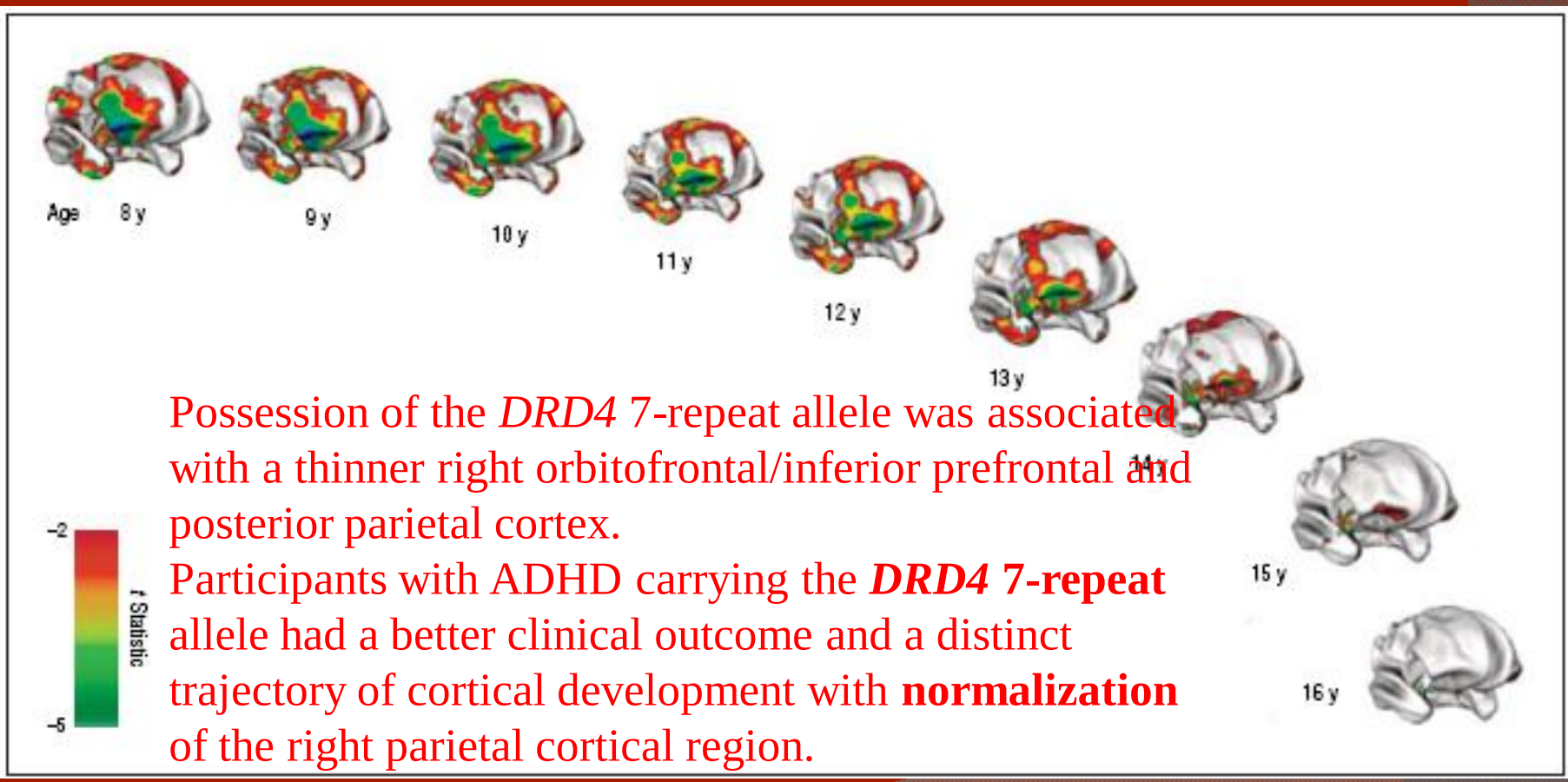
Developmental Neuroanatomy: Cortical thickness



ADHD ~ delay in cortical maturation
And: differential clinical outcome ~ differential trajectories

Shaw ea 2007

Developmental neuroanatomy: genetic mediation ?



Possession of the *DRD4* 7-repeat allele was associated with a thinner right orbitofrontal/inferior prefrontal and posterior parietal cortex.

Participants with ADHD carrying the ***DRD4* 7-repeat** allele had a better clinical outcome and a distinct trajectory of cortical development with **normalization** of the right parietal cortical region.

