Why is Phillip so fidgety and Johnny such an airhead?

Prof Dave Coghill
University of Melbourne

Tel Aviv April 2016
"Let me see if Philip can
Be a little gentleman;
Let me see if he is able
To sit still for once at
table."

The Story of Fidgety Philip
by Dr. Heinrich Hoffmann
1845
As he trudged along to school,
It was always Johnny's rule
To be looking at the sky
And the clouds that floated by;
But what just before him lay,
In his way,
Johnny never thought about;
So that everyone cried out,
"Look at little Johnny there,
Little Johnny Head-in-Air!"
Diagnostic criteria

• **What is ADHD**
  
  A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development

• **What is not ADHD**
  
  The symptoms are not solely a manifestation of oppositional behaviour, defiance, hostility, or failure to understand tasks of instructions

Criteria for ADHD Diagnosis: 
DSM-5

**Inattention**
- Lack of attention to details, makes careless mistakes
- Difficulty sustaining attention
- Does not listen when spoken to directly
- Trouble completing or finishing job tasks
- Problems organizing tasks and activities
- Avoids or dislikes sustained mental effort
- Loses and misplaces things
- Easily distracted
- Forgetful in daily activities

**Hyperactivity**
- Fidgetiness b(hands or feet) or squirming in seat
- Leaves seat when not supposed to
- Restless or overactive
- Difficulty engaging in leisure activities quietly
- Always ‘on the go’
- Talks excessively

**Impulsivity**
- Blurs out answers before questions have been completed
- Difficulty waiting in line or taking turns
- Interrupts or intrudes on others when they are working or busy

American Psychiatric Association. Diagnostic and Statistical Manual (DSM) of Mental Disorders. 5th Edition 2013
Defining adult ADHD (DSM-5)

- **Criteria A**: 5 or more symptoms of inattention or hyperactivity-impulsivity
- **Criteria B**: Several symptoms present by the age of 12
- **Criteria C**: Several symptoms present in two or more settings
- **Criteria D**: Symptoms interfere with or reduce quality of social, educational or occupational functioning
- **Criteria E**: Symptoms are not better explained by another condition, such as mood disorder

American Psychiatric Association. Diagnostic and Statistical Manual (DSM) of Mental Disorders. 5th Edition 2013
### Domains of ‘IMPAIRMENT’

1. *Work Functions*  
2. *Social relationships*  
3. *Coping with daily activities*  
4. Driving accidents (increased mortality)  
5. *Behavioural problems*  
6. *Distress from the symptoms*  
7. *Low self-esteem*  
8. Emotional instability  
9. Sleep problems  
10. *Risk for comorbid disorders (substance abuse, anxiety, depression, personality disorder)*  
11. Cognitive impairments, including general and specific learning difficulties (dyslexia, dyspraxia, autism spectrum disorder)

* *NICE definition of impairment 2008*

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Inter rater Reliability of Diagnoses From the Initial DSM-5 Field Trials

Kappa

0 0.2 0.4 0.6 0.8 1

Major Neurocognitive disorder
Autism
PTSD
ADHD
Bipolar 1
Schizophrenia
Conduct Disorder
ODD
Major Depressive Disorder
Disruptive Mood Dysregulation Disorder
Generalised Anxiety Disorder

Thanks to Sam Chung

Am J Psych 2013
ADHD is common

Prevalence of ADHD in China (Shanghai)

- Two stage assessment
  - ADHD-RS-IV parent reported questionnaire
  - KIDDIE SADS diagnostic interview

- Questionnaires
  - 15,412 distributed
  - 12,954 returned
  - 9,900 valid (64.2%)
  - 5,648 eligible for interview stage (several schools opted out of this stage)

- Interviews
  - 1187 were interviewed
  - Overall prevalence 4.6%
  - Gender ratio 2.5 : 1
    - Boys 6.6%
    - Girls 2.7%
  - Type
    - Combined type 1.8%
    - Inattentive type 2.4%
    - Hyperactive/Impulsive type 0.4%
  - Age
    - 5-6 years 5.2%
    - 7 – 10 years 6.3%
    - 11 – 15 years 2.4%

Polanczyk et al 2007

Coghill, Du, Su in preparation
Percent of Youth Aged 4-17 with Current Attention-Deficit/Hyperactivity Disorder in USA by State: National Survey of Children's Health – CDC 2011

But not this common!

