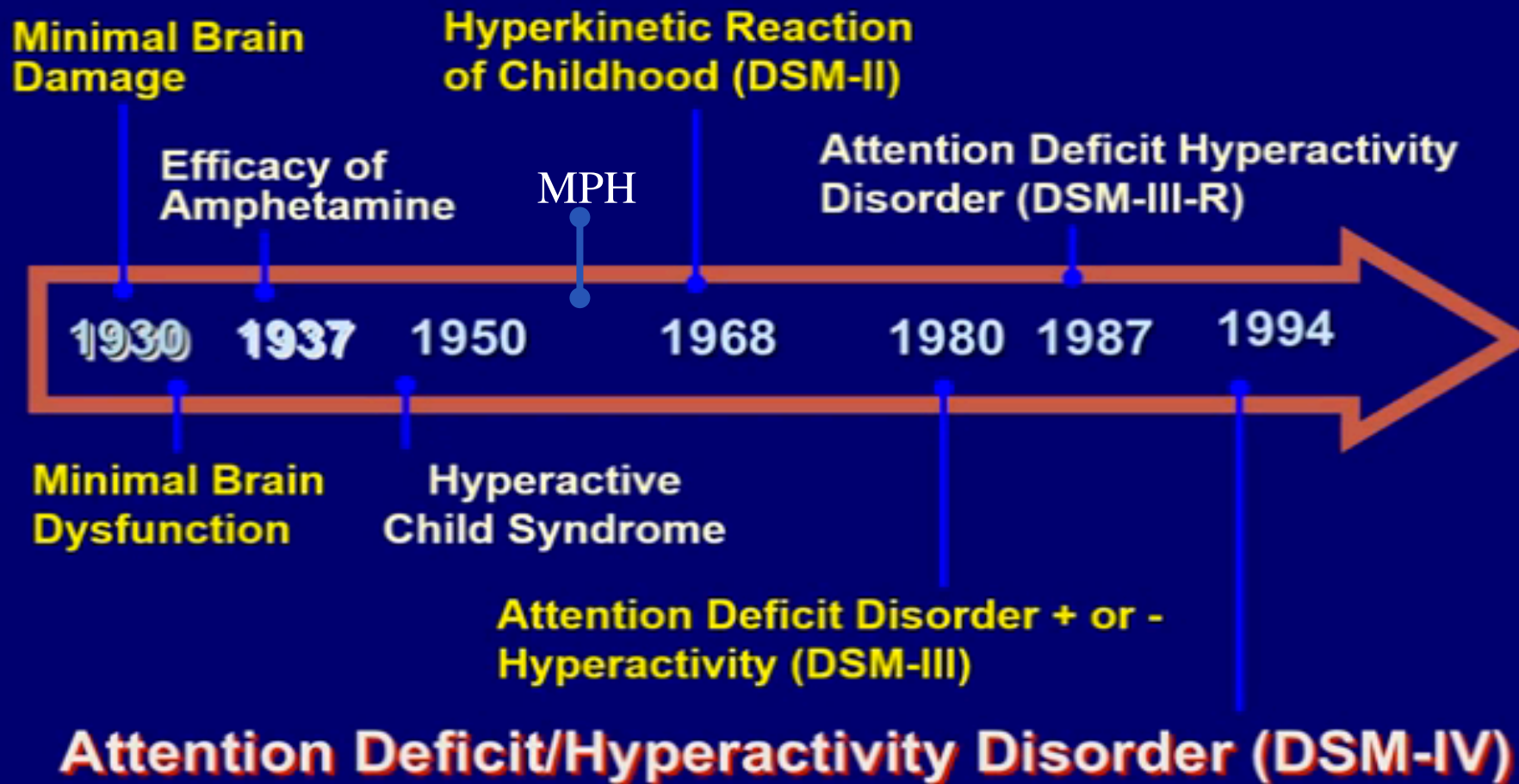


Apport de la neuroimagerie à la compréhension des symptômes du TDAH: de l'inhibition à l'aversion du délai.

Michel Habib
CHU de Marseille

ADHD

Historical Timeline



Attention Deficit Hyperactive Disorder

Must meet **at least 6** of the criteria within A1 and/or A2, and have experienced for at least the past 6 months.

A1: Inattention

- a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).
- b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or reading lengthy writings).
- c. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).
- d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked; fails to finish schoolwork, household chores, or tasks in the workplace).
- e. Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized, work; poor time management; tends to fail to meet deadlines).
- f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, or reviewing lengthy papers).
- g. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, or mobile telephones).
- h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).
- i. Is often forgetful in daily activities (e.g., chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

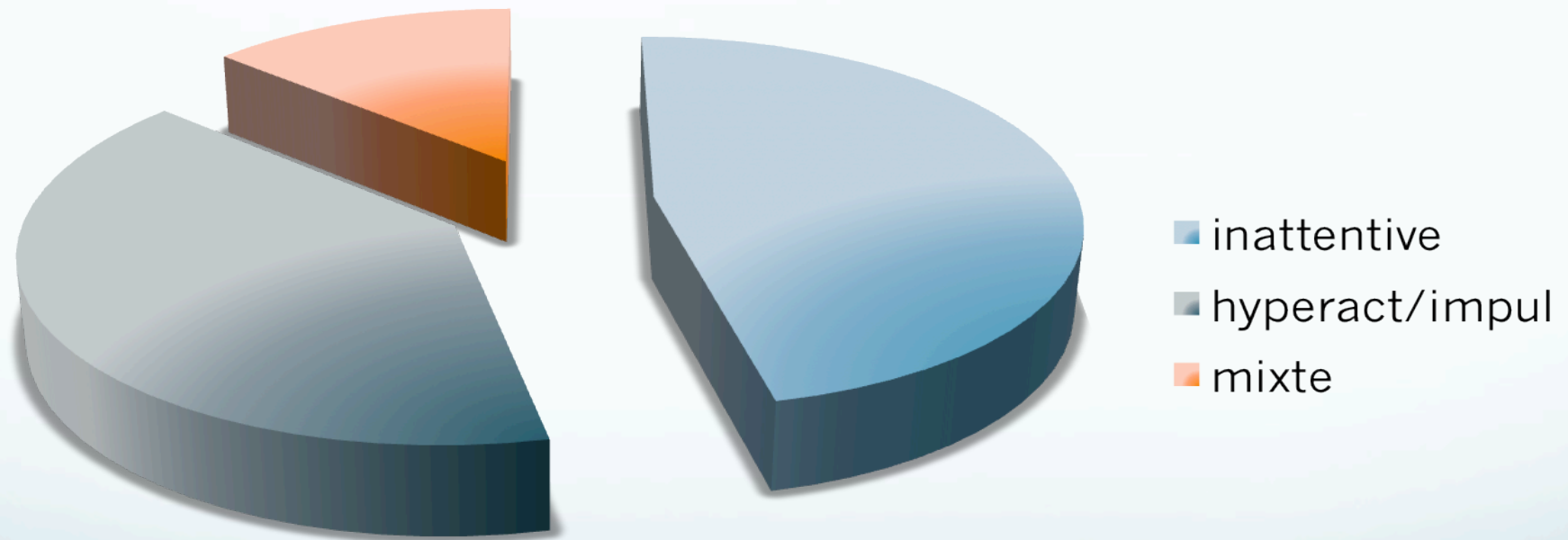
A2: Hyperactivity and Impulsivity

- a. Often fidgets with or taps hands or feet or squirms in seat.
- b. Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, office or other workplace, or in other situations that require remaining seated).
- c. Often runs about or climbs in situations where it is inappropriate. (In adolescents or adults, may be limited to feeling restless).
- d. Often unable to play or engage in leisure activities quietly.
- e. Is often "on the go," acting as if "driven by a motor" (e.g., is unable or uncomfortable being still for an extended time, as in restaurants, meetings, etc; may be experienced by others as being restless and difficult to keep up with).
- f. Often talks excessively.
- g. Often blurts out an answer before a question has been completed (e.g., completes people's sentences and "jumps the gun" in conversations, cannot wait for next turn in conversation).
- h. Often has difficulty waiting his or her turn (e.g., while waiting in line).
- i. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people's things without asking or receiving permission, adolescents or adults may intrude into or take over what others are doing).

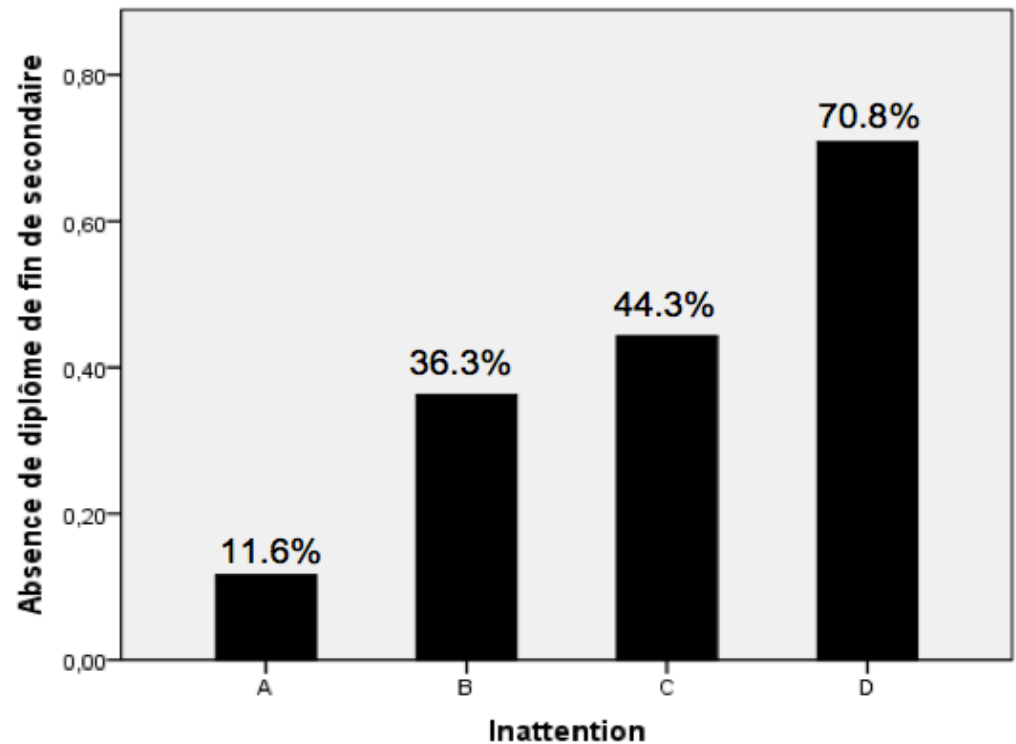
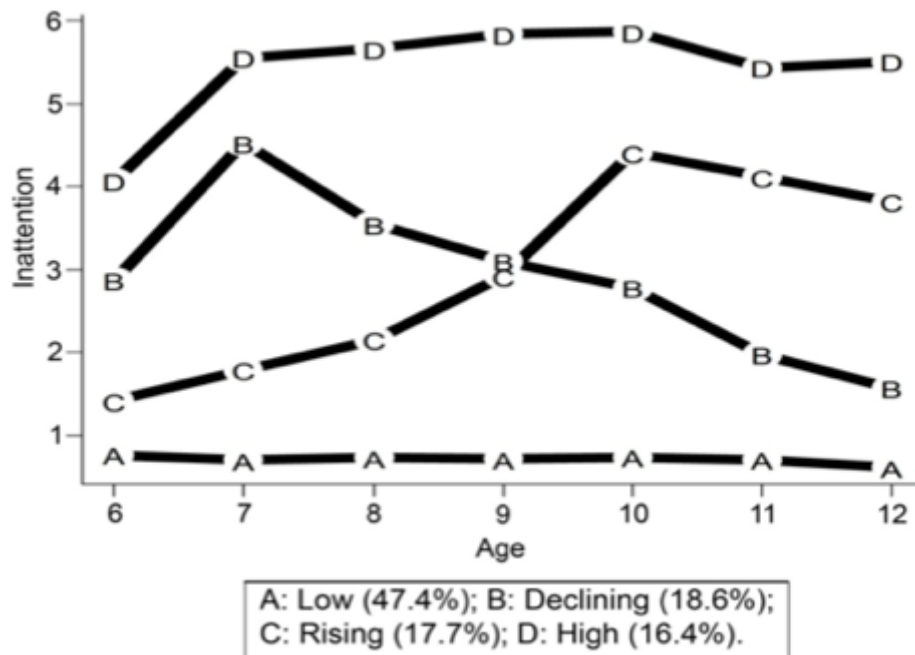
- B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12.
- C. Criteria for the disorder are met in two or more settings (e.g., at home, school or work, with friends or relatives, or in other activities).
- D. There must be clear evidence that the symptoms interfere with or reduce the quality of social, academic, or occupational functioning.
- E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).