Shaw ea 2007, Arch Gen Psychiatry

Developmental neuroanatomy: Outcome ~ brain development

Persistent anatomical differences in persistent ADHD / worse outcome

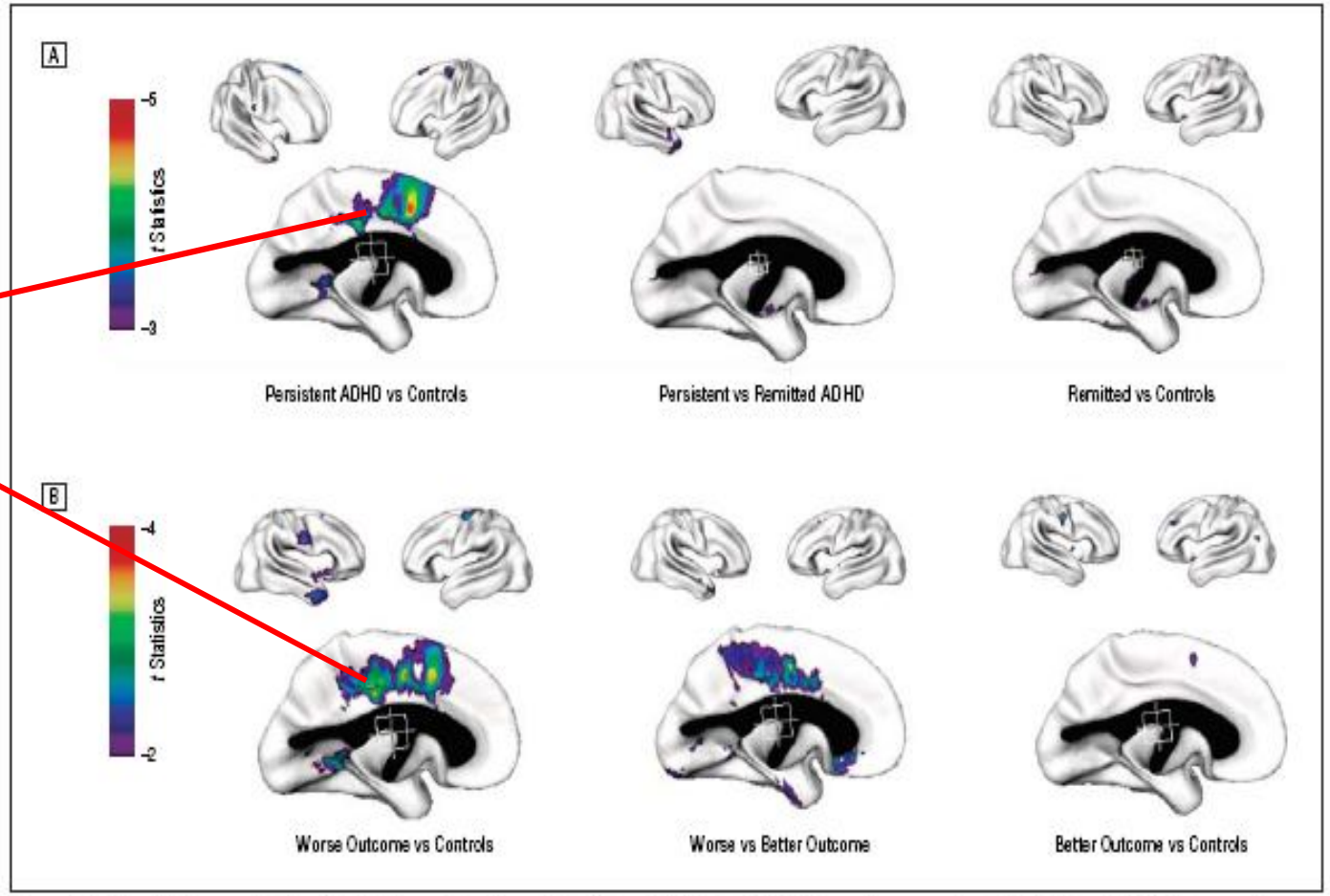


Figure 2. Contrasts between patients with attention-deficit/hyperactivity disorder (ADHD) with differing outcomes and controls. A, The *t* statistical maps of pairwise contrasts using persistence/remission of ADHD as the outcome measure. B, The *t* maps using Children's Global Assessment Scale scores as the outcome measure. Adjustment is made for IQ and mean cortical thickness.

