ADHD in Adolescents

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Disclosures

	Advisor	Lecturer
Eli Lilly and Company	x	x
Flynn	x	x
Janssen-Cilag	x	x
Medice	x	x
Neuropharm	x	
Novartis	x	x
Otsuka	x	
Shire	x	x
UCB	x	x

Traditional View of Adolescence 1

There is an interaction between biological development

- Rapid physical growth
- Pubertal sexual changes, endocrine and physical
- Acquisition of formal operational (abstract) thought

and various social challenges

- Individuation with a move away from parental values
- General autonomy including financial independence, leaving home, etc
- Adopting peer group values and social acceptance
- Exercising judgment and self-restraint
- Various age-related social maturity tasks: exams, school-leaving age, etc

Traditional View of Adolescence 2

this results in an identity crisis, not uncommonly a rebellious conflict with family or wider society

which is in turn associated with increased emotional and behavioural symptomatology, partly stress related, partly endocrine-fuelled

Adulthood is recognised towards the end of the teens, roughly in parallel with cessation of body growth

Myth 1: Adolescent Behaviour Is Governed by Raging Hormones

- Very little to support this
  - "Empirical evidence confirming this link is almost nonexistent"[1]
  - "Less than 5% of variance"[2]

1. Susman EJ, et al. *Child Dev.* 1987;58(4):1114-1134.
2. Hill P. *J Child Psychol Psychiatry.* 1993;34(1):69-99.

Myth 2: Adolescence Characterised by Identity Conflicts

- Yet most teenagers have stable identities ('foreclosed' in Marcia's terms)[1,2]
- Identity conflict/uncertainty more of an issue for young adults[3]

1. Archer SL. *Child Dev.* 1982;53:1551-1556.
2. Allison BN, Schultz JB. *Adolescence.* 2001;36(143):509-523.
3. Adams G, Adams C. In: Hsu G, et al., eds. *Recent Developments in Adolescent Psychiatry*; 1989.

Myth 3: Rebellion Against Parental Values and Distancing from Family

- In fact, continuing identification with parental values is usual

- Peer group values may well be in conflict, but do not usually replace parental values; there is a trade-off

Steinberg L, Silverberg SB. *Child Dev.* 1986;57(4):841-851.

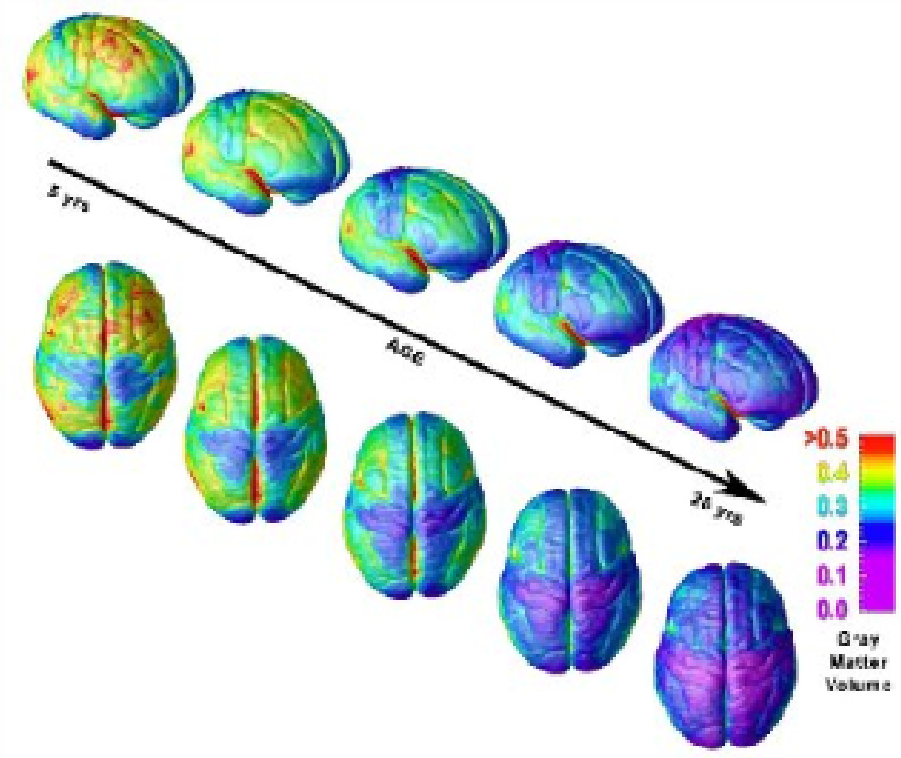
Emerging neurocognitive perspective

Current View of Adolescence Revolves Around Three Main Issues

- Brain cortex/white matter changes
- Change in balance of dopamine circuits
- Increasing importance of peer group standards and involvement in self-esteem

Spear LP. In: Cicchetti D, et al., eds. *Neurodevelopmental Mechanisms in Psychopathology*; 2003.

Grey Matter Growth: Proliferation Followed by Pruning



Grey matter develops quickly during childhood, but slows during adolescence.

↓

Grey matter volume peaks at age 11 in **girls** and at age 13 in **boys**.

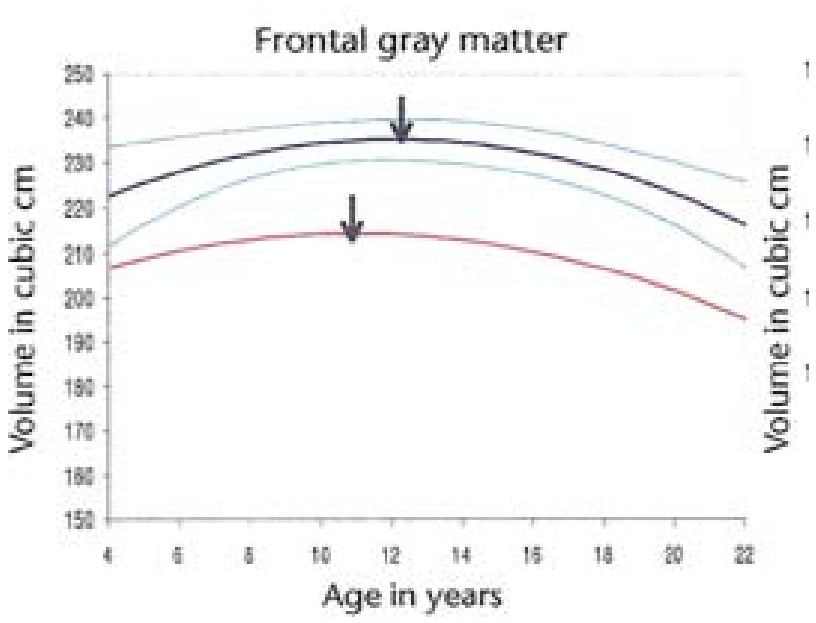
↓

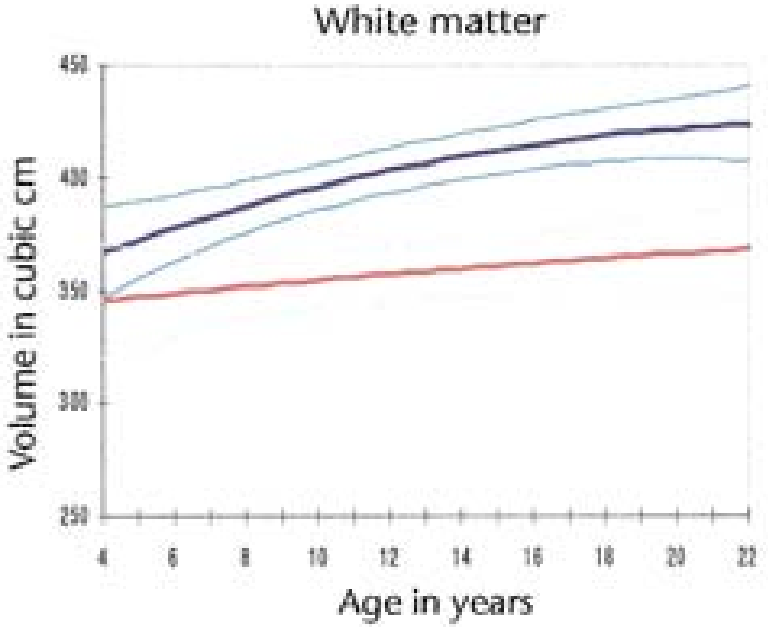
Then, the volume of grey matter begins to decline.

