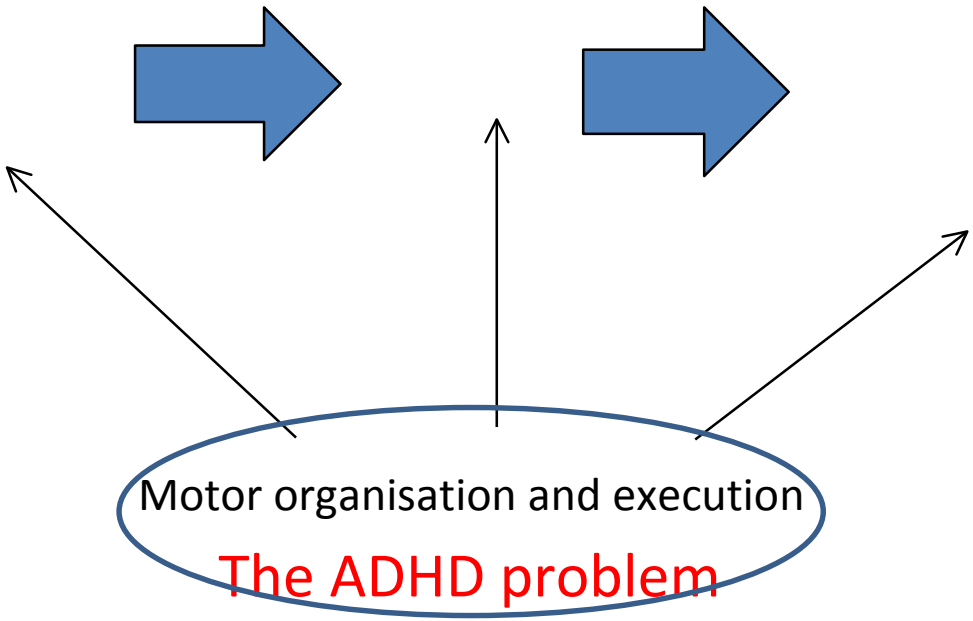
ADHD, STATE REGULATION, DEFAULT MODE NETWORK, AND NEGATIVE ACADEMIC EMOTIONS

Jaap J. van der Meere

The Sternberg reaction time model

- Encoding Memory Search Decision



The meaning of additive reaction-time effects: Frontiers in Psychology, 2013, 4, 744

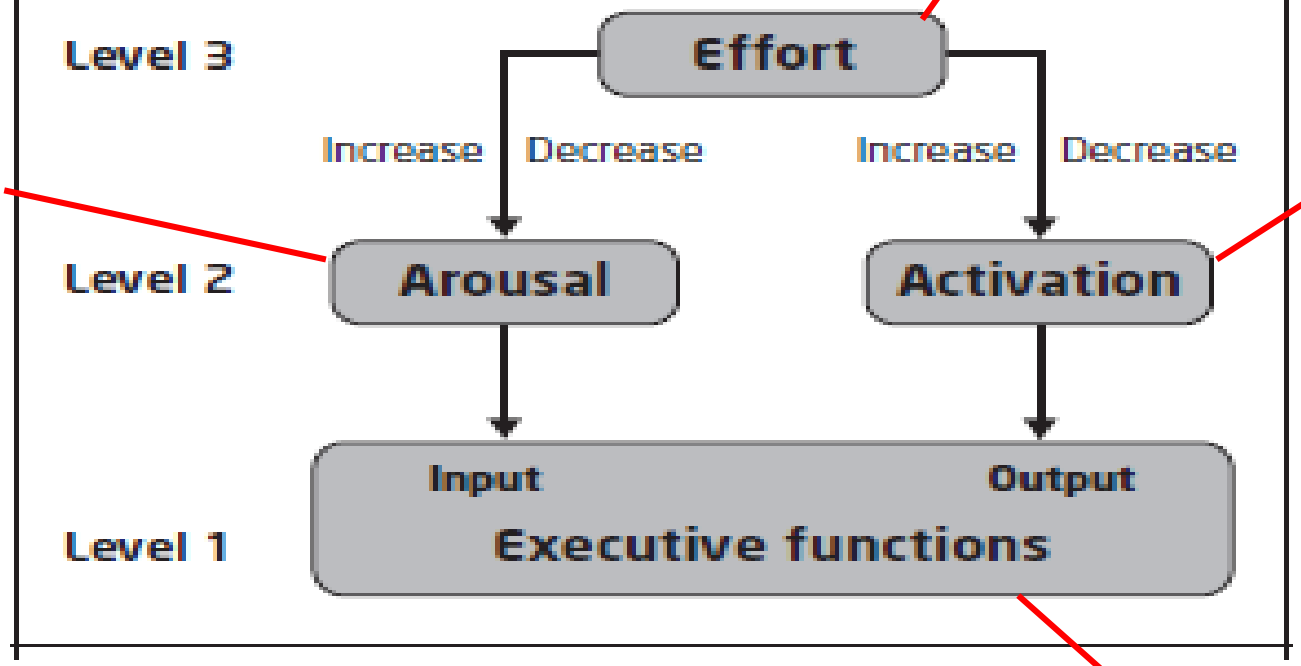
ADHD: State Regulation and Motivation

Jaap J van der Meere, Prof, PhD[1], Norbert A Börger, PhD[1], and Jan R Wiersema, PhD[2]
[1]Department of Clinical Neuropsychology, University of Groningen, The Netherlands, and
[2]Department of Experimental Clinical and Health Psychology, Ghent University, Belgium

CML – Psychiatry 2010;21(1):1–7.

Reward

Figure 1. The state regulation model.



Noise

Event rate

Task difficulty

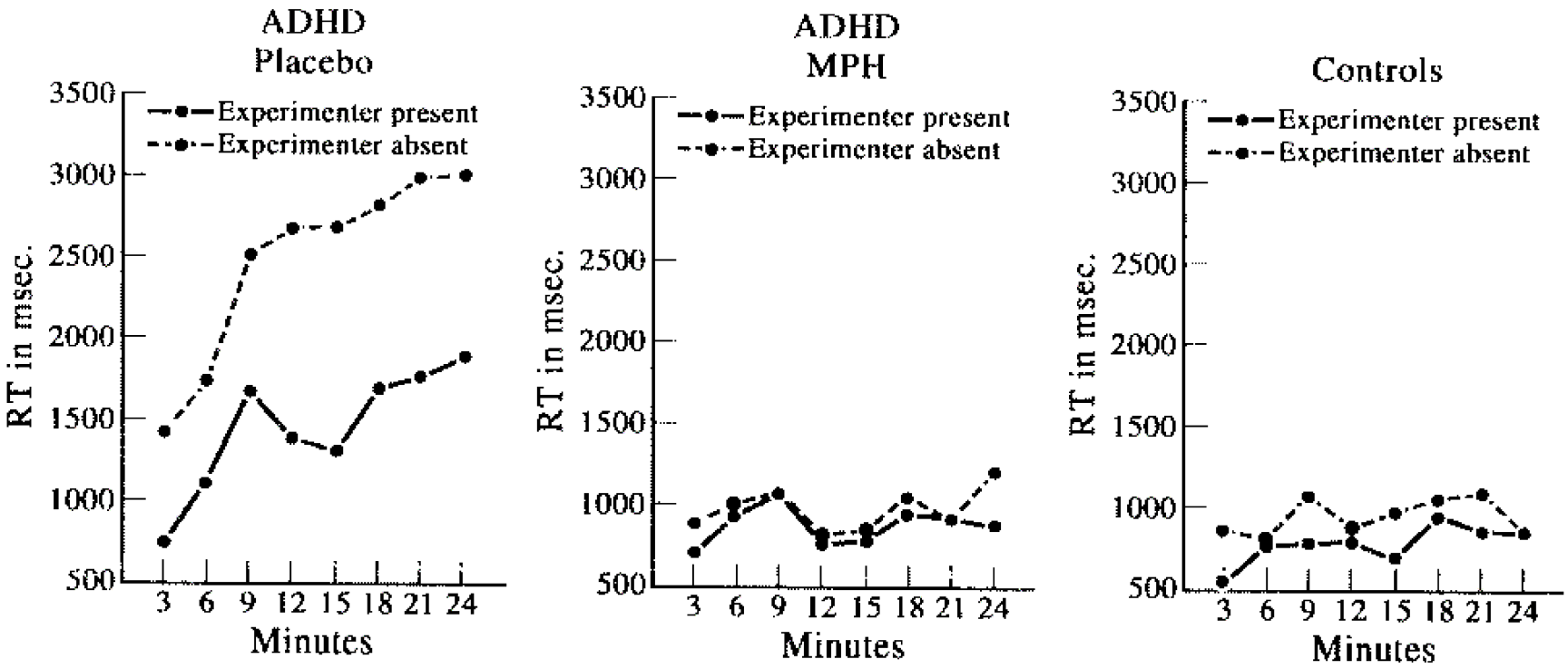


Fig. 1 Mean reaction time as function of task duration for the experimenter present and absent condition across nine periods of three minutes.

Different Effects of Adding White Noise on Cognitive Performance of Sub-, Normal and Super-Attentive School Children

Suzannah K. Helps[1], Susan Bamford[1], Edmund J. S. Sonuga-Barke[1,3]*, Göran B. W. Söderlund[2]*

PLOS | ONE

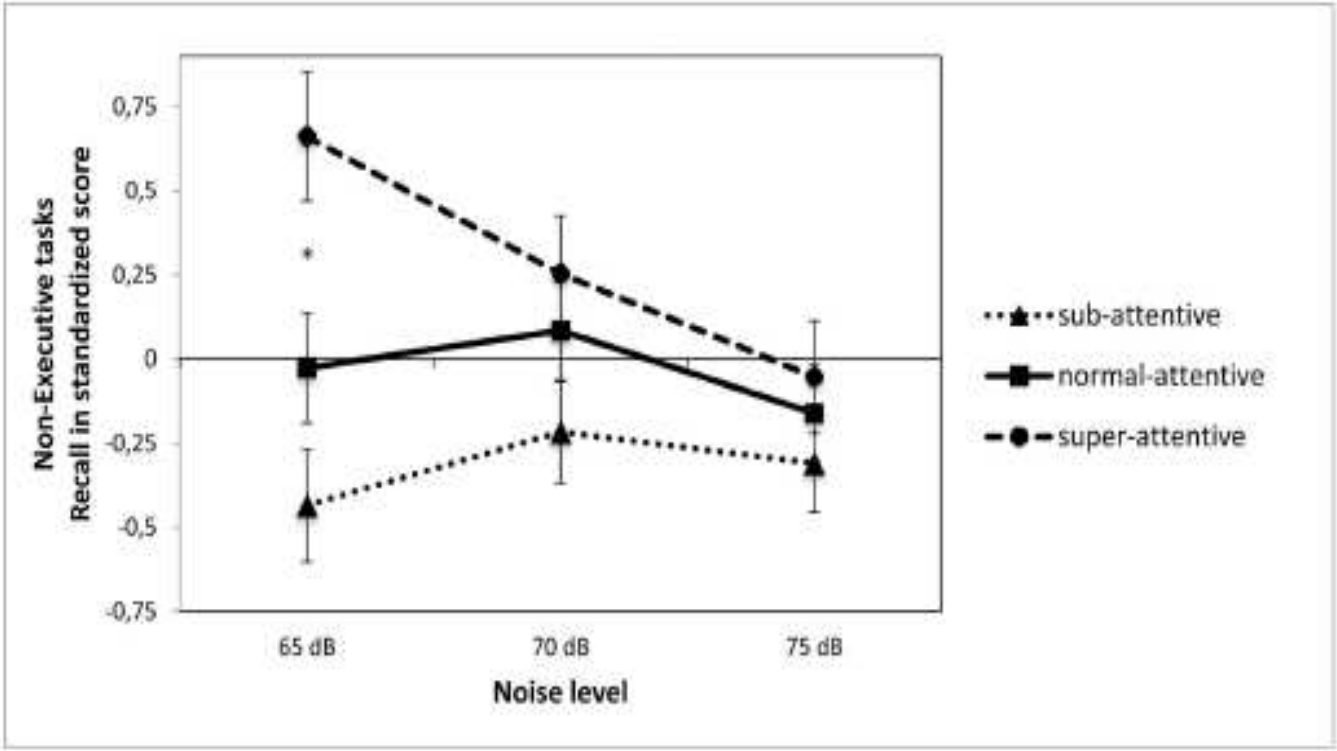
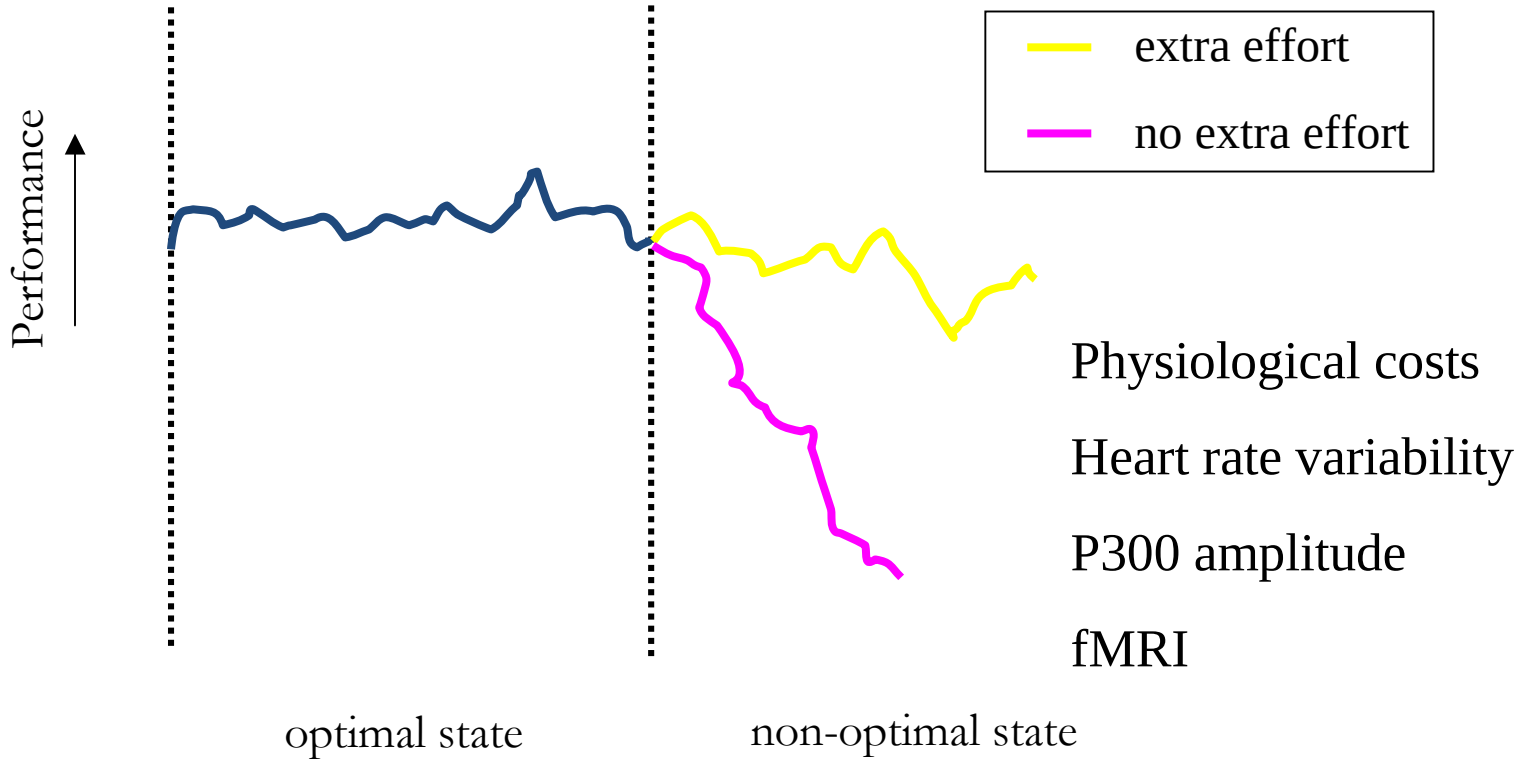


Figure 1. Performance on executive function tasks as a function of attention ability and noise level. *Note: White noise levels were 65, 75, 85 dB; * indicates a significant difference between groups in the 65 dB condition ($F(2,86) = 6.36$, $p = .003$).*
doi:10.1371/journal.pone.0112768.g001

Theory of state regulation

- Actual state vs. required (target) state – effort allocation

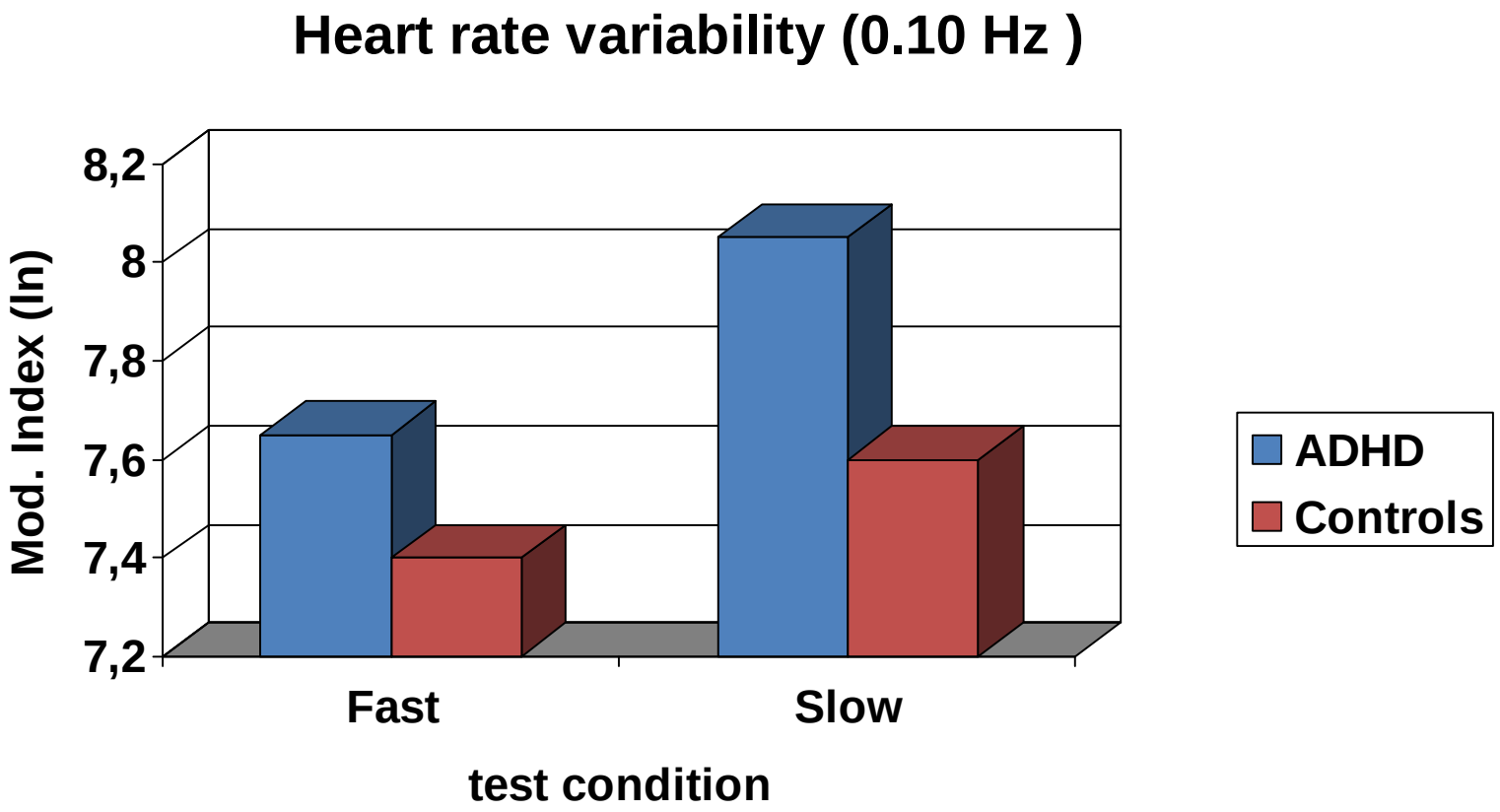


Physiological costs

Heart rate variability

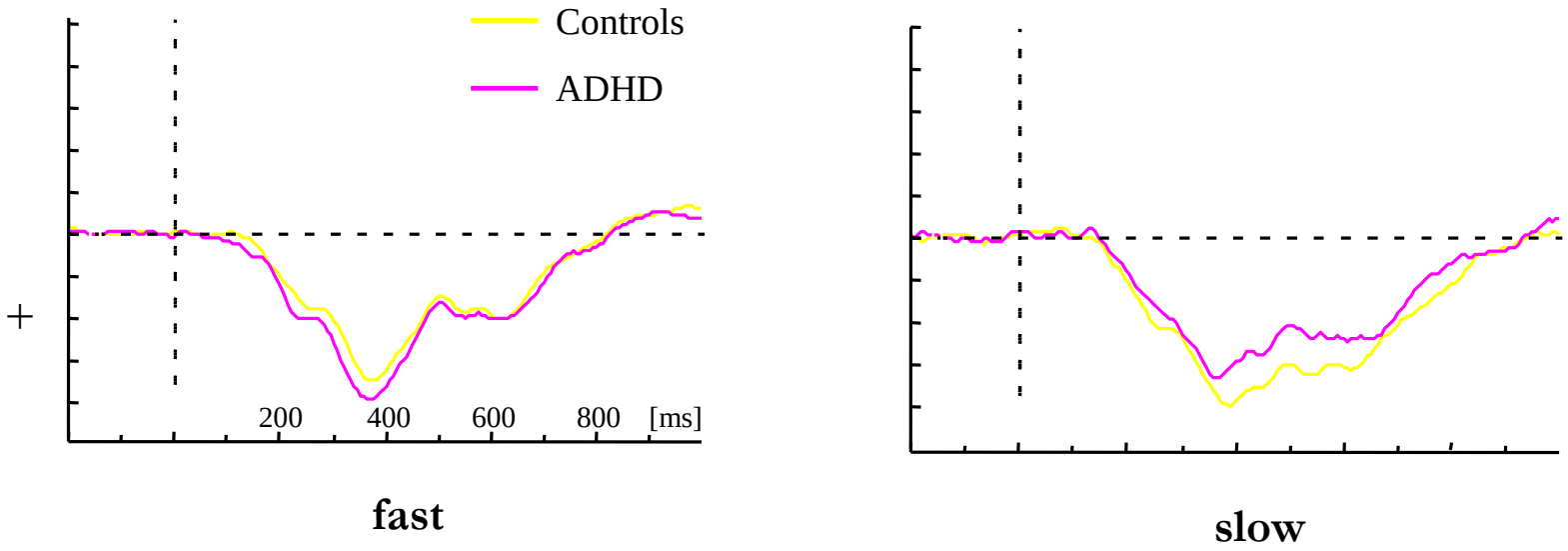
P300 amplitude

fMRI


Heart rate variability (0.10 Hz)
Mod. Index (ln)
8,2
8
7,8
7,6
7,4
7,2
Fast
Slow
test condition
ADHD
Controls