Incidence en France : 3,5%

Lecendreau et al., 2010



Trajectoires des symptômes d'inattention et résultats scolaires dans le TDAH (Pingault et al., Am Journal of Psychiatry, 2011)



« Inattention rather than hyperactivity during elementary school significantly predicts long-term educational attainment. Children with attention problems, regardless of hyperactivity, need preventive intervention early in their development. »

Neurologie du TDAH

- Deux modèles qui s'opposent
 - modèle classique : TDAH = défaut d'inhibition de l'action (Barkley)
 - Ref : systèmes de contrôle exécutif : "cool" executive*
 - Modèle plus récent : TDAH = défaut de capacité à différer la récompense (delay aversion = "hot executive*")
 - Ref : modèle des circuits de la récompense
 - Cf. comorbidité troubles des conduites (CD) ~ 50%
- Les pistes actuelles : défaut de connectivité

*Zelazo & Müller, 2002

Impulsivité : une définition bio-psycho-sociale

- **A predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to themselves or others**

(Moeller et al., Am J Psychiatry, 2001).

- Implique:
 - Une prédisposition, en partie génétique
 - Une réaction rapide, voire brutale
 - Non planifiée ou empêchée d'être planifiée
 - Aux stimuli externes mais aussi internes
 - Constituant une prise de risques pour soi et les autres
 - Sans bénéfice secondaire attendu

L'impulsivité dans le TDAH

cognitive



Conners'
CPT II
Continuous Performance Test II

comportementale



affective

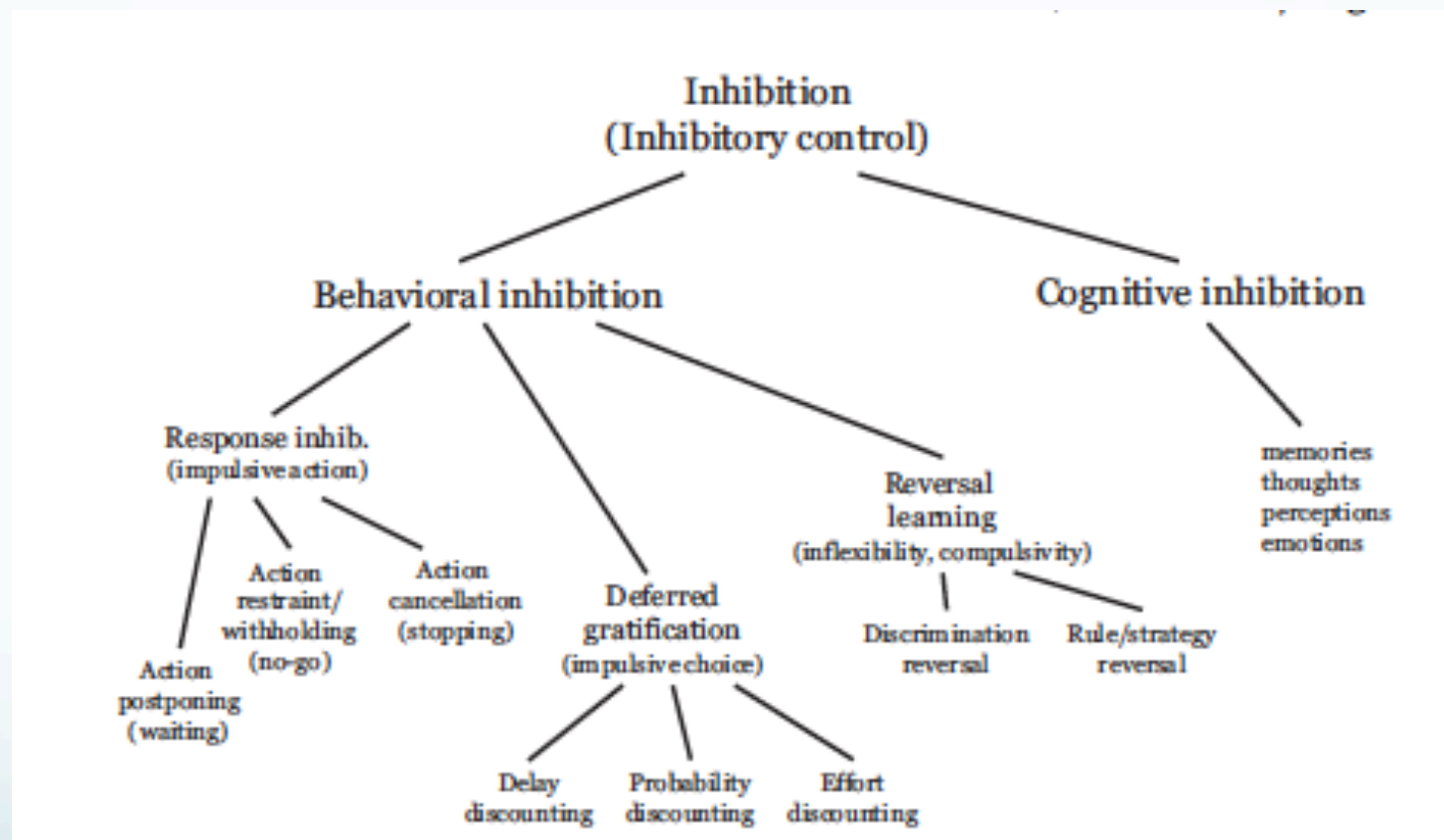


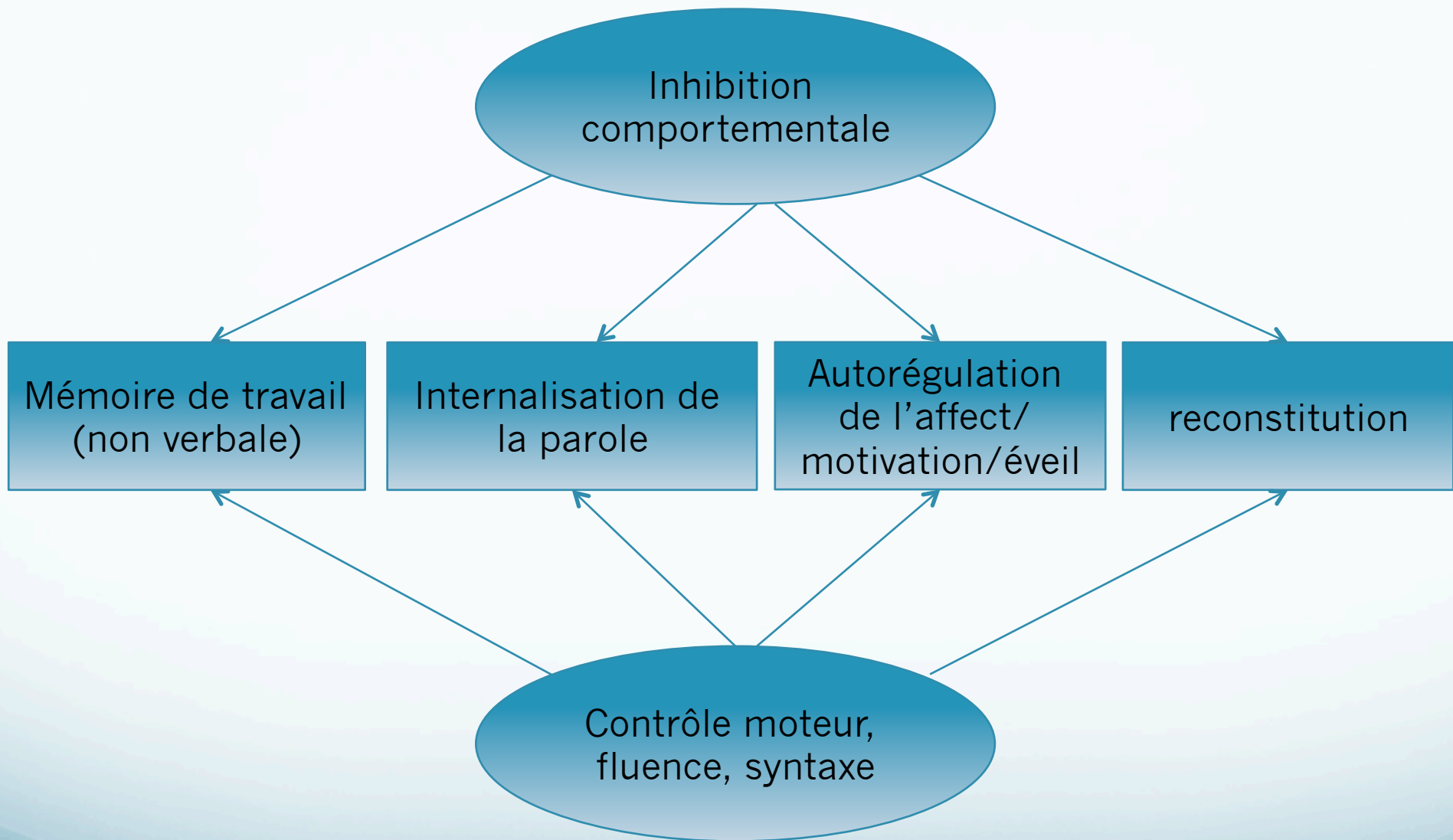
I/ Le modèle classique

= inhibition de l'action (Barkley)

Imagerie fonctionnelle dans des protocoles d'inhibition (go-no-go, stop signal, flanker, Stroop....)