Changes Across Adolescence

Gray matter volume diminishes (synaptic pruning)

White matter volume increases (myelination)





Giedd JN, et al. *Nat Neurosci.* 1999;2(10):861-863.

Synaptic Pruning in Adolescence

- 30,000 synapses lost *per second* during the adolescent period

Rakic P, et al. In: van Pelt J, et al., eds. *Progress in Brain Research. The Self-Organizing Brain: From Growth Cones to Functional Networks*; 1994:227-243.

These changes are associated with improvements in …

- Inhibitory control[1]
- Processing speed[2]
- Working memory[3]
- Decision making[4]

Executive function tasks generally correlate with fMRI prefrontal cortex development[5-7]

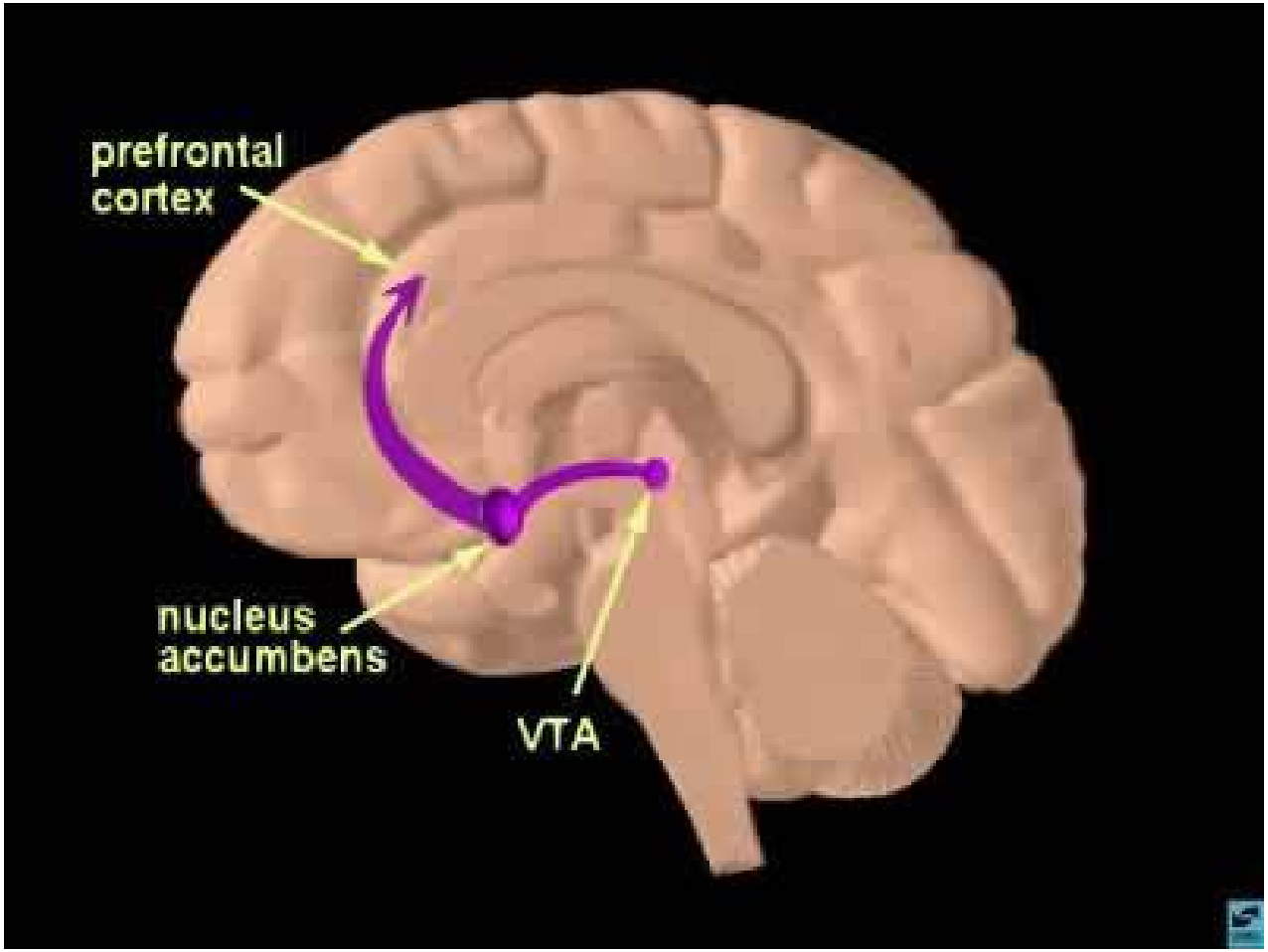
1. Leon-Carrion J, et al. *Int J Neurosci.* 2004;114(10):1291-1311.
2. Luna B, et al. *Child Dev.* 2004;75(5):1357-1372.
3. Anderson P, et al. *Clin Neuropsychol.* 2001;15(1):81-94.
4. Hooper CJ, et al. *Dev Psychol.* 2004;40(6):1148-1158.
5. Luna B, et al. *Neuroimage.* 2001;13(5):786-793.
6. Tamm L, et al. *J Am Acad Child Adolesc Psychiatry.* 2002;41(10):1231-1238.
7. Bjork JM, et al. *J Neurosci.* 2004;24(8):1793-1802.

… as well as improved social cognition

Allows perspective taking, accurate emotion recognition, higher order theory of mind, and the creation of the ‘imaginary audience’ of Elkind (1967)

Choudhury S, et al. *Soc Cogn Affect Neurosci.* 2006;1(3):165-174.

Dopamine pathways of interest



Changes in Dopamine Pathway Activity During Adolescence

- Decline in D_2, D_4 and probably D_1 receptors in striatum, but not in prefrontal cortex; *high* DA activity in mesocortical tract

- DA synthesis and turnover rates *low* in nucleus accumbens (mesolimbic)

Imbalance Produces a 'Reward Deficiency Syndrome' so That Adolescents Seek Out[1] …

- Environmental novelty and risk
- Sensation
- Drug thrills

… And may experience lowering of mood because less pleasure obtained from apparently positive experiences[2]

1. Spear LP. In: Cicchetti D, et al., eds. *Neurodevelopmental Mechanisms in Psychopathology*; 2003.
2. Larson R, Richards MH. *Divergent Realities: The Emotional Lives of Mothers, Fathers and Adolescents*; 1994.