- ≤ 5.0%
- 5.1% – 7.0%
- 7.1% – 9.0%
- 9.1% – 11.0%
- ≥ 11.0%
But not this common!

Percent of Youth Aged 4-17 with Current Attention-Deficit/Hyperactivity Disorder in USA by State: National Survey of Children's Health – CDC 2011
Numbers of prescriptions of ADHD medications per year across Australia range from 382 to 28,642 per 100,000 children under the age of 17 years.

Prescriptions are only for a maximum of 1 month = 12 per year.

Suggests that in the top prescribing areas around 2.4% of children and young people under 17 years of age are receiving medication for ADHD.

It is easy to focus on the increase rather than the actual numbers. Maximum prevalence of prescribing is under 1% of the population. For adults 25 – 45 yrs. the maximum prevalence is 0.01%.

Error bars indicate 95% confidence intervals
Age-dependent decline and persistence of ADHD throughout the lifetime

- At follow-up, although an age-dependent decline in ADHD was observed, ADHD is a highly persistent disorder when defined by ‘persistence of functional impairment’ or persistence of subthreshold (three or fewer) impairing symptoms. By contrast, many patients remit full diagnostic criteria.
ADHD is a persistent disorder: Follow-up after 6 years - Netherlands

Participants with relapse, %

- Persistent (n=178): 86.5%
- Subthreshold (n=17): 8.4%
- Remittent (n=11): 5.1%

Participants with relapse:

- Persistent (n=178)
- Subthreshold (n=17)
- Remittent (n=11)

Number of ADHD symptoms:

Hyperactivity/Impusivity

Inattention

Baseline Follow-up


ADHD: attention-deficit hyperactivity disorder.
Tax Issues & Relationship Problems

Substance use problems

Several Issues!

Several High Profile Buisness Failures

Teenage Pregnancy and aggressive behaviour
ADHD IS IMPAIRING
Pre-treatment mean domain T-scores for HRQoL in three ADHD study populations and controls

<table>
<thead>
<tr>
<th>CHIP CE Domains</th>
<th>Study SPD489-326</th>
<th>ADORE study</th>
<th>Pooled ATX studies</th>
<th>Diabetes mellitus</th>
<th>Control</th>
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<tbody>
<tr>
<td>Achievement</td>
<td>30.2</td>
<td>30.2</td>
<td>30.5</td>
<td>49.7</td>
<td>48.6</td>
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<tr>
<td>Risk Avoidance</td>
<td>32.3</td>
<td>29.9</td>
<td>30.2</td>
<td>50.0</td>
<td>50.5</td>
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<td>Resilience</td>
<td>36.8</td>
<td>36.0</td>
<td>36.0</td>
<td>45.3</td>
<td>44.6</td>
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<td>Satisfaction</td>
<td>35.5</td>
<td>32.8</td>
<td>34.4</td>
<td>45.5</td>
<td>42.8</td>
</tr>
<tr>
<td>Comfort</td>
<td>44.5</td>
<td>42.5</td>
<td>43.7</td>
<td>50.8</td>
<td>53.5</td>
</tr>
</tbody>
</table>

Dundee Data
Impact of untreated and undertreated ADHD on patients and their families

**School and occupation**
- 60% suspended\(^\text{12}\)
- 32% drop out\(^\text{12}\)
- Lower occupational status\(^\text{5}\)

**Family**
- 3–5-fold ↑ parental divorce or separation\(^\text{4,10}\)
- ↑ risk of teenage pregnancy\(^\text{12}\)

**Healthcare system**
- ↑ in ED visits\(^\text{2}\)
- 50% ↑ in bike accidents\(^\text{1}\)
- 4-fold more motor vehicle crashes\(^\text{3}\)

**Employer**
- ↑ parental absenteeism and ↓ productivity\(^\text{11}\)

**Society**
- Substance use disorders:
  - 2-fold risk\(^\text{6}\)
  - Earlier onset\(^\text{7,8}\)
  - Less likely to quit smoking in adulthood\(^\text{9}\)

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Adult outcomes of ADHD

- Grade point average
- Class rank (%)
- Suspended during high school
- Special education during high school
- Retained in grade
- Graduated high school
- Enrolled in college
- Currently full-time student
- Total years of education

