Determining Medication Treatment Response in ADHD: Does Neuropsychological Impairment Matter?

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What is ADHD?
"Cool" and "Hot" Brain Boss Circuits in Learning, Emotions, and Behaviour

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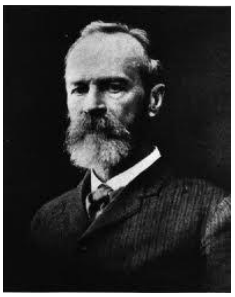
What is Attention?

"Everyone knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed, scatterbrained state."



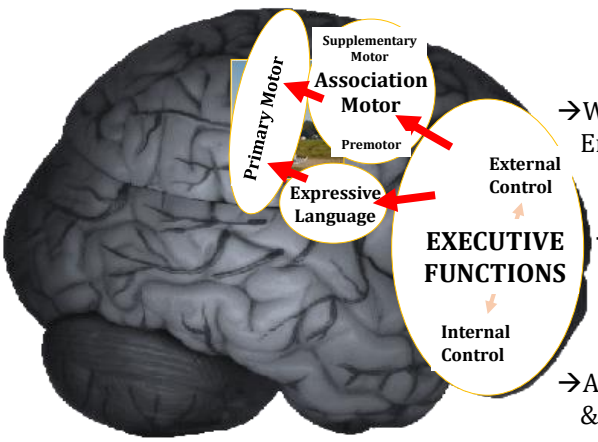
William James
Principles of Psychology (1890)

→Is this primary attention or executive function?

→How do we separate cortical tone, primary attention, and executive attention?

Executive Function

Programming, Regulating, and Verifying Mental Activity



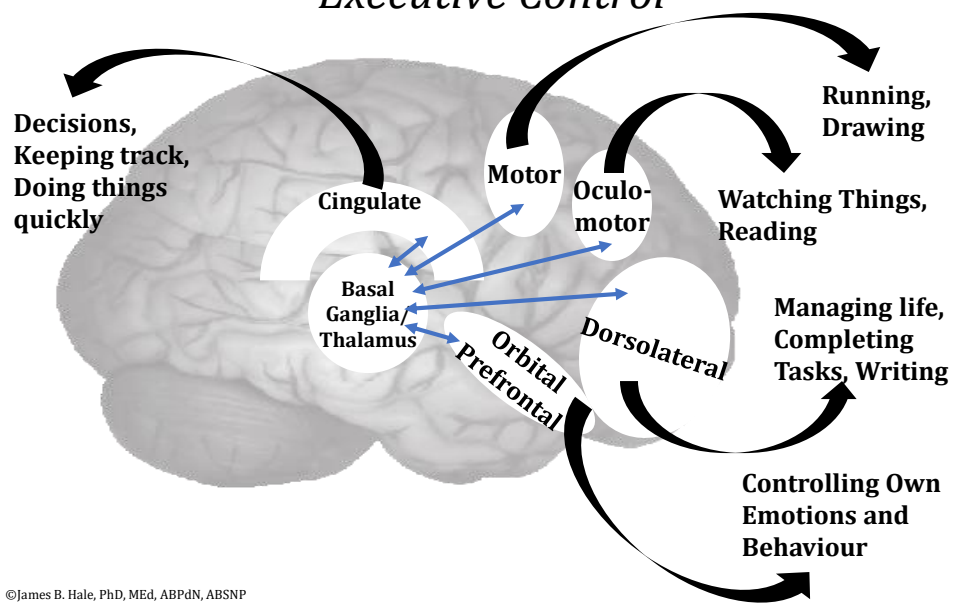
→Working Memory, Memory Encoding & Retrieval (HERA)

→Plan, Organize, Strategize, Monitor, Evaluate, Modify, & Change Behavior

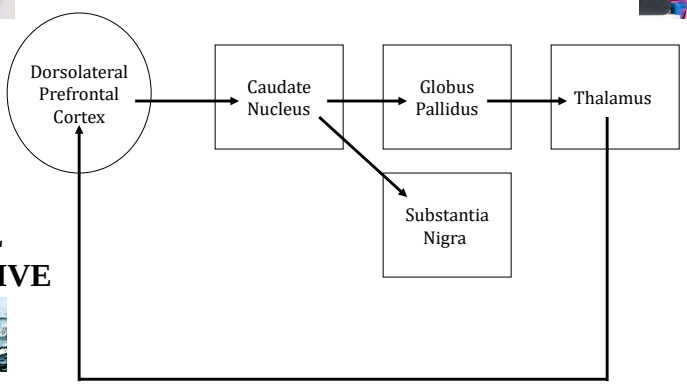
→Attention, Concentration, & Impulse Control

The Brain Manager

Frontal-Subcortical Circuits: Executive Control



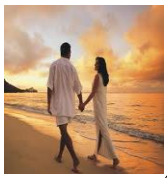
Dorsolateral Circuit: "Cool" Executive Functions



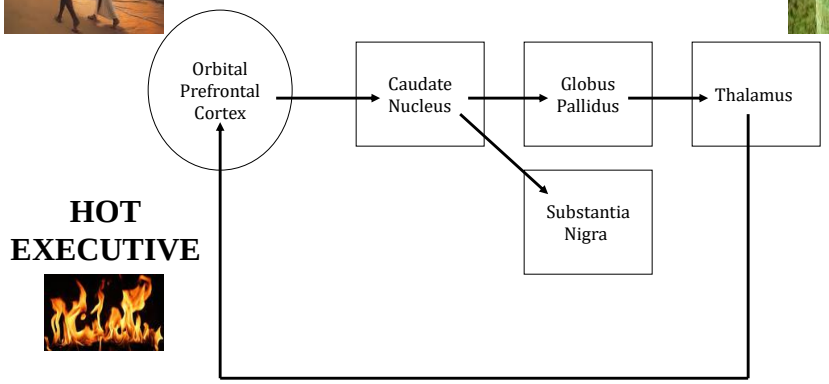
COOL EXECUTIVE

→Planning, organizing, monitoring, evaluating, shifting, and modifying behaviour, including COGNITIVE response inhibition

→Working memory, memory encoding, and retrieval



Orbital Circuit
"Hot" Executive Functions



→Behaviour regulation – EMOTIONAL response inhibition

→Reward processing and theory of the mind-empathy (perception of emotional state more posterior)

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"Cool" and "Hot" Circuits and Psychopathology: The Search for Balance

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Frontal-Subcortical Circuits and Psychopathology: Are the Scales Tipped?