Importance of Integration Into Peer Group

- Comes to rival parents as source of self-esteem[1]
- And development of peer group involvement depends on group social skills[2]

1. Armsden GC, Greenberg MT. *J Youth Adolesc.* 1987;16(5):427-454.
2. Tarrant M. *Soc Devel.* 2002;11:110-123.

Extension of Adolescence Beyond Teenage Years

- If one takes a neuromaturational perspective, recognisable adult brain not achieved until mid-20s[1,2]

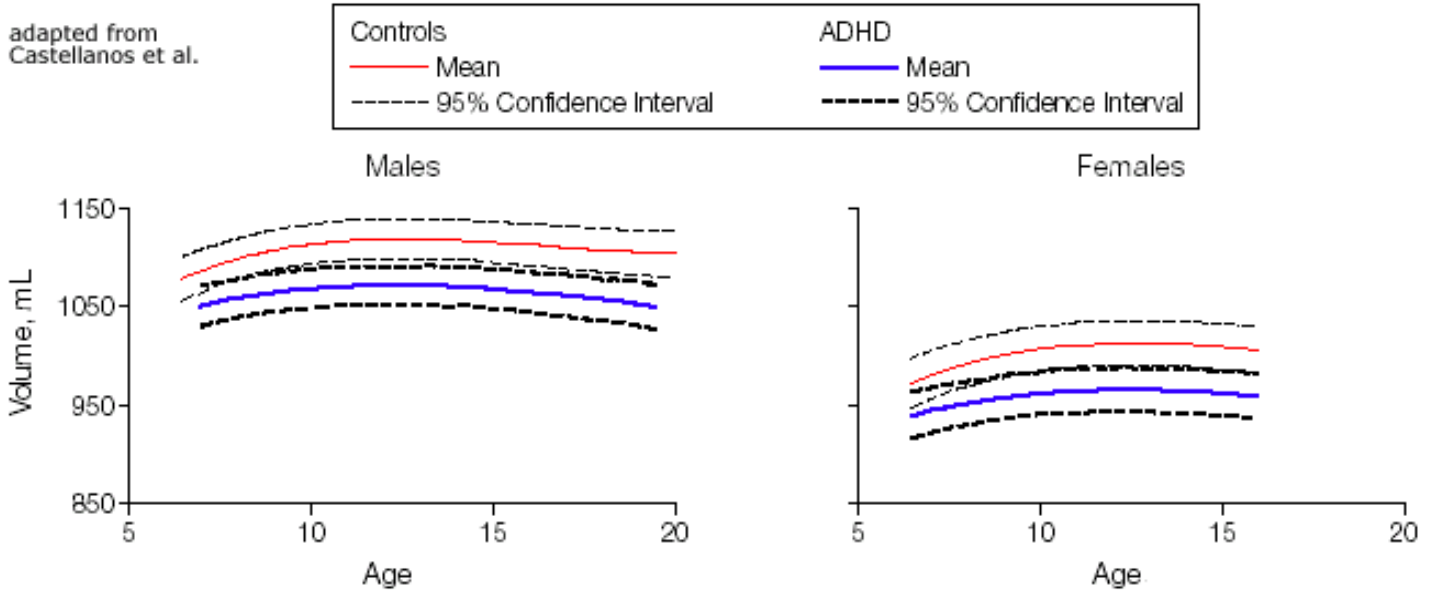
- And synaptic change continues, perhaps until age 70-80[3]

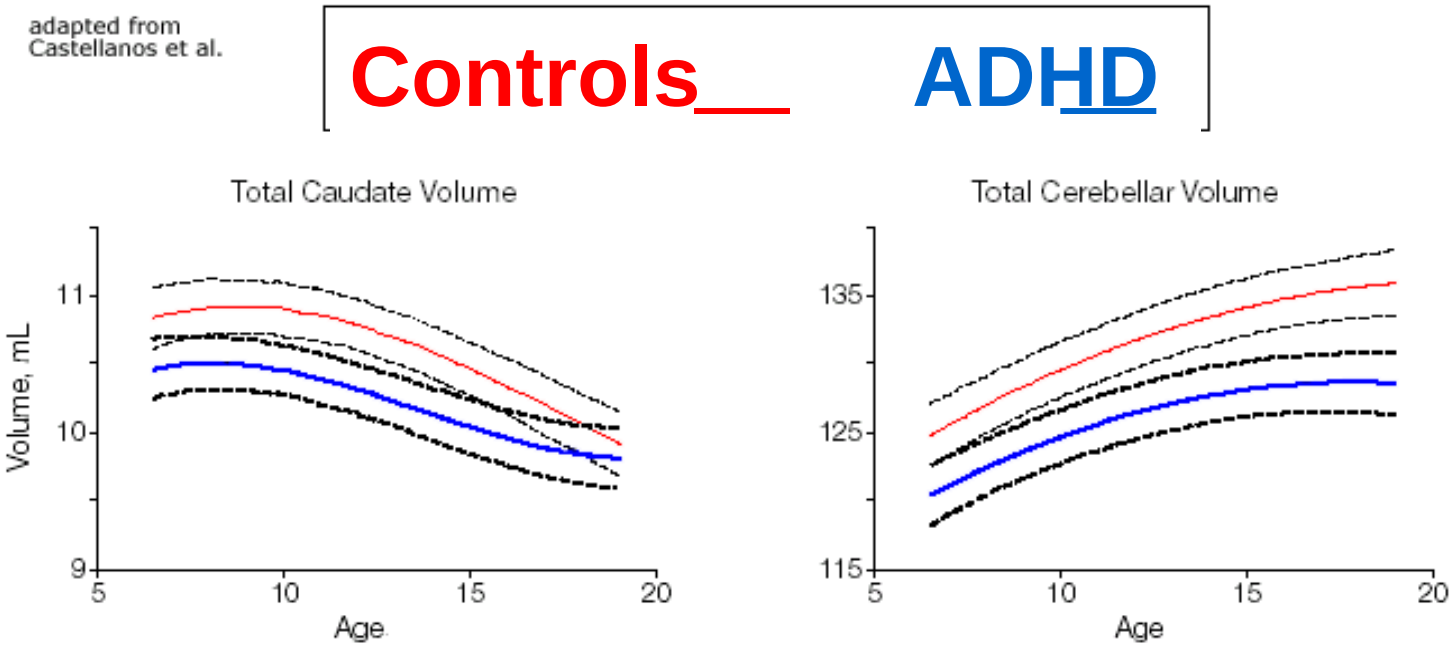
1. Jernigan TL, Sowell ER. In: Keshavan MS, et al., eds. *Neurodevelopment & Adult Psychopathology*; 1997:63-70.
2. Luna B. *Brain and Cognitive Processes Underlying Cognitive Control of Behavior in Adolescence.* PhD Thesis. University of Pittsburgh, 2005.
3. Nowakowski RS, Hayes NL. *Dev Psychopathol.* 1999;11(3):395-417.