- Hypofonctionnement du cortex frontal
- Notion de dysfonctionnement exécutif





Barkley, R.A. (1997; 2007)

ADVANCING THE NEUROSCIENCE OF ADHD

Structural Brain Imaging of Attention-Deficit/Hyperactivity Disorder

Larry J. Seidman, Eve M. Valera, and Nikos Mal

♦ Human Brain Mapping 31:904–916 (2010) ♦

ELSEVIER
SAUNDERS

Psychiatr Clin N Am
27 (2004) 323–347

Brain function and structure
attention-deficit/hyperactiv

Larry J. Seidman, PhD^{a-f,*}, Eve M.
George Bush, MD, MS



278

Neuropsychopharmacology **REVIEWS** (2010) 35, 27
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www.neuropsychopharmacol

Is the ADHD Brain Wired Differently? A Review on Structural and Functional Connectivity in Attention Deficit Hyperactivity Disorder

Kerstin Konrad,^{1,2,3*} and Simon B. Eickhoff^{2,3,4}

¹Child Neuropsychology Section, Department of Child and Adolescent Psychiatry and Psychotherapy, University Hospital of the RWTH Aachen, Germany

²Institute of Neuroscience and Medicine (INM-2, INM-3), Research Center Juelich, Germany

³JARA – Translational Brain Medicine, Germany

⁴Department of Psychiatry and Psychotherapy, University Hospital of the RWTH Aachen University, Germany

Attention-Deficit/Hyperactivity Disorder and Attention Networks

George Bush^{*,1,2,3,4}

Eur Arch Psychiatry Clin Neurosci (2006) 256 [Suppl 1]:I/32–I/41

Marc Schneider · Wolfgang Retz · Andrew Coogan · Johannes Thome · Michael Rösler

Anatomical and functional brain imaging in adult attention-deficit/hyperactivity disorder (ADHD) – A neurological view

MENTAL RETARDATION AND DEVELOPMENTAL DISABILITIES
RESEARCH REVIEWS 9: 184–195 (2003)

A REVIEW OF THE BIOLOGICAL BASES OF ADHD: WHAT HAVE WE LEARNED FROM IMAGING STUDIES?

Sarah Durston^{*}

Department of Child and Adolescent Psychiatry, University Medical Center Utrecht, the Netherlands and Sackler Institute for Developmental Psychobiology, Weill Medical College of Cornell University, New York, New York

Réseau fronto-pariétal dorsal (bilatéral) : attention endogène; génération d'un « set attentionnel » applicable lors du traitement du stimulus dans une tâche donnée

Sillon intra-pariétal/
Lobule pariétal supérieur

Frontal Eye Field

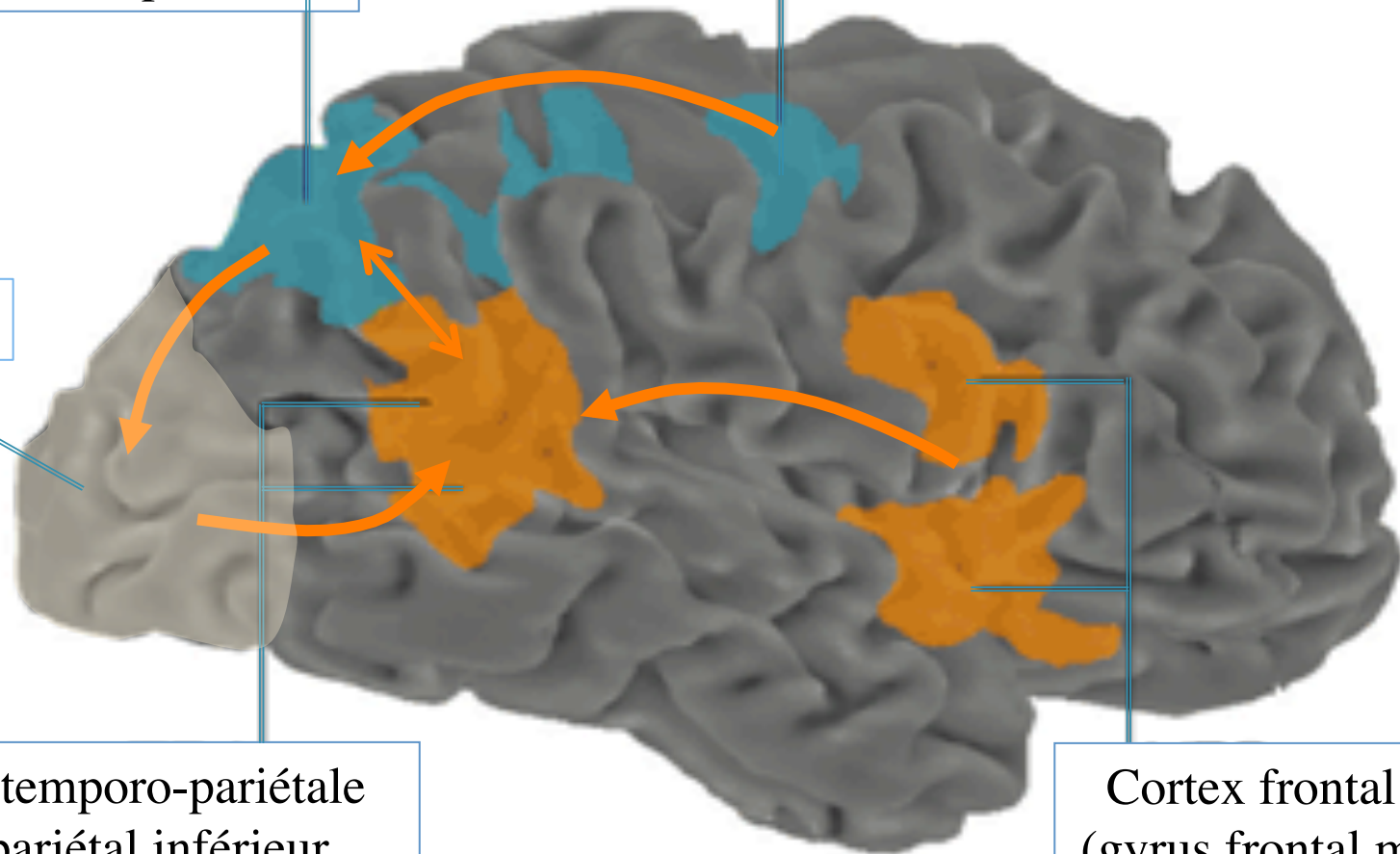
Cortex visuel

Jonction temporo-pariétale
(lobule pariétal inférieur,
gyrus temporal supérieur)

Cortex frontal ventral
(gyrus frontal moyen et
inférieur)

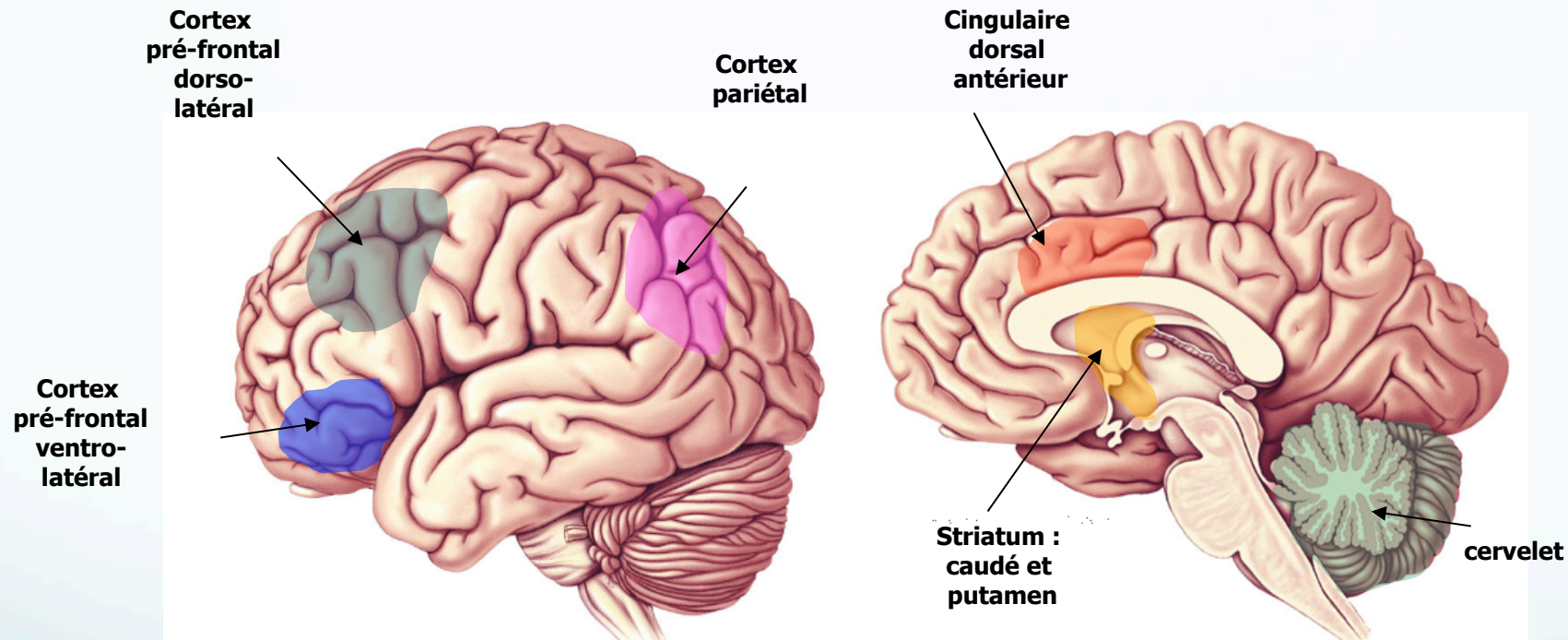
Corbetta et al., 2002

Réseau fronto-pariétal ventral (fortement latéralisé à droite) : attention exogène; détection de stimuli comportementalement pertinents. Système d'alerte pour le système dorsal.