CHAPTER 11

Assessment and Intervention Practices for Children with ADHD and Other Frontal-Striatal Circuit Disorders

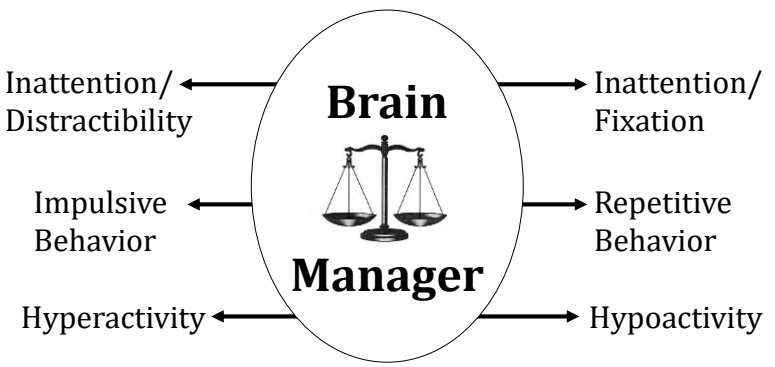
JAMES B. HALE, LINDA A. REDDY, GABRIELLE WILCOX, AMY MCLAUGHLIN, LISA HAIN, AMY STERN, JULIE HENZEL, and ELEAZAR EUSEBIO

MOST CHILDREN REFERRED for a school neuropsychological evaluation present with an attention problem, and when behavioral criteria are gathered by informant report, many will meet criteria for Attention Deficit Hyperactivity Disorder (ADHD). No longer considered *just* a "disruptive behavior disorder," ADHD is now widely understood to be a frontal-subcortical circuit disorder (Castellanos et al., 2002), with affected brain regions potentially contributing to both cognitive and behavioral symptom expression (Voeller, 2001). Although this clarifies the nature and manifestation of ADHD, most frontal-subcortical circuit disorders lead to impaired attention (see Lichter & Cummings, 2001), suggesting differential diagnosis of ADHD can be difficult using only behavioral criteria (Hale, Fiorello, & Brown, 2005). In fact, the conflicting evidence regarding frontal-subcortical-executive causes of ADHD may be due to considerable population heterogeneity found when behavioral diagnostic criteria are used (Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008).

All Emotional and Behavioural Disorders Have Attention Problems!

Circuit Balance Theory

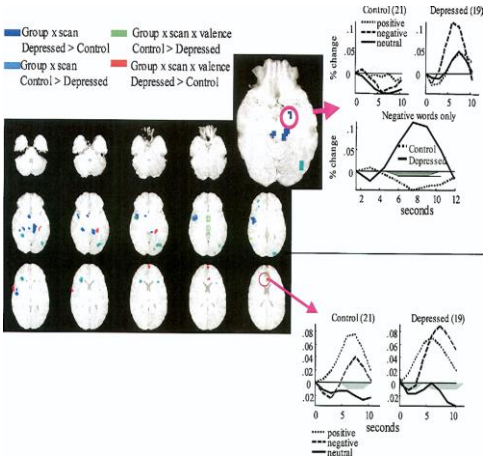
(Hale et al., 2009)



Regulation problem of cortical-subcortical circuits

Balance Theory and Comorbidity

- Does one circuit problem lead to compensatory balance?
- Example: Anxiety comorbid with depression
- Decreased dorsolateral and increased amygdala in depression (Siegle et al., 2007)
- Increased orbital frontal, amygdala, and anterior cingulate in GAD (McClure et al., 2007)



→Optimal Executive Function Requires Frontal-Subcortical Circuit Balance!

Emotional Executive Function and Self-Control

APPLIED NEUROPSYCHOLOGY: CHILD, 0: 1–10, 2015

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Routledge
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Evaluating Orbital-Ventral Medial System Regulation of Personal Attention: A Critical Need for Neuropsychological Assessment and Intervention

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Attention to self and environment form the basis of effective social exchange and relationships. Although implicit in this basic social competency is the ability to be self-aware and responsive to circumstances of others, many neuropsychologists have yet to understand or measure its basic functions, let alone recognize the brain–behavior relationships that govern this area. Several years ago, interest in "emotional intelligence" rose to the forefront of popular psychology, but we are still unraveling the cortical, subcortical, and neurocellular interactions that produce this nebulous construct, and we are determining how dysfunctional frontal-subcortical and cortico-cerebellar circuitry can lead to aberrant social dynamics and ultimately psychopathology when maladaptive patterns become routinized. In this article, we explore the orbital-ventral medial circuitry thought to govern emotional attention, personal self-regulation, social concern and exchange, and affective aspects of interpersonal relationships. Our examination notes both the dearth of and need for neuropsychological research on the biological basis and measurement of executive regulation of emotional attention, behavioral regulation, and social competence. We conclude with a call for development of neuropsychological measures and methods that can foster differential diagnosis and targeted treatment strategies for children with orbital-ventral medial circuit dysfunction.

Key words: *emotional, orbital, self-regulation, social competence, ventral-medial*

Orbital Prefrontal Circuit and Theory of Mind

Hale & Fitzer, 2015; *Applied Neuropsychology: Child*

- Theory of Mind – Taking the perspective of others (e.g., empathy)
- Is empathy about perception or action?
- Posterior brain areas linked to affect perception
  →Parietal lobe and "mirror" neurons
  →Temporal lobe and face recognition
- But theory of mind linked to frontal systems
  →Pars opercularis and imitation
  →Medial orbital cortex and theory of mind
- Balancing orbital critical, too little or too much is a problem!
- Balancing perception and action in social relationships

Frontal-Subcortical Circuits and Psychosocial Functioning: An ALE Meta-analysis

(Lee et al., 2017)

Behavioural Brain Research 325 (2017) 117–130

Contents lists available at ScienceDirect

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Research report

Frontal-subcortical circuitry in social attachment and relationships: A cross-sectional fMRI ALE meta-analysis

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HIGHLIGHTS

- We examined EF neurocircuitry associated with effective social bonds.
- ALE meta-analysis of PET and fMRI studies conducted on "cool" and "hot" EF tasks.
- Dissociation of networks between "cool" and "hot" EF tasks were observed.
- Differences within "hot" EF circuit between reward and empathy were shown.
- Implications for a social executive control circuit related to attachment discussed.