Recent Social Changes Clouding the Boundary Between Childhood and Adulthood

- Protracted dependency on parents
- Fewer financial and employment opportunities
- Drug and alcohol recreational culture
- Diffusion of boundary between teenage and adult culture in music, clothes, fashion etc

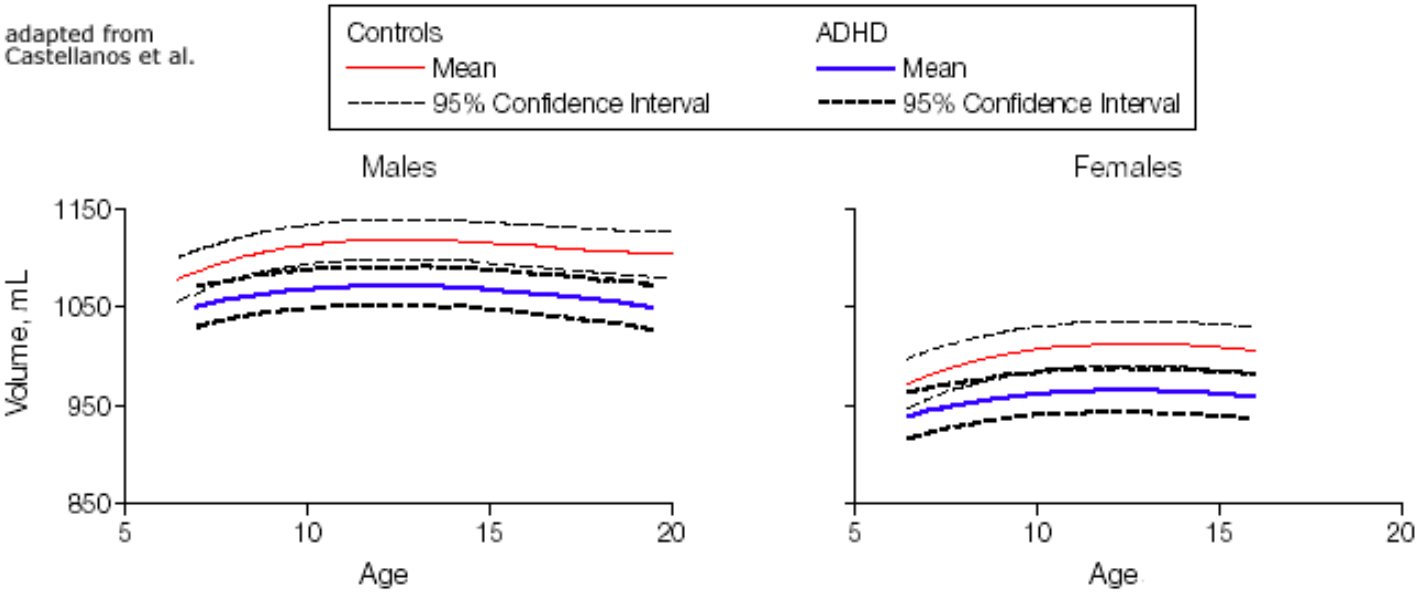
ADHD in Adolescence: neurodevelopmental





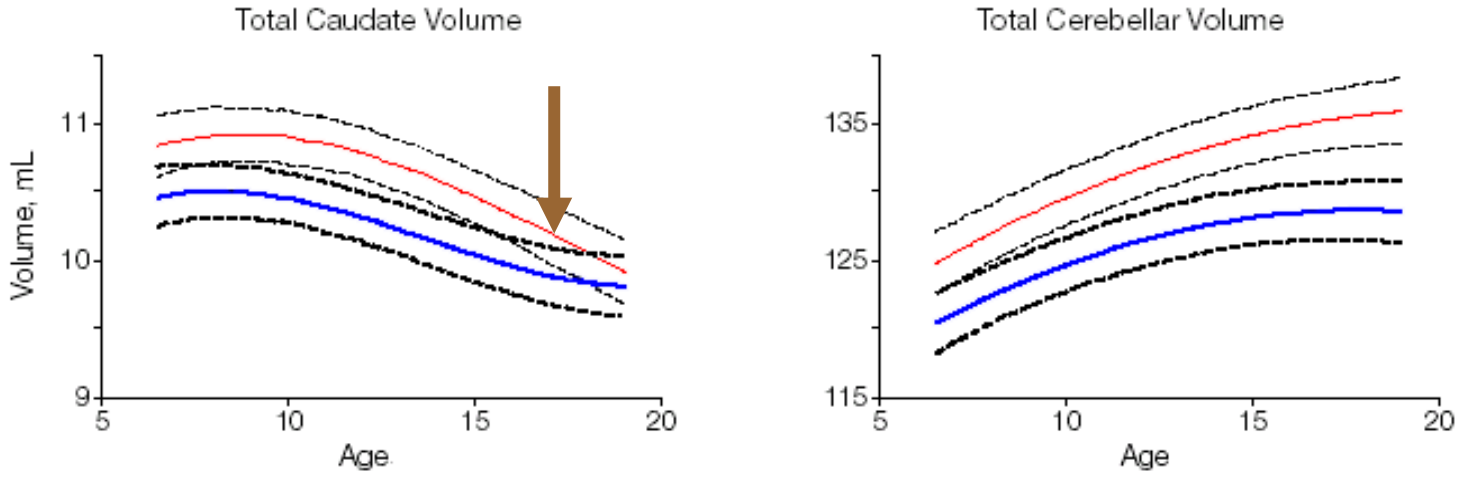
Castellanos FX et al. : JAMA 2002; 288:1740–1748

adapted from
Castellanos et al.



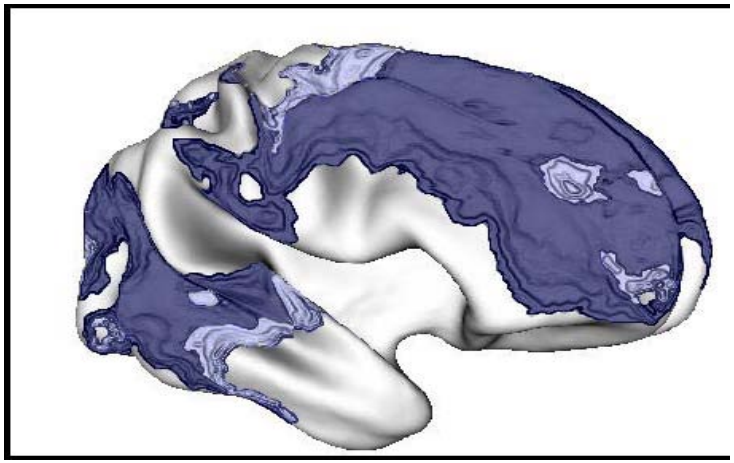
adapted from
Castellanos et al.