- Number of full-time jobs
- Ever fired from employment
- Number of lifetime moves
- Close friends now
- Ever fired from employment
- % Jobs fired from employment
- Ever had a credit card
- Have a savings account
- Have trouble saving to pay bills
- Driving offences and accidents
- No. of sex partners
- No. of sex partners in past year
- Time spent watching TV

High rates of crime
High rates of substance misuse
High rates of psychiatric disorder
# ADHD and Mortality

<table>
<thead>
<tr>
<th>Age at ADHD-diagnosis (years)</th>
<th>No. of deaths</th>
<th>Person-years</th>
<th>Mortality rate per 10 000 person-years</th>
<th>Fully adjusted model MRR (95% CI)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRR according to age at first diagnosis vs those without ADHD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-5</td>
<td>10</td>
<td>29 944</td>
<td>3.34</td>
<td>1.86 (0.93–3.27)</td>
</tr>
<tr>
<td>6-17</td>
<td>59</td>
<td>136 048</td>
<td>4.34</td>
<td>1.58 (1.21–2.03)</td>
</tr>
<tr>
<td>&gt;17</td>
<td>38</td>
<td>24 724 510</td>
<td>22.28</td>
<td>4.25 (3.03–5.78)</td>
</tr>
<tr>
<td>No ADHD</td>
<td>5473</td>
<td>24 724 510</td>
<td>2.21</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>p value§</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Overall cohort</td>
<td>5580</td>
<td>24 907 560</td>
<td>2.24</td>
<td></td>
</tr>
</tbody>
</table>

Indivduals diagnosed with ADHD in adulthood had a greater risk of death than those diagnosed in childhood and adolescence.

*adjusted for age, calendar year, and sex. †adjusted for age, calendar year, sex, parental history of psychiatric disorders, and maternal and paternal age at time of delivery. ‡adjusted for age, calendar year, sex, parental history of psychiatric disorders, maternal and paternal age at time of delivery, parental educational, and parental employment status. P value is overall effect of being diagnosed with ADHD at different ages vs individuals without ADHD. ADHD: Attention-deficit hyperactivity disorder; MRRs: Mortality rate ratio. Dalsgaard S, et al. 2015 Lancet;385: 2190–96
Is there consistent evidence of genetic, environmental or neurobiological risk factors associated with ADHD?

Causal pathways to ADHD

- Genes
- Brain Structure and Function
- Cognition
- Symptoms
Genetics of ADHD

Heritability of ADHD consistently around 75%

It seems very likely that much of the other 50 or so percent of the gene effects relate to interactions between genes and environmental factors

BUT

We don’t yet know what these might be
ADHD Meta-analysis:
17,516 cases 94,414 controls

Preliminary analyses suggest one genome-wide significant locus

Raymond Walters
Ditte Demontis
<table>
<thead>
<tr>
<th>Cohort</th>
<th>Cases</th>
<th>Controls</th>
<th>Design</th>
<th>PGC Batch</th>
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</thead>
<tbody>
<tr>
<td>CHOP</td>
<td>262</td>
<td>262</td>
<td>Trios</td>
<td>PGC ADHD1</td>
</tr>
<tr>
<td>IMAGE-I</td>
<td>700</td>
<td>700</td>
<td>Trios</td>
<td>PGC ADHD1</td>
</tr>
<tr>
<td>IMAGE-II</td>
<td>624</td>
<td>1755</td>
<td>Case/control</td>
<td>PGC ADHD1</td>
</tr>
<tr>
<td>PUWMa</td>
<td>635</td>
<td>635</td>
<td>Trios</td>
<td>PGC ADHD1</td>
</tr>
<tr>
<td>Toronto, Canada</td>
<td>109</td>
<td>109</td>
<td>Trios</td>
<td>PGC CDG</td>
</tr>
<tr>
<td>Barcelona, Spain</td>
<td>572</td>
<td>425</td>
<td>Case/control</td>
<td>PGC CDG</td>
</tr>
<tr>
<td>Cardiff, UK</td>
<td>721</td>
<td>5081</td>
<td>Case/control</td>
<td>PGC CDG</td>
</tr>
<tr>
<td>Germany</td>
<td>487</td>
<td>1290</td>
<td>Case/control</td>
<td>PGC CDG</td>
</tr>
<tr>
<td>Beijing, China</td>
<td>1012</td>
<td>925</td>
<td>Case/control</td>
<td>Solo (Yang et al. 2013)</td>
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<tr>
<td>Bergen, Norway</td>
<td>295</td>
<td>202</td>
<td>Case/control</td>
<td>New (Zayas et al. 2015)</td>
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<tr>
<td>Yale-Penn</td>
<td>182</td>
<td>1315</td>
<td>Case/control</td>
<td>New</td>
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<tr>
<td>Denmark iPSYCH</td>
<td>14584</td>
<td>22492</td>
<td>Case/control</td>
<td>New</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>20183</strong></td>
<td><strong>35191</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Is there consistent evidence of genetic, environmental or neurobiological risk factors associated with ADHD?