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ABSTRACT

Researchers have explored the concept of attachment in multiple ways, from animal studies examining imprinting to abnormal attachment in psychopathology. However, until recently, few have considered how neural circuitry develops the effective social bonds that are subsequently replicated in relationships across the lifespan. This current cross-sectional study undertook a fMRI Activation Likelihood Estimation (ALE) meta-analyses to examine the neurocircuitry that governs emotional and behavioural functions critical for building effective social relationships in children and adults. Results suggest that dissociable dorsal cognitive ("cool") and ventral – affective ("hot") frontal-subcortical circuits (FSC) work together to govern social relationships, with repeated social consequences leading to potentially adaptive – or maladaptive – relationships that can become routinized in the cerebellum. Implications for forming stable, functional, social bonds are considered, followed by recommendations for those who struggle with cool and hot FSC functioning that can hinder the development of adaptive prosocial relationships.

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"Cool" and "Hot" Frontal-Subcortical Circuits and Stimulant Response in ADHD

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American Academy of Pediatrics Standard of Care ADHD Medical Practice

1) Primary care physician evaluates **any** child with academic or behavioural problems and ADHD symptoms
2) ADHD diagnosis: ***DSM-V*** criteria, 2 settings, and multisource information
3) Coexisting conditions **assessment**
4) Treatment includes medications **and/or** evidence-based behavior therapy, both best
5) Titrate **maximum medication dose** with **minimum adverse effects**

Childhood's Greatest "Behaviour Problem": Persistent Academic Achievement Deficits

- ADHD is a neurodevelopmental disorder, but defined by behaviour?
- Are *academic deficits* the common problem in all types of attention problems?

WHAT CAUSES ADHD ACADEMIC DEFICITS?

OR

Poor Availability For Learning?

Executive Deficits Impair Learning?

Methylphenidate (MPH) Treatment and ADHD

- MPH effective in 60 to 90% of children with ADHD
- Increaeses excitatory neurotransmitter dopamine (block DA reuptake to reduce frontal-striatal hypoactivity)
- Improves classroom behaviour and peer interactions, but not academic achievement over time
- Few serious side effects, but can cause "zombie effect"

→Best dose for <u>cognition</u> appears to be **lower** than best dose for <u>behavior</u> in good responders

(see Arnsten & Pliszka, 2011; Berridge et al., 2006; Hale et al., 2011; Kubas et al., 2012)

Modeling the Frontal-Subcortical Circuits

Determining medication treatment effects using teacher ratings and classroom observations of children with ADHD: Does neuropsychological impairment matter?

James B. Hale, Catherine A. Fiorello & Lucy L. Brown

Abstract

Children with attention deficit hyperactivity disorder (ADHD) often experience significant academic and behavioural problems in the classroom and other settings, but clinicians often rely on qualitative judgements and informant reports to formulate diagnostic impressions and make treatment recommendations rather than on direct measurement of child performance or behaviour. Although there is mounting evidence for a neuropsychological model of ADHD, the disorder remains largely a behavioural one, which could limit diagnostic accuracy and intervention efficacy, especially for academic problems in the classroom. In this study of 49 children diagnosed with ADHD, robust medication treatment effects were observed, with increasing dose resulting in better teacher ratings and direct observations of classroom academic performance and behaviour. However, when participants were classified according to level of neuropsychological impairment, only those children who showed significant deficits in executive function and self-regulation responded to medication, according to teacher report. Children who showed minimal or no response were more likely to be classified with the inattentive type of ADHD, but those who showed dramatic medication effects were more likely to be diagnosed with the combined type ADHD. Results suggest that neuropsychological impairment, but not baseline teacher ratings or classroom observations, can help clinicians determine the likelihood of medication response in children with ADHD. Implications for classroom academic performance and behaviour are addressed.

CHILDREN WITH attention deficit hyperactivity disorder (ADHD) display developmentally inappropriate levels of attention, impulse control and motor activity that lead to both indirect and direct school-based difficulties (Landau & Burcham, 1995). Diagnostic definitions differ for the disorder, with ICD-10 and DSM-IV criteria the most commonly used (McKenzie & Wurr, 2004), and symptoms vary in severity and pervasiveness across environments (Shelton & Barkley, 1995), but academic achievement difficulties (Hinshaw, 1992) and the subsequent need for special education services (Reid *et al.*, 1994) are common outcomes. It remains unclear whether academic difficulties are due to neuropsychological deficits (Hale & Fiorello, 2004; Hale *et al.*, 1998) and/or limited availability for learning (Silver, 1990). Although academic failure may be the final common pathway for many children with ADHD (Shaywitz & Shaywitz, 1988), psychostimulant medication has not been effective in improving academic outcomes for children with ADHD, despite demonstrating consistent behavioural treatment efficacy (MTA, 1999; Purdie *et al.*, 2002; Schachter *et al.*, 2001). Although stimulant medication is prescribed for a relatively high proportion of children with ADHD in the United States, its use in the United Kingdom is not as prevalent (Kewley, 1998), with both countries experiencing controversy about whether ADHD is under-, over- or mis-