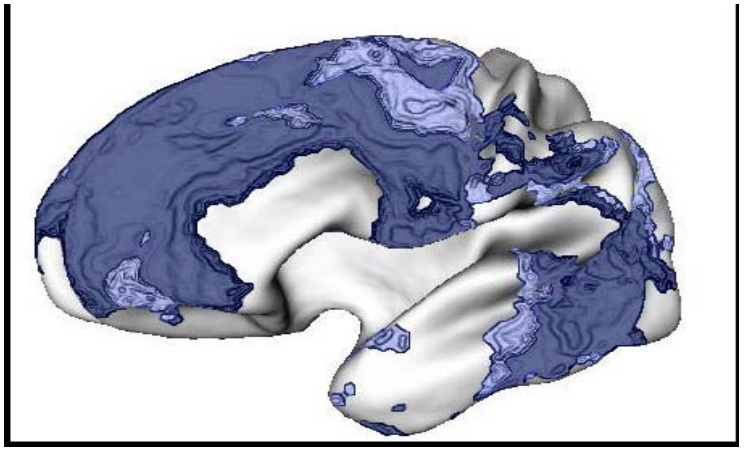
Controls **ADHD**

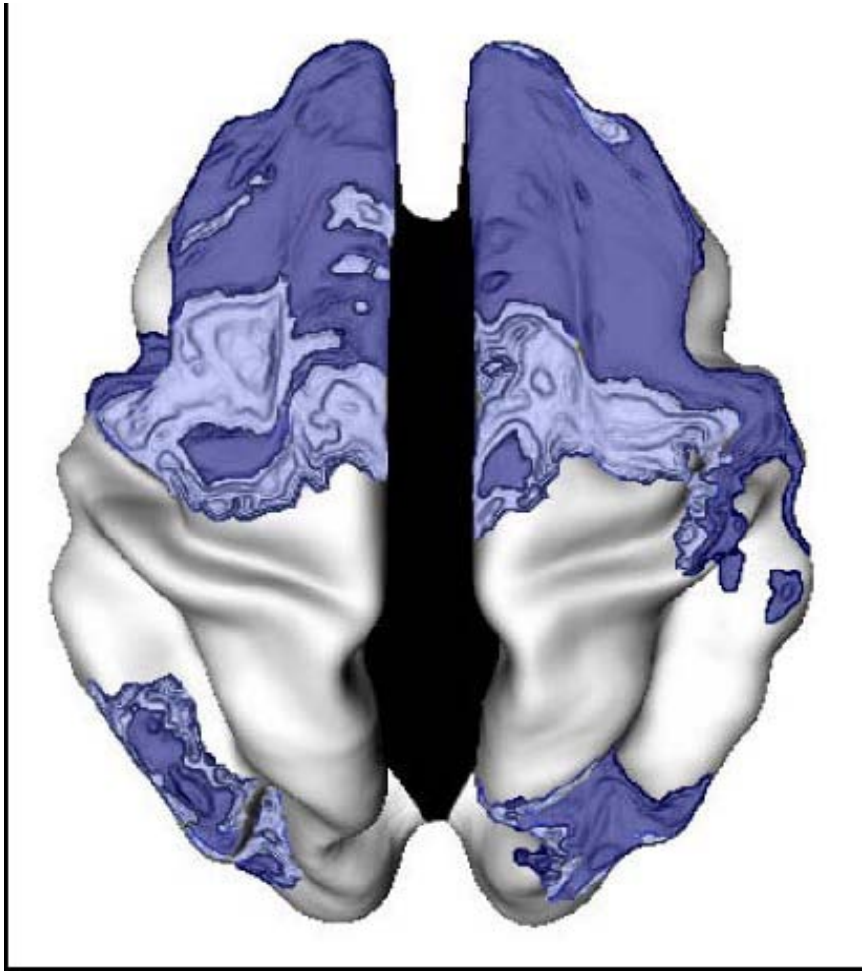


Castellanos FX et al. : JAMA 2002;

Delay in cortical maturation in ADHD (2+ years)







Shaw et al 2007

Delay > of 2 years

Delay of at least 2 years

Delay in cortical maturation in ADHD (2+ years)

From Shaw, P. et al. (2007). ADHD is characterized by a delay in cortical maturation

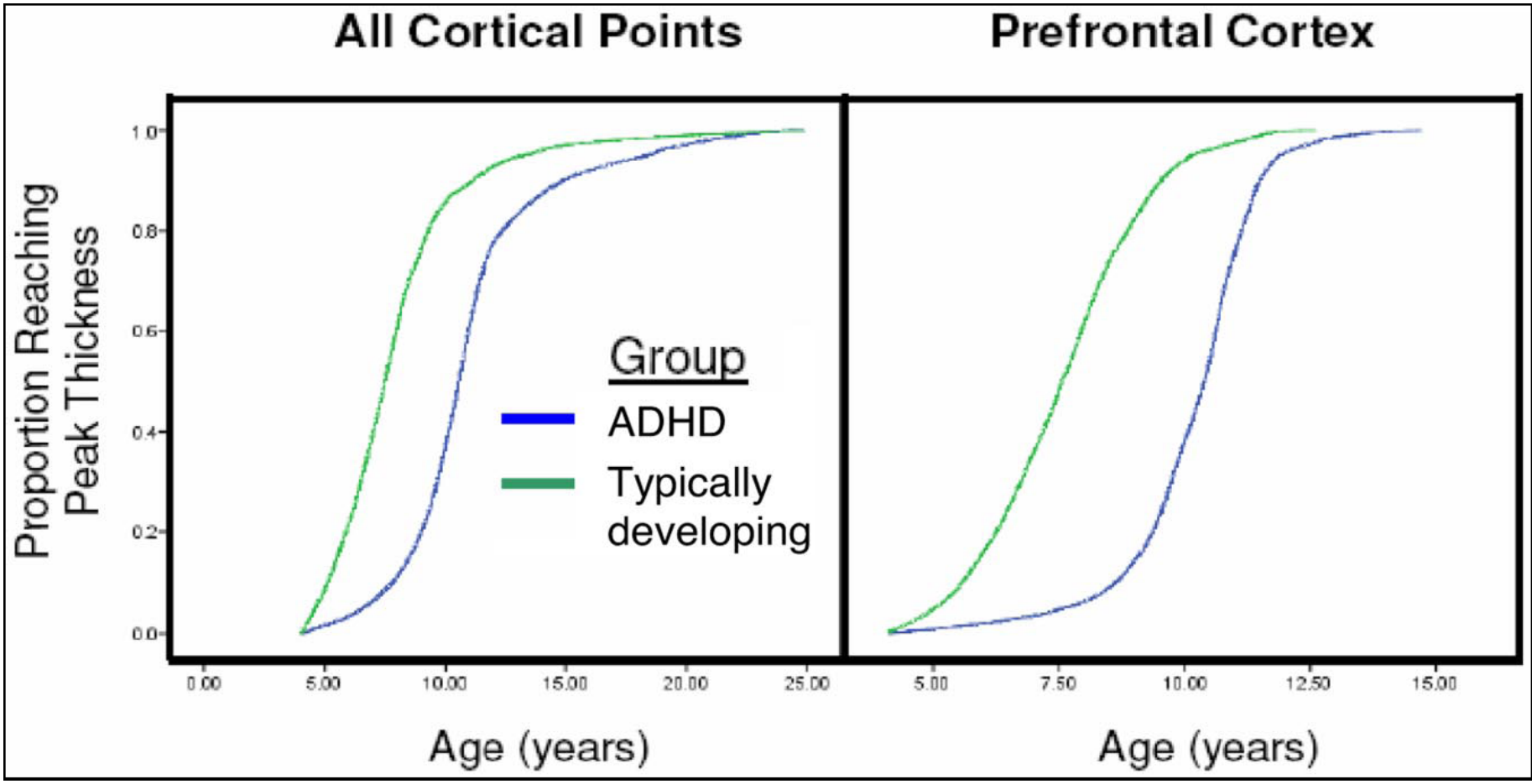
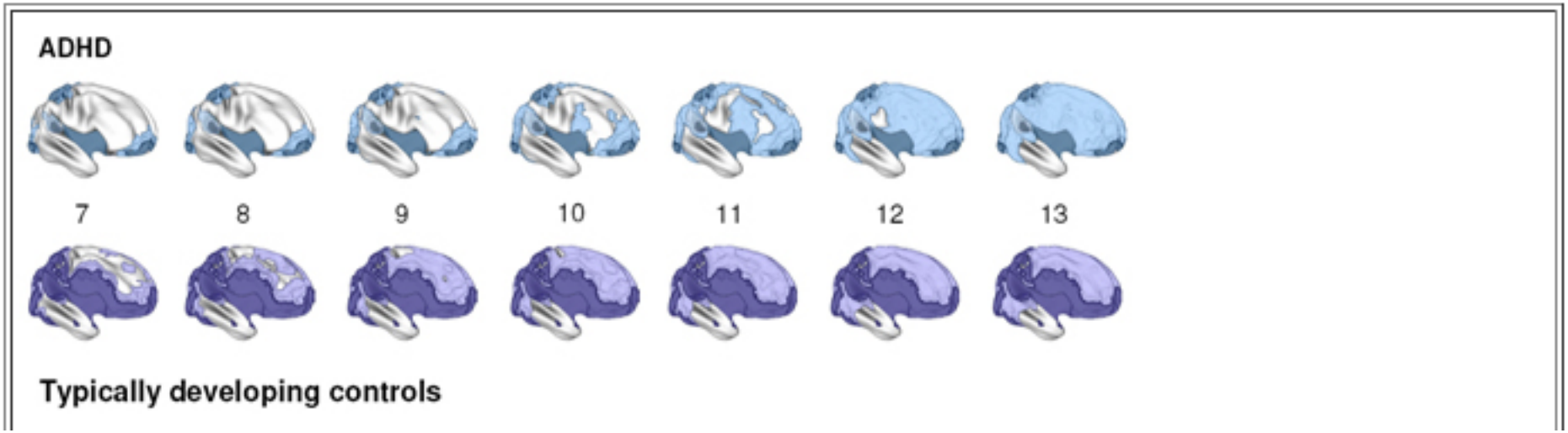