• **A: Sufficient Evidence of a Causal Relationship**
  • No risk factor met these criteria

• **B: Sufficient Evidence of a Temporal Association**
  • Premature birth

• **C: Limited or Suggestive Evidence**
  • Maternal smoking during pregnancy
  • Low birth weight
  • DNA variants in *DAT1, DRD4, DRD5, 5HT1B, 5HT transporter* and *SNAP25*

The grade B DNA altogether explain only 3.2% of the overall variance of ADHD and only 4.2% of the disorder’s heritability

(Coghill et al in preparation)
BUT!

• Other there are still other possible explanations for these associations that can not be excluded from these traditional designs (Thapar and Rutter 2009)

• Need to utilize designs that can
  • separate pre and post natal effects
  • use genetically sensitive designs to take into account the relationship between maternal and offspring genomes
## Systematic Review - Maternal smoking in pregnancy

<table>
<thead>
<tr>
<th>Biologically Plausible?</th>
<th>Studies included</th>
<th>Odds Ratio</th>
<th>Consistent findings?</th>
<th>Evidence Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2 systematic reviews that included a total of 9 studies</td>
<td><strong>2.4 - meta analytic</strong>&lt;br&gt;Range 1.5 - 4.0</td>
<td>Not Consistent</td>
<td>Initially C (Limited evidence of temporal association) Downgraded to D (Inadequate or insufficient evidence) following further studies</td>
</tr>
<tr>
<td></td>
<td>24 additional studies (total n=1,059,416)</td>
<td></td>
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</tbody>
</table>

- A meta analysis of five case control studies and half of the 24 subsequent cohort and case control studies showed a significant association between maternal prenatal smoking and risk of ADHD.
- A few studies suggested a possible dose response relationship.

Very few studies reported that smoking data was collected prospectively systematically. This may lead to inaccuracies and recall bias in many studies.
Obel et al 2011 - Genetically sensitive assessment of the impact of smoking during pregnancy on HKD

• A cohort study that included all singletons born in Finland 15 year period between 1989 and 2001
• Participants were followed up until 1 January 2006 based on linkage of national registers.
• Data were available for 97% (N = 868 449) of the population.
• Compared children of smoking and non-smoking mothers and identified whether or not they received an ICD-10 diagnosis of hyperkinetic disorder
• Used sibling-matched Cox regression analyses to control for social and genetic confounding. This involved identifying sibling pairs that were discordant for smoking and therefore allows for the dissociation of genetic and environmental effects.

Obel et al 2011
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Obel et al 2011
## Hazard Ratios for HKD according to smoking during pregnancy

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>n(%)</th>
<th>HRcrude</th>
<th>HRadjusted</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Non-smokers</td>
<td>733 174</td>
<td>4971 (0.7)</td>
<td>Ref.</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>135 275</td>
<td>2052 (1.5)</td>
<td>2.22</td>
<td>2.01</td>
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</tr>
<tr>
<td><strong>Boys</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
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<td>374 074</td>
<td>4286 (1.1)</td>
<td>Ref.</td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>69 002</td>
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<td>2.17</td>
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<td>1.85–2.08</td>
</tr>
<tr>
<td><strong>Girls</strong></td>
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<td></td>
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<tr>
<td>Non-smokers</td>
<td>359 100</td>
<td>685 (0.2)</td>
<td>Ref.</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>66 273</td>
<td>325 (0.5)</td>
<td>2.55</td>
<td>2.28</td>
<td>1.99–2.63</td>
</tr>
</tbody>
</table>