Attention-Deficit/Hyperactivity Disorder and Attention Networks

George Bush^{*,1,2,3,4}



Les principales régions cérébrales dysfonctionnelles dans le TDAH (méta-analyse)

Anterior Cingulate Cortex Dysfunction in Attention-Deficit/Hyperactivity Disorder Revealed by fMRI and the Counting Stroop

George Bush, Jean A. Frazier, Scott L. Rauch, Larry J. Seidman, Paul J. Whalen, Michael A. Jenike, Bruce R. Rosen, and Joseph Biederman

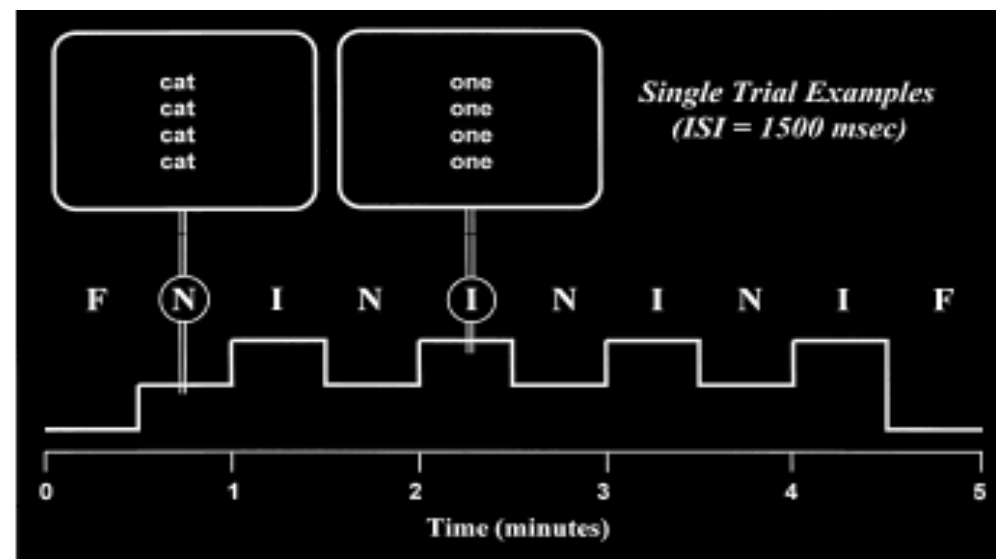
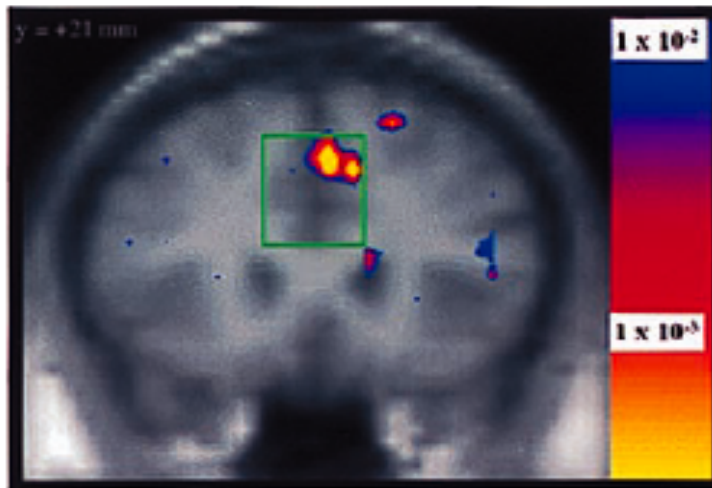
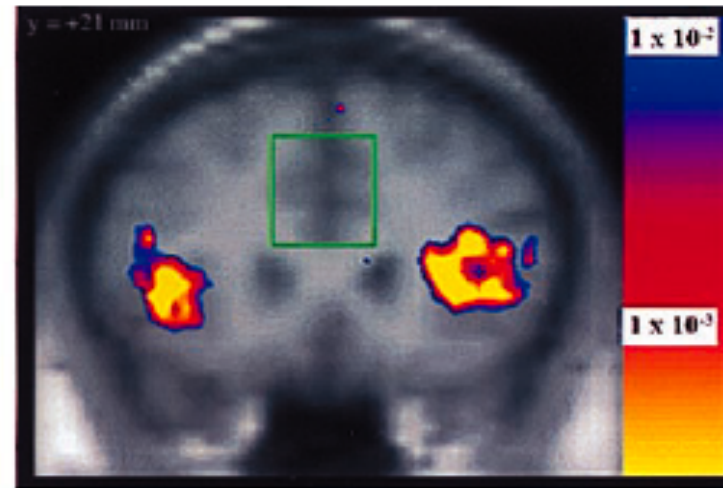


Figure 1. The Counting Stroop task: trial examples and block design. The top portion of this combination figure depicts examples of single trials for the two types of stimuli. Subjects were told that they would see sets of one to four identical words appear on the screen, and were instructed to report, via button-press, the number of words in each set, regardless of word meaning. During “neutral” trials, common animal names (dog, cat, bird, or mouse) were used. During “interference” blocks, the words consisted of number names (one, two, three, or four).

Normal Controls



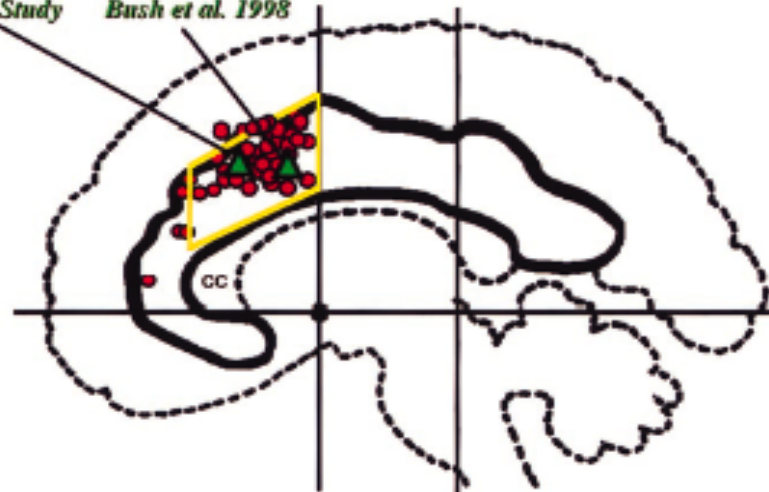
ADHD



Counting Stroop Studies

Present Study

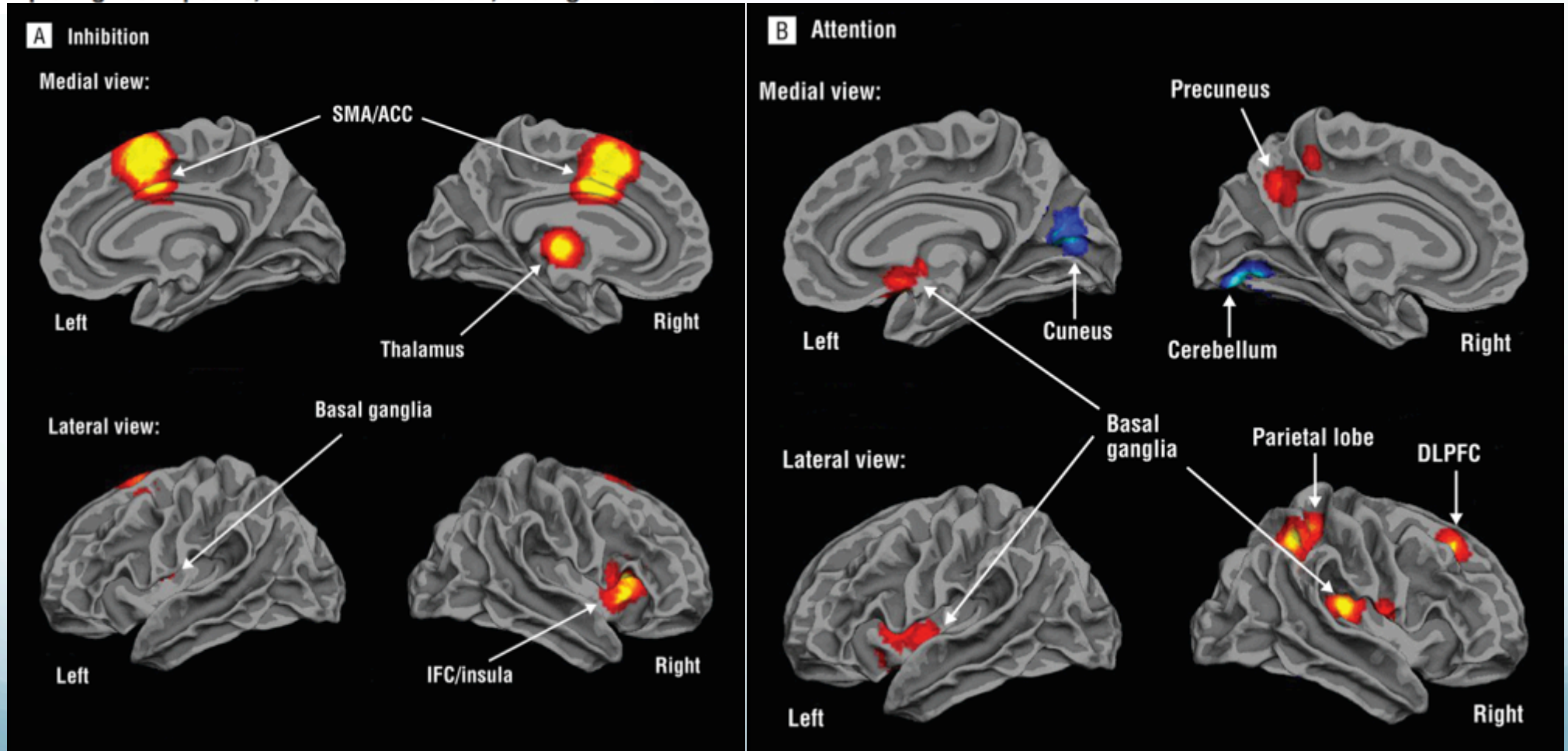
Bush et al. 1998



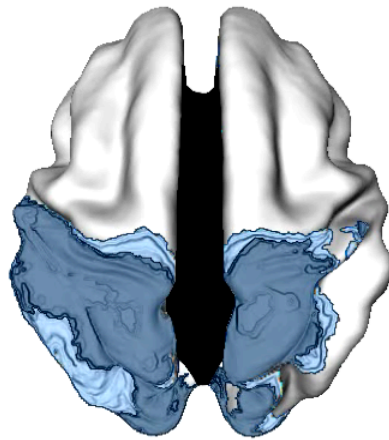
Meta-analysis of Functional Magnetic Resonance Imaging Studies of Inhibition and Attention in Attention-deficit/Hyperactivity Disorder

Exploring Task-Specific, Stimulant Medication, and Age

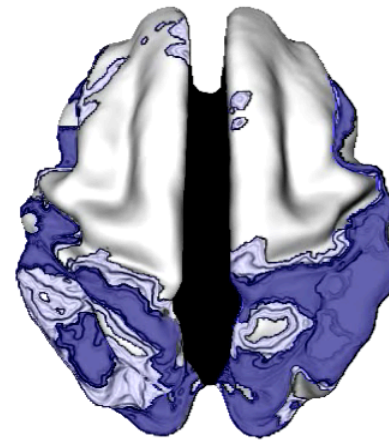
Twenty-one data sets were included for inhibition (287 patients with ADHD and 320 control subjects), and 13 data sets were included for attention (171 patients with ADHD and 178 control subjects).