Shaw ea 2006

Relationship developmental course & outcome

- Proal ea 2012: 33y follow-up:
  - Continuing grey matter deficits
    - Cortical thinning in dorsal attentional networks
    - N. Caudatus, Cerebellar hemispheres
  - No relationship with caseness

Problem: Continuity /discontinuity

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A TRIPLE PATHWAY HYPOTHESIS

CORTICO-VENTRAL STRIATAL LOOP DISTURBANCE

IMPAIRED SIGNAL DELAYED REWARD

DELAY AVERSION

CORTICO-DORSAL STRIATAL LOOP DISTURBANCE

INHIBITORY DEFICITS

EXECUTIVE DEFICITS

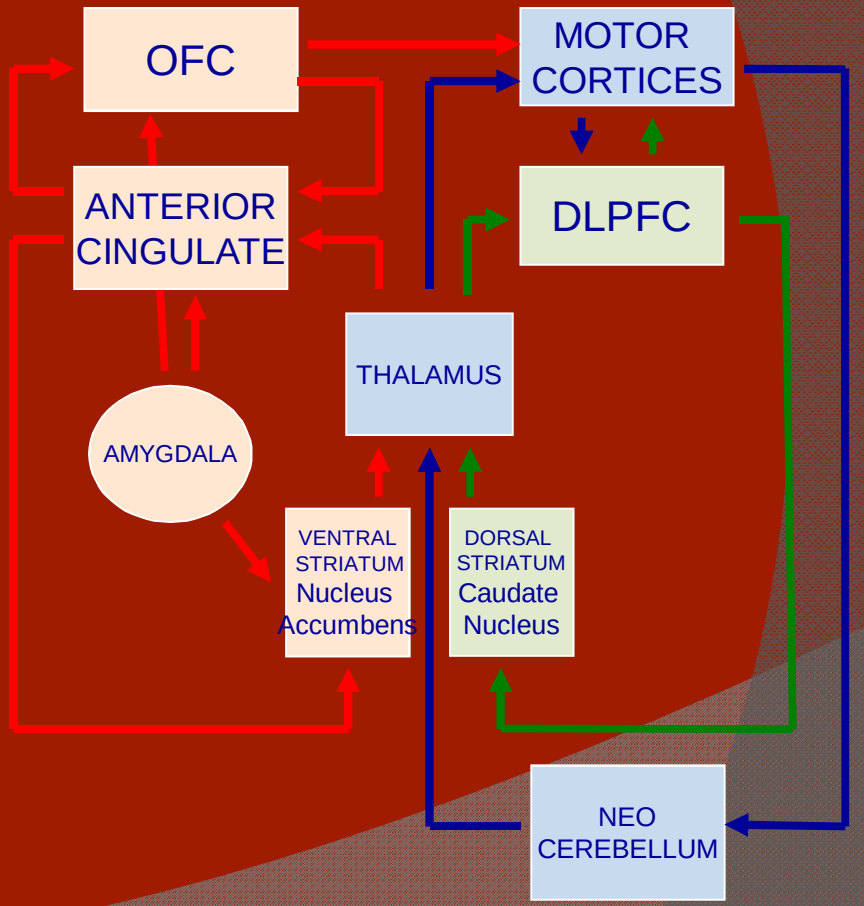
CORTICO-CEREBELLAR LOOP DISTURBANCE

TEMPORO-SENSORY-MOTOR INTEGRATI'N DEFICITS

MOTOR ASYNCHRONY

ADHD

SIMPLIFIED FUNCTIONAL NEUROANATOMY



Developmental genetics

- Cross sectional twin studies:
  - High heritability in childhood : 0.70 – 0.80
  - Lower heritability in adulthood: 0.30 – 0.40