Fig. 3. Kaplan–Meier curves illustrating the proportion of cortical points that had attained peak thickness at each age for all cerebral cortical points (*Left*) and the prefrontal cortex (*Right*). The median age by which 50% of cortical points had attained their peak differed significantly between the groups (all *P* 1.0 1020)

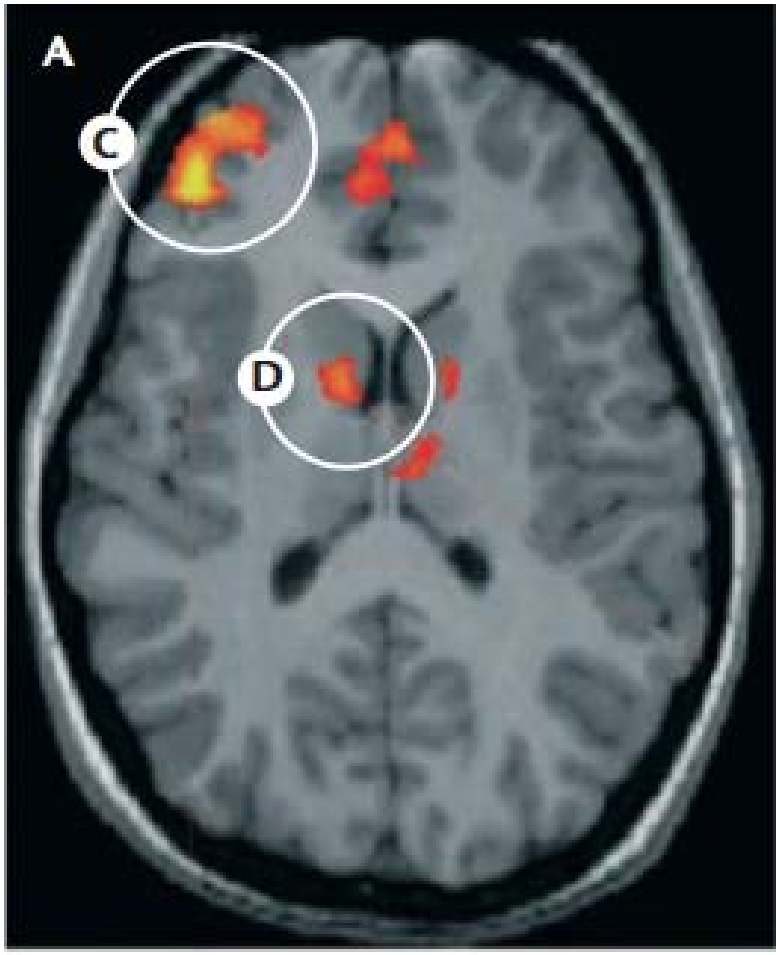
Put more simply……..



Shaw 2007
Replication Almeida 2010

Immature Frontostriatal Hypofunction in ADHD

Hypofunction in ADHD relates to equivalent lower age in adolescents and adults



Rubia K, et al. *Neurosci Biobehav Rev.* 2000;24(1):13-19.

ADHD in Adolescence: clinical

Clinical Issues in ADHD Management in Adolescence

- Issue of ‘emerging’ ADHD
- Change in clinical picture
- Change in impairment domains
- Re-examination/revision of earlier treatment strategy
- Compliance/adherence
- Preparation for transition to adult services
- Ethics

Emerging ADHD

- Latent ADHD may be thrown into focus by increasingly analytical schoolwork

Age of onset

- Currently age 7 years (why?)
- Previous arguments and data showing little effect on clinical picture, response to treatment etc when age of onset is increased[1–3] and adults with childhood onset later than age 7 years no different from those with onset before age 7[4]

1. Applegate B et al. *J Am Acad Child Adolesc Psychiatry* 1997;36:1211–21; 2. Barkley RA, Biederman J. *J Am Acad Child Adolesc Psychiatry* 1997;36:1204–10; 3. Kieling C et al. *Am J Psychiatry* 2010;167:14–16; 4. Faraone SV et al. *Am J Psychiatry* 2006;163:1720–9.

Discussions in DSM-V: Age of onset

- Change from 7 to 12?
  - Changing age of onset to before age 12 years does not affect prevalence[1]

- Need to look out for new cases of ADHD in teens

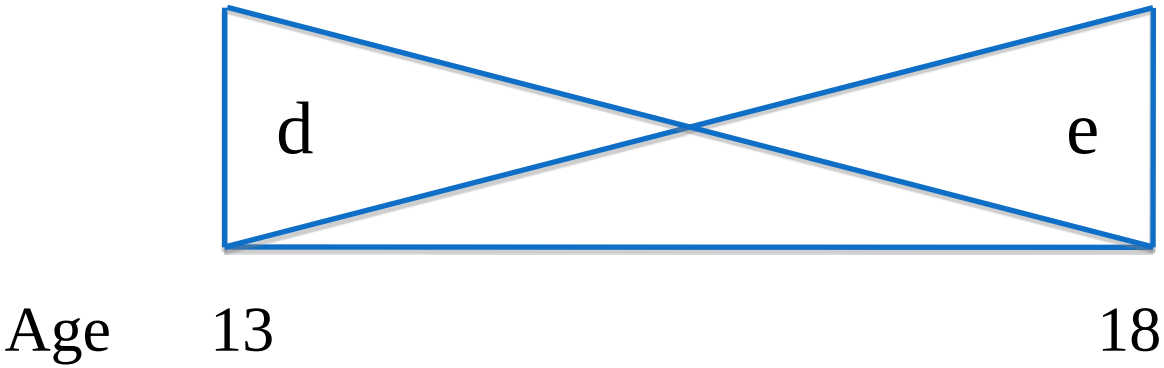
1.Polanczyk G et al. *J Am Acad Child Adolesc Psychiatry* 2010;49:210–16.

Clinical issues in ADHD management in adolescence

- Issue of ‘emerging’ ADHD
- Change in clinical picture

Clinical picture

- Diminishing hyperactivity
- Emergence of emotional (e) rather than developmental (d) comorbidities



Hart EL et al. *J Abnorm Child Psychol* 1995;23:729–49.

Clinical issues in ADHD management in adolescence

- Issue of ‘emerging’ ADHD
- Change in clinical picture
- Change in impairment domains

Impairment 1: Schoolwork

- Schoolwork
  - Homework
    - Poor listening to instructions
    - Forgetting to take books home or hand in completed work
    - Extended work-day
    - Does not understand urgency

Impairment 1: Schoolwork

- Schoolwork
  - ‘Coursework’ and projects
    - Difficulty stopping an activity in order to start work
    - Impulsive starting without thinking through or reading
    - Poor organisation; files in a mess
    - Poor planning; cannot get things in order
    - Cannot get books, notes, etc together in one place
    - Distraction by internal as well as external elements
    - Failure to sustain attention
    - Trouble with deadlines

Impairment 1: Schoolwork

- Examinations
  - Inefficient revision
  - Impulsive answering
  - Poor time judgement
  - Failure to sustain attention

Impairment 2: Social relationships

- Peer group
  - Rejection/isolation
  - Association with antisocial friends[1]
  - (Opposite) sex relationships[2,3]
    - pregnancy (impulsiveness, forgetfulness)
    - sexually transmitted diseases

1. van Lier PA et al *Dev Psychopathol* 2007;19:167–85; 2. Barkley RA et al. *J Am Acad Child Adolesc Psychiatry* 2006;45:192–202; 3. Barkley RA. *J Clin Psychiatry* 2002;63(Suppl 12):10–5.