AGE: 5

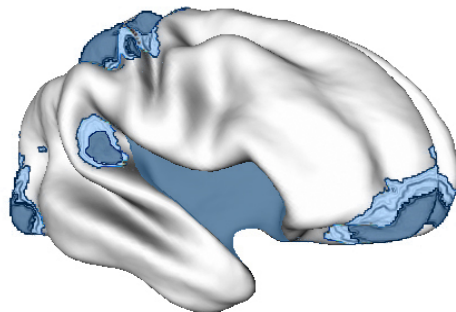


ADHD

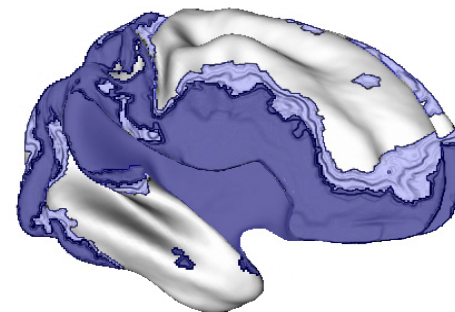


**TYPICALLY DEVELOPING
CONTROLS**

AGE: 6



ADHD

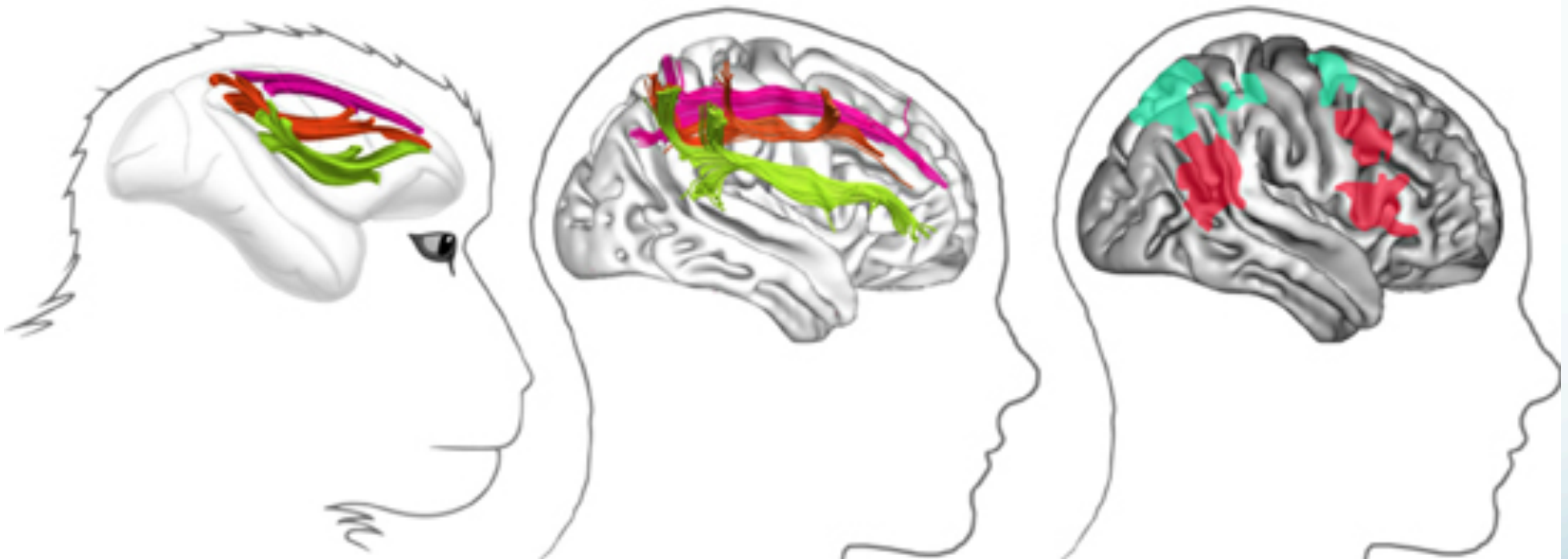


**TYPICALLY DEVELOPING
CONTROLS**

Bilatéral et
symétrique

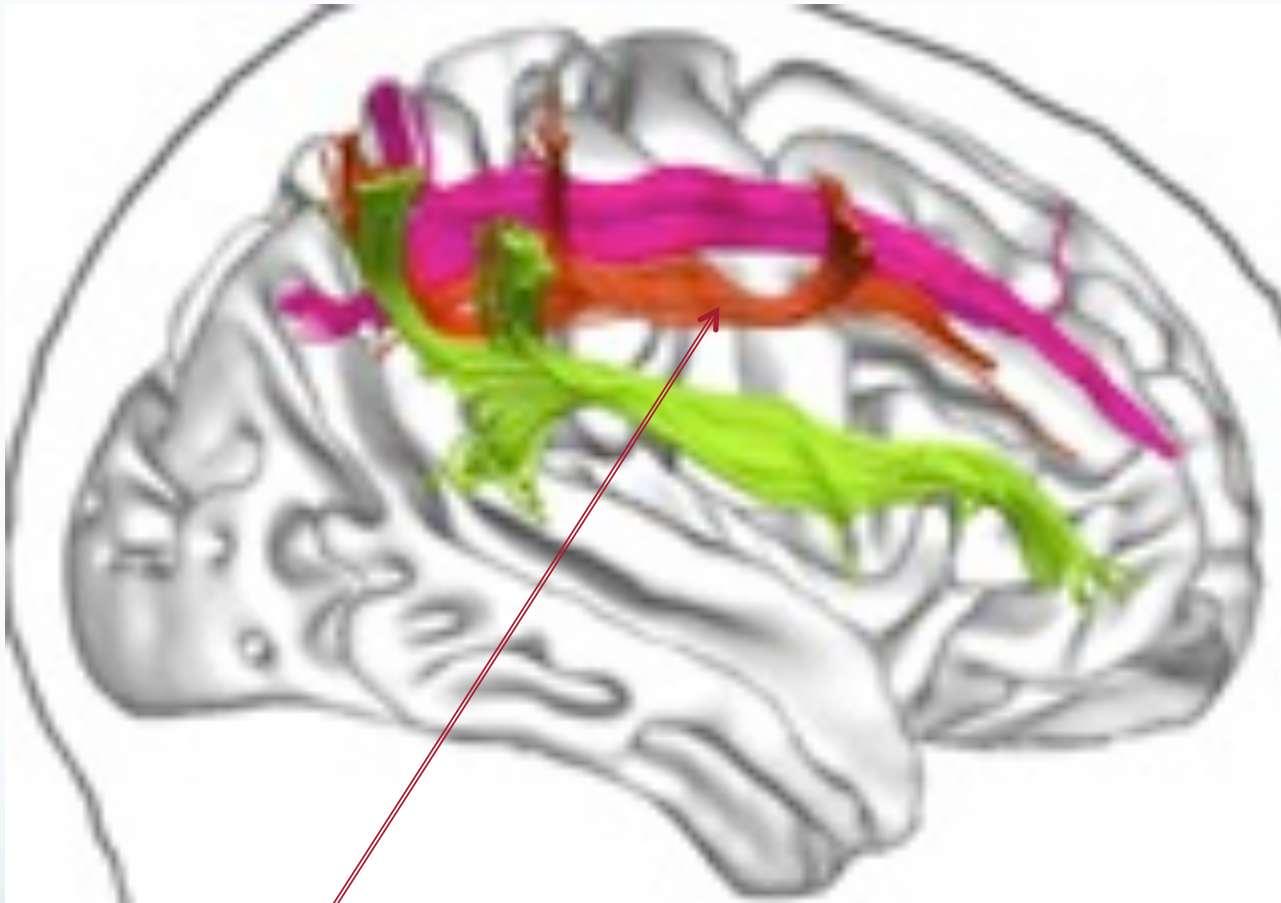
« Dorsal attentional
network » : *orientation
spatiale*

SLF I SLF II SLF III DAN VAN



Fortement
latéralisé à droite

« Ventral attentional
network » : *détection
événements motivants*



The SLF II connects the parietal component of the VAN to the prefrontal component of the DAN

Review

Diffusion tensor imaging in attention deficit/hyperactivity disorder: A systematic review and meta-analysis

Hanneke van Ewijk^{a,*}, Dirk J. Heslenfeld^{a,b}, Marcel P. Zwiers^c, Jan K. Buitelaar^{c,d}, Jaap Oosterlaan^a

^a Department of Clinical Neuropsychology, VU University Amsterdam, The Netherlands