Parent & Teacher ratings

Self-ratings

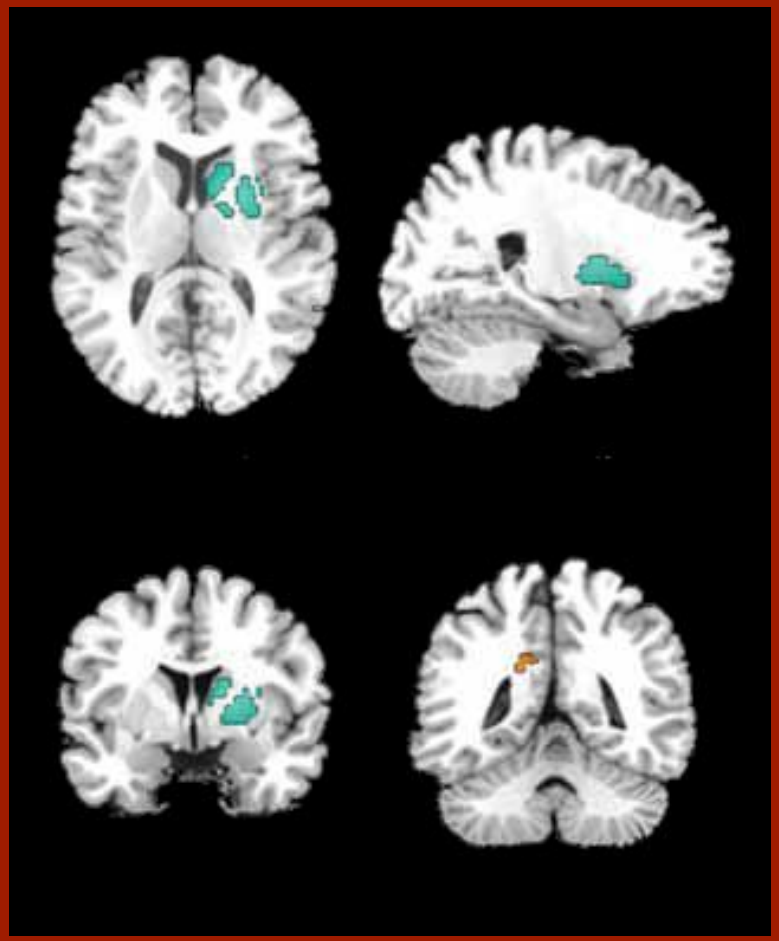
- Prospective twin studies:
  - When cross-informant ratings are used: higher heritability is found in adult ADHD: 0.80
  - Both developmentally stable and dynamic (i.e. different genetic effects operating at different ages) are demonstrated

Chang ea, CJAMA Psychiatry., Published online January 2, 2013

Treatment effects on continuity / discontinuity ?

Medication effects on brain development

Meta-analysis: 14 datasets: 378 ADHD (202 ch&adol) vs 344 CON; 55% on medication



- In general: decreased grey matter; most consistent in n.caudatus:
- AGE and USE OF MEDICATION were independent predictors of normal volumes