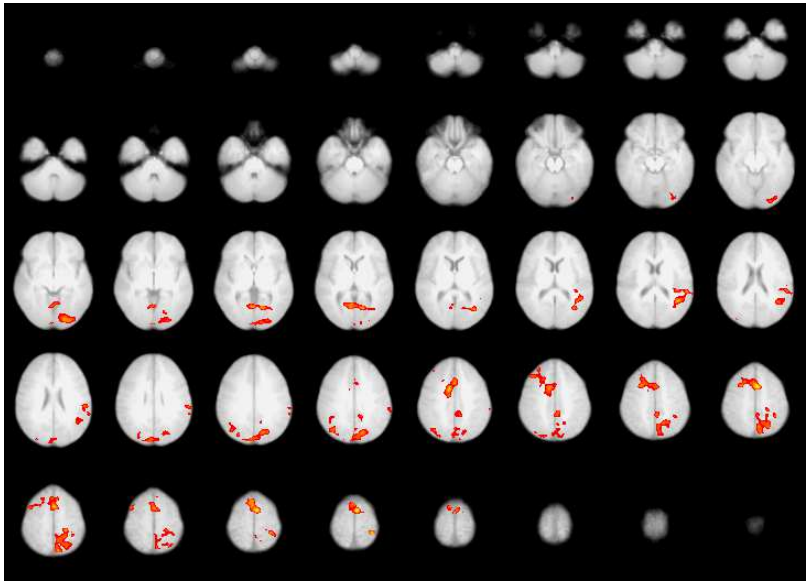
P300 amplitude – a measure of effort

Performance decrement of children with ADHD most pronounced in slow condition (slower responding) accompanied by smaller P3 amplitudes

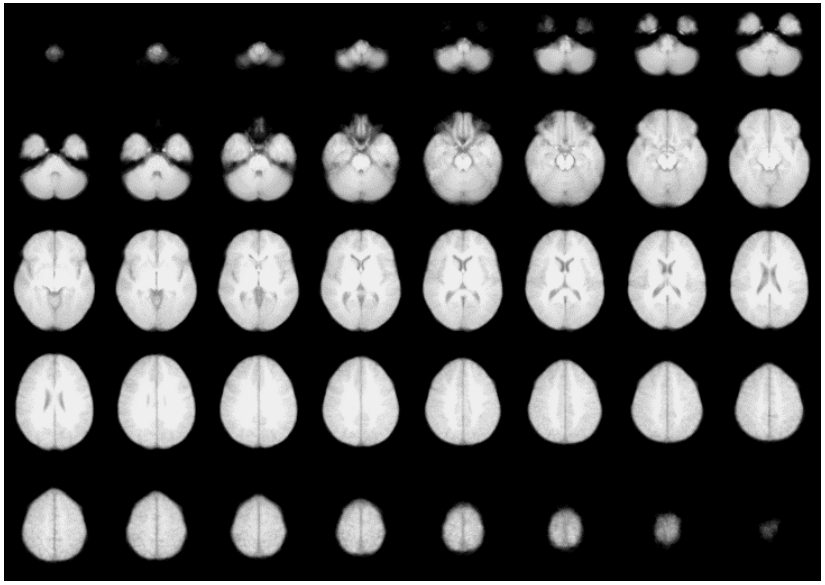


Children with ADHD do not allocate enough extra effort in order to adjust their under-activated state

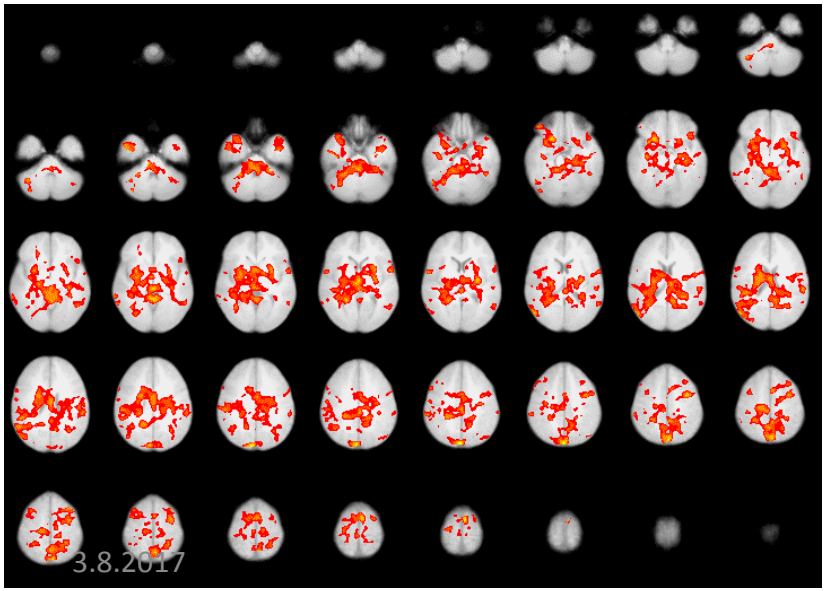
Controls > ADHD: Fast Go Correct



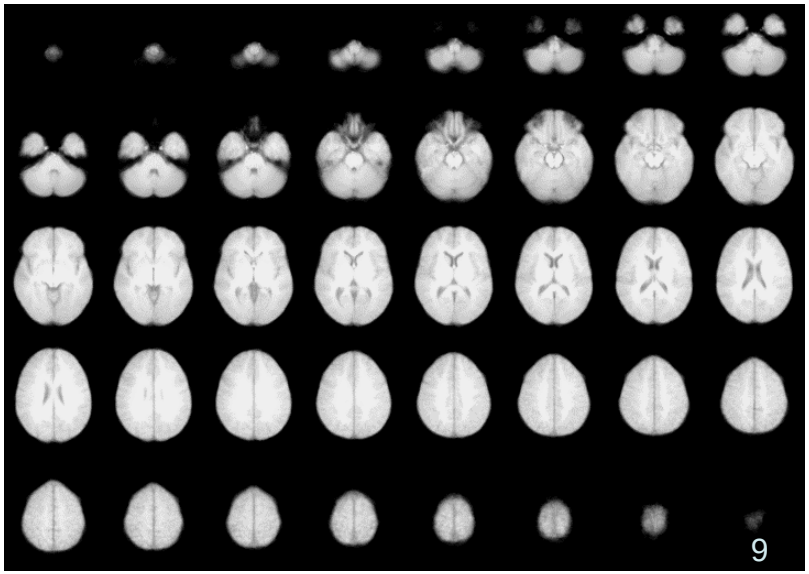
ADHD > Controls: Fast Go Correct



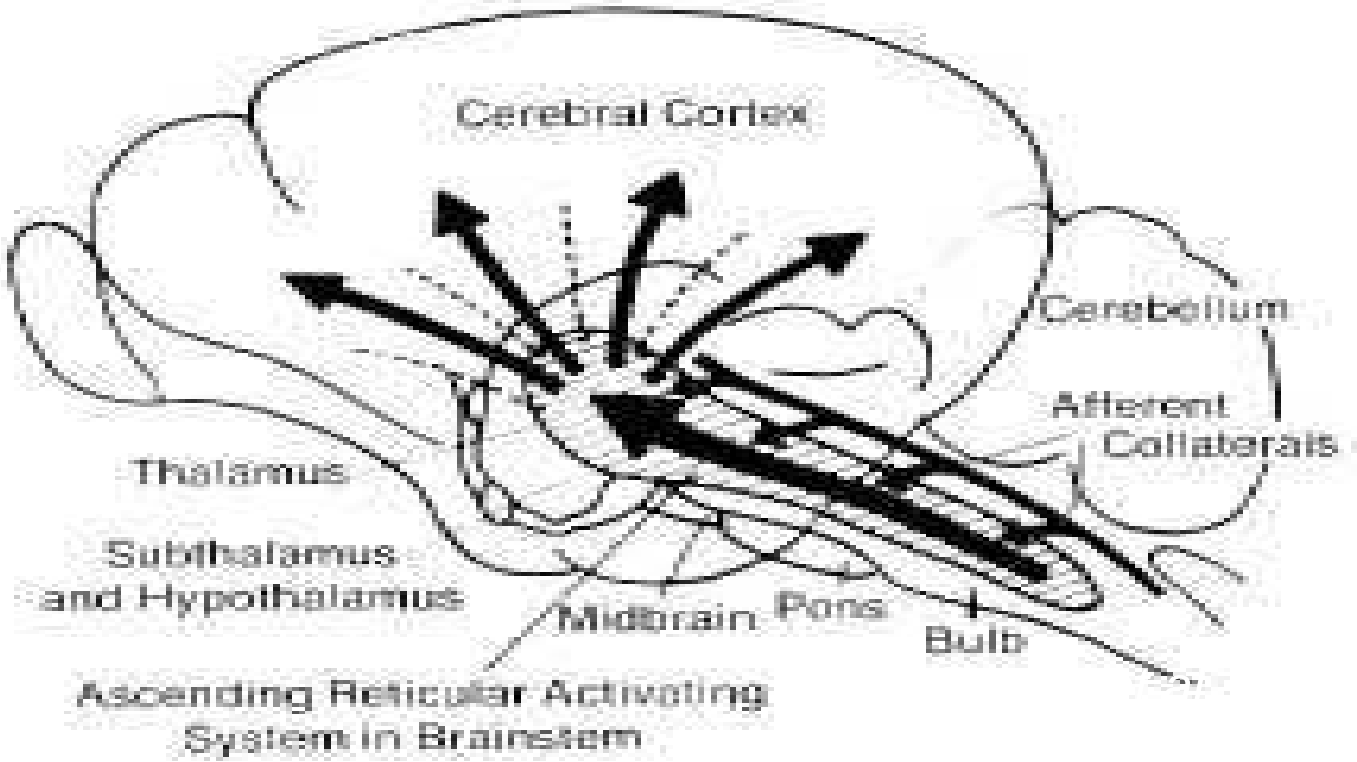
Controls > ADHD: Slow Go Correct



ADHD > Controls: Slow Go Correct



Nucleus Reticularis Thalami

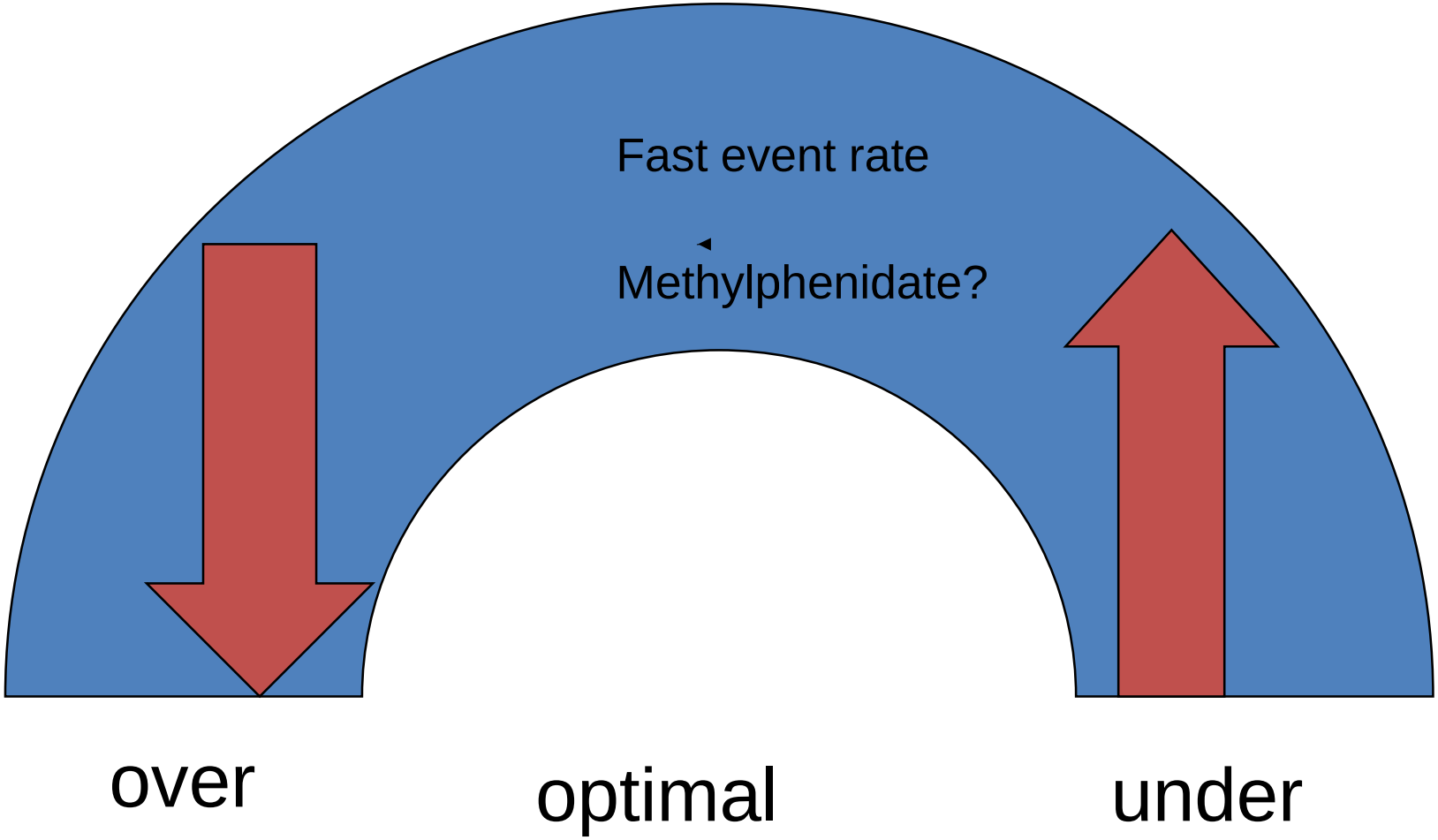


In conclusion

- According to the state regulation theory, ADHD is a motivation deficit, related to an insufficient energy allocation to control motor activation

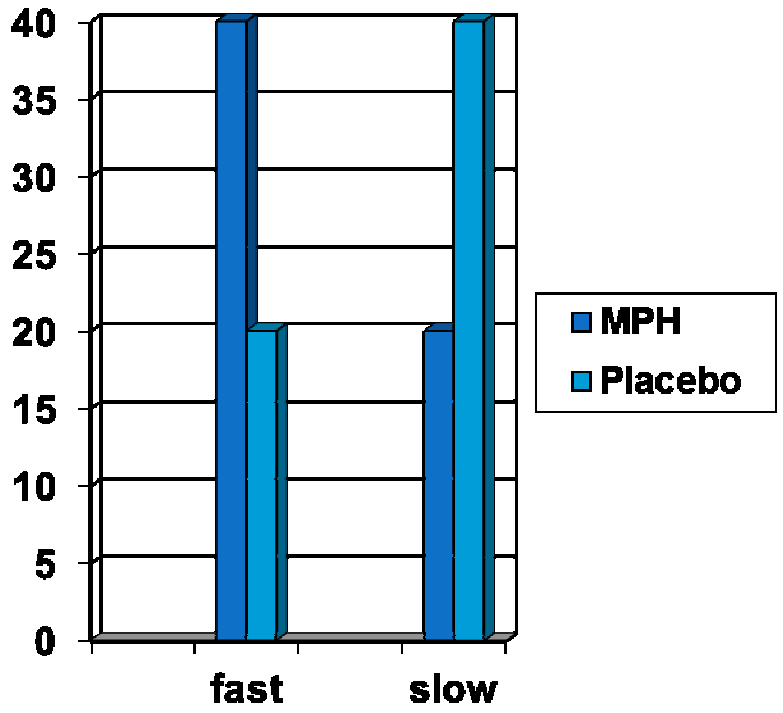
- Relation state regulation and dopamine (see next slides)

event rate and MPH act on dopamine

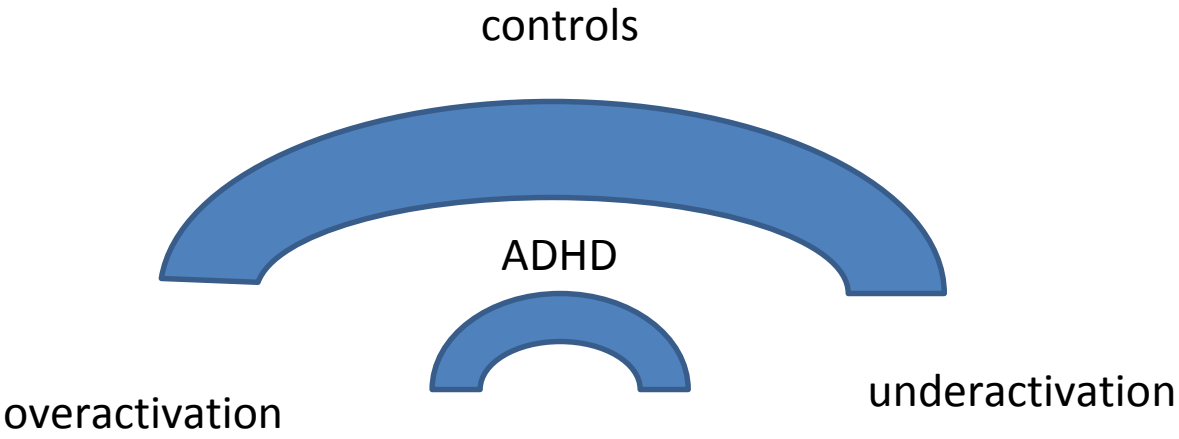


Children with ADHD on or off mediation

- Two energizers result in over-activation



Activation function



Event rate and reaction time performance in ADHD: Testing predictions from the state regulation deficit hypothesis using an ex-Gaussian model

Baris Metin, Jan R. Wiersema, Tom Verguts, Roos Gasthuys, Jacob J. van Der Meere, Herbert Roeyers & Edmund Sonuga-Barke

Routledge
Taylor & Francis Group

Child Neuropsychology

A Journal on Normal and Abnormal Development in Childhood and Adolescence

ISSN: 0929-7049 (Print) 1744-4136 (Online) Journal homepage: http://www.tandfonline.com/loi/ncny20