^b Department of Cognitive Psychology, VU University Amsterdam, The Netherlands

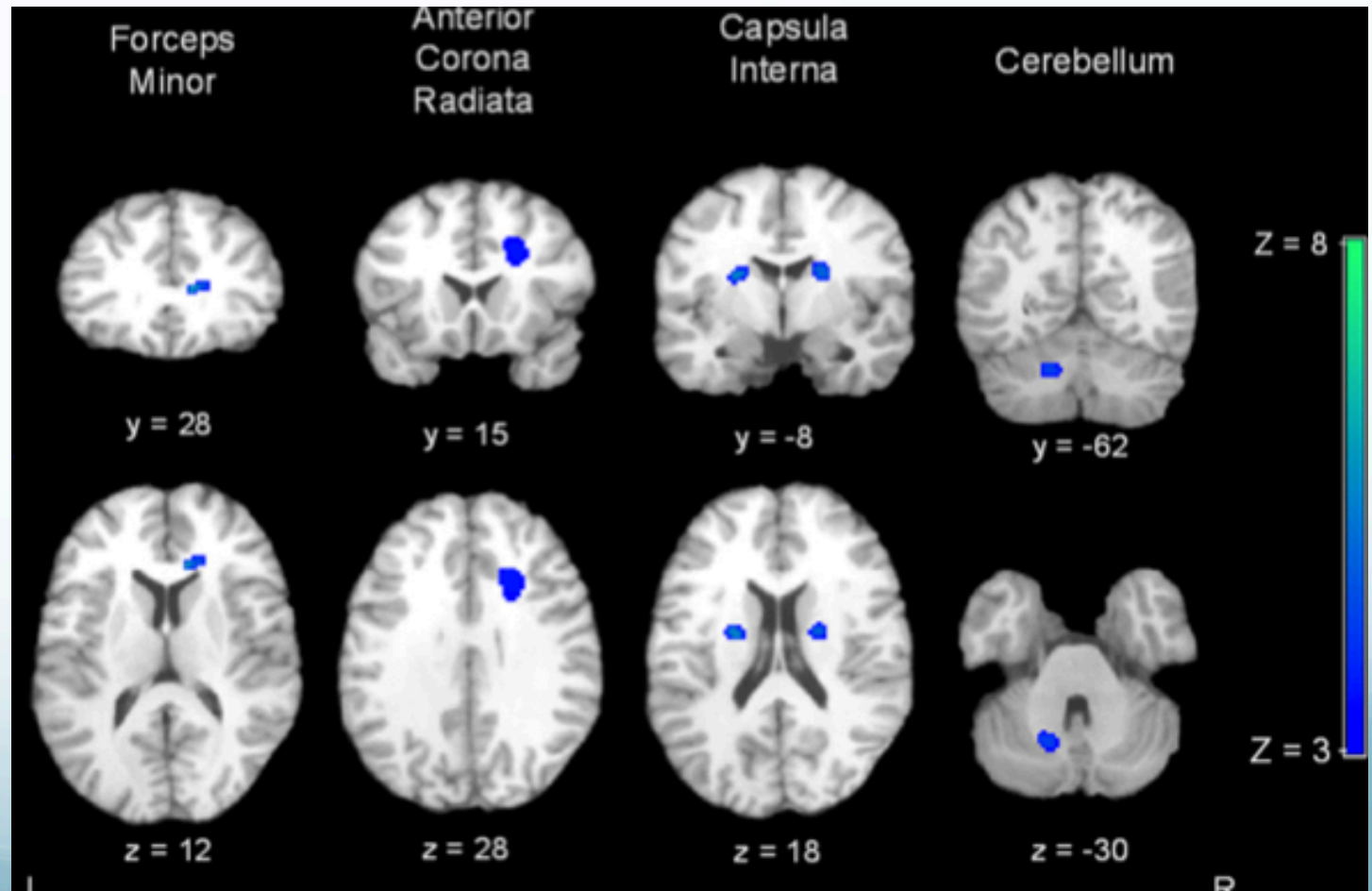
^c Department of Cognitive Neuroscience, Donders Institute for Brain, Cognition and Behavior, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

^d Karakter, Child and Adolescent Psychiatry University Center Nijmegen, Nijmegen, The Netherlands

Méta-analyse « ALE » de 15
études DTI publiées à 2011:173
ADHD patients and 169 healthy
control subjects

Diminution d'anisotropie

- faisceau long. sup
- f. cortico-spinal
- connexions
fronto-striées
- Cervelet gauche



Research article

Open Access

Structural brain change in Attention Deficit Hyperactivity Disorder identified by meta-analysis

Ian Ellison-Wright^{*1,3}, Zoë Ellison-Wright² and Ed Bullmore³

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Email: Ian Ellison-Wright* - ian.ew@inbex.com; Zoë Ellison-Wright - zoe.ellison-wright@dchft.nhs.uk; Ed Bullmore - etb23@cam.ac.uk

* Corresponding author

Published: 30 June 2008

Received: 7 May 2008

Méta-analyse de 7 études de la substance grise (143 témoins vs 114 patients TDAH) : seule significativité = putamen/pallidum droit

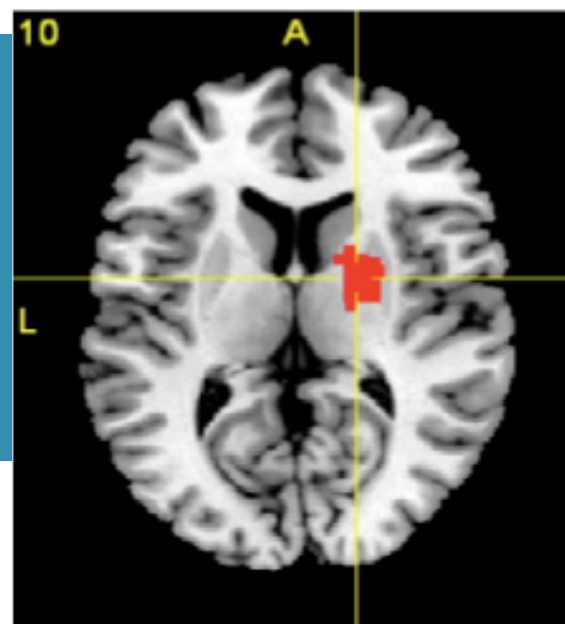


Figure 1
Gray Matter Decreases in ADHD. A transverse section at Talairach space level $z = 10$ showing gray matter reduction in ADHD in the right putamen/globus pallidus region, displayed on a template brain. The right side of the section represents the right side of the brain. Significant clusters were thresholded with a false discovery rate (FDR) at $P < 0.05$.

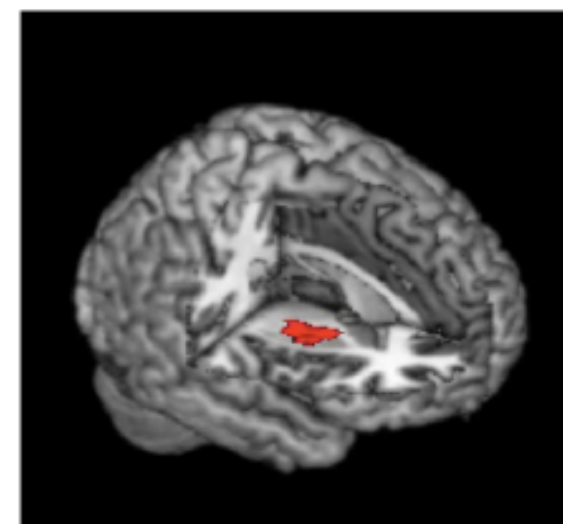


Figure 2
Gray Matter Decreases in ADHD. Gray matter signal decrease in ADHD in the right putamen/globus pallidus region, displayed on a three-dimensional rendered brain with right frontal lobe removed.

ADHD had more lesions localized in the right putamen [23]. Another study of ADHD symptoms in twenty-five children with focal stroke lesions found that the symptoms were most commonly associated with lesions of the

Le TDAH lié à une anomalie neurologique du système de la motivation

PsychoMédia - Publié le 09 septembre 2009

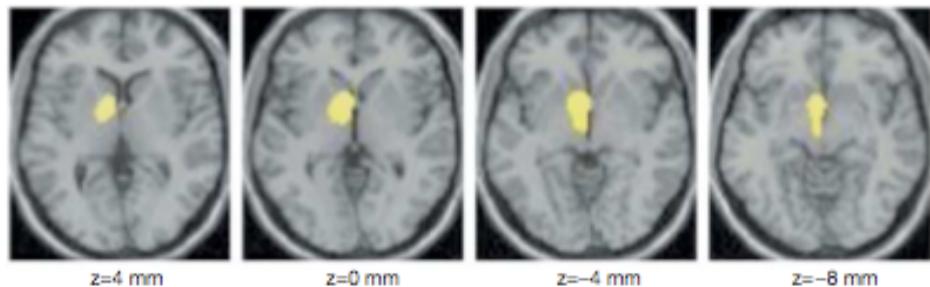


L'inattention associée au trouble déficit d'attention et hyperactivité (TDAH) pourrait s'expliquer en partie par la sous-stimulation des centres du cerveau dits de la récompense, impliqués dans la motivation, selon une étude publiée dans le Journal of the American Medical Association.

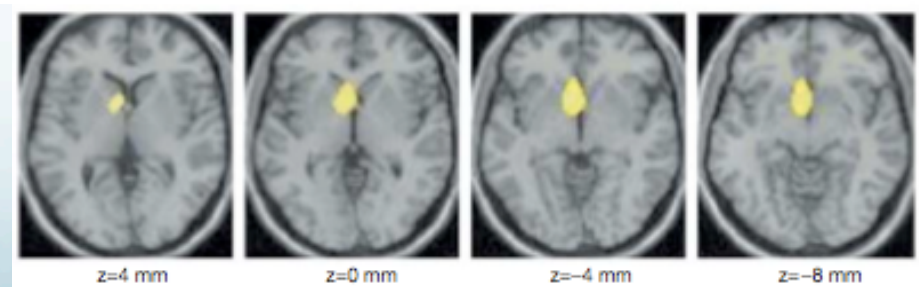
Les chercheurs ont comparé des images cérébrales de 53 adultes atteints du TDAH, ne prenant pas de médicaments, et 44 personnes n'ayant pas le TDAH.

Les personnes ayant le TDAH présentaient de faibles niveaux de certains récepteurs du neurotransmetteur dopamine dans le mésencéphale et le noyau accumbens, des régions clés du circuit dopaminergique de la récompense, ont constaté Nora D. Volkow du National Institute on Drug Abuse (États-Unis) et ses collègues. De bas niveaux des récepteurs de la dopamine étaient associés avec des résultats plus faibles à des tests d'attention.

"Cela peut expliquer pourquoi les déficits d'attention des personnes atteintes du TDAH sont plus importants dans des tâches qui sont considérées comme ennuyantes, répétitives et inintéressantes ainsi qu'expliquer la propension aux complications telles que la toxicomanie et l'obésité (la dopamine étant impliquée dans les addictions)", écrivent les auteurs.



Dopamine D 2/D3 receptor availability



Dopamine transporter availability

PRELIMINARY COMMUNICATION

Evaluating Dopamine Reward Pathway in ADHD Clinical Implications

Nora D. Volkow, MD
Gene-Jack Wang, MD
Scott H. Kolins, PhD
Tim L. Wigal, PhD
Jeffrey H. Newcorn, MD
Frank Telang, MD
Joanna S. Fowler, PhD
Wei Zhu, PhD
Jean Logan, PhD

Context Attention-deficit/hyperactivity disorder (ADHD)—characterized by symptoms of inattention and hyperactivity-impulsivity—is the most prevalent childhood psychiatric disorder that frequently persists into adulthood, and there is increasing evidence of reward-motivation deficits in this disorder.