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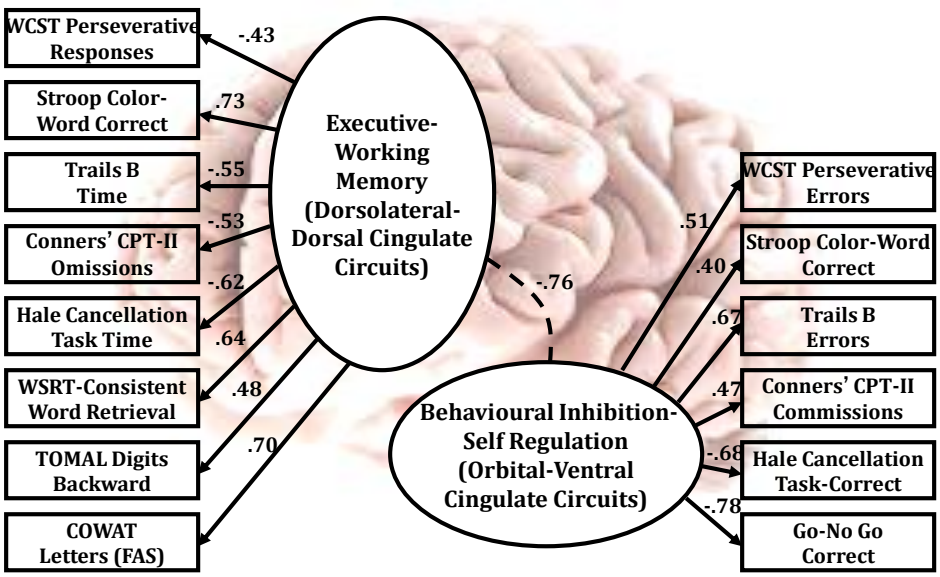
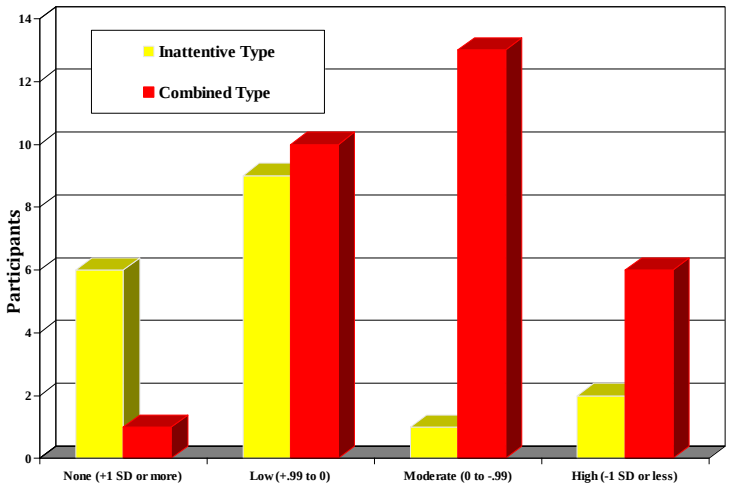
Relevance of ADHD Executive Deficits and Medication Response: Cortical-Subcortical Circuit Confirmatory Factor Analysis



Sources: Hale et al., (2011) *Journal of Learning Disabilities.* Kubas et al. (2012) *Postgraduate Medicine*

Frontal-Subcortical Impairment and Diagnosis



Is DSM All You Need?

APPLIED NEUROPSYCHOLOGY: CHILD, 0: 1–9, 2015

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Reconsidering "Inattention" in Attention-Deficit Hyperactivity Disorder: Implications for Neuropsychological Assessment and Intervention

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Attention-deficit hyperactivity disorder (ADHD) does not exist. This explicit statement needs elucidation of course given ADHD is a common neurodevelopmental disorder, but it provides the reader with the impetus to reconsider long-held beliefs about this condition and its treatment. Surely, there is a disorder called ADHD from which this thesis is framed, but primary attention and hyperactivity-impulsivity problems are mediated by different albeit interrelated brain systems. Like many neurodevelopmental disorders (e.g., learning disabilities, autism spectrum disorder), the medical and psychological professions have used a single, large inclusive ADHD diagnostic category to represent children with different etiologies for their overt symptoms. Despite neurobiological differences among children diagnosed with ADHD, the clinical position that attention-deficit or primary attention problems are sufficient for ADHD identification undermines clinical practice. This commonly accepted dubious position not only

Neuropsychological Tests and DSM-V Criteria Correlations

Carmichael et al., 2015; *Applied Neuropsychology: Child*

	DSM-V Criteria		
Baseline Executive Measures	Inattention $r\ (r^2)$	Hyper-Impulsive $r\ (r^2)$	Total Symptoms $r\ (r^2)$
HDCT Correct	-.15 (.021)	-.08 (.006)	-.15 (.023)
SRTM Consistent Retrieve	.03 (.001)	**-.32 (.104)**	**-.27(.072)**
Go-No Go	-.08 (.006)	**-.22 (.048)**	**-.24 (.058)**
CPT Omissions	.17 (.030)	.13 (.016)	**.21 (.044)**
CPT Commissions	.13 (.018)	-.06 (.004)	.02 (.000)
CPT Block Change	.19 (.035)	**.20 (.038)**	**.28 (.078)**
Stroop Raw	-.17 (.030)	**-.31 (.096)**	**-.37 (.138)**
Stroop Errors	.01 (.000)	.15 (.022)	.13 (.018)
TMTB Time	**.33 (.106)**	.19 (.036)	**.35 (.125)**
TMTB Errors	**.41 (.170)**	**.31 (.096)**	**.51 (.258)**
Back Digits	.18 (.031)	**-.28 (.076)**	-.15 (.021)

→Low correlations between DSM-IV and neuropsychological measures, BUT

Neuropsychological Data, DSM-V Criteria, and MPH Response

(Carmichael et al., in press; *Applied Neuropsychology: Child*)

Measure	Cognitive Medication Response $r\ (r^2)$	Behavioural Medication Response $r\ (r^2)$
DSM-IV Inattention Ratings (Parent Report)	.09 (.008)	.03 (.000)
DSM-IV Hyperactivity-Impulsivity Ratings (Parent Report	**.30* (.090)**	.25 (.063)
Dorsolateral-Dorsal Cingulate "Cool" Circuit Functions Factor	**.44** (.194)**	**.33* (.109)**
Orbital-Ventral Cingulate "Hot" Circuit Functions Factor	**.45** (.203)**	**.31* (.097)**

Differential ADHD Dose-Response Relationships

HAMMILL INSTITUTE ON DISABILITIES

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.sagepub.com
SAGE

Executive Impairment Determines ADHD Medication Response: Implications for Academic Achievement