EVENT RATE EFFECTS ON VARIABILITY IN ADHD 105

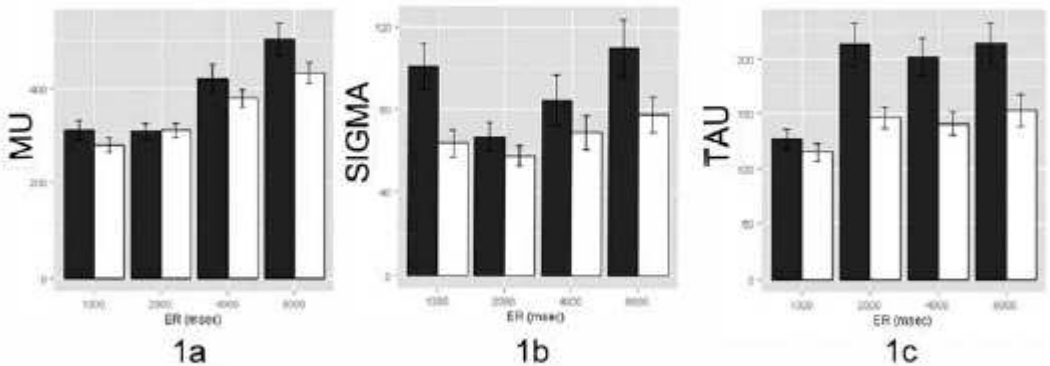
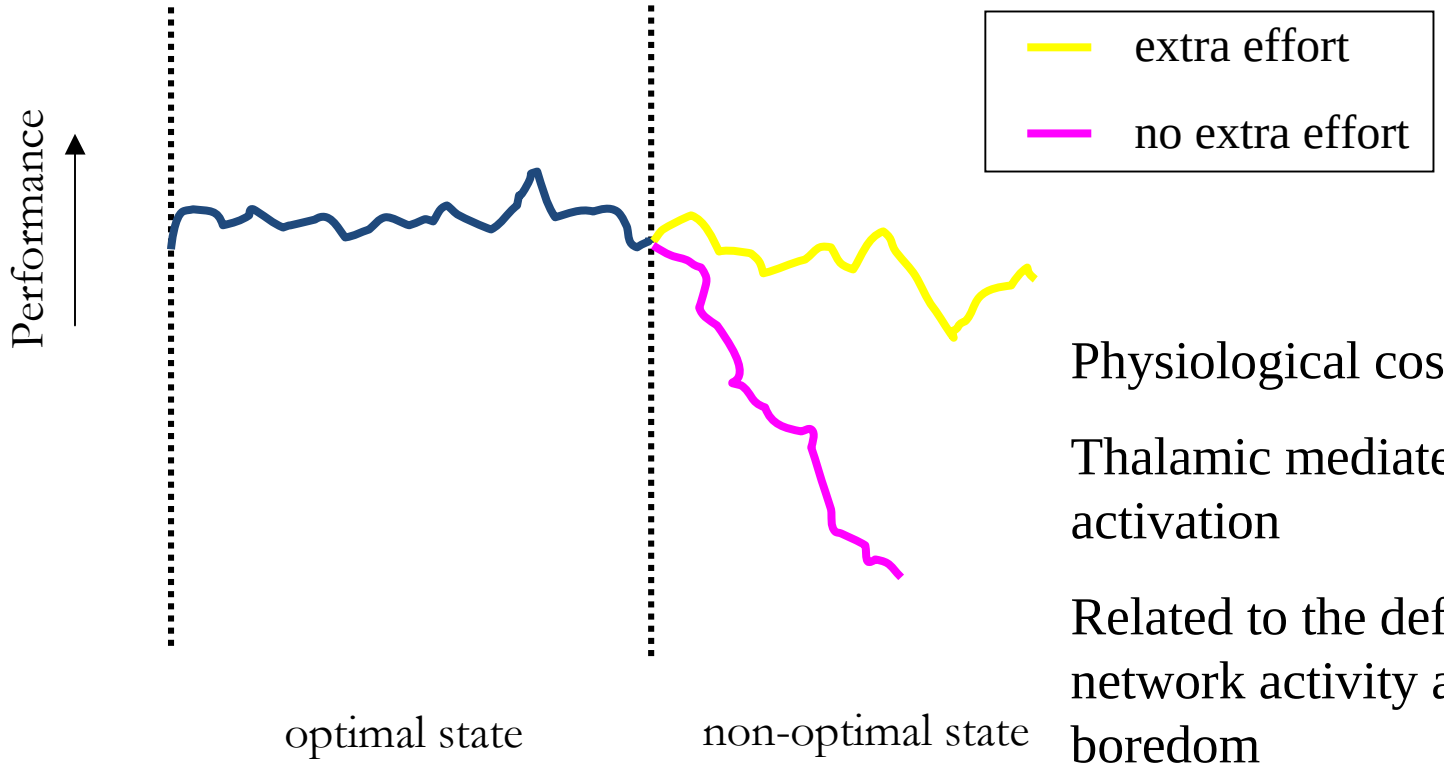


Figure 1 The effect of event rate on (a) *mu*, (b) *sigma*, and (c) *tau* for each group. Error bars = Standard error of the mean.

Mu = normal variation
Sigma = motor preparation
Tau = attentional lapses

Theory of state regulation and the default mode network

Actual state vs. required (target) state – effort allocation



Physiological costs

Thalamic mediated activation

Related to the default network activity and boredom

fMRI indicates two anticorrelational networks in the brain

- The task **positive** frontal parietal attention network (active task state)

- The task **negative** default mode network (passive task state)

- Raichle et al (2001). Proceedings National Academy of Science USA, 98, 676-682

Task negative default mode network

- The wandering mind
- Day dreaming
- Internally focused tasks
- **Suboptimal motivational states**

Theory of state regulation and the default mode network

Actual state vs. required (target) state – effort allocation

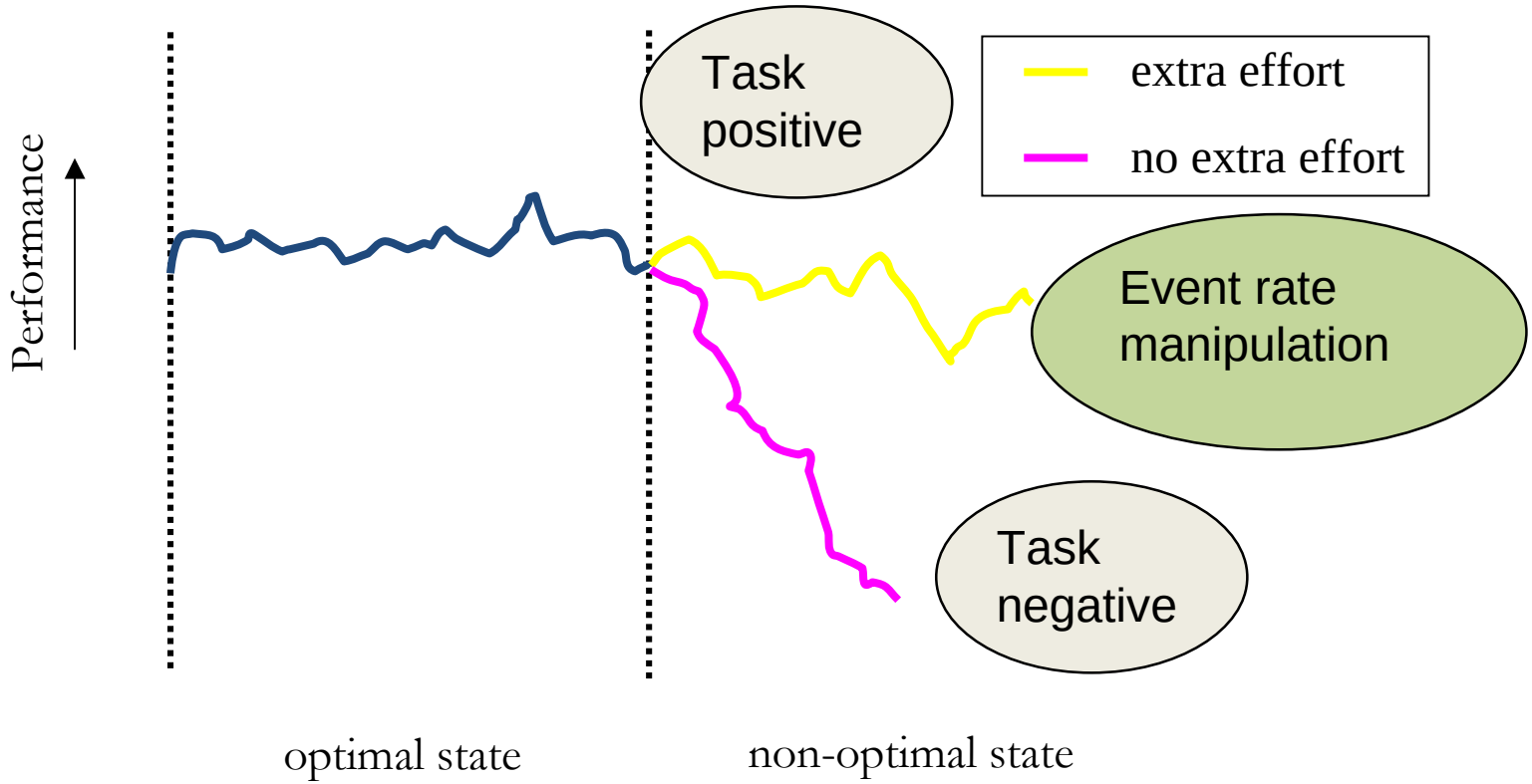
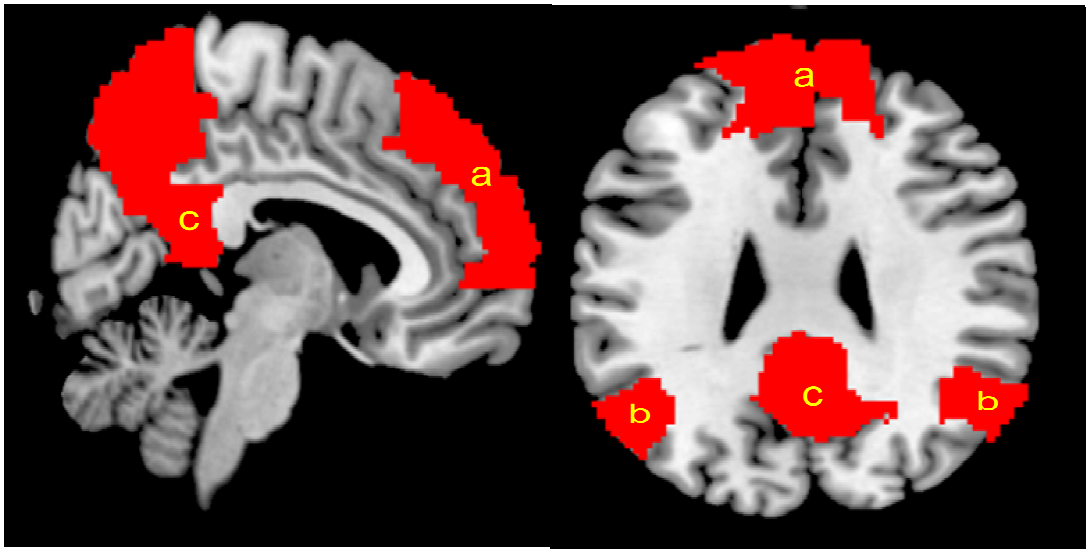


Figure 1. Regions included in the default mode network mask:

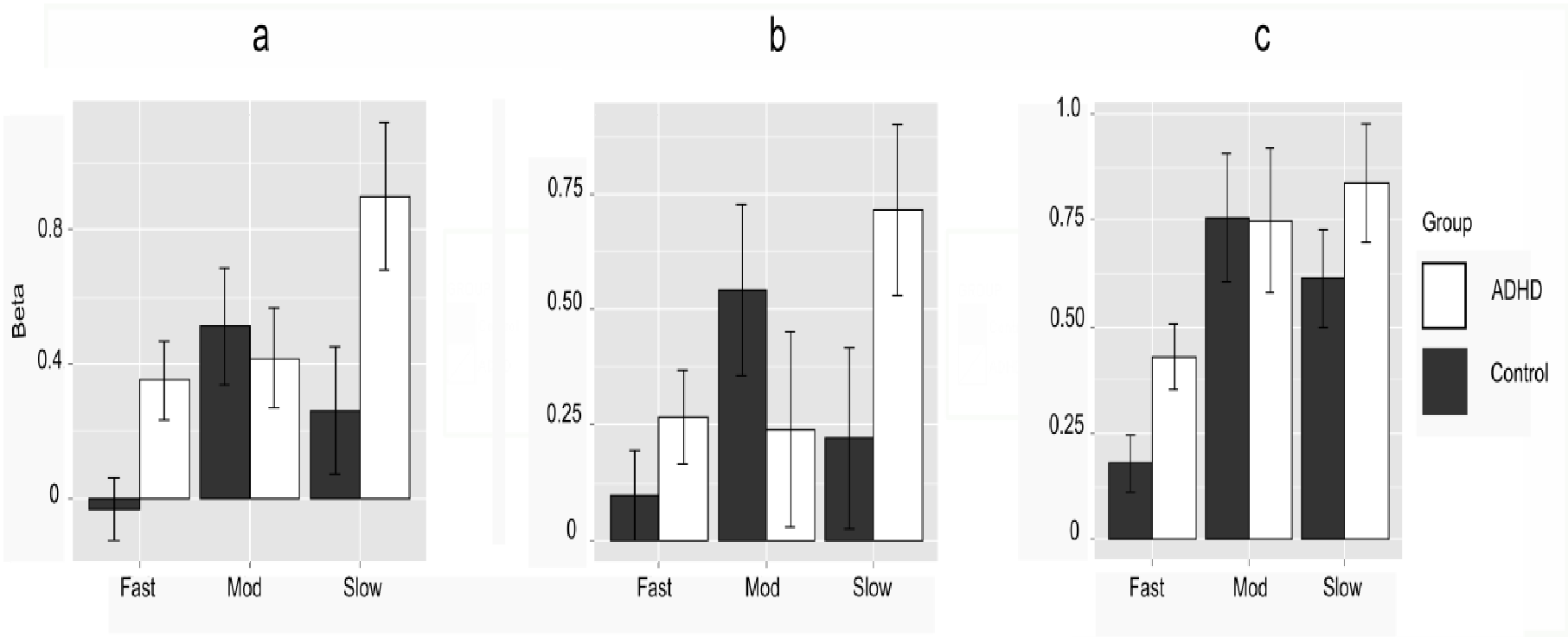
a: superior and medial prefrontal cortex (anterior component),

b: angular gyrus (lateral component)

c: posterior cingulate cortex/precuneus masks (posterior component).



Brain activity of the default mode network during three event rates for anterior (**a**), lateral (**b**) and posterior DMN (**c**) masks.
Error bars: SE of the mean



Conclusion: default mode network in ADHD is most active in the slow condition: is this an expression of boredom?

In conclusion

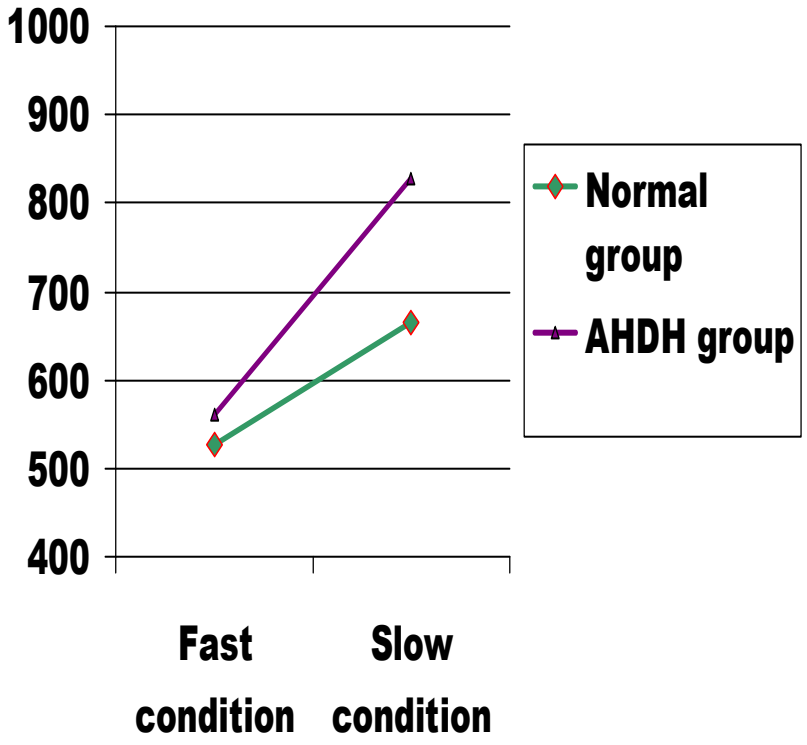
- Psychophysiological indices (heart rate variability, P300 amplitude, and fMRI activity) point in the direction of diminished effort allocation in ADHD children.
- In other words, their task positive attention network becomes *less* active and their default network mode becomes *more* active

Problem 1

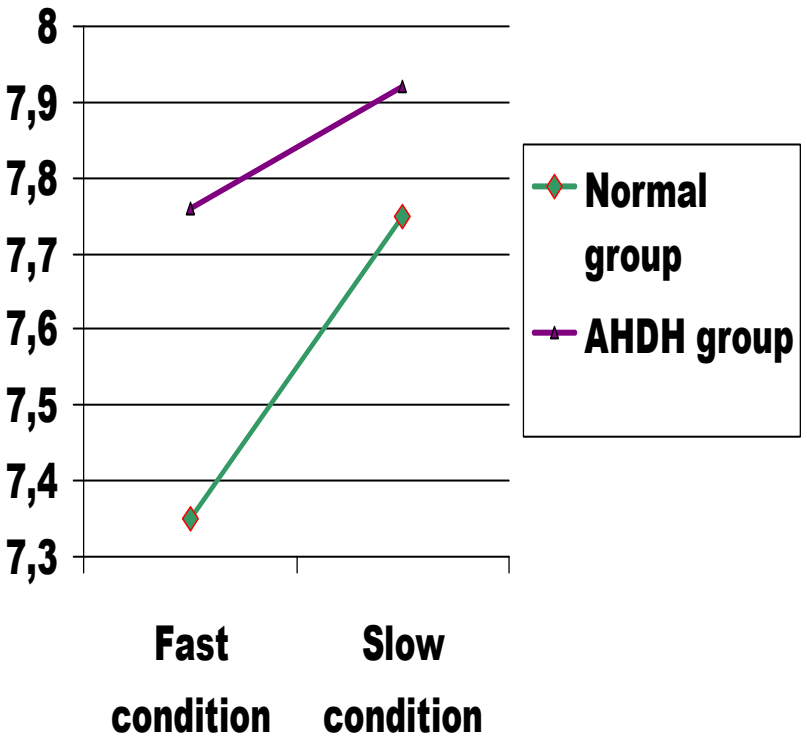
What is fast and what is slow?