Impairment 2: Social relationships

- Problems with authority beyond home and school

- Workplace issues
  - Punctuality
  - Instructions and procedures
  - Distractibility and distracting
  - Poor task performance
  - Anger

Impairment 3: Disorganisation

- General disorganisation
  - Medication
  - Self-care
  - Things not in order
  - Time management
  - Keeping appointments
  - Paying bills
  - Honouring commitments and promises

Impairment 4: Substance misuse

- Higher rates of substance misuse, especially if comorbid oppositional defiant disorder/conduct disorder (ODD/CD)
  - Smoking
  - Alcohol
  - Illicit drugs

Impairment 5: Associated behaviour

- Risk-taking or sensation-seeking behaviour generally
- Driving
  - Speeding
  - Rage
  - Risk taking

Barkley R.A *Attention Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment* 3rd Ed, New York: Guilford Press 2006.

Clinical issues in ADHD management in adolescence

- Issue of ‘emerging’ ADHD
- Change in clinical picture
- Change in impairment domains
- Re-examination/revision of earlier treatment strategy

When would you generally encourage a male teenager to start taking responsibility for his ADHD medication?

1. 14
2. 16
3. 18

Re-examine treatment strategy: Issues

- Use of problem-focused targets rather than rating scales (and difficulties with teacher reports from multiple subjects)
- Longer waking day compared with childhood
- Sleep
- Relevance of neuropsychology (working memory, non-verbal learning difficulties, etc)
- Possible use of cognitive approaches in older teenagers[1]
- Higher rates of poor medication adherence than in childhood[2]

1. Young S, Bramham J. *ADHD in Adults: A Psychological Guide to Practice*, 2007;
2. Gau S et al. *J Clin Psychiat* 2008;69:131-40 .

Clinical issues in ADHD management in adolescence

- Issue of ‘emerging’ ADHD
- Change in clinical picture
- Change in impairment domains
- Re-examination/revision of earlier treatment strategy
- Compliance/adherence

What rate of non-adherence to ADHD medication would you expect among adolescents?

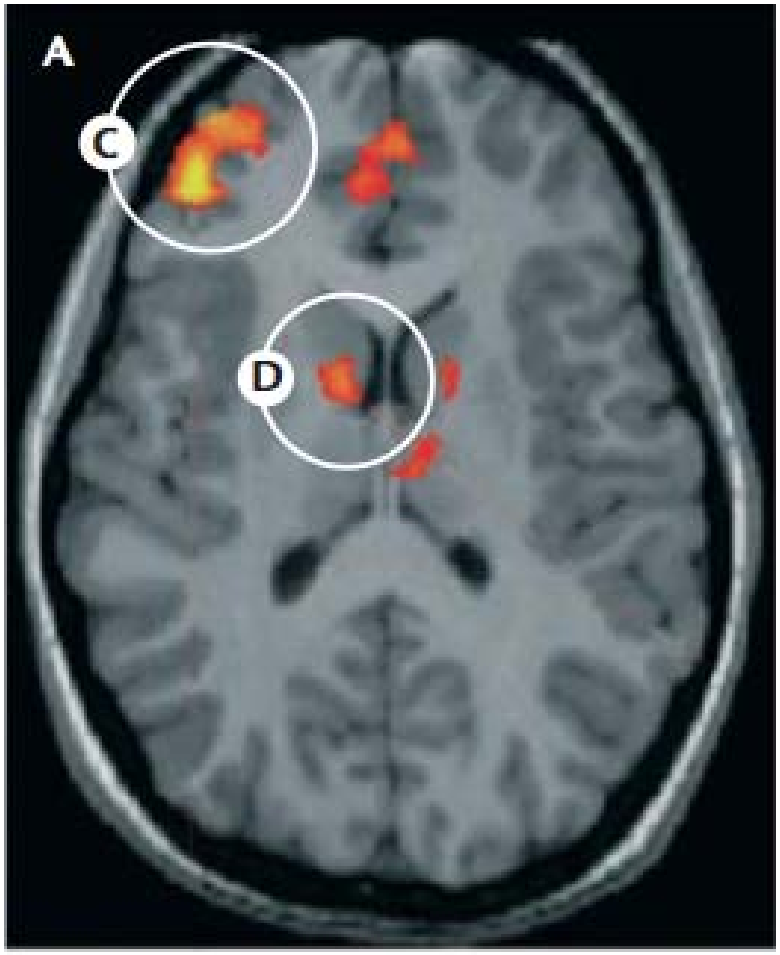
1. 13%
2. 24%
3. 37%
4. 64%

Adler L, Nierenberg A. *Postgrad Med* 2010;122:184–91..