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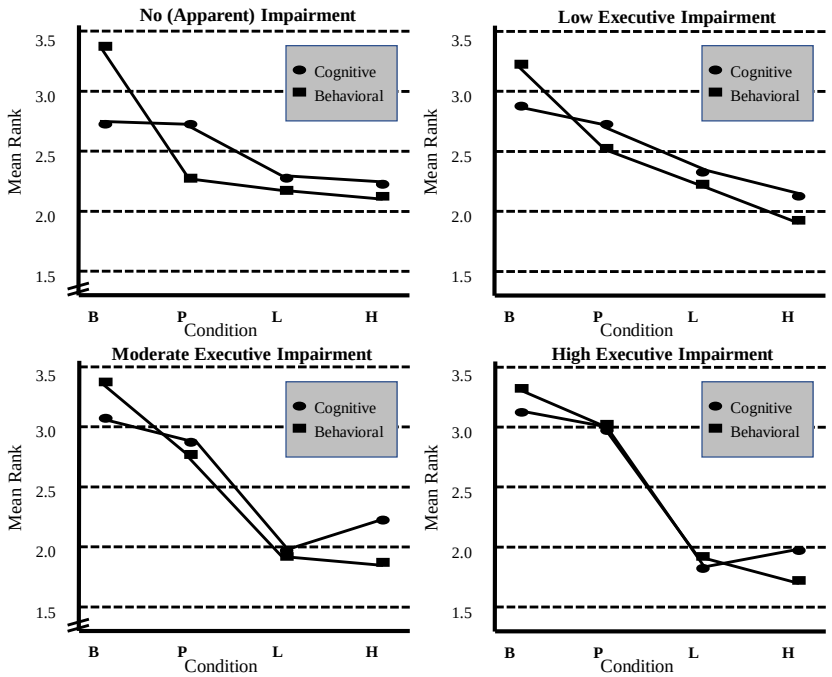
Abstract

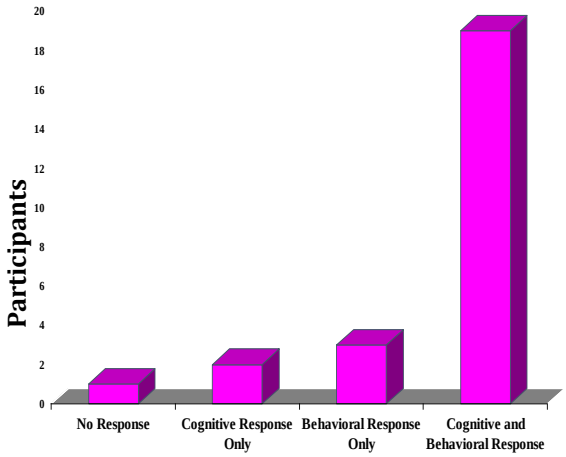
Methylphenidate (MPH) often ameliorates attention-deficit/hyperactivity disorder (ADHD) behavioral dysfunction according to *indirect* informant reports and rating scales. The standard of care behavioral MPH titration approach seldom includes *direct* neuropsychological or academic assessment data to determine treatment efficacy. Documenting "cool" executive-working memory (EWM) and "hot" self-regulation (SR) neuropsychological impairments could aid in differential diagnosis of ADHD subtypes and determining cognitive and academic MPH response. In this study, children aged 6 to 16 with ADHD inattentive type (IT; $n = 19$) and combined type ($n = 33$)/hyperactive-impulsive type ($n = 4$) (CT) participated in double-blind placebo-controlled MPH trials with baseline and randomized placebo, low MPH dose, and high MPH dose conditions. EWM/SR measures and behavior ratings/classroom observations were rank ordered separately across conditions, with nonparametric randomization tests conducted to determine individual MPH response. Participants were subsequently grouped according to their level of cool EWM and hot SR circuit dysfunction. Robust cognitive and behavioral MPH response was achieved for children with significant baseline EWM/SR impairment, yet response was poor for those with adequate EWM/SR baseline performance. Even for strong MPH responders, the best dose for neuropsychological functioning was typically lower than the best dose for behavior. Findings offer one possible explanation for why long-term academic MPH treatment gains in ADHD have not been realized. Implications for academic achievement and medication titration practices for children with behaviorally diagnosed ADHD will be discussed.

Keywords



B = Baseline; P = Placebo; L = Low Dose MPH; H = High Dose MPH. Lower ranks = better performance and behavior (see Hale et al., 2011).

Moderate and Severe Frontal-Subcortical Impairment And Statistical Medication Response



Medication Response

What Neuropsychological Functions Are Most Impaired on High Dose Stimulants? Working Memory

CLINICAL FOCUS: ADHD, DEPRESSION, PAIN, AND NEUROLOGICAL DISORDERS

The Effects of Methylphenidate on Cognitive Function in Children with Attention-Deficit/ Hyperactivity Disorder

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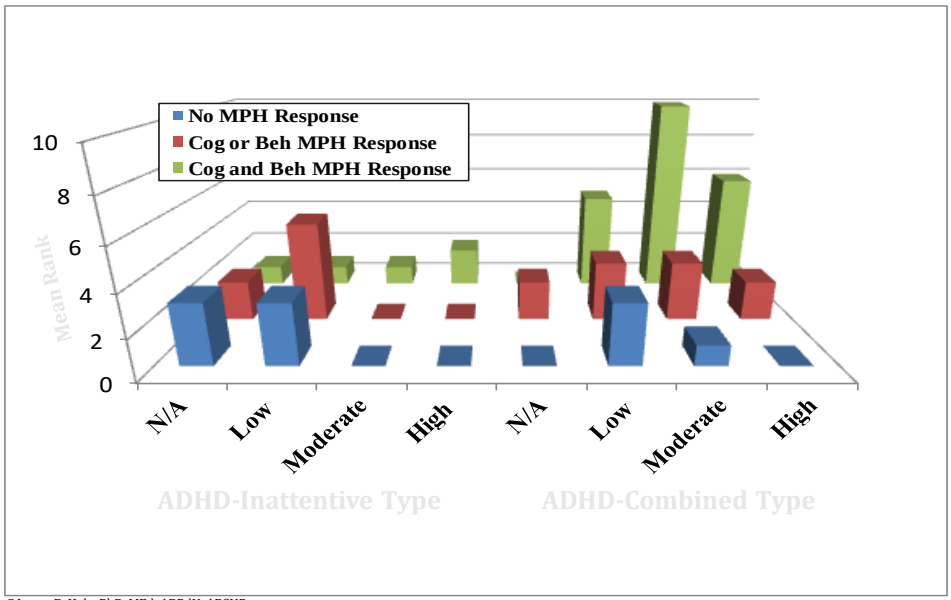
DOI: 10.3810/pgm.2012.09.2592