Young age group (7-8 years)

Mean reaction time

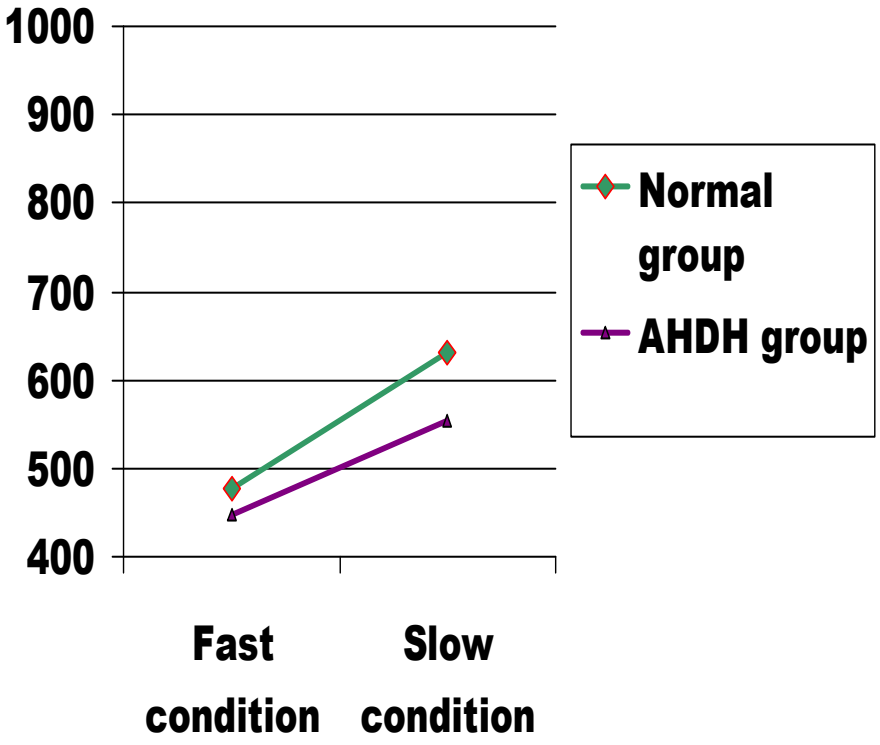


Heart rate variability

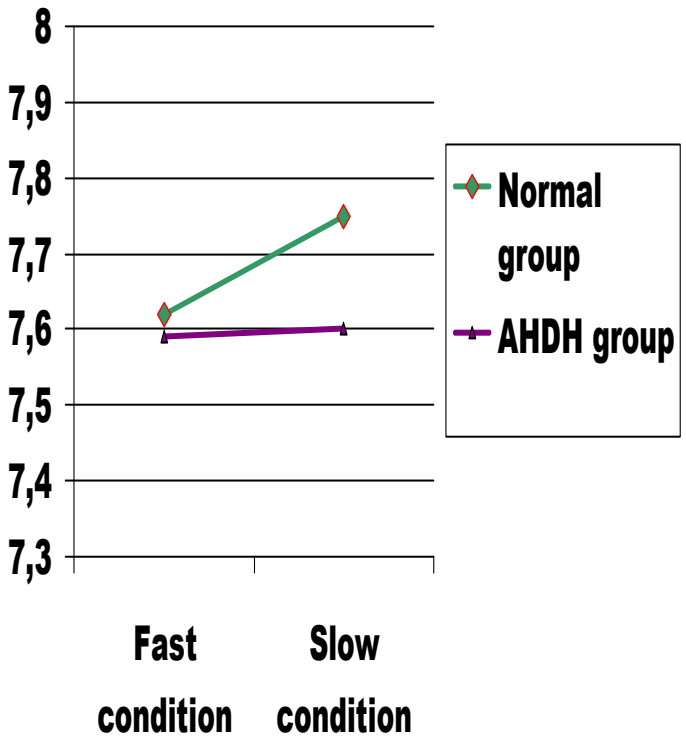


Old age group (9-13 years)

Mean reaction time



Heart rate variability



Answer 1

What is fast, what is slow depends on the type of task and the age of the child

A Meta-Analytic Study of Event Rate Effects on Go/No-Go Performance in Attention-Deficit/Hyperactivity Disorder

Baris Metin, Herbert Roeyers, Jan R. Wiersema, Jaap van der Meere, and Edmund Sonuga-Barke

994 BIOL PSYCHIATRY 2012;72:990–996

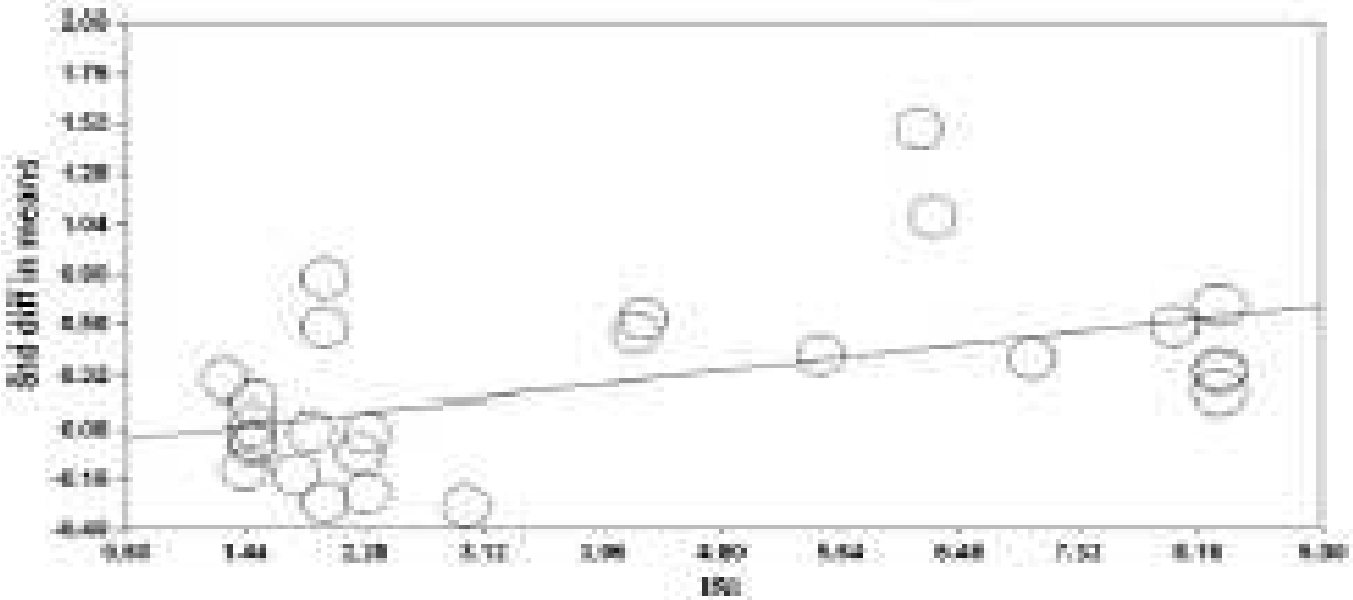


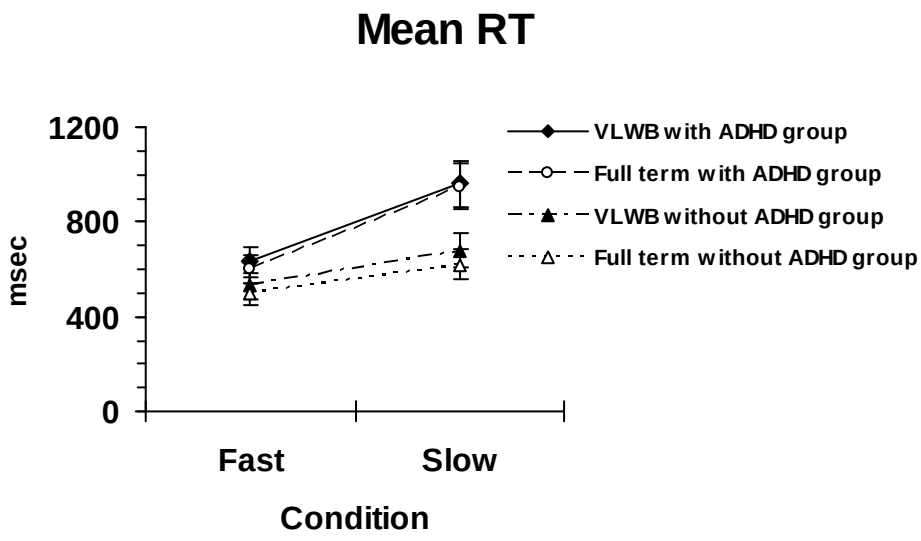
Figure 5. Scatter plot for regression of interstimulus interval (ISI) on effect size for mean reaction time. Std diff, standard difference.

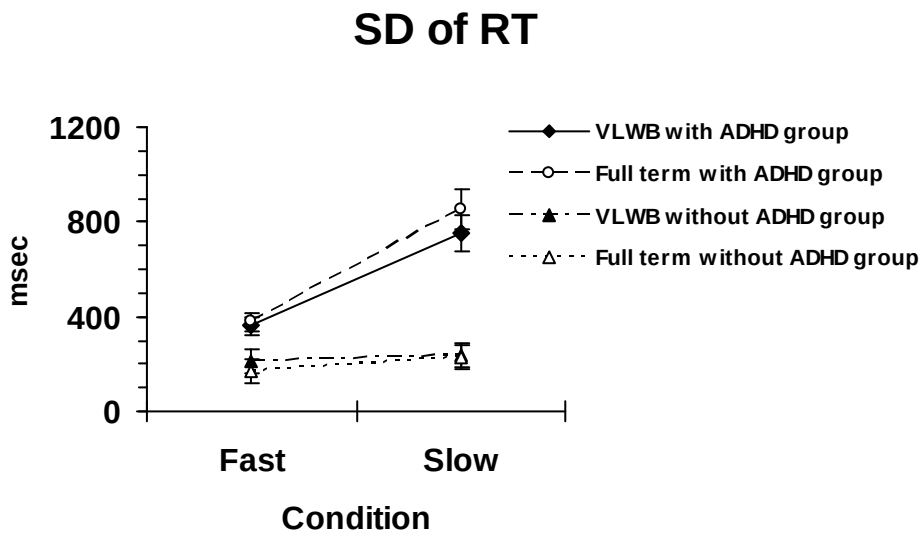
Problem 2

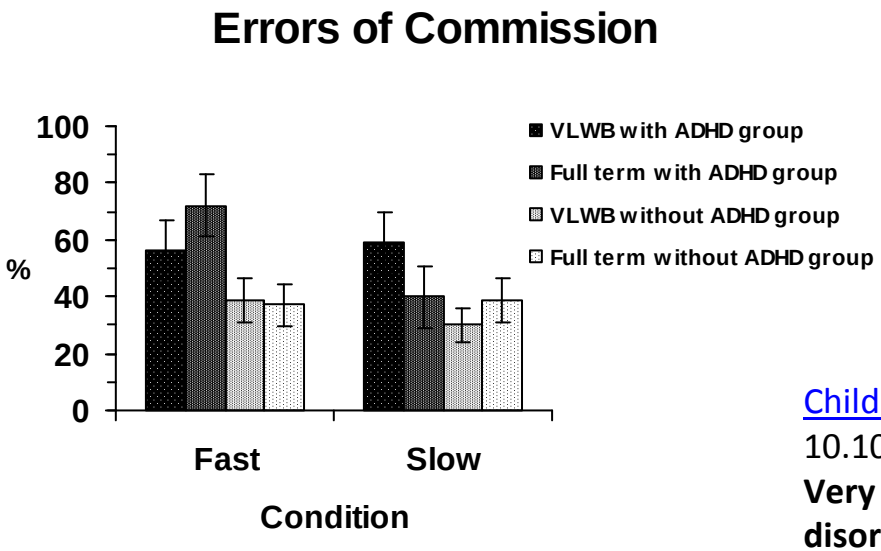
State regulation problems and its etiology?

Main group characteristics

Group (n)	Age (means and sd)	IQ (means and sd)	SES[1] (median and range)	Boys: girls
VLBW (n = 31)	8 years and 5 months (1.23)	104 (2.01)	3 (2-5)	11:20
VLBW + ADHD (n = 12)	8 years and 0 months (1.99)	102 (3.27)	3.5 (2-5)	5:7
Full term + ADHD (n = 10)	8 years and 0 months (1.91)	102 (3.13)	4.5 (3-5)	8:2
Full term (n = 31)	8 years and 3 months (1.27)	105 (2.12)	4 (1-5)	18:13







Child Neuropsychol. 2009 Nov;15(6):605-18. doi: 10.1080/09297040902984482.

Very low birth weight and attention deficit/hyperactivity disorder.

van der Meere J[1], Börger NA, Potgieter ST, Pirila S, De Cock P.

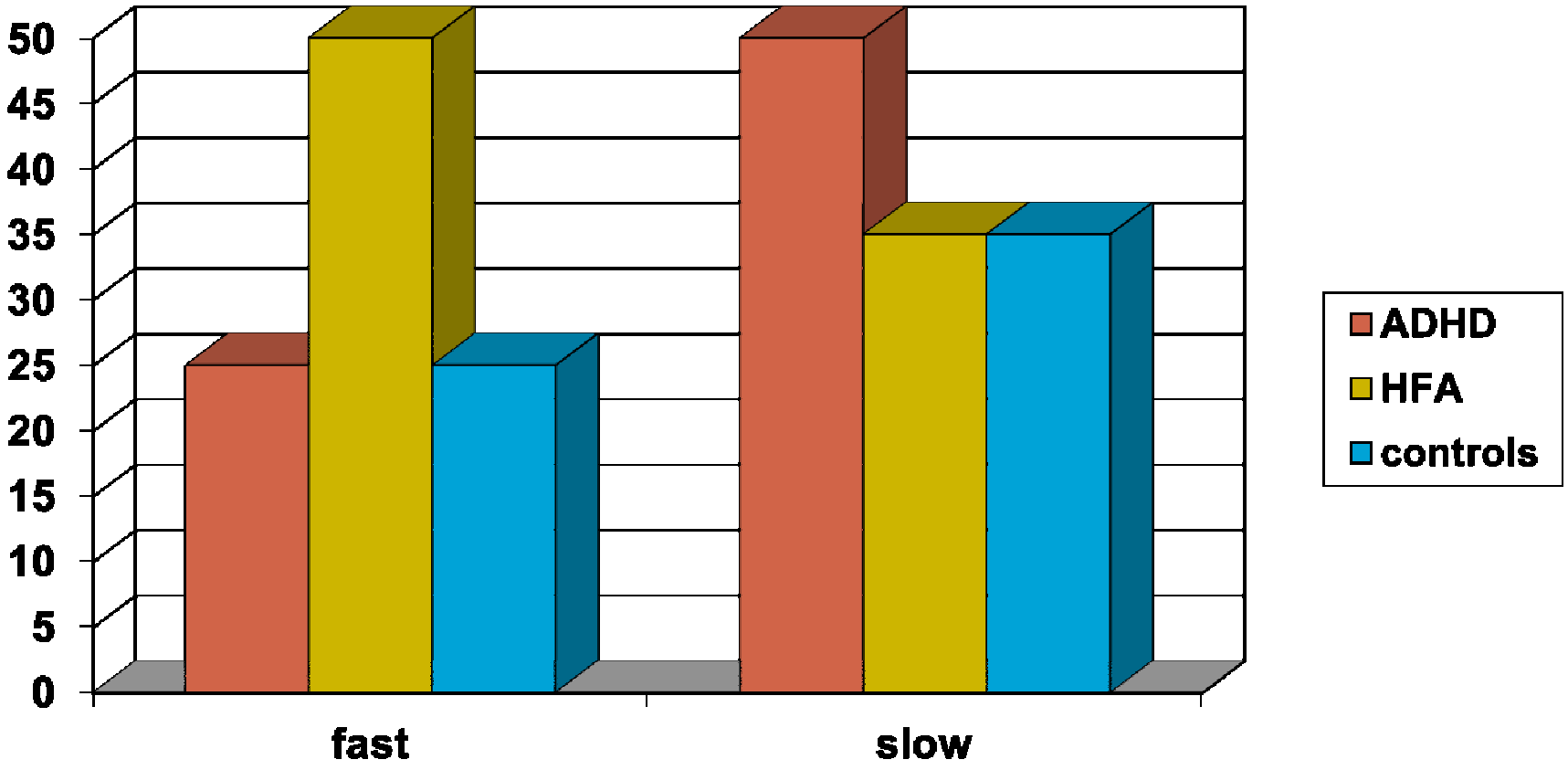
Answer 2

Origins of state regulation deficts are associated with classical etiological factors such as prematuritas and maternal stress during pregnancy

Problem 3

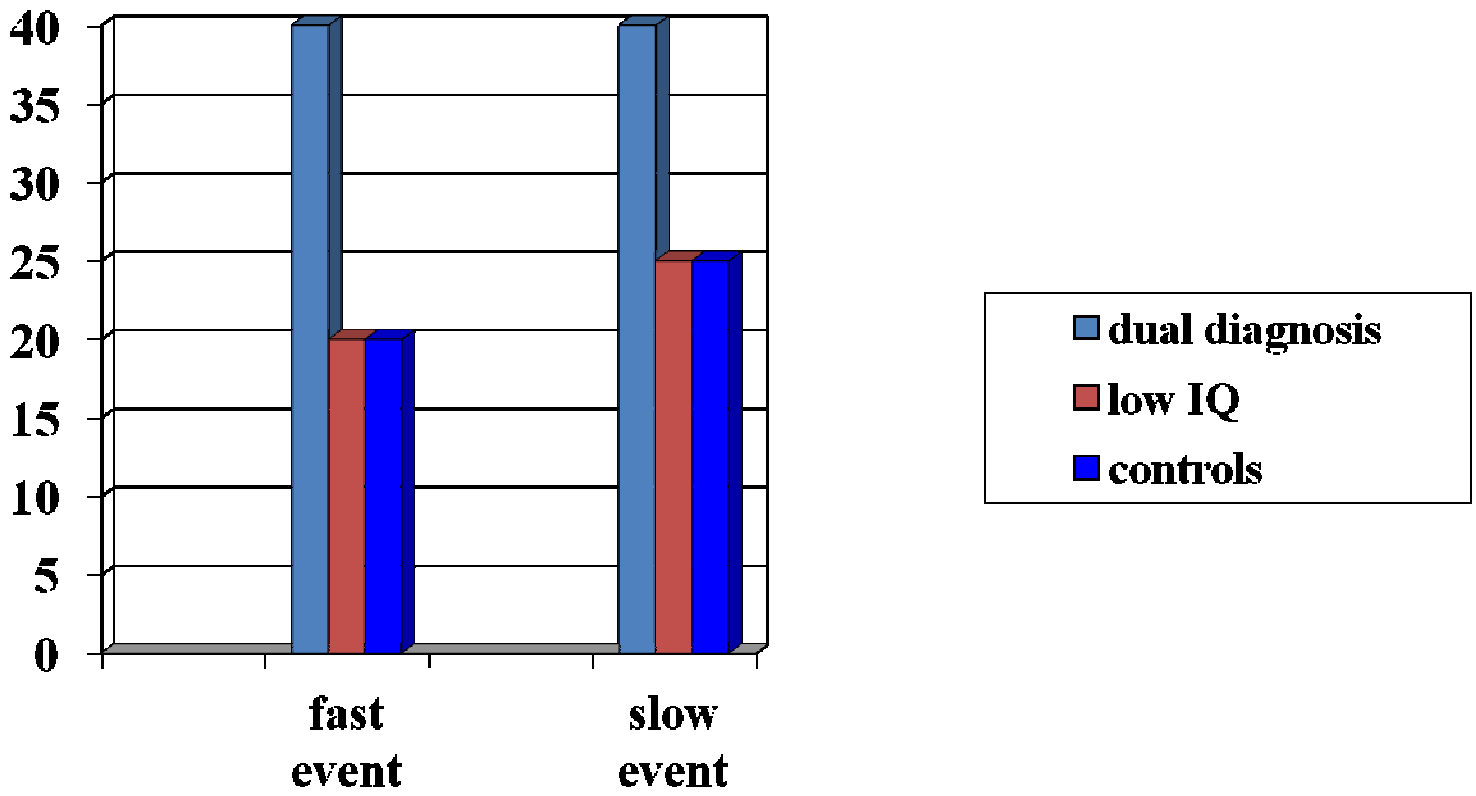
How specific is the state regulation deficit?

Autism and state regulation



Double dissociation? HFA = overactivation ADHD underactivation

CD plus low IQ and state regulation



Inhibition errors independent of event rate manipulation
Children with low IQ outperform children with the dual diagnosis

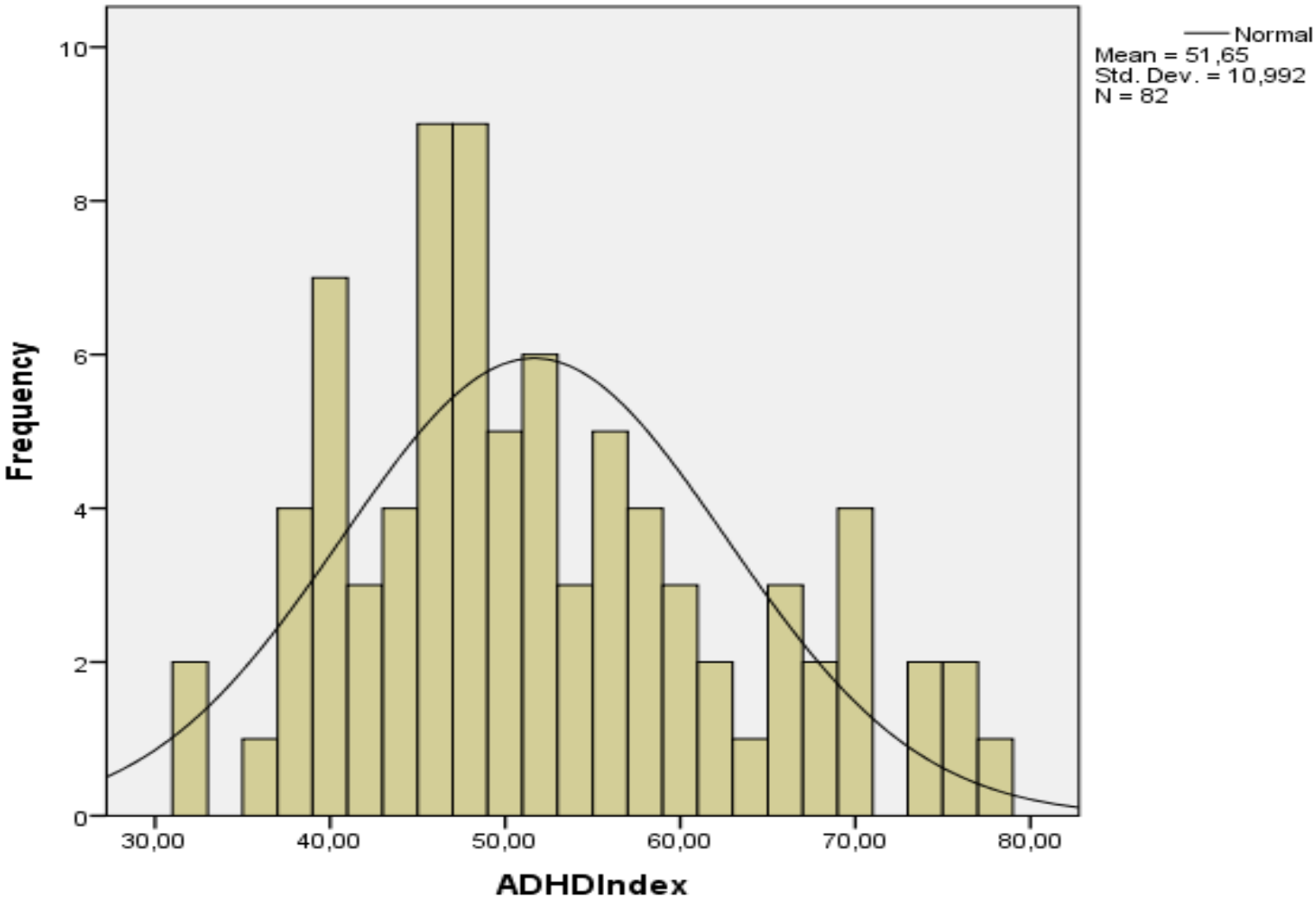
Answer 3

The state regulation deficit is rather specific for ADHD

Problem 4

How is the state regulation deficit postulated in the normal population?