Objective To evaluate biological bases that might underlie a reward/motivation deficit by imaging key components of the brain dopamine reward pathway (mesoaccumbens).

Design, Setting, and Participants We used positron emission tomography to measure dopamine synaptic markers (transporters and D₂/D₃ receptors) in 53 nonmedicated adults with ADHD and 44 healthy controls between 2001-2009 at Brookhaven National Laboratory.

Main Outcome Measures We measured specific binding of positron emission tomographic radioligands for dopamine transporters (DAT) using [¹¹C]cocaine and for D₂/D₃ receptors using [¹¹C]raclopride, quantified as binding potential (distribution volume ratio -1).

Results For both ligands, statistical parametric mapping showed that specific binding was lower in ADHD than in controls (threshold for significance set at $P < .005$) in regions



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Contents lists available at SciVerse ScienceDirect

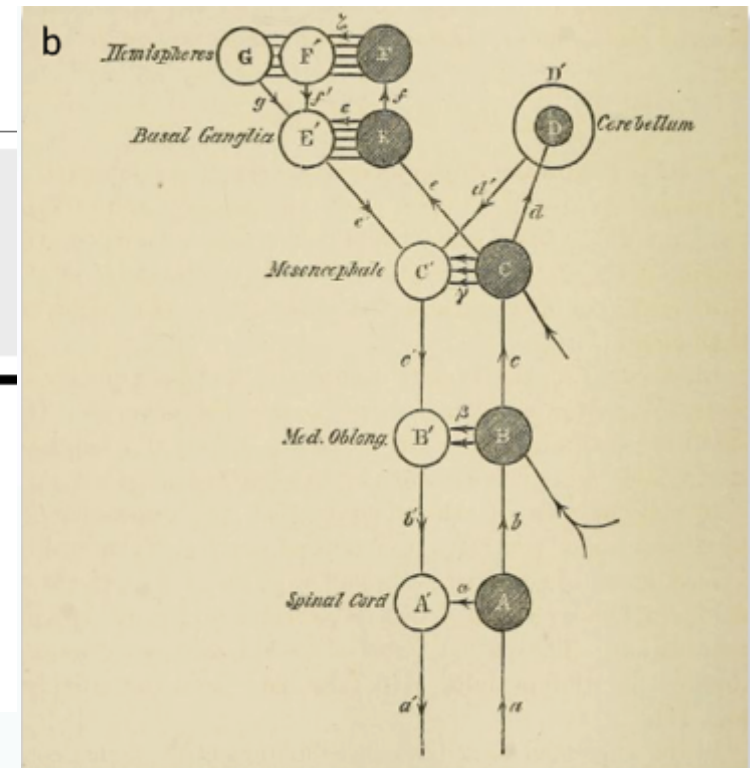
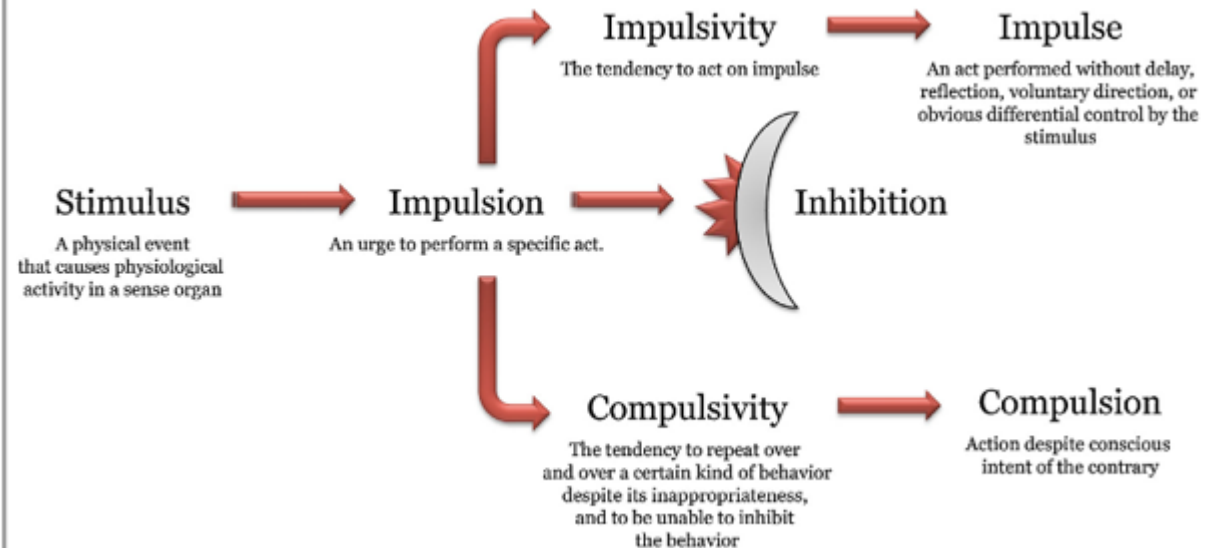
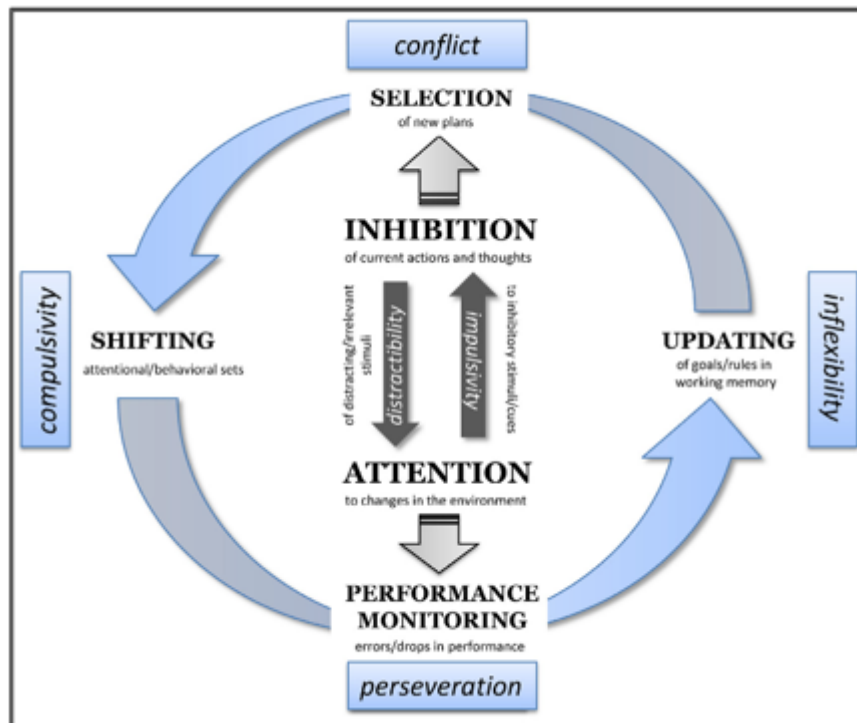
Progress in Neurobiology

journal homepage: www.elsevier.com/locate/pneurobio

Inhibition and impulsivity: Behavioral and neural basis of response control

Andrea Bari *, Trevor W. Robbins

Behavioral and Clinical Neuroscience Institute, Department of Experimental Psychology, University of Cambridge, Cambridge CB2 3EB, UK



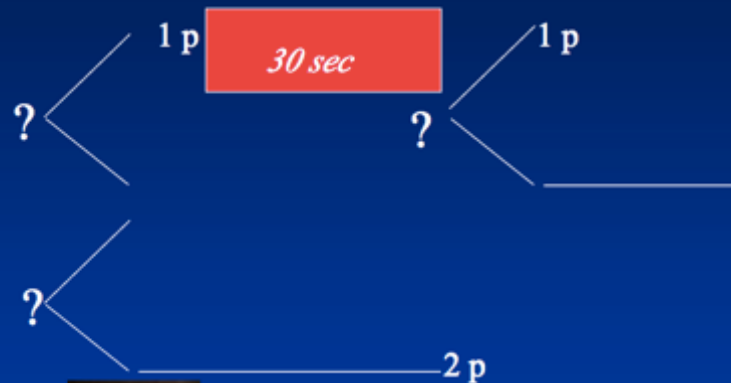


II/ Le modèle alternatif

= défaut des systèmes de la récompense (Sonuga-Barke)
Imagerie fonctionnelle dans des protocoles de récompense

→ Dysfonctionnement des circuits cortico-striés

Post - reward delay



Experiments by Edmund Sonuga-Barke

Delay aversion v inhibition

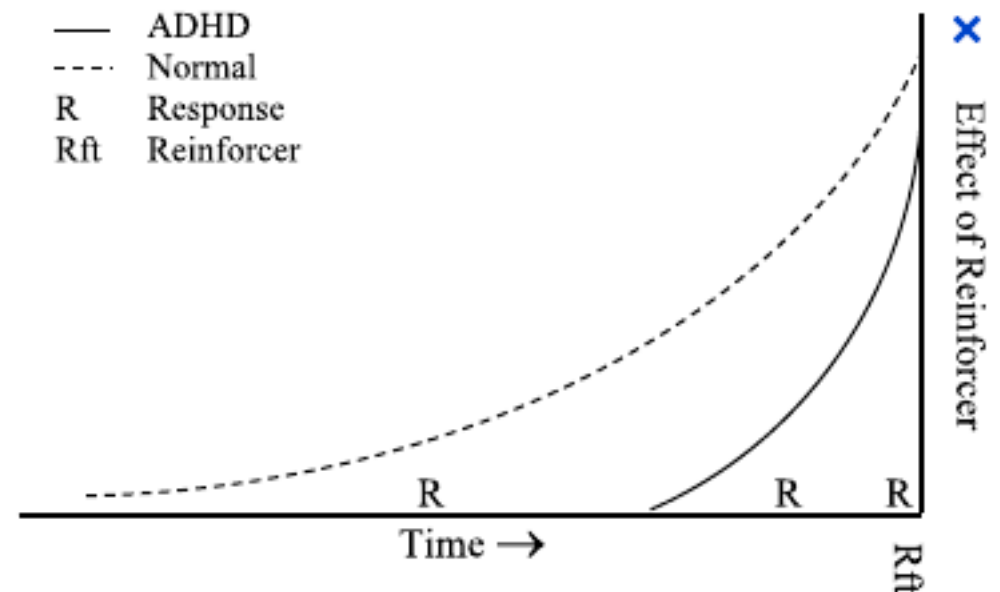
Evidence for both; inhibitory failure in more severe cases

Combination of both predicts behavior much more strongly than either alone (Solanto et al)