Abstract: Focusing on behavioral criteria for attention-deficit/hyperactivity disorder (ADHD) diagnosis leads to considerable neuropsychological profile heterogeneity among diagnosed children, as well as variable response to methylphenidate (MPH) treatment. Documenting "cold" executive working memory (EWM) or "hot" self-regulation (SR) neuropsychological impairments could aid in the differential diagnosis of ADHD subtypes and may help to determine the optimal MPH treatment dose. In this study, children with ADHD inattentive type (n = 19), combined type (n = 33), and hyperactive-impulse type (n = 4) underwent randomized controlled MPH trials; neuropsychological, behavioral, and observational data were collected to evaluate the children's responses. Those with moderate or significant baseline EWM/SR impairment showed robust MPH response, whereas response for those with lower baseline impairment was equivocal. Implications for medication use and titration, academic achievement, and long-term treatment efficacy are examined.

Keywords: attention-deficit/hyperactivity disorder; methylphenidate; frontal-subcortical circuits; executive function; achievement

Neuropsychological Impairment, Behavioural Diagnosis, and ADHD Medication Response



What Can A Busy Clinican Do? Use DSM-V, Behavioural Ratings, and Screen for Executive Deficits

JOURNAL OF CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY
2009, 31 (8), 897–912

Psychology Press
Taylor & Francis Group

Development and validation of an attention-deficit/ hyperactivity disorder (ADHD) executive function and behavior rating screening battery

James B. Hale,[1] Linda A. Reddy,[2] Scott L. Decker,[3] Rebecca Thompson,[4] Julie Henzel,[1] Annemarie Teodori,[1] Elizabeth Forrest,[1] Eleazar Eusebio,[1] and Martha Bridge Denckla[5]

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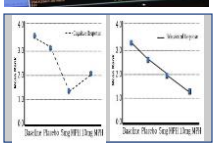
Attention problems are ubiquitous in clinical practice, commonly found in many childhood learning and behavior disorders. Practitioners need cost- and time-effective methods for determining whether children have attention problems due to attention-deficit/hyperactivity disorder (ADHD) or numerous other conditions. This study examined the utility of a 15-minute ADHD screening battery designed to differentiate ADHD (including inattentive, IT, and combined, CT, subtypes), specific learning disability (SLD), and typical child samples. Results for the 368 children (age 6 to 12 years) revealed that the Trail Making Test–Part B (Time/Errors), Hale–Denckla Cancellation Test (Time/Correct), and Child Attention Profile (Inattention/Overactivity) teacher ratings discriminated between typical and ADHD groups (87% correct classification; sensitivity = .64; specificity = .92) and differentiated between IT, CT, and SLD groups (80% correct classification; IT sensitivity = .82, and specificity = .96; CT sensitivity = .84, and specificity = .82). Discriminant function and Bonferroni post hoc results revealed different neuropsychological and behavioral patterns among groups.

Double-Blind Placebo Biphentin Protocol

- Children diagnosed by physician and psychologist, consent, and random assignment
- Standard of Care control group = baseline, best dose, 6 months; open trial
- Experimental group = baseline, randomized placebo, low dose, high dose, best dose, 6 months, blinded trial
- Neuropsychological tests, academic tests, and parent/teacher behaviour ratings
- Data rank ordered across conditions with nonparametric randomization to judge response y
- Graphic and statistical response reported to physician/parent for clinical decision-making



Drug Trial Example: Lisa

- 11 year, 7 month-old friendly and outgoing girl with love for adventure and being outdoors
- Academic and social concerns:
  - →Inattentive, easily distracted, fidgety
  - →Frequently off-task
  - →Poor writing skills
  - →Noncompliant behaviour
  - →Limited social skills
- Comprehensive evaluation revealed Lisa had ADHD
- Pediatrician then referred Lisa to our medication trial

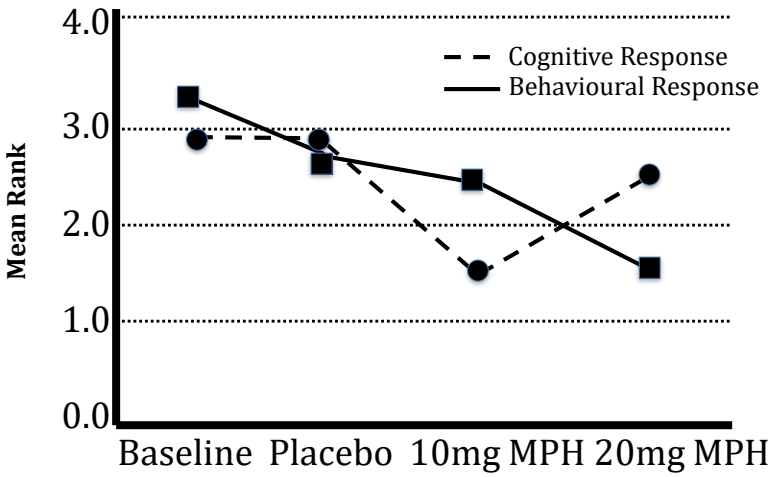
Lisa's Neuropsychological Response to Stimulant Medication