ADHD-Index in student population
Connors Adult ADHD Rating Scale (1999)



The goal is to investigate brain laterality and its association with state regulation and error monitoring with ADHD symptomatology

Participants

- Right handed university students
- Mean age: 21.6 (SD = 2.6, 18-31 years)
- 38 males, 39 females (study 1)
- 25 males, 31females (study 2)

JOURNAL OF CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY, 2016
http://dx.doi.org/10.1080/13803395.2016.1167174
Routledge Taylor & Francis Group

Linking state regulation, brain laterality, and self-reported attention-deficit/hyperactivity disorder (ADHD) symptoms in adults

Saleh M. H. Mohamed [a,b], Norbert A. Börger[a], Reint H. Geuze[a] and Jaap J. van der Meere[a]

[a]Department of Clinical and Developmental Neuropsychology, University of Groningen, Groningen, The Netherlands; [b]Department of Psychology, Beni-Suef University, Beni-Suef, Egypt

Brain and Cognition 108 (2016) 11–19
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journal homepage: www.elsevier.com/locate/b&c
ELSEVIER

Post-error adjustments and ADHD symptoms in adults: The effect of laterality and state regulation

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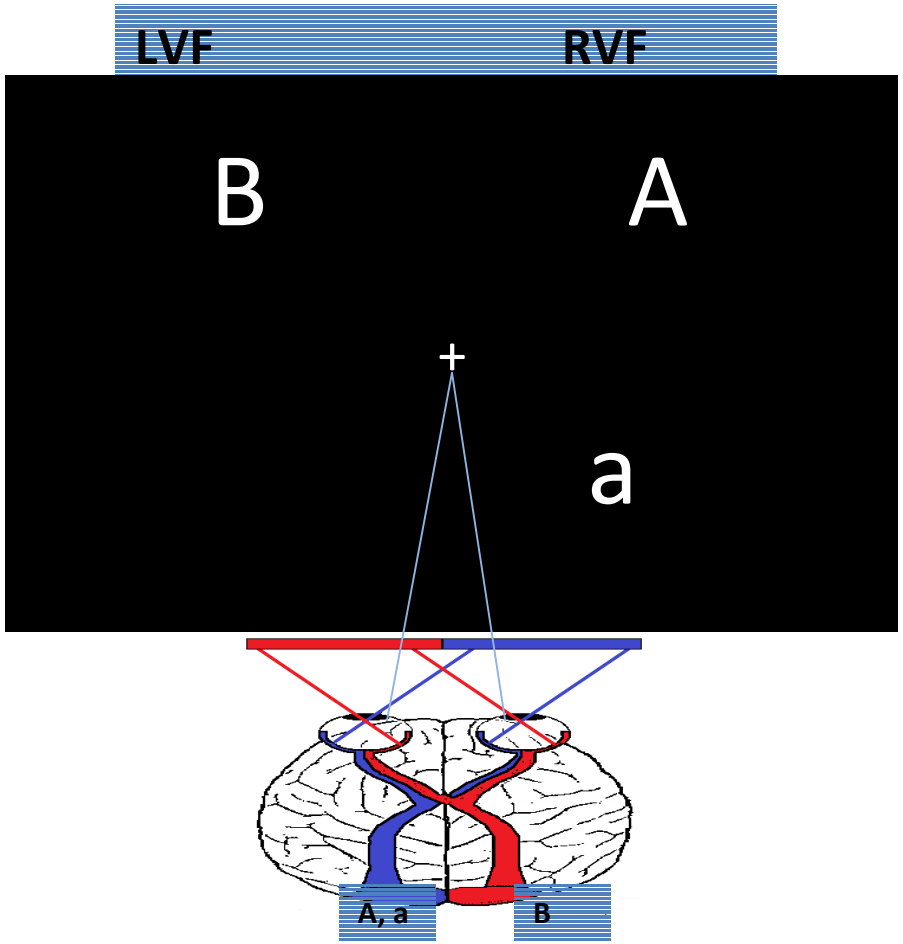
[a] University of Groningen, Faculty of Behavioural and Social Sciences, Clinical & Developmental Neuropsychology Department, Grote Kruisstraat 2/1, 9712 TS Groningen, The Netherlands
[b] Beni-Suef University, Department of Psychology, Salah Salem Street, 62511 Beni-Suef, Egypt

Banich Task: Brain laterality

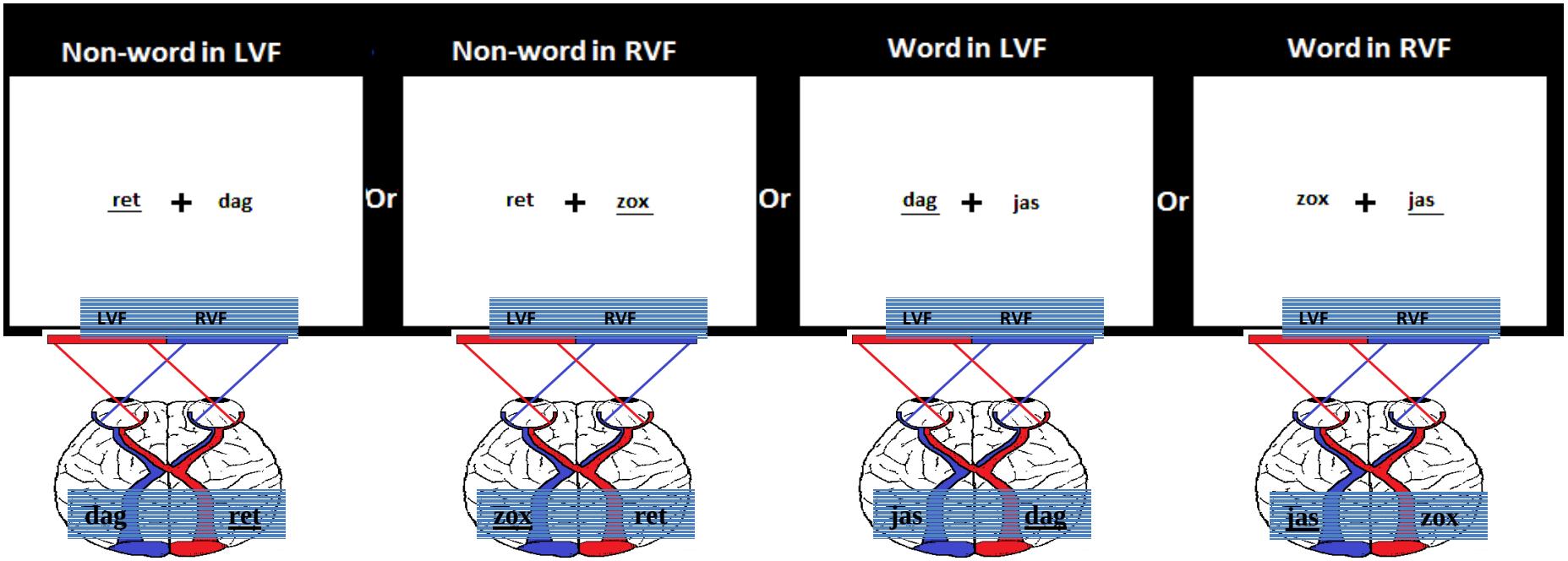
- Here is a RVF stimulus.

- Brain laterality is measured by RT LVF versus RT RVF.



Lateralized lexical decision task

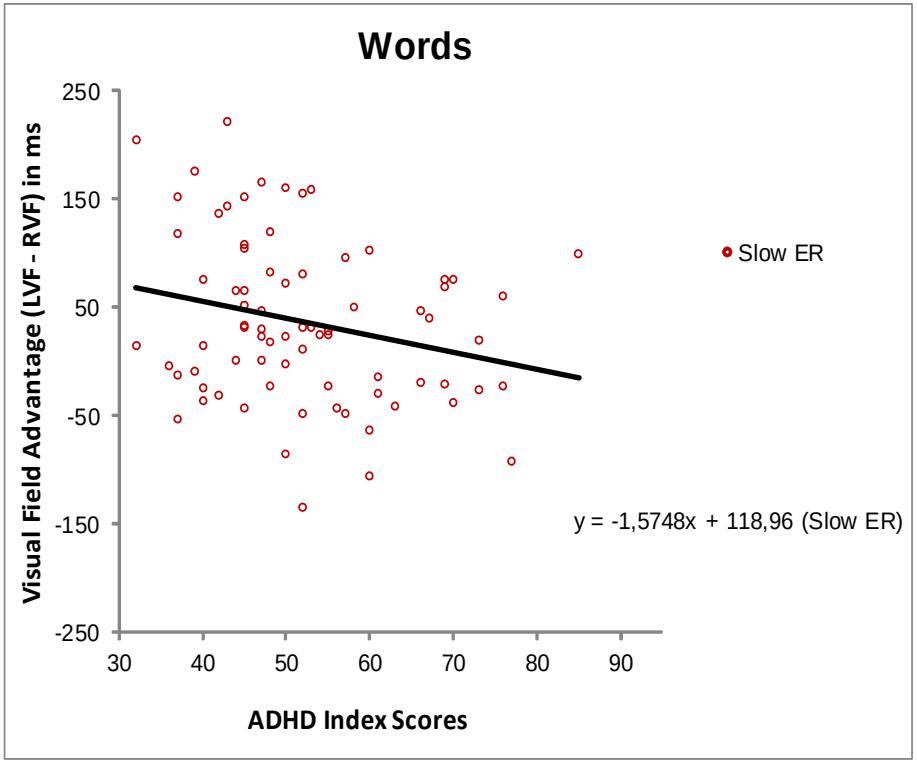
- Four types of stimuli were presented.



- Stimuli were presented at a fast and a slower rate. It has been reported that slower presentation rate of stimuli induces a lower motor activation state, which in turn leads to poor performance. To prevent a decline in performance, subjects must allocate extra effort. (Metin et al., 2012, *Biological Psychiatry*)

- Error-monitoring was measured in terms of post-error adjustments. If participants are aware that they just have made an error, they will adjust their responses accordingly. Typical participants slow down their responses to increase the chance of having a correct response on the subsequent trial. (Danielmeier et al., 2011, *Frontiers in Psychology*)

Slow presentation rate



- It appeared that especially during the slow presentation rate adults with higher levels of ADHD symptoms have a reduced left hemisphere word processing, ($F(1, 75) = 10.782$, $p = .002$, $\eta 2 = .13$).

Error monitoring

- During a slower presentation rate and RVF trials, subjects with lower ADHD symptoms did slow down their RT after errors ($F(1,54) = 4.134$, $p = 0.047$, $\eta 2 = 0.07$). They also tended to increase response accuracy after errors ($F(1,54) = 3.965$, $p = 0.052$, $\eta 2 = 0.07$).

- In contrast, subjects with higher ADHD symptoms did not adjust their responses after error making.

- Thus, the left hemisphere ability to compensate for errors seems to be affected when extra effort allocation is needed.

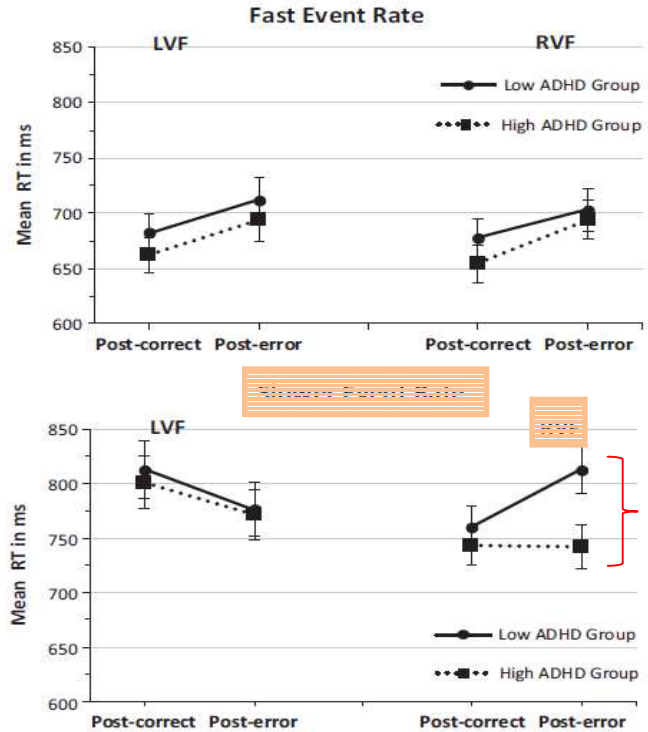


Fig. 1. Mean reaction times of correct trials following correct and incorrect responses in each visual field and presentation rate. Note; Post-correct = RT for correct responses after correct trials; Post-error = RT for correct responses after errors; Fast Event Rate = the fast stimulus presentation rate condition; Slow Event Rate = the slower stimulus presentation rate condition; High ADHD Group = participants with scores fall in the third tertile of ADHD index scores; Low ADHD Group = participants with scores fall in the first tertile of ADHD index scores; LVF = left visual field; RVF = right visual field; Error bars indicate SE values.

Answer 4

The state regulation concept is normally distributed in the general population and postulated in the left hemisphere

Problem 5

What is the ecological validity
of the state regulation concept?

Answer 5

The ecological relevance of our findings

- Academic Achievement Test
- Weis Functional Impairment Rating scale
- Executive Function index Scale
-
- A moderate correlation between executive functioning and left hemisphere processing at slow stimulus presentation rate (**N = 77, *r* = .25, *p* = .029**): subjects with more severe ADHD symptoms and decreased left hemisphere processing manifested decreased executive functioning in daily life contexts.

- A moderate correlation between functional impairments in daily life and post-error slowing for RVF stimuli presented at slower rate (**N = 56, *r* = -.28 , *p* = .043**): subjects with more severe ADHD symptoms and decreased post-error slowing demonstrate more daily life functional impairments.

Problem 6

Where are the emotions?

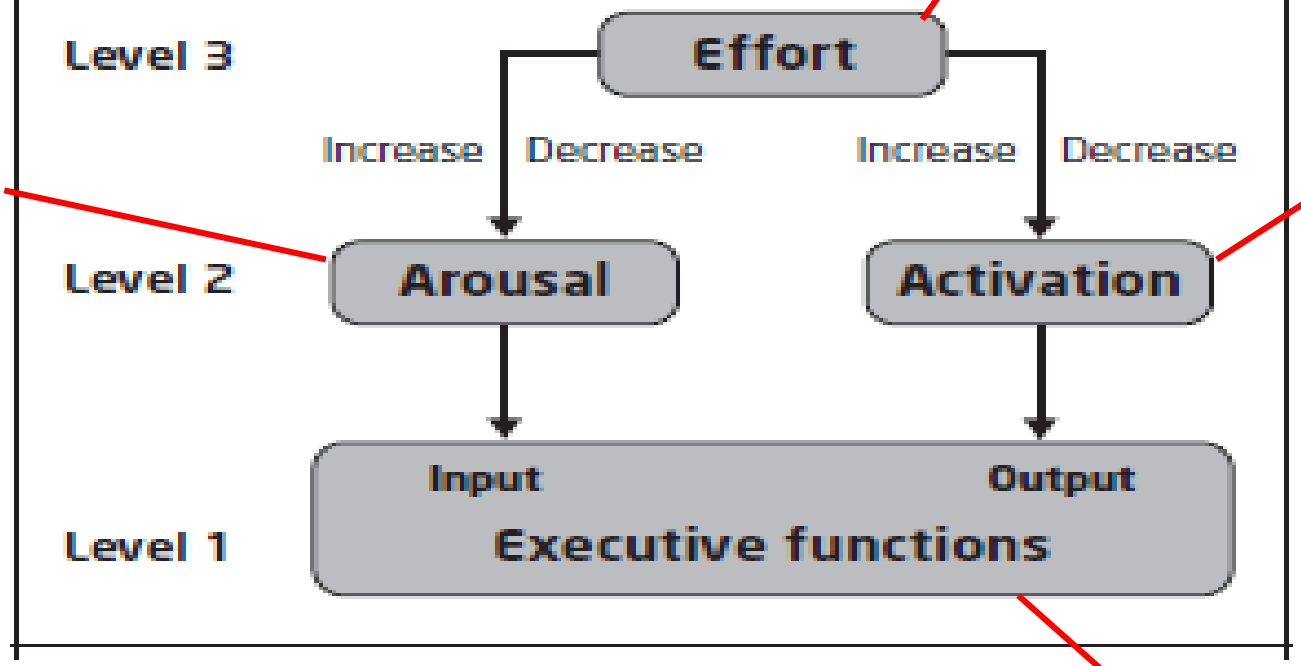
ADHD: State Regulation and Motivation

Jaap J van der Meere, Prof, PhD[1], Norbert A Börger, PhD[1], and Jan R Wiersema, PhD[2]
[1]Department of Clinical Neuropsychology, University of Groningen, The Netherlands, and
[2]Department of Experimental Clinical and Health Psychology, Ghent University, Belgium

CML – Psychiatry 2010;21(1):1–7.

Negative emotions

Figure 1. The state regulation model.

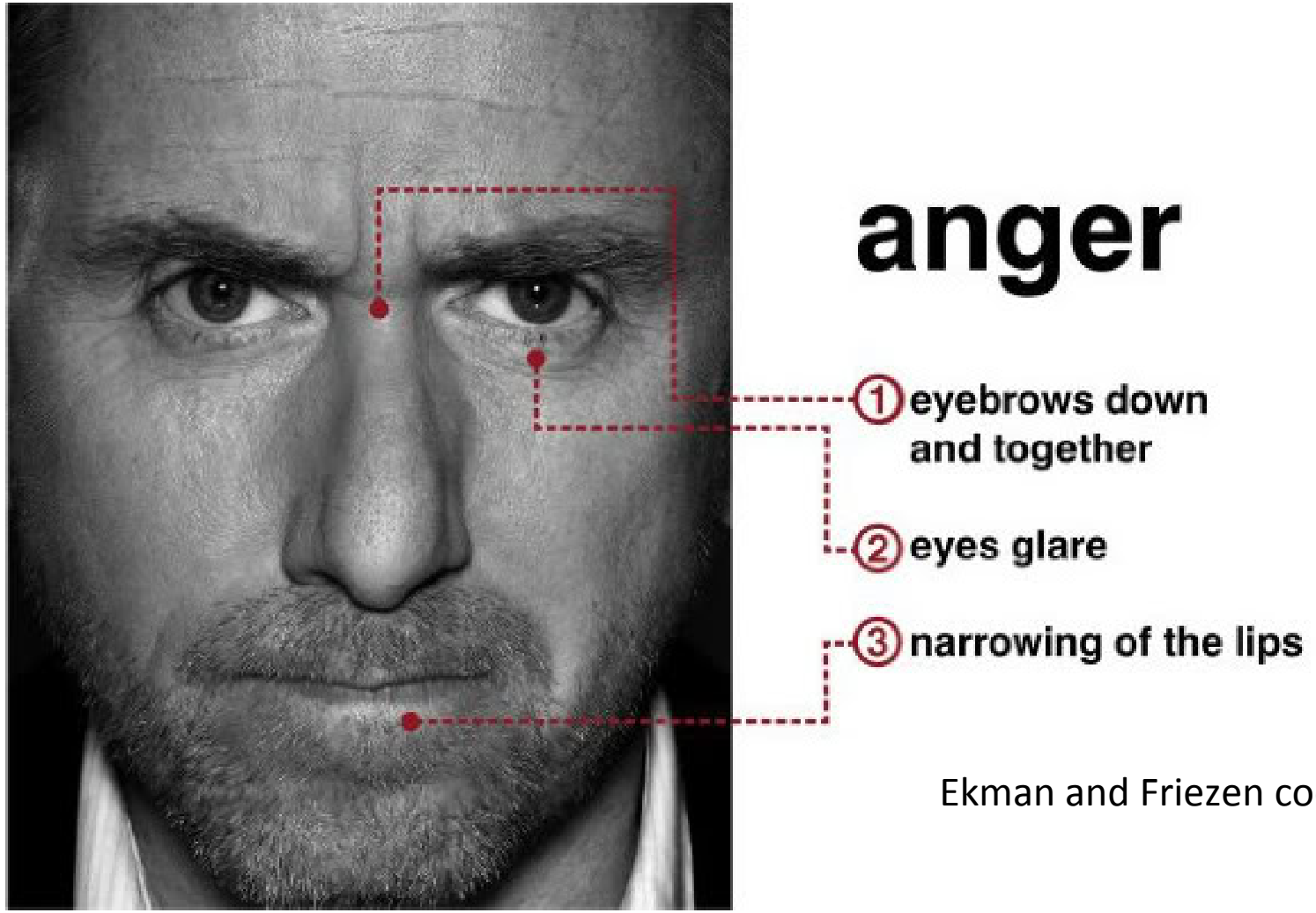


Noise

Event rate

Task difficulty

Tell me the emotion. How to observe?