Obel et al 2011
Hazard Ratios for HKD according to smoking during pregnancy adjusted for sibling relationships in sibling pairs discordant for prenatal exposure to smoking

<table>
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<tr>
<th></th>
<th>N</th>
<th>n(%)</th>
<th>HRcrude</th>
<th>HRadjusted</th>
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<td>0.97–1.49</td>
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<td><strong>Boys</strong></td>
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<td>1.85–2.08</td>
<td>1.19</td>
<td>1.21</td>
<td>0.93–1.59</td>
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<td><strong>Girls</strong></td>
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<td>1.51</td>
<td>0.71–3.19</td>
</tr>
</tbody>
</table>

Obel et al 2011
Red indicates more gray matter, blue less gray matter. Gray matter wanes in a back to front wave as the brain matures and neural connections are pruned. Areas performing more basic functions mature earlier; areas for higher-order functions (emotion, self-control) mature later. The pre-frontal cortex, which handles reasoning and other "executive" functions, emerged late in evolution, and is among the last to mature.
Red indicates more gray matter, blue less gray matter. Gray matter wanes in a back to front wave as the brain matures and neural connections are pruned. Areas performing more basic functions mature earlier; areas for higher-order functions (emotion, self-control) mature later. The pre-frontal cortex, which handles reasoning and other "executive" functions, emerged late in evolution, and is among the last to mature.
Brain development is delayed in ADHD

Maturation of the brain, as reflected in the age at which a cortex area attains peak thickness, in ADHD (above) and normal development (below). Lighter areas are thinner, darker areas...

Shaw et al PNAS (2007)
Is there consistent evidence of genetic, environmental or neurobiological risk factors associated with ADHD?

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).

Shaw P et al. PNAS 2007;104:19649-19654

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Effects of stimulant medication on brain activity in ADHD

- Meta-analysis results in three-dimension showing brain regions of increased (red/orange) and decreased (blue) activation after a single dose of stimulant medication in children and adolescents with ADHD compared with placebo or off-medication.

- Increased activation is shown in right inferior prefrontal cortex extending deep into the insula and bordering superior temporal lobe.

- Decreased activation in anterior cingulate cortex and supplementary motor area.

Rubia et al (2014) Biological Psychiatry
Effects of age and stimulants

Meta-analysis, Nakao et al., 2011
Brain-based diagnostics?

Patients with ADHD had significantly reduced grey matter in the putamen (P) and cerebellum (C) and significantly reduced white matter in the brainstem (B) and cerebellum (C).

Using Feature Selection with a Gaussian SVM resulted in individual scan predictive accuracies of 91% using grey matter alone and 97% using grey and white matter data (p<0.001).

Johnston et al., 2014
Neuropsychology of ADHD

- Understanding Heterogeneity
- Impact of medication
  - Acute
  - Chronic
- Impact of development
- Inter relationships between cognition, symptoms and impairment
“Single cause” model of ADHD

Genetic factors

Dopaminergic and Noradrenergic abnormalities in Fronto / striatal pathways

1° Behavioural Inhibition deficits

2° Broader Executive Dysfunctions e.g. Working memory, planning

ADHD Symptoms

Biological

Cognitive

Behaviour

Genes and Environment

Brain Structure and Function

Cognition

Symptoms

Impairment

Recognition and Referral

Assessment and Diagnosis

Initiation of treatment

Monitoring treatment
Genetic factors

Dopaminergic and Noradrenergic abnormalities in Fronto / striatal pathways

Behavioural Inhibition deficits

ADHD Symptoms and Impairments

Environmental factors

Temporal lobe, amygdalo / hippocampal circuits

Acetylcholine

Working Memory Deficits

Non-Working Memory Deficits
Organization of Memory

Central Executive

Visuospatial Sketchpad

Episodic Buffer

Phonological Loop

Visual Semantics ↔ Episodic LTM ↔ Language
ADHD is associated with significant deficits in both executive and non-executive aspects of working memory

Rhodes, Coghill and Matthews 2004, 2005

Short-term memory in children with untreated ADHD resembles that of elderly with Alzheimer's