Subtest	Baseline No Medication	Week 2 Placebo	Week 1 10 mg	Week 3 20 mg
Auditory-Verbal Measures				
WSRT Long-term Storage	72 (3)	73 (1.5)	73 (1.5)	65 (4)
WSRT Consistent LT Retrieval	72 (2)	56 (3)	73 (1)	39 (4)
WSRT LTS-CLTR Ratio	100%(1.5)	77%(3)	100%(1.5)	60%(4)
Go-No Go Correct (30 Possible)	25 (4)	28 (2.5)	28 (2.5)	30 (1)
WISC-IV-I Digit Span Backward	20 (4)	33 (1)	28 (2)	26 (3)
D-KEFS Inhibition Time	85" (4)	66" (3)	63" (2)	52" (1)
D-KEFS Inhibition # of Errors (raw)	8 (4)	2 (3)	1 (1.5)	1 (1.5)
Visual-Motor Measures				
Hale-Denckla Cancellation (Correct)	26 (4)	30 (2)	30 (2)	30 (2)
Hale-Denckla Cancellation (Time)	**87" (2)**	**99" (3)**	**71"(1)**	**130" (4)**
WISC-IV-I Spatial Span Backward	43 (2)	23 (4)	28 (3)	44 (1)
Trail Making Test-Part B Errors	1 (3.5)	1 (3.5)	0 (1.5)	0 (1.5)
Trail Making Test-Part B Time	30" (3.5)	30" (3.5)	19" (1)	20" (2)
CPT-II Omissions	47 (2)	49 (4)	47 (2)	47(2)
CPT-II Commissions	50 (3)	49 (2)	47 (1)	56 (4)
CPT-II Reaction Time	57 (3)	58 (4)	56 (2)	55 (1)
CPT-II Reaction Time Standard Error	47 (1)	55 (4)	48 (2)	49 (3)
CPT-II Hit Reaction Time Block Change	54 (4)	45 (2.5)	42 (1)	45 (2.5)
CPT-II Hit Reaction Time ISI Change	48 (3)	55 (4)	43 (1)	45 (2)
AVERAGE COGNITIVE RANK	2.97	2.97		2.42

Lisa's Behavioural Response to Stimulant Medication

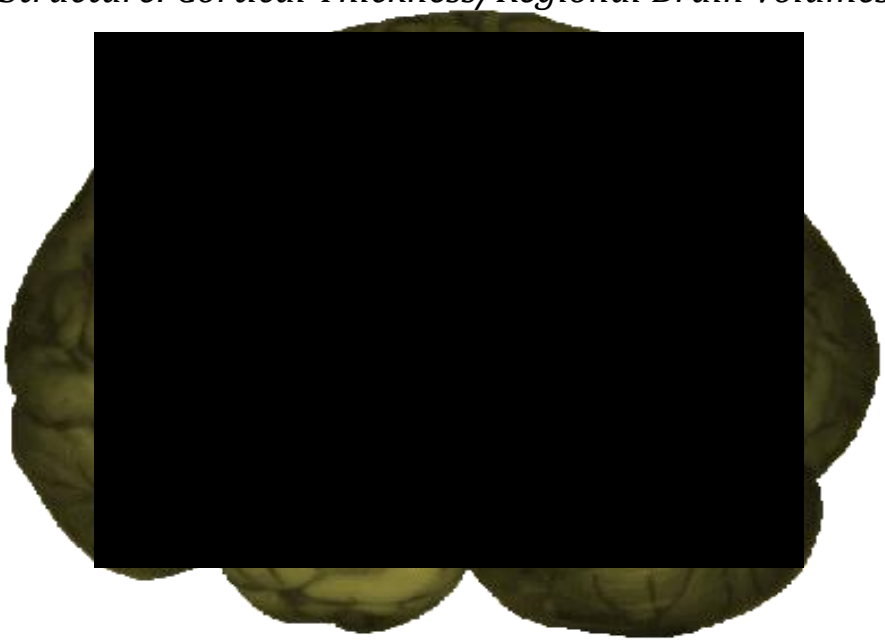
Parent Behavior Ratings				
Scale/Subscale	Baseline	Placebo	10 mg	20 mg
BRIEF				
Inhibit	86 (3)	84 (2)	89 (4)	68 (1)
Shift	77 (3)	81 (4)	66 (1.5)	66 (1.5)
Emotional Control	83 (3)	85 (4)	71 (2)	61 (1)
Initiate	73 (2.5)	73 (2.5)	76 (4)	66 (1)
Working Memory	74 (2)	82 (3.5)	82 (3.5)	65 (1)
Plan/Organize	84 (4)	66 (2)	80 (3)	62 (1)
Organization of Materials	70 (3.5)	70 (3.5)	67 (2)	55 (1)
Monitor	79 (4)	67 (2)	73 (3)	61 (1)
HSQR Number of Problems	9 (1.5)	13 (4)	9 (1.5)	11 (3)
Mean Severity	5.89 (3)	5.92 (4)	5.67 (2)	2.27(1)
Teacher Behaviour Ratings				
BRIEF				
Inhibit	53 (4)	49 (2.5)	49 (2.5)	45 (1)
Shift	49 (2.5)	49 (2.5)	49 (2.5)	49 (2.5)
Emotional Control	46 (2.5)	46 (2.5)	46 (2.5)	46 (2.5)
Initiate	65 (3.5)	58 (2)	65 (3.5)	54 (1)
Working Memory	68 (4)	61 (2)	65 (3)	54 (1)
Plan/Organize	70 (3.5)	58 (2)	70 (3.5)	49 (1)
Organization of Materials	69 (3)	69 (3)	57 (1)	69 (3)
Monitor	66 (3.5)	52 (2)	66 (3.5)	49 (1)
SSQR Number of Problems	3 (3.5)	2 (1.5)	3 (3.5)	2 (1.5)
Mean Severity	1.7 (3)	2.0 (4)	1.0 (1.5)	1.0 (1.5)
APRS Learning	14 (4)	17 (1)	16 (2.5)	16 (2.5)
Impulse Control	18 (3.5)	18 (3.5)	20 (1.5)	20 (1.5)
Academic Performance	21 (3.5)	21 (3.5)	24 (2)	25 (1)
Social Interest	16 (4)	18 (2)	18 (2)	18 (2)
Classroom Observation – Restricted Academic Task				
RAT Off-Task	43% (4)	33% (2)	30% (1)	37% (3)
Fidgeting	10% (1.5)	20% (3)	10% (1.5)	37% (4)
Vocalization	3% (2)	13% (4)	7% (3)	0% (1)
Plays with Objects	17% (2.5)	27% (4)	10% (1)	17% (2.5)
Out-of-Seat	33% (4)	10% (2)	13% (3)	7% (1)
AVERAGE BEHAVIOURAL RANK	3.18	2.78	2.44	1.60