Ekman and Friezen coding system

Facial movements and negative emotions

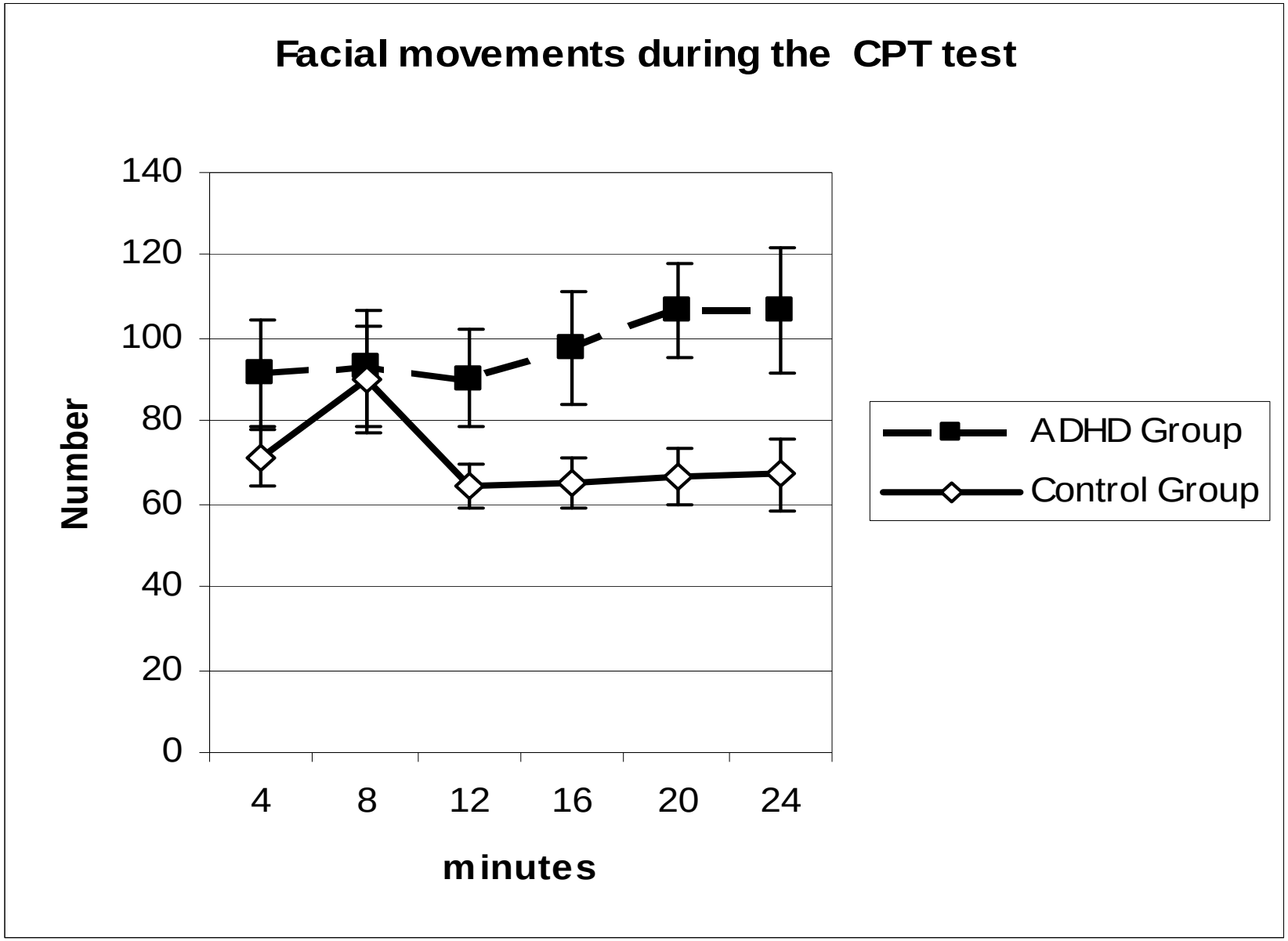
- Brow raiser
- Brow lowerer
- Blink
- Eyes down
- Lip corner puller
- Tongue show
- Lip presser
- Lips part / Mouth stretch
- Lips suck
- Jaw sideways
- Puff

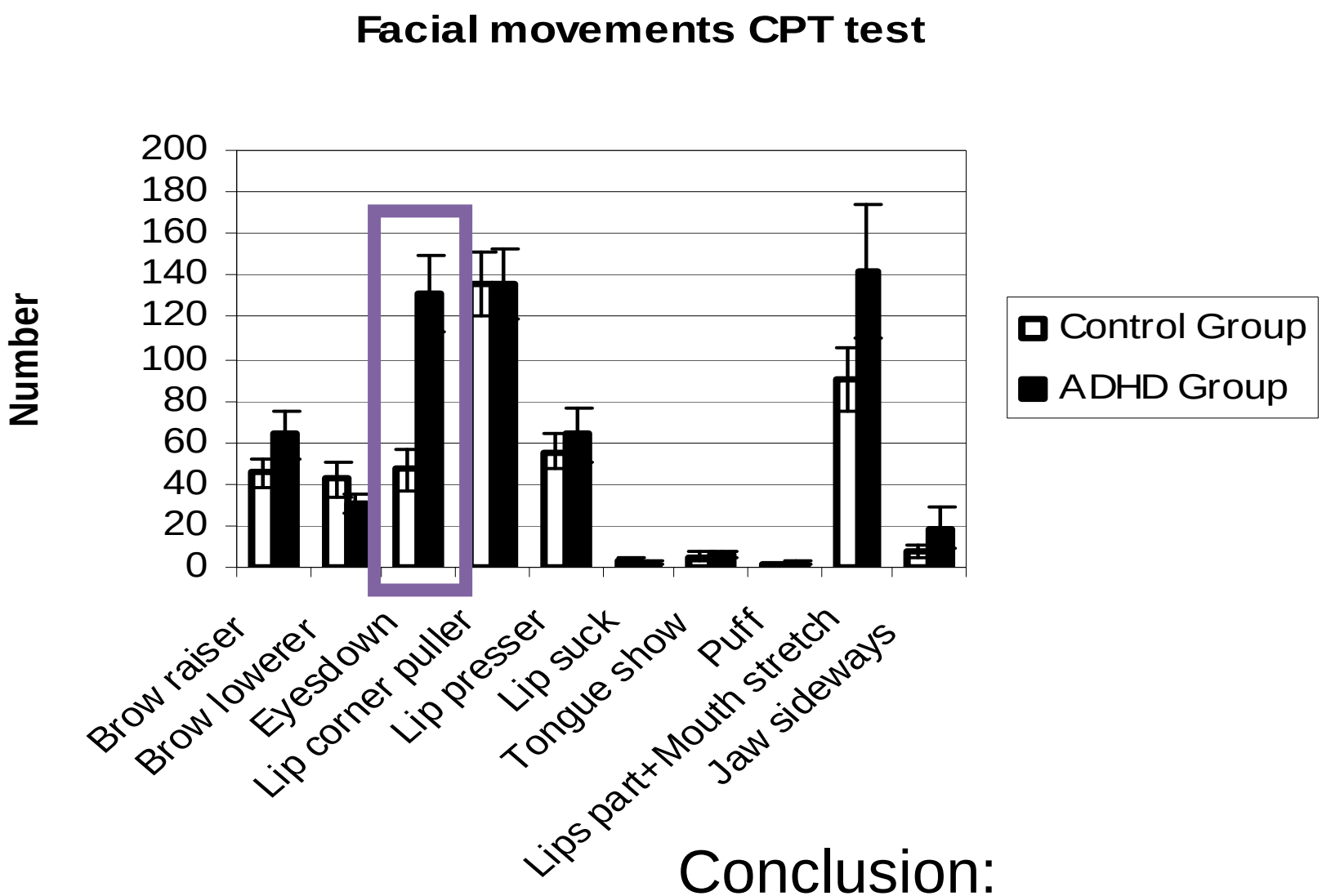
Fear and anger

boredom

disgus
t

disgus
t


Facial movements during the CPT test
140
120
100
80
60
40
20
0
Number
4
8
12
16
20
24
minutes
ADHD Group
Control Group



Conclusion:
children are easily bored

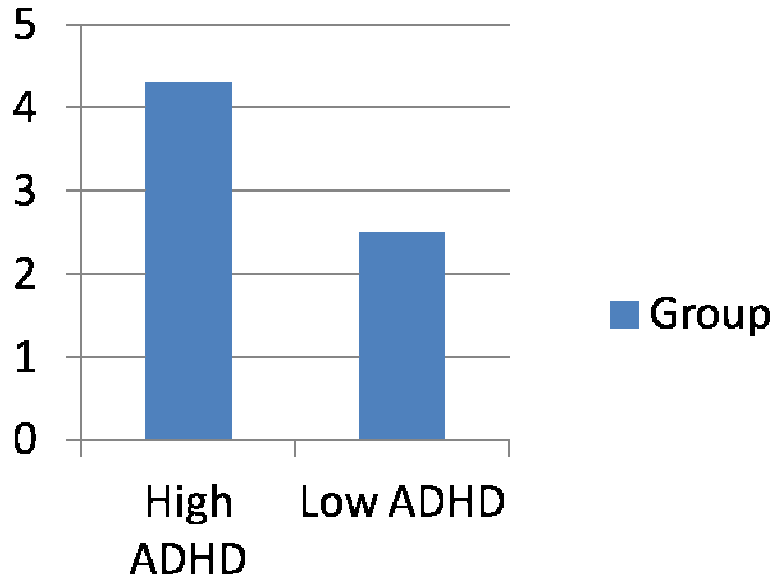
Negative-task related emotions

Emotion	Craig et al. (2004a)	McDaniel et al. (2007)	Graesser & D'Mello (2012)
Boredom 	-AU43 (eye closure) -Eye blinks and mouth movements -neutral face	-AU4 (brow lowerer) -AU7 (lid tightener) -AU12 (lip corner puller) -AU45 (blink) -expressionless face	-expressionless face
Frustration 	-AU1 (inner brow raise) -AU2 (outer brow raise)* -14 (dimpler)	-AU12 (lip corner puller)* -AU43 (eye closure)* -most difficult to detect	-AU12 (lip corner puller)* -often disguised
Confusion 	-AU4 (brow lowerer) -AU7 (lid tightener) -AU12 (lip corner puller)	-AU1 (inner brow raise) -AU4 (brow lowerer)* -AU7 (lid tightener)* -AU12 (lip corner puller)* most likely to be detected	-AU4 (lowered brow)* -AU7 (tightening of the eye lids)* -AU12 (lip corner puller)*

ADHD and task-related emotions

Sumscore of negative task-related emotions:

- Frustration
- Confusion
- Boredom
- Stress



P < .005

0 = not present
5 = much present (a lot)

Observed facial expressions

Upper face movements:

(1) eye closure, (2) outer brow raisor (3) inner brow raiser, (4) brow lowerer, (5) lid tightener, (6) upper lid raisor (7) looking down, (8) looking up,

Lower face movements:

(9) lip corner puller, (10) dimpler, (11) mouth opener, (12) nostril dilator.

Association with the sum of the negative emotions:

Upper face: (2), (3), (4), (5) and (8): correlations from .32 to .35

i.e.: diverse brow movements and looking down

Lower face: (9), (10), (11): tendencies ($P<.10$), $r= .27$ to .29

i.e. lips/mouth

{yes: $p < .05$, tendency: $p< .10$}

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- Mohamed, S. M., Börger, N. A., Geuze, R. H., & Meere, J. J. (2016). Linking state regulation, brain laterality, and self-reported attention-deficit/ hyperactivity disorder (ADHD) symptoms in adults. *Journal of Clinical and Experimental Neuropsychology*. doi:10.1080/13803395.2016.1167174

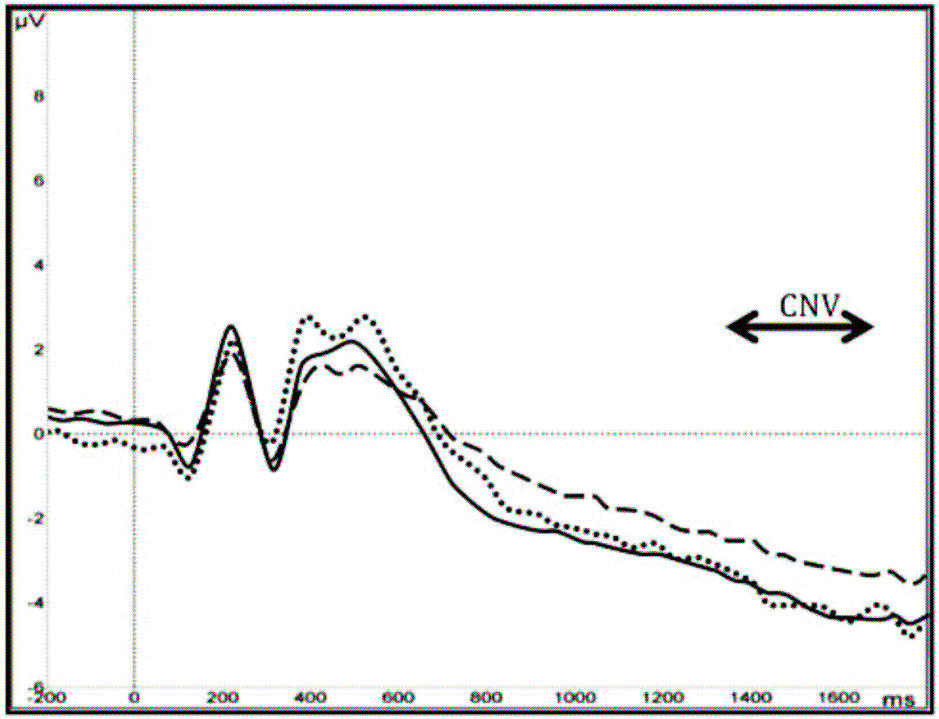
Answer 6

Where are the emotions?

- NEW DIRECTIONS CAN’T HARDLY WAIT

CNV neurophysiological marker of ADHD persistence

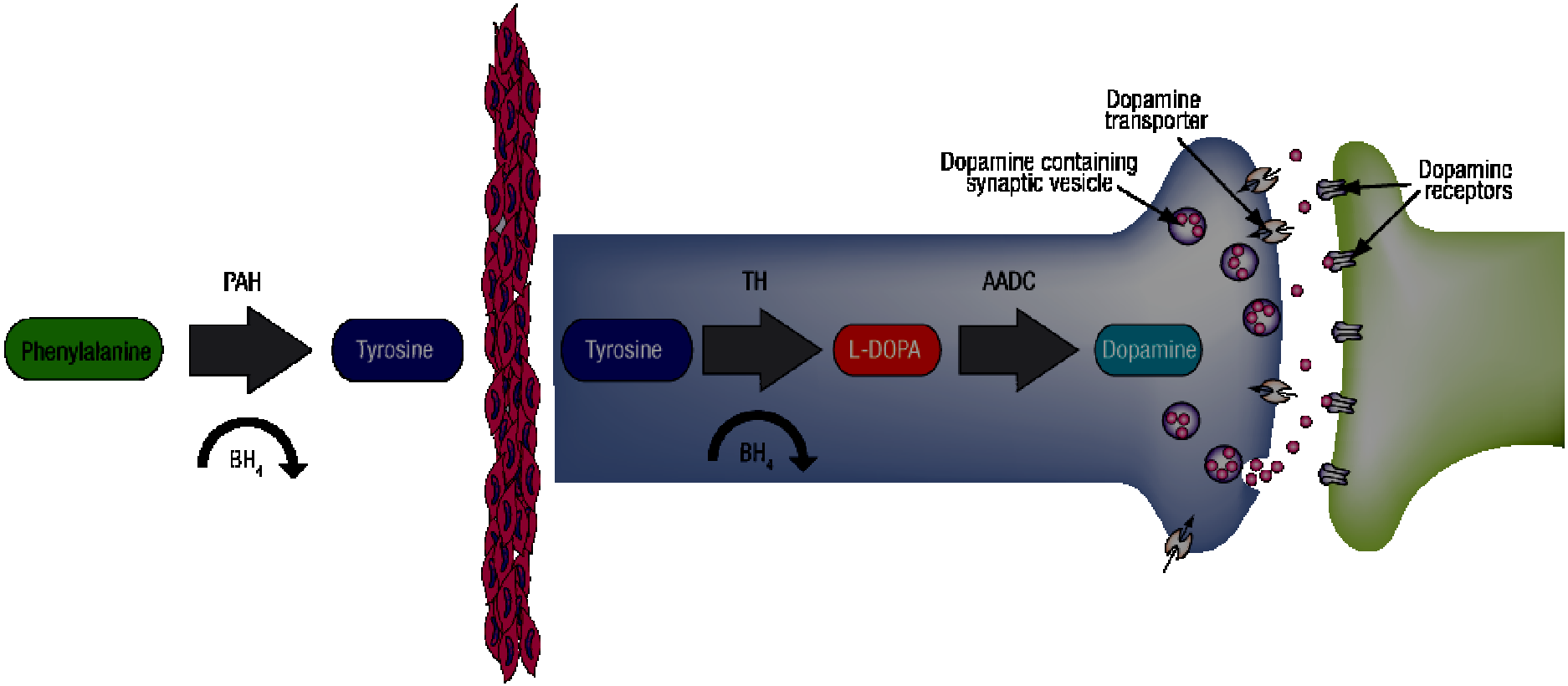
- ADHD persisters (dash), ADHD remitters (dot) and controls (solid)



Celeste H. M. et al. Cognitive and neurophysiological markers of ADHD persistence and remission. The British Journal of Psychiatry, 1–8. doi: 10.1192/bjp.bp.114.145185

Early treated phenylketonuria (PKU) is an interesting contrast group

Low dopamine availability links PKU and ADHD


Phenylalanine
PAH
Tyrosine
BH4
Tyrosine
TH
L-DOPA
AADC
Dopamine
BH4
Dopamine transporter
Dopamine containing synaptic vesicle
Dopamine receptors

Dopamine Is Critically Involved in Executive Function, Emotion, and Social Behavior

- Neurotransmitter related to attention, mood, and movement
- Precursor to norepinephrine and epinephrine

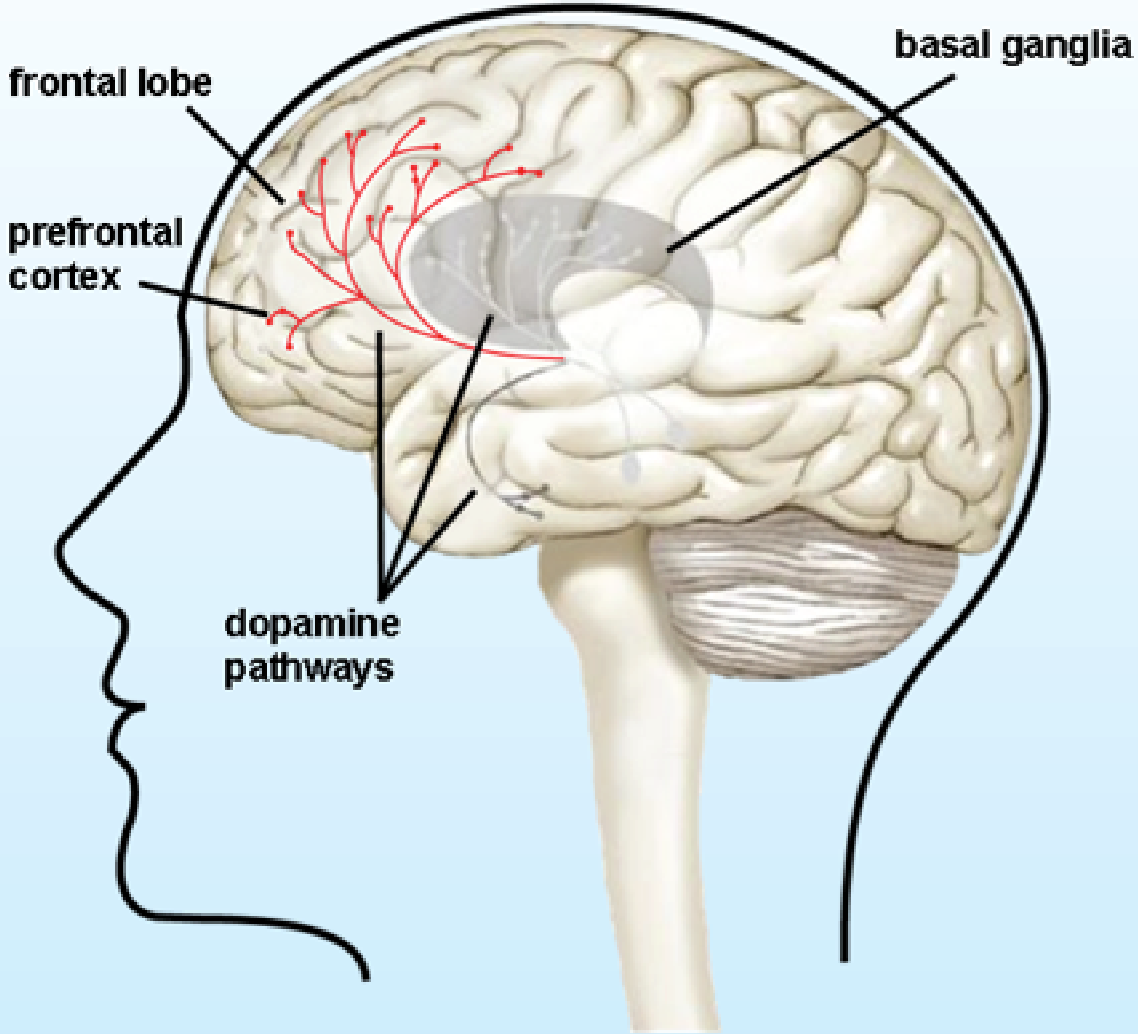


Image from http://nobelprize.org/nobel_prizes/medicine/laureates/2000/press.html

Figure 1. Executive functioning deficits; figure adapted from Anderson VA, et al. *Child Neuropsychol.* 2002;8(4):231-240.