Nakao ea. Am J P sychiatry 2011, 168, 1154-1163

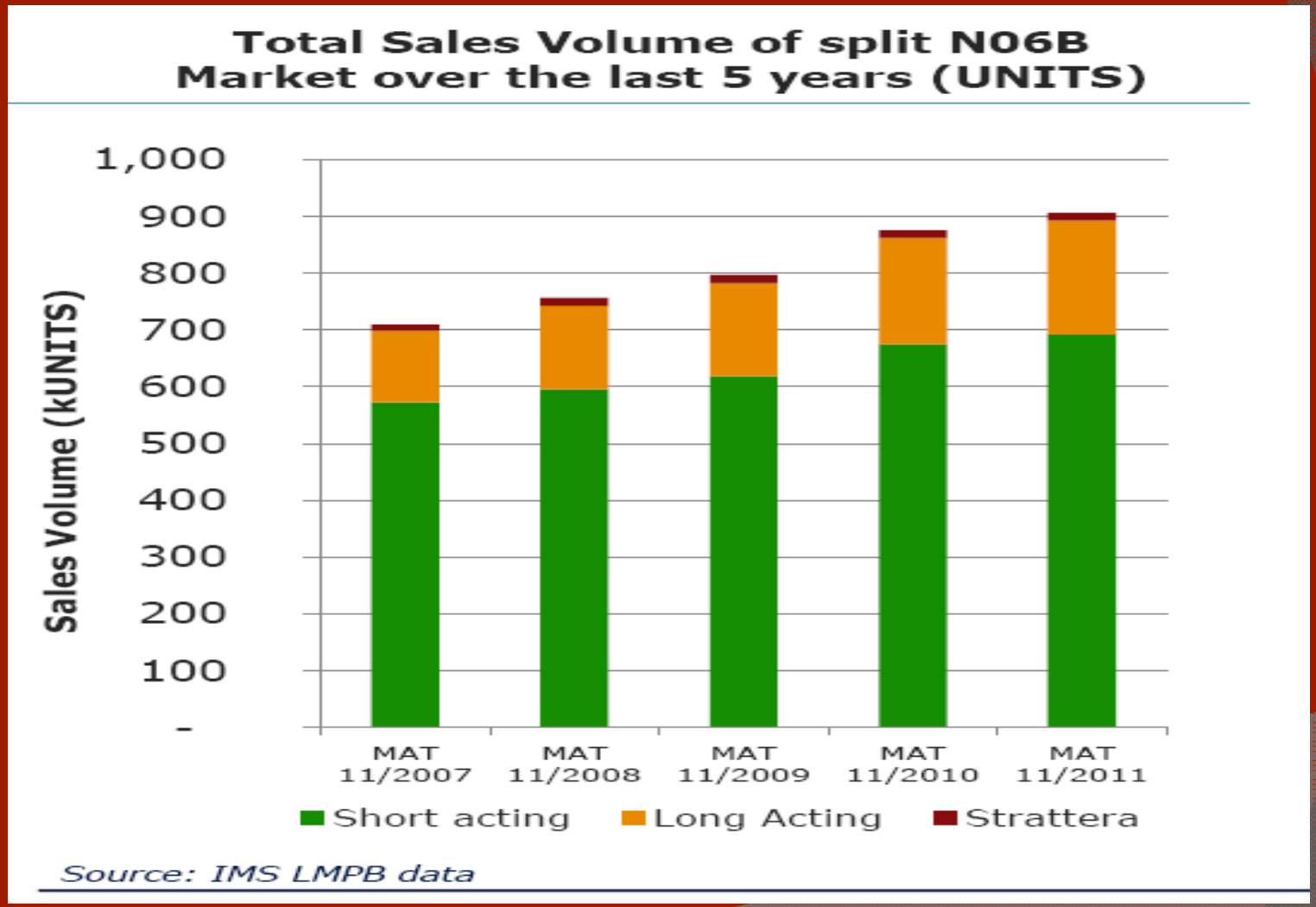
Medication effects on brain development

6 studies > 10 months: ADHD +/- medication:

- 2 no neuro-anatomical differences
- 4 more normalisation with medication:
  - N. caudatus
  - White matter
  - Cortex thickness
  - G. cingularis anterior
- None of the studies shows deterioration

- Mechanism? Direct effect or “use it or loose it” ?

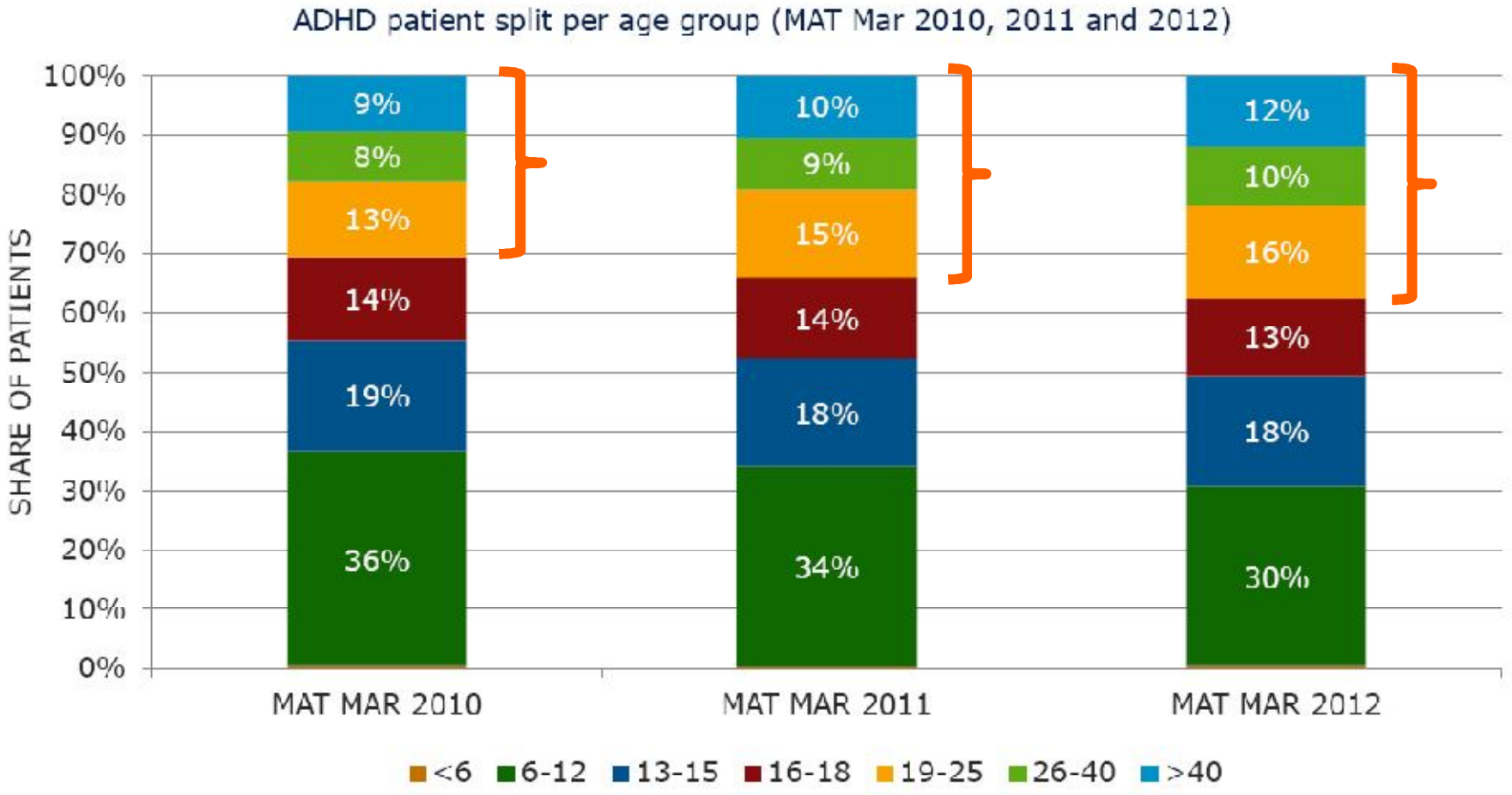
Belgium: Pharmaco-epidemiology: 2007-2011