Contrasting Lisa's Neuropsychological and Behavioural Response to Stimulant Medication

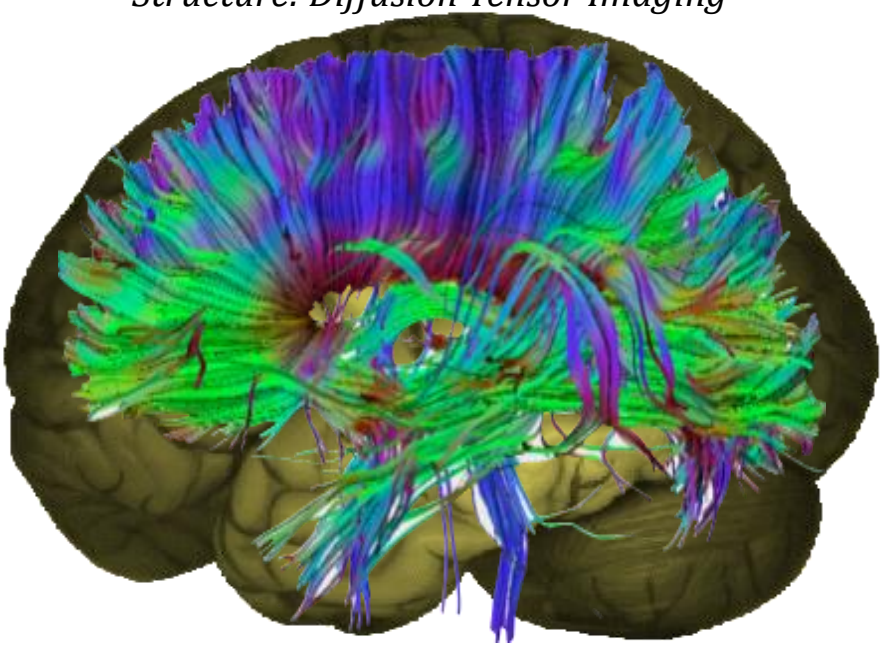


Note. Lower Ranks = Better performance and behaviour;
Order of conditions = Baseline, Low Dose, Placebo, High Dose

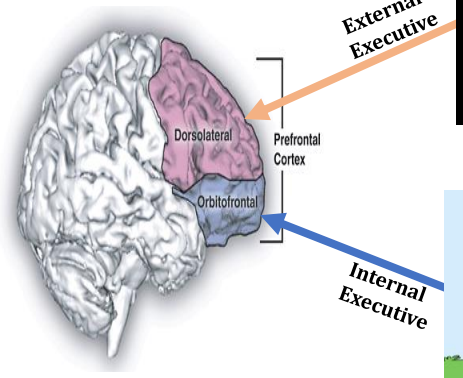
Structure: Cortical Thickness/Regional Brain Volumes



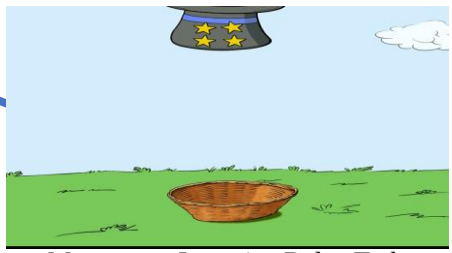
Structure: Diffusion Tensor Imaging



Is Cognitive or Behavioural MPH Response More Relevant for Academic Achievement? fMRI Tasks



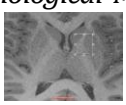
Multi-Source Interference Task
(Bush, Shin)

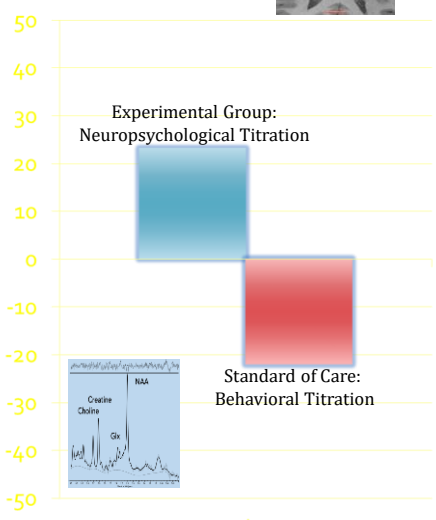


Momentary Incentive Delay Task
(Helfinstein, Kirwan, Benson, Hardin, Pine, Ernst, Fox)

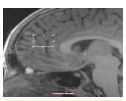
Is "Dopamine Insufficiency" Insufficient?
Neuropsychological Medication Response and Glutamate

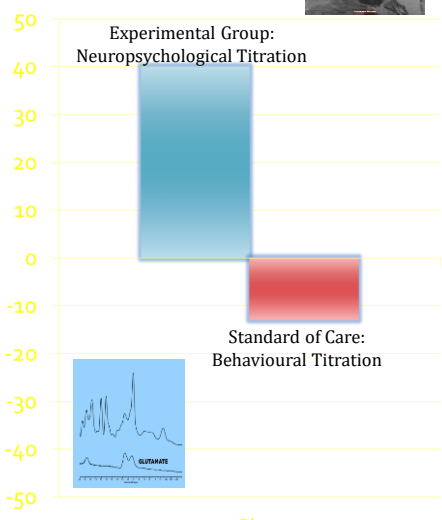
Left Striatum





Right Prefrontal





Discussion

- **Academic achievement deficits due to poor availability or executive deficits?**
- **Medication trials detect neuropsychological and behavioral response**
- **Children with executive impairment and ADHD-Combined Type show robust medication response**
- **Children with low impairment and ADHD-Inattentive Type less likely to respond**
- **Differential "brain boss" executive circuits could explain why best dose for cognition lower than best dose for behaviour**
- **Using combination of medicine and other inteventions could optimize both *academic* and *behavioural* outcomes**

NANYANG TECHNOLOGICAL UNIVERSITY

Teaching Brain Literacy Initiative

CRADLE
Centre for Research and Development in Learning

Questions? Comments?

Were YOU paying attention? ☺

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