Rhodes, Coghill and Matthews 2004, 2005
Causal heterogeneity in ADHD

Multiple Environmental Factors ↔ Multiple Genetic Factors

Mesolimbic reward circuits

Fronto Cerebellar circuits

Dopaminergic and Noradrenergic abnormalities in Fronto / striatal pathways

Temporal lobe, amygdalo / hippocampal circuits

Delay aversion

Timing deficits

Behavioural Inhibition deficits

Working Memory Deficits

Non-Working Memory Deficits

ADHD Symptoms

Coghill, Seth and Matthews, 2014
A direct comparison of neuropsychological functioning across the six key domains in ADHD

<table>
<thead>
<tr>
<th>Factor</th>
<th>ADHD Mean (SD)</th>
<th>TYP Mean (SD)</th>
<th>p</th>
<th>Effect Size (δ)</th>
<th>% with deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>-0.43 (1.00)</td>
<td>0.54 (1.04)</td>
<td>&lt; .001</td>
<td>0.95</td>
<td>30.1</td>
</tr>
<tr>
<td>Inhibition</td>
<td>-0.12 (0.44)</td>
<td>0.15 (0.44)</td>
<td>&lt; .001</td>
<td>0.61</td>
<td>22.9</td>
</tr>
<tr>
<td>Delay Aversion</td>
<td>-0.37 (0.96)</td>
<td>0.47 (1.10)</td>
<td>&lt; .001</td>
<td>0.82</td>
<td>36.1</td>
</tr>
<tr>
<td>Decision Making</td>
<td>-0.20 (0.85)</td>
<td>0.25 (0.79)</td>
<td>&lt; .001</td>
<td>0.55</td>
<td>20.5</td>
</tr>
<tr>
<td>Timing</td>
<td>-0.36 (1.16)</td>
<td>0.43 (1.07)</td>
<td>&lt; .001</td>
<td>0.71</td>
<td>31.3</td>
</tr>
<tr>
<td>Variability</td>
<td>-0.10 (0.79)</td>
<td>0.13 (0.40)</td>
<td>.029</td>
<td>0.37</td>
<td>18.1</td>
</tr>
</tbody>
</table>

Coghill, Seth and Matthews, 2014
A direct comparison of neuropsychological functioning across the six key domains in ADHD

Coghill, Seth and Matthews, 2014
Clinical question

Despite generally good symptom outcomes why are many children and young people still struggling at home, school and in the community?
Systematic review and meta analysis of the effects of MPH on cognition

Effect Size Methylphenidate

- Symptoms
- RT Variability
- RT
- Non-Exec Memory
- Exec Memory
- Response Inhibition

Coghill et al 2013
Genes & Environment

Brain Structure and Function

Cognition

Symptoms

Methylphenidate

Coghill et al 2007 Biological Psychiatry

Coghill et al 2007 Biological Psychiatry
Supported by
• Our work
  • Neuropsychopharmacological studies
  • Developmental Studies
• Other findings
  • Dutch systematic review relationship between developmental trajectory of cognition and remission
  • Effects of cognitive training on cognition but not ADHD symptoms
  • Findings in other disorders e.g. schizophrenia, depression, Alzheimer's

Potential Impacts

- Can explain why cognitive training approaches (e.g. working memory training) does not impact on symptoms but may still improve functioning
- A need to measure both symptom and cognitive outcomes
- Presents and opportunity to provide more concrete evidence as to why the FDA and EMA should consider cognitive outcomes when licensing medications

WM TRAINING CAN IMPROVE WM IN THOSE WITH WM DEFICITS AND WITH ADHD

Figure 1 Impact of training on working memory.

Holmes et al., 2009

Holmes et al., 2010
Impact of working memory training on memory – for ADHD small but significant

Effect Sizes pre vs post: all reported as significant (but no control)

Holmes et al, 2009, 2010
Effects of Cognitive Training on ADHD Symptoms

SMD 0.24 NS

Overall SMD=0.24, 95% CI=−0.24, 0.72
Test for overall effect: Z=0.96, p=0.34
Heterogeneity: $\chi^2=13.78$, df=4, p=0.008, $I^2=71%$

Sonuga-Barke et al 2013
Genes

Brain Structure and Function

Symptoms

Impairment

Cognition