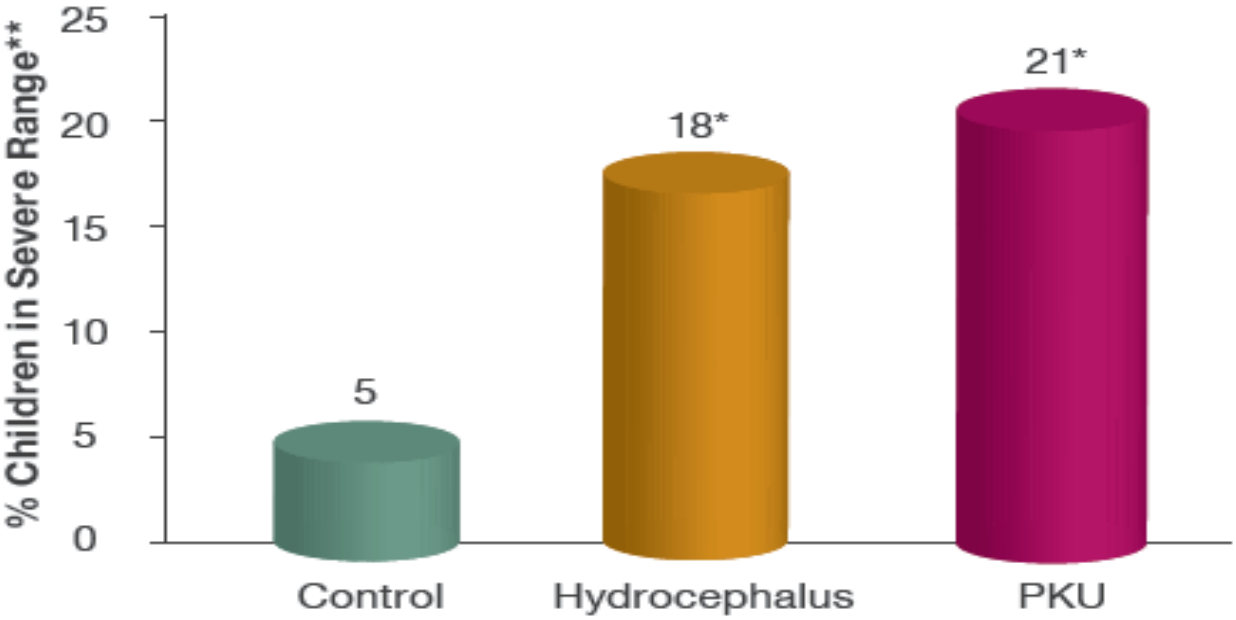


Figure 2. Attention problems in individuals with PKU; figure adapted from Arnold GL, et al. *J Inherit Metab Dis.* 2004;27:137–143.

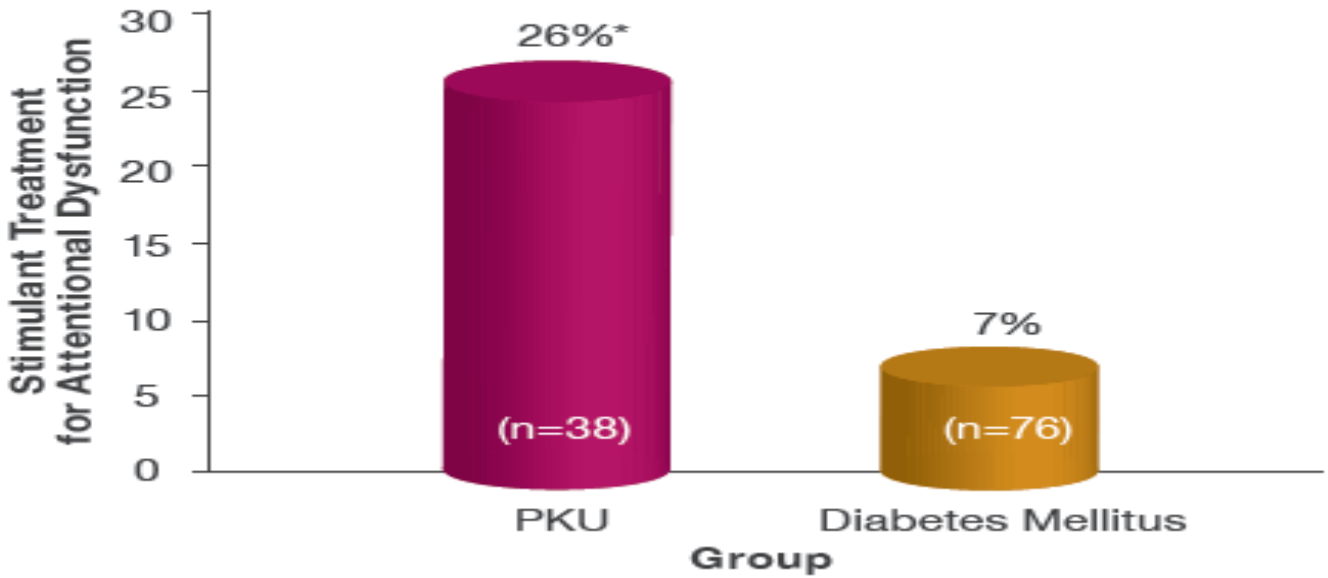
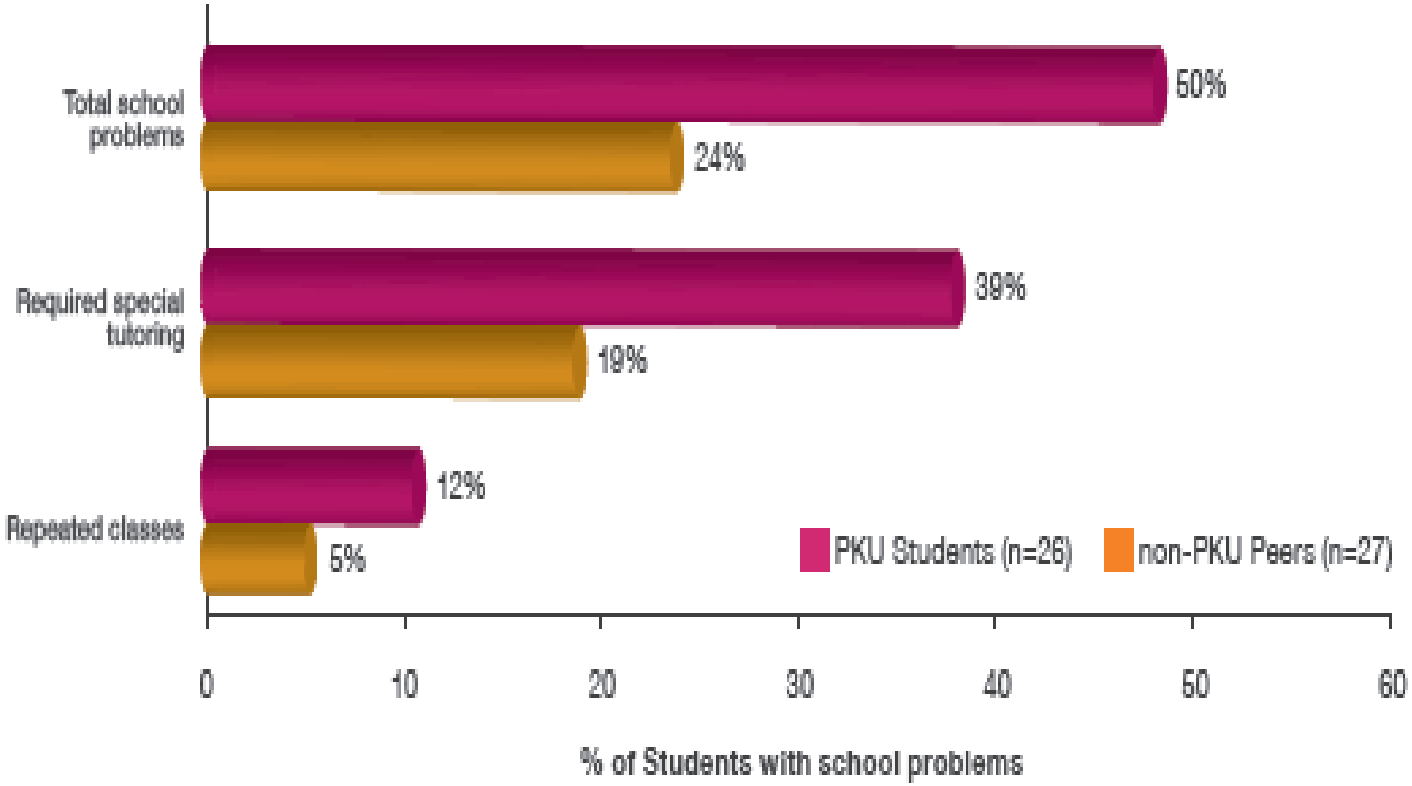
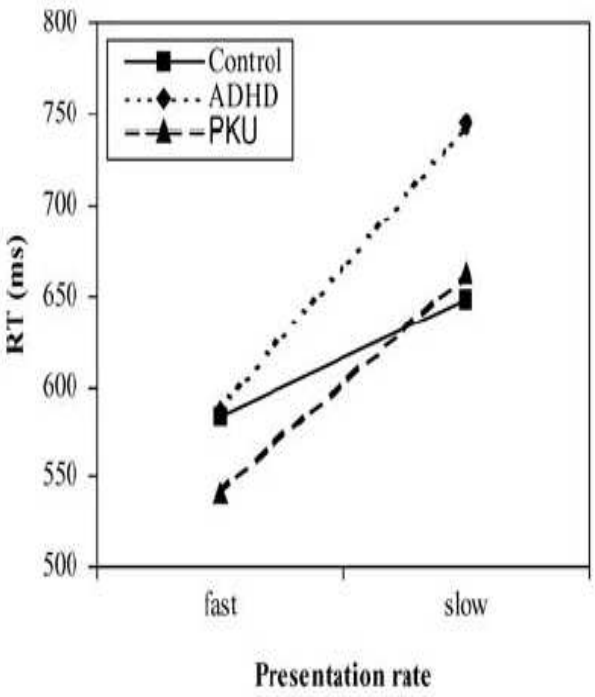
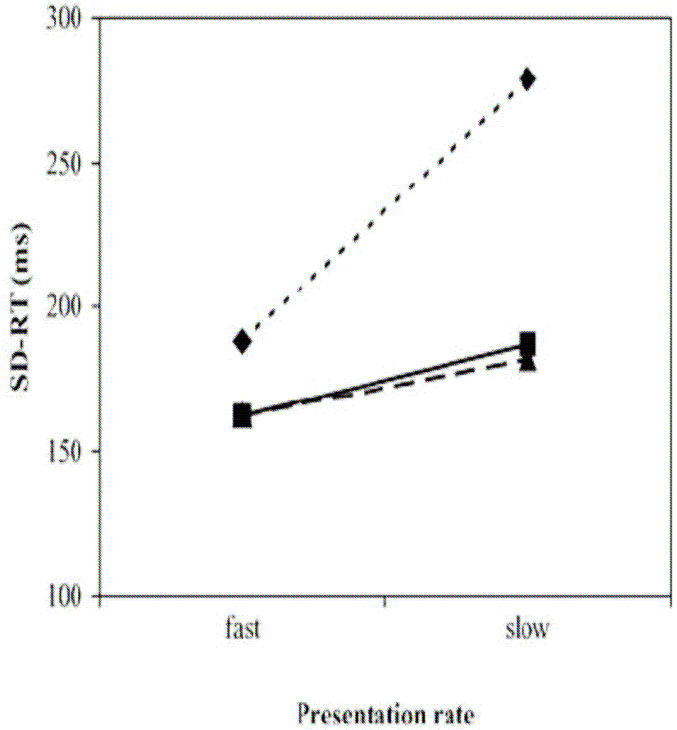


Figure 3. School problems in individuals with PKU.



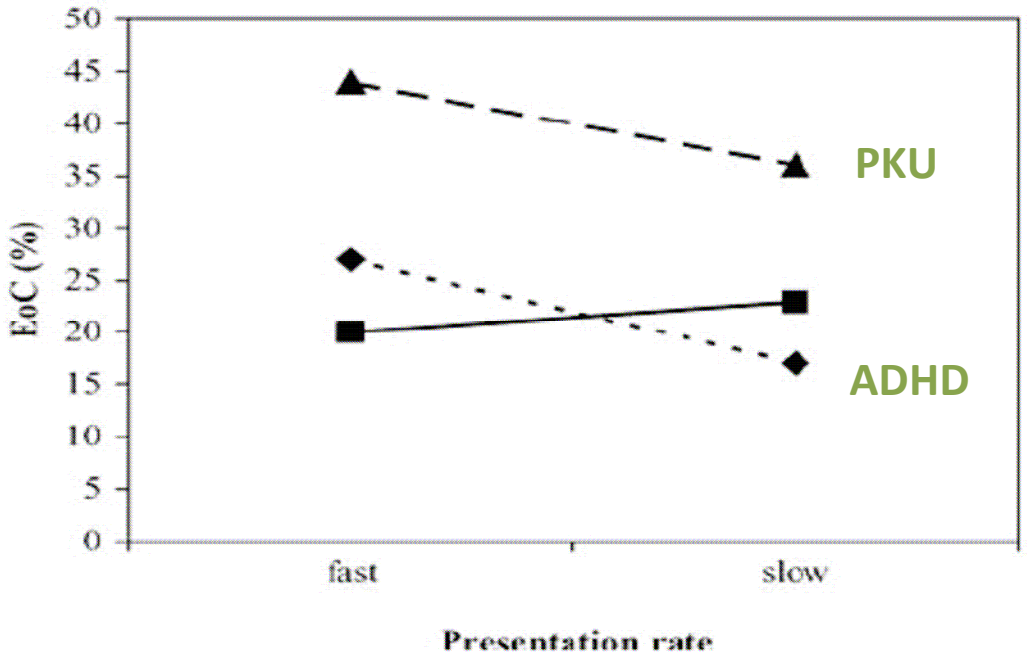
Direct comparison between ADHD and PKU



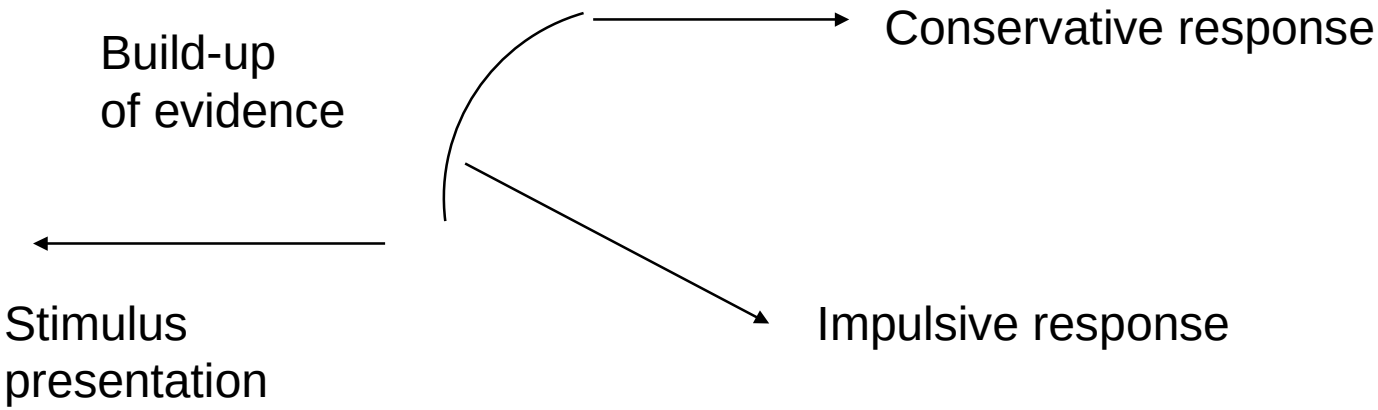


J Inherit Metab Dis. 2005;28(6):831-43.
State regulation and response inhibition in children with ADHD and children with early- and continuously treated phenylketonuria: an event-related potential comparison.
Wiersema JR[1], van der Meere JJ, Roeyers H.

Errors of the groups

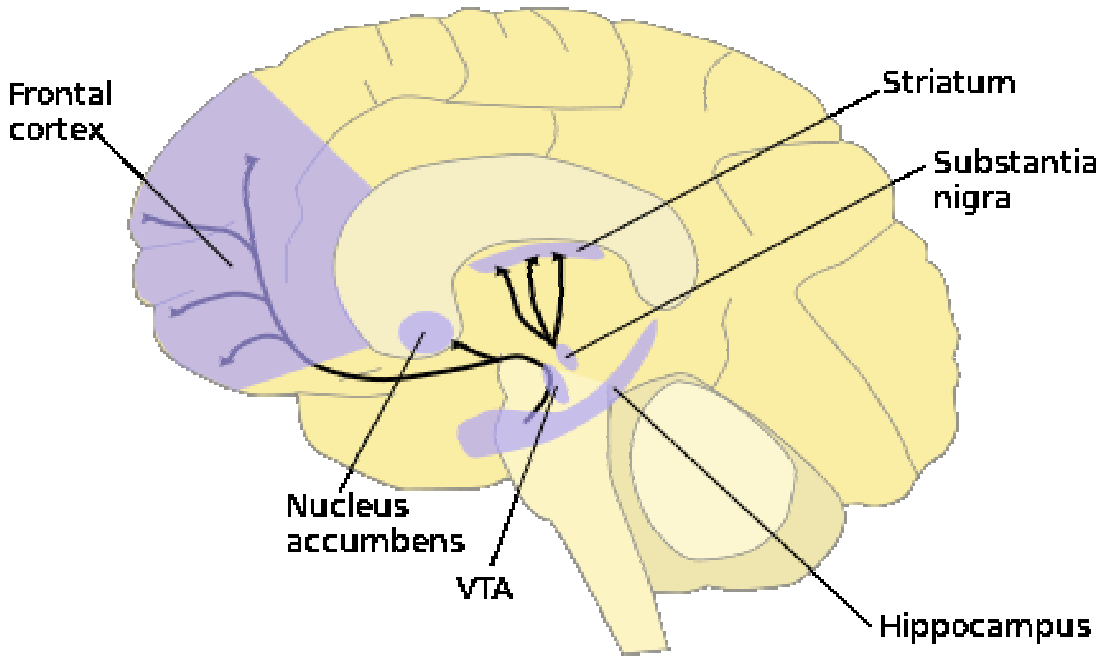


In conclusion:
PKUs fast but inaccurate responders: Pew Curve



Speed-accuracy trade-off

Is ADHD different from ETPKU in a particular dopamine circuit?



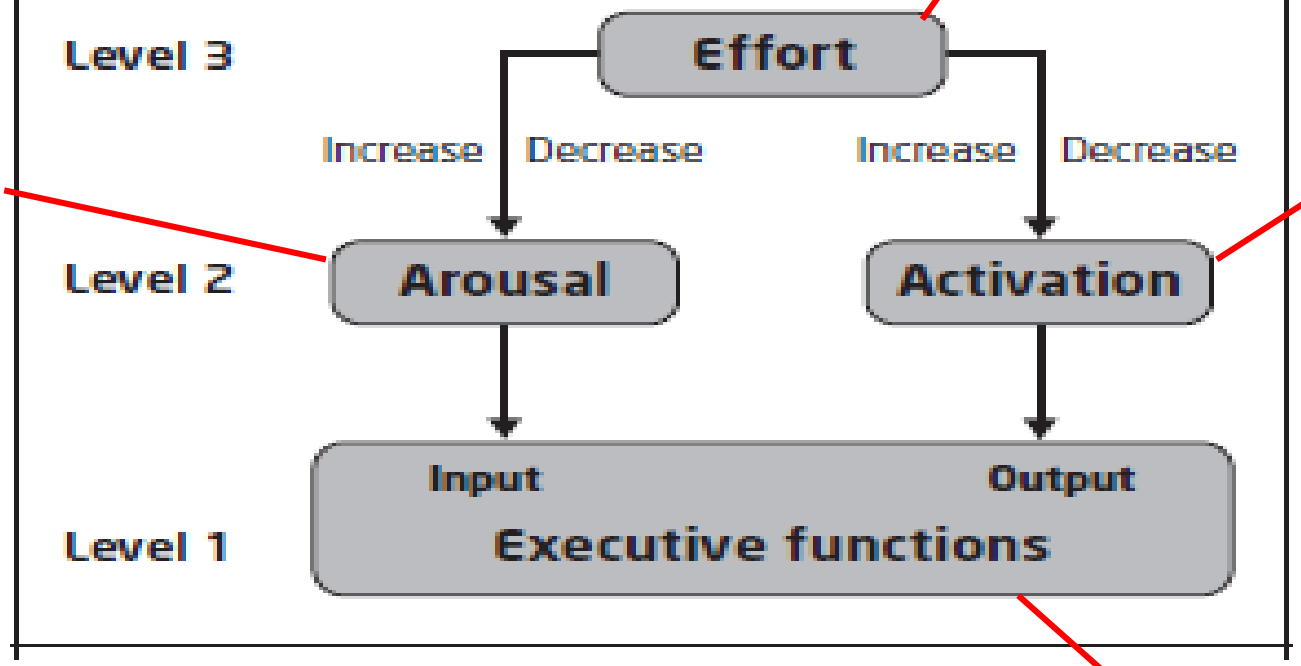
ADHD: State Regulation and Motivation

Jaap J van der Meere, Prof, PhD[1], Norbert A Börger, PhD[1], and Jan R Wiersema, PhD[2]
[1]Department of Clinical Neuropsychology, University of Groningen, The Netherlands, and
[2]Department of Experimental Clinical and Health Psychology, Ghent University, Belgium

CML – Psychiatry 2010;21(1):1–7.