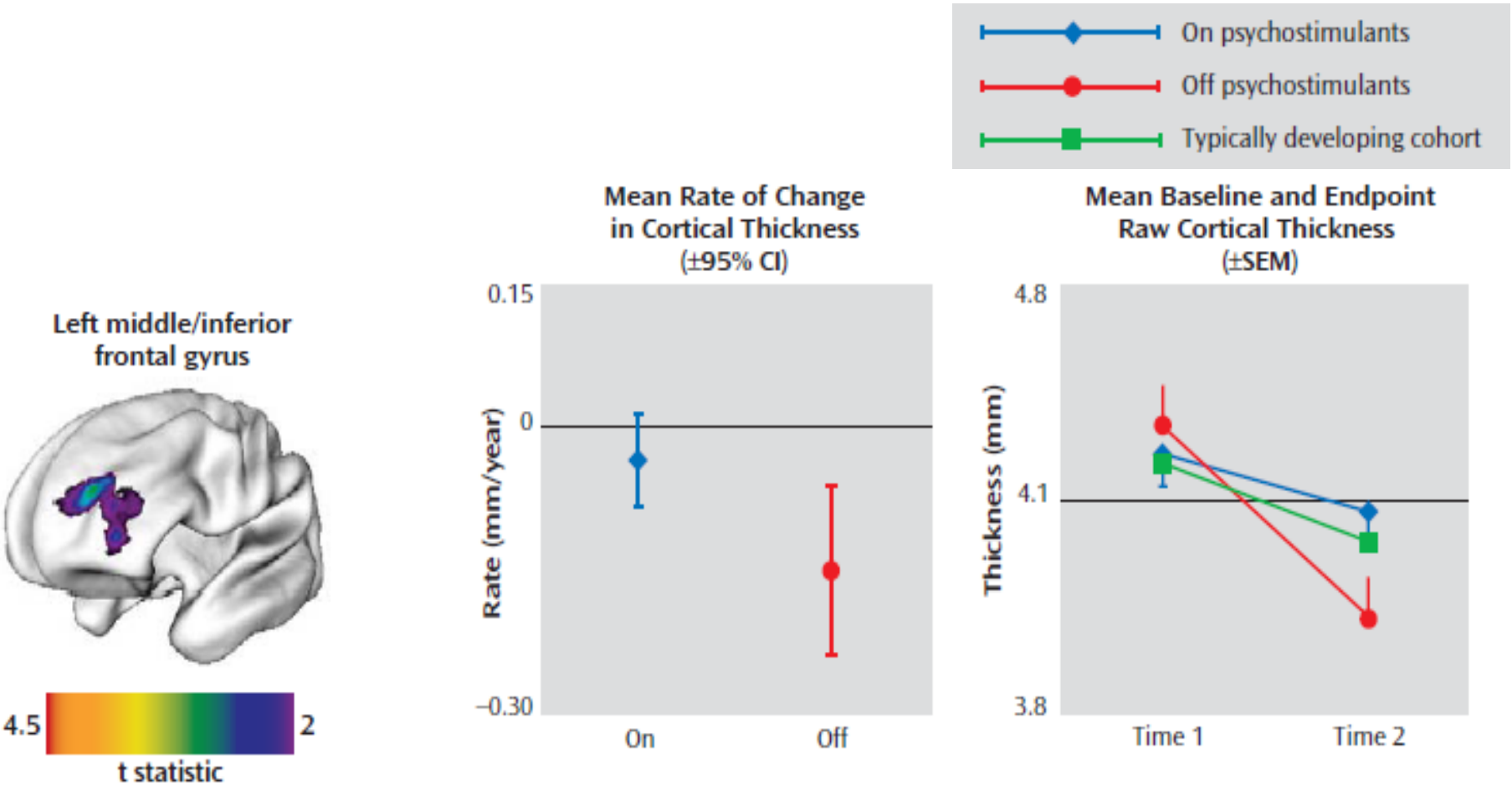
Promoting compliance/adherence

- Talk directly with adolescent
- Use visual aids

Immature frontostriatal hypofunction in ADHD



Rubia K et al. *Neurosci Biobehav Rev* 2000;24:13–19.



•Left: Brain template showing regions where the two groups had a significantly different rate of cortical growth

•Middle: rate of change in raw cortical thickness in these regions

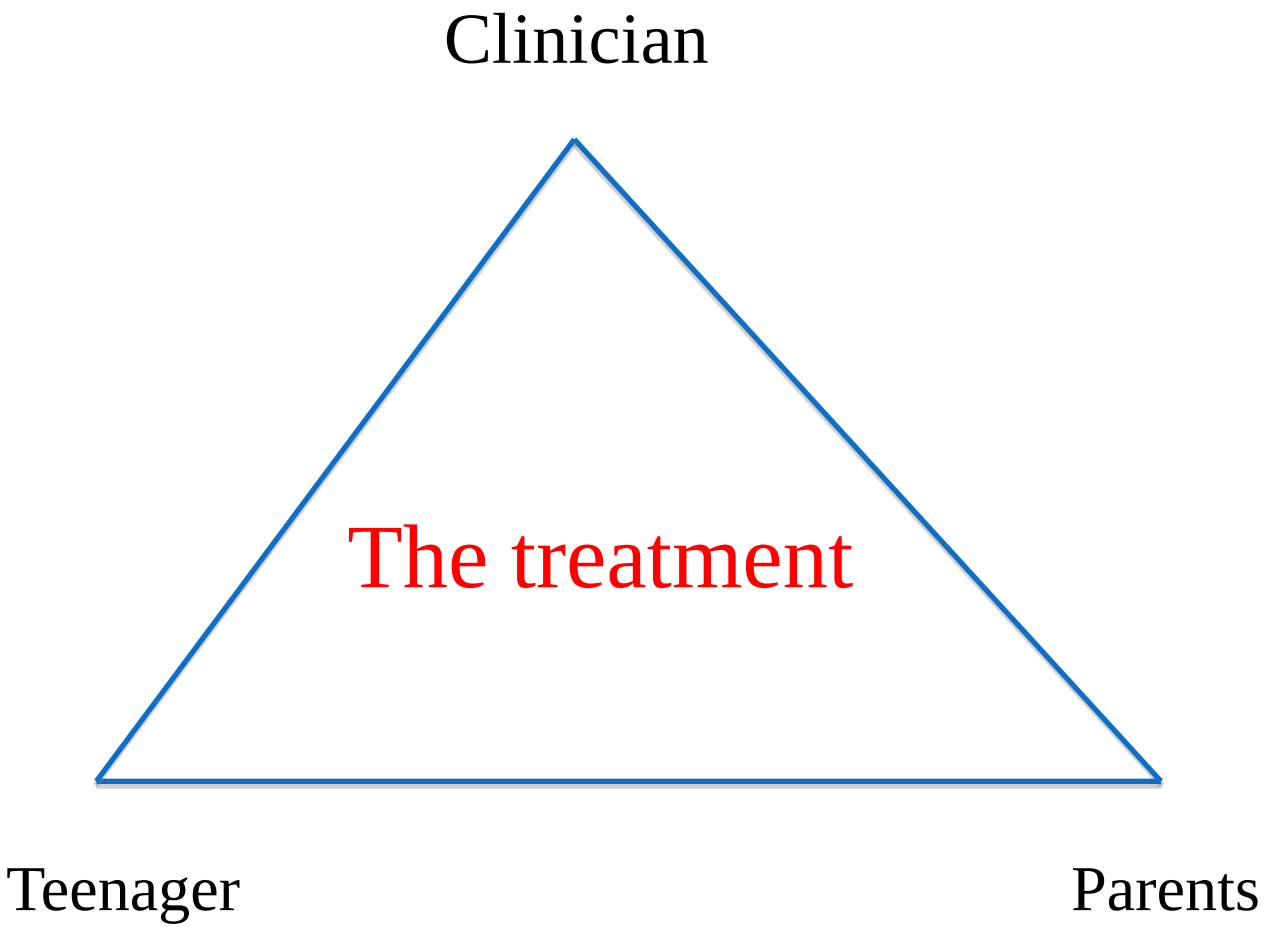
•Right: baseline and endpoint raw cortical thickness for each group and the age-expected values for a typically developing adolescent

Shaw P et al. *Am J Psychiatry* 2009;166:58–63.

Promoting compliance/adherence

- Talk directly with adolescent
- Use visual aids
- Motivational interviewing stance
  - Mild scepticism “How do we know this medicine is working?”
  - Is it worth it?

The triangle of discussion



Clinical issues in ADHD management in adolescence

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- Compliance/adherence
- Preparation for transition to adult services

Preparation for transition to adult services

- Know local structure of services
  - At what age is transition expected?
  - To whom (adult psychiatry, student health, etc)?
  - How to make referral
- Move towards placing adolescent progressively more in charge of own diagnosis and treatment

Change in patient–doctor contract

- Shift from parental referral basis to patient acceptance basis
- Balance of focus of complaint: parent and teacher towards the patient
- Open discussion of adverse effects (eg, loss of spontaneity, appetite reduction, growth)
- Change of authority/responsibility within the family
- Some will discontinue attendance but return later

Use of medication

- Pressure from marketing authorisation (‘licensing’) regulations
- Possible move from regular to pulsed or p.r.n. (when necessary) pattern or *vice versa*
- Need for patient to develop expertise in how to titrate against situational demands
- Advice about combining with alcohol, cannabis, etc
- How can patient handle controlled drugs?

Clinical issues in ADHD management in adolescence

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Ethical dilemmas

- Autonomous decisions
- Confidentiality
- Examinations (‘cosmetic neurology’)
- Medication misuse and diversion

Tensions in management of ADHD in adolescents: Summary

- Balancing development (brain immaturity issue) and expectations
- Impairment (need to seek out)
- Compliance/adherence: Whose problem?
- Transition issues (possibly service development)
- Ethical dilemmas

Frustrating – or rewarding?

Thank You

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