Belgium: proportion of +18y increases

Half of the patients taking ADHD drugs are under the age of sixteen, with 30% of them between six and twelve

The share and amount of older patients seems to be increasing, looking at the shift in age over the previous 3 years

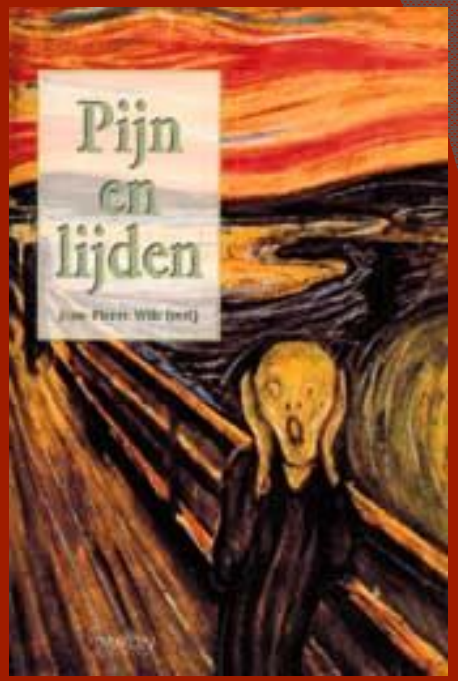


Conclusions:

- Problematic developmental outcome of childhood ADHD
- Applying same criteria: discontinuity & continuity
- Discontinuity seems a linear process starting in early adolescence
- DSM-5 adaptations will (artificially ?) increase “continuity”
- Neurodevelopment suggests partial normalization or compensation
- Twin studies suggest rater bias and new genes coming into action
- Treatment may foster some normalization
- Proportion of “treated” adults in Belgium increases

“In the patiënt’s best interest ?

- How much “disfunctioning” / “suffering” is necessary to reach the threshold of caseness?



“Zolang men gezond is, existeert men niet”

De wreedheid van de pijn – genieten van het lijden, omdat je geniet van je eigen, met het wezen van het leed verbonden persoonlijkheid. Het laatste toevluchtsoord voor de honger naar leven en de dorst naar genot (F. Pessoa)

Transition of care from adolescence to adulthood

- UK 3-tier model based on complexity:
  - Tier 1: follow-up by GP (specialist back-up)
  - Tier 2: follow-up by GP + coach
  - Tier 3: follow-up by specialist
- Re-assessment at school leaving age
- Transition period
- Autonomy / dependence

Young et al. BMC Psychiatry 2011, 11:174