Reward

Figure 1. The state regulation model.



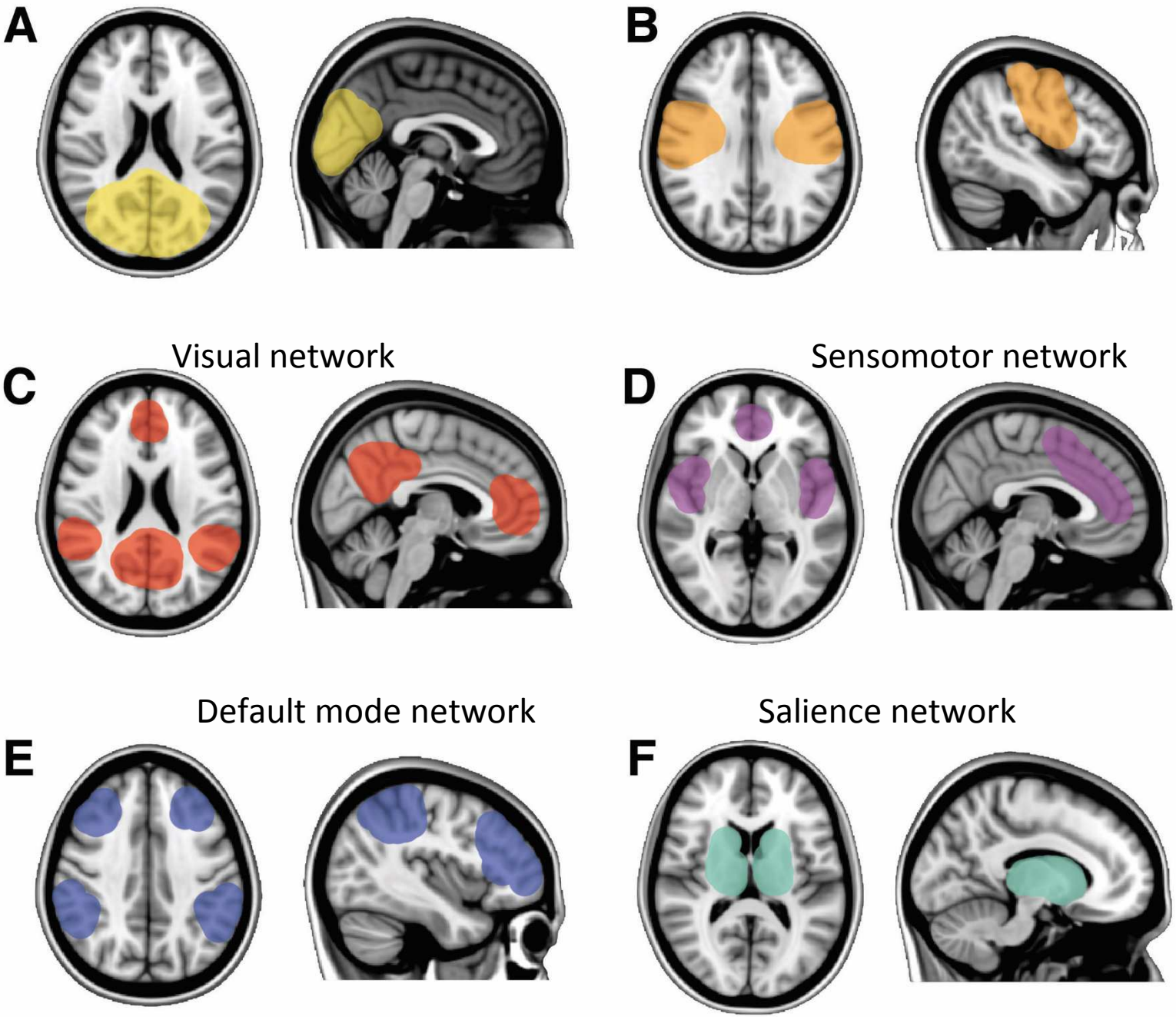
Noise

Event rate

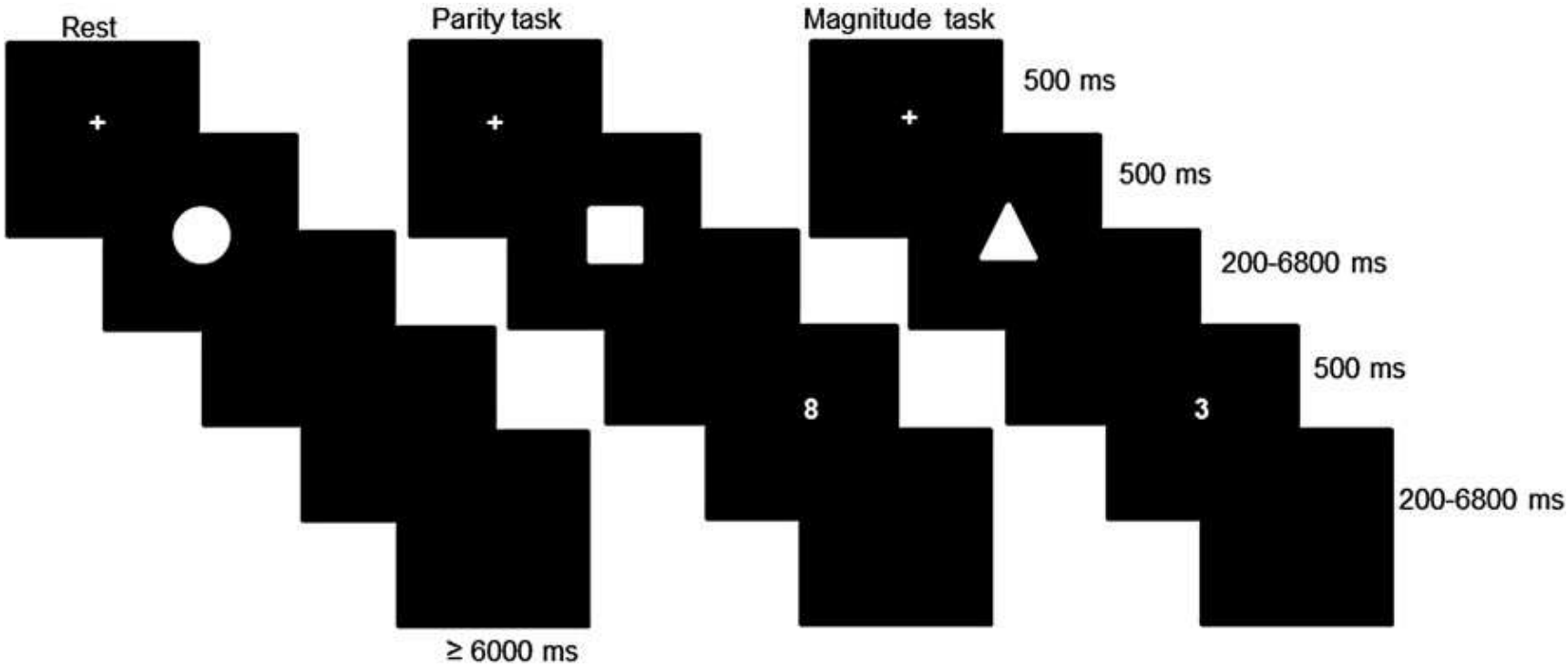
Task difficulty

NEW DIRECTIONS

ADHD BRAIN NETWORKS


A
B
Visual network
Sensomotor network
C
D
Default mode network
Salience network
E
F
Executive network
Striatum

State-to-state switching



Psychological Medicine (2016), **46**, 519–528. © Cambridge University Press 2015
doi:10.1017/S0033291715002019

ORIGINAL ARTICLE

Default mode network abnormalities during state switching in attention deficit hyperactivity disorder

J. Sidlauskaite[1*], E. Sonuga-Barke[1,2], H. Roeyers[1] and J. R. Wiersema[1]

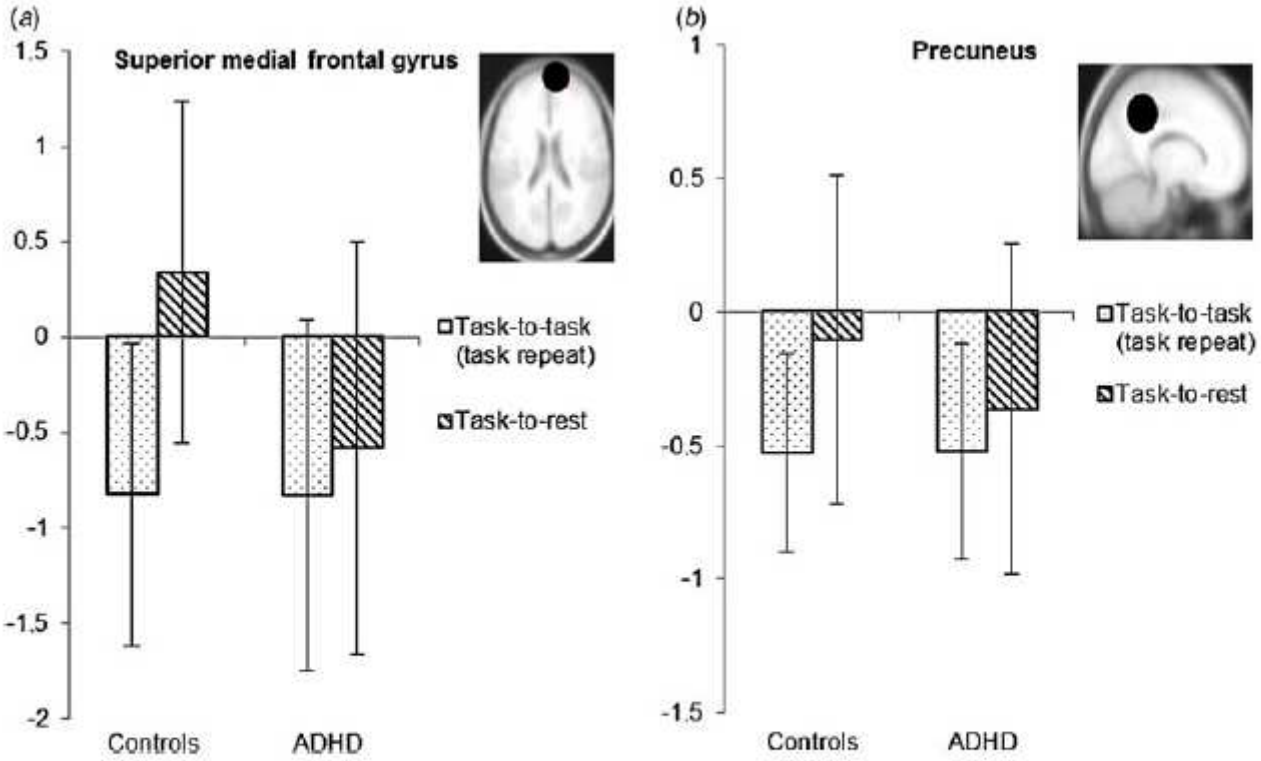


Fig. 3. Default mode network modulation anticipating task-to-task (task repeat) and task-to-rest switches in adults with ADHD and controls. The average parameter estimates (beta values ± S.D.) for the ADHD and control groups extracted from default mode network (DMN) regions. (*a*) Region of interest (ROI) analysis of the DMN superior medial frontal gyrus during task-to-task (task repeat) and task-to-rest cues. (*b*) ROI analysis of the posterior DMN precuneus during task-to-task (task repeat) and task-to-rest cues.

Danckert et al., Boredom, sustained attention and the default mode network. Exp Brain Res 2016.

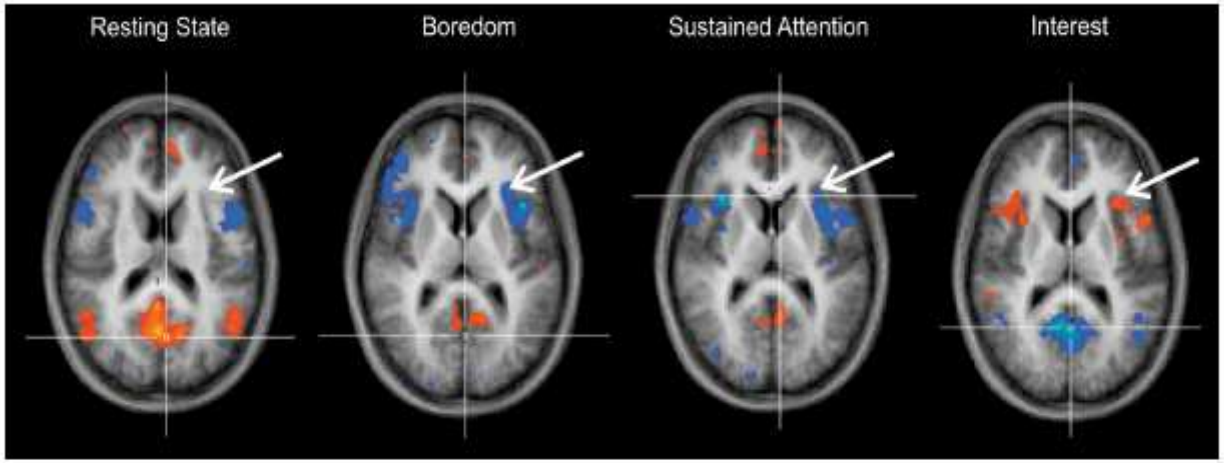
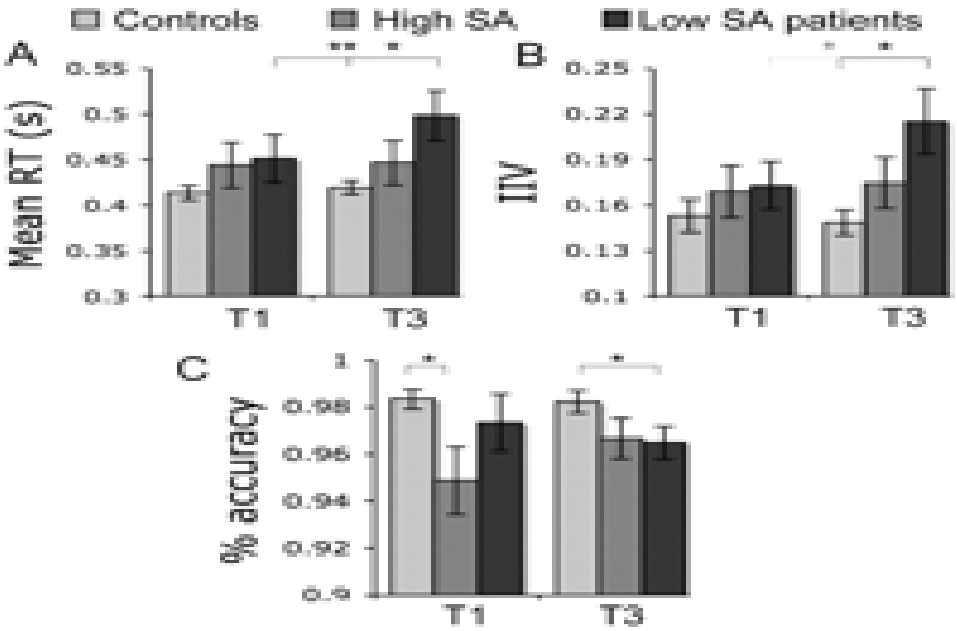
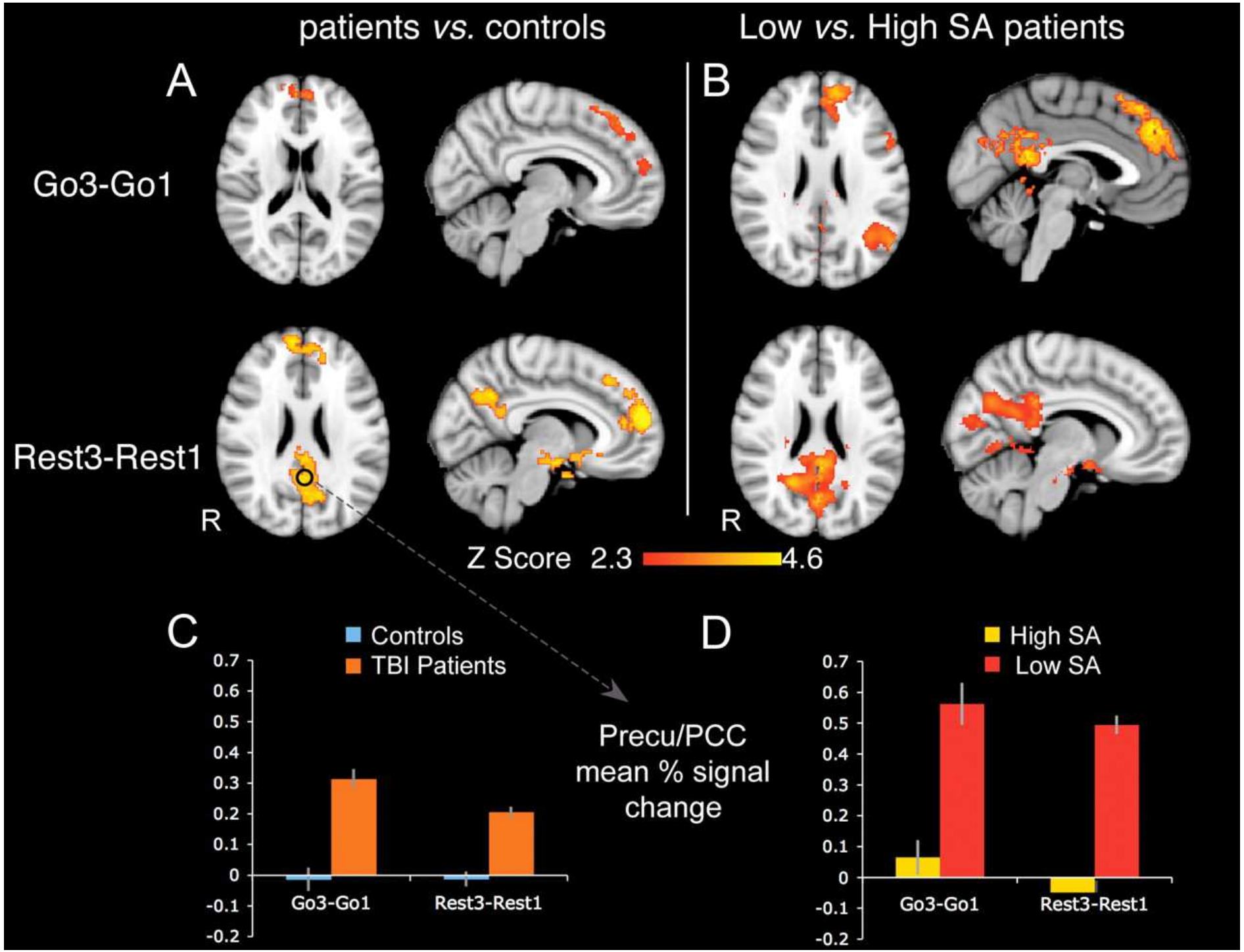


Fig. 3 Axial images for each condition showing the absence of any activity in the anterior insula for the resting state scan, activity that was anticorrelated with DMN clusters in the boredom mood induction and sustained attention scans, and finally, correlated activity in the same region for the interest mood induction

Default Mode Network connectivity predicts sustained attention deficits after traumatic brain injury. Bonnelle et al., J Neuroscience, 2011, 31.




patients vs. controls
Low vs. High SA patients
A
B
Go3-Go1
Rest3-Rest1
R
R
Z Score 2.3
4.6
C
Controls
TBI Patients
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
Go3-Go1
Rest3-Rest1
Precu/PCC
mean % signal
change
D
High SA
Low SA
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
Go3-Go1
Rest3-Rest1