Inhibition (5-choice serial RT; 5HT_{2A,C}) and preference for delayed reward (5HT_{2C,B}) show double dissociation with 5-HT receptor (Talpos et al)

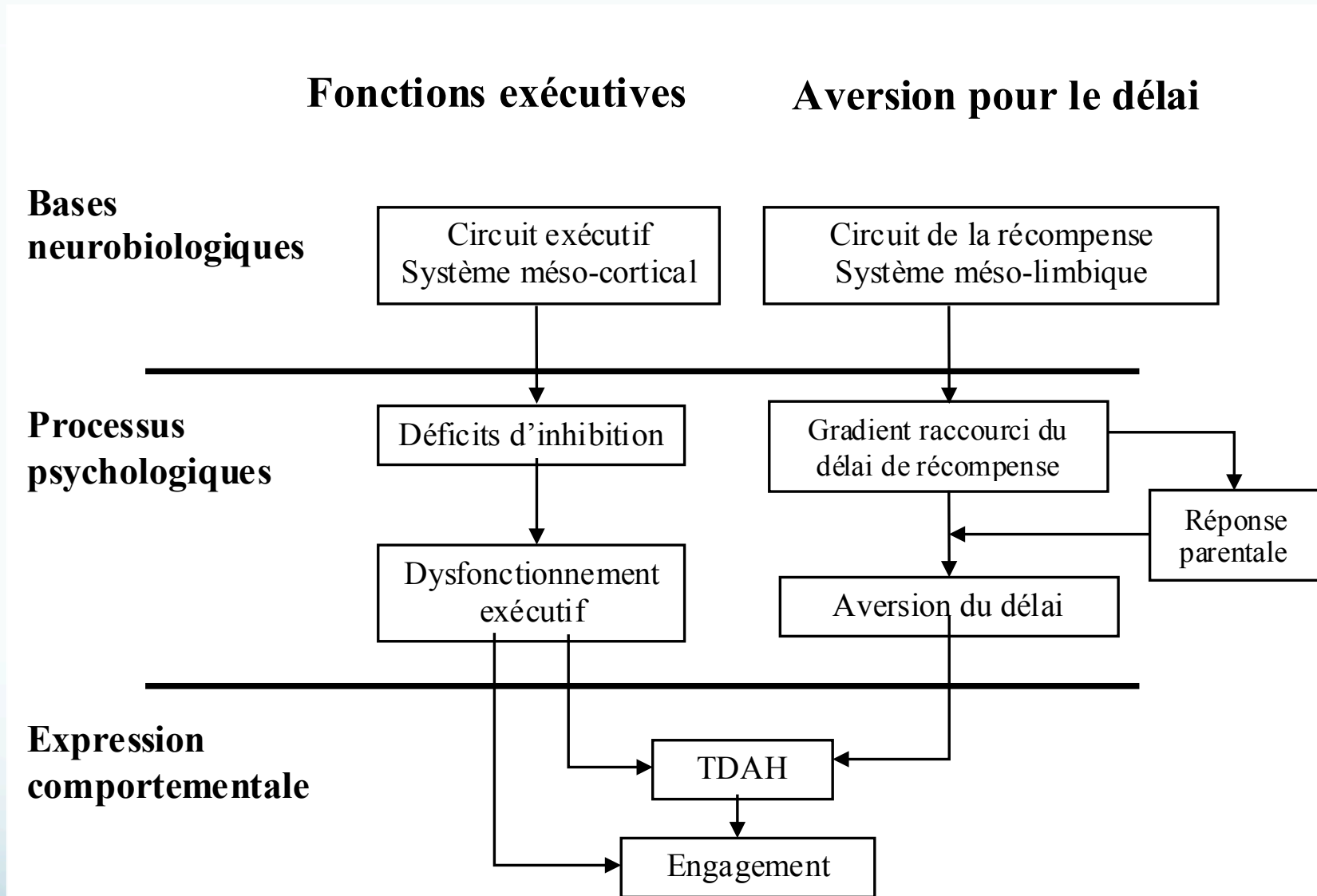
Fig. 2. Theoretical delay-of-reinforcement ('reward') gradients. The effect of a reinforcer is more potent when the delay between the response and the reinforcer is short than when the delay is long. The delay gradient may be steeper and shorter in children with ADHD than in normal children.

— ADHD
 ---- Normal
 R Response
 Rft Reinforcer



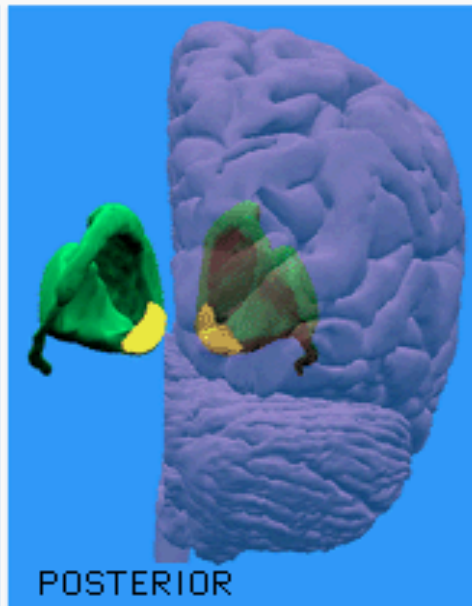
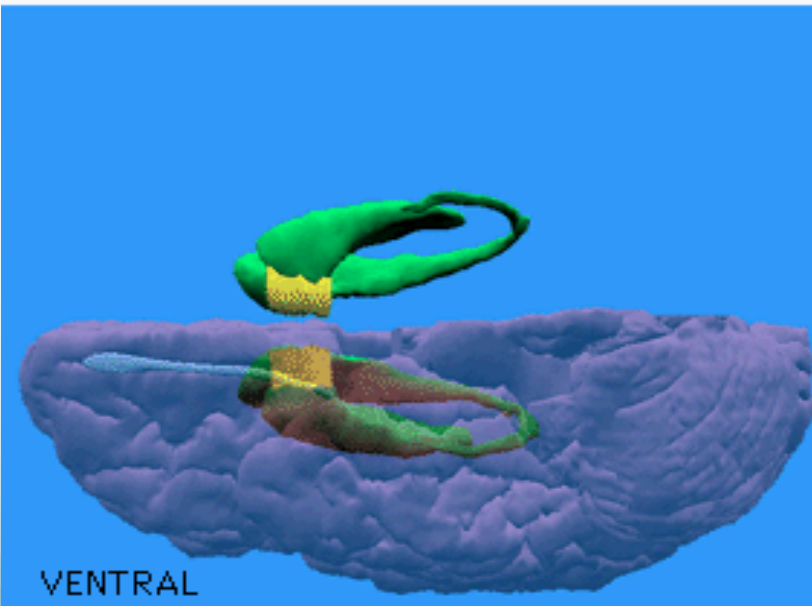
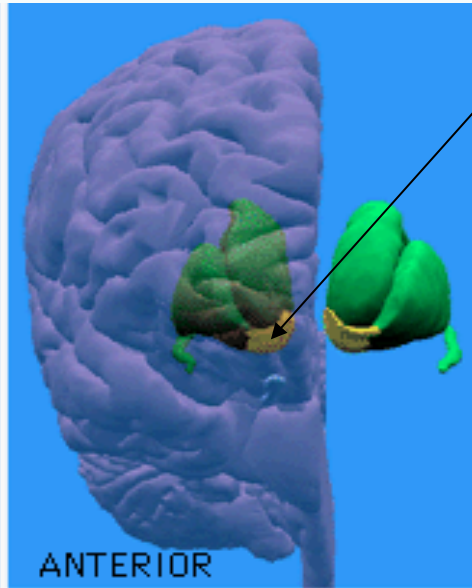
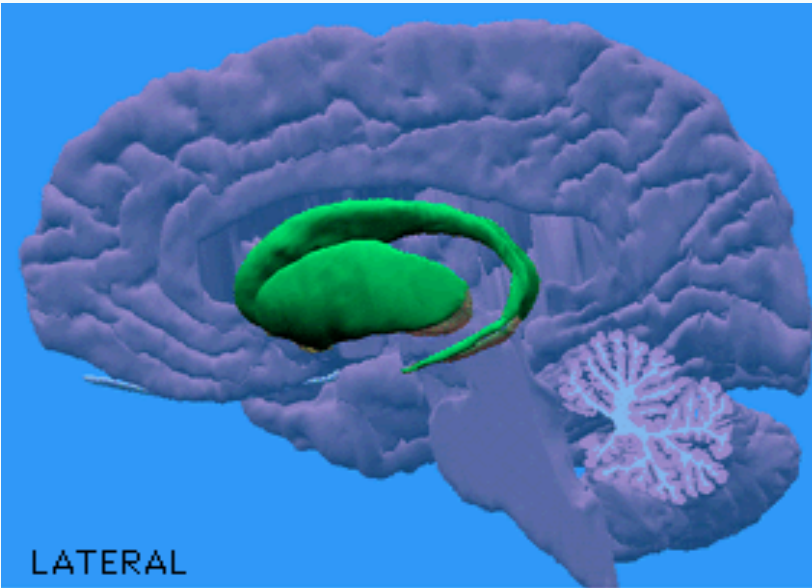
Théorie du « gradient de délai de renforcement » (Sagvolden et al.) : le délai de gradient serait plus court et plus abrupt chez les enfants TDAH

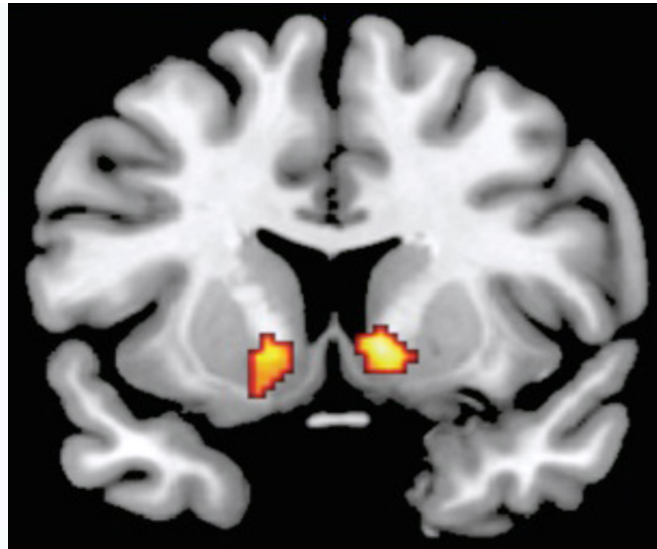
Sagvolden T, Aase H, Zeiner P, Berger DF. Altered reinforcement mechanisms in attention deficit/hyperactivity disorder. Behav Brain Res 1998;94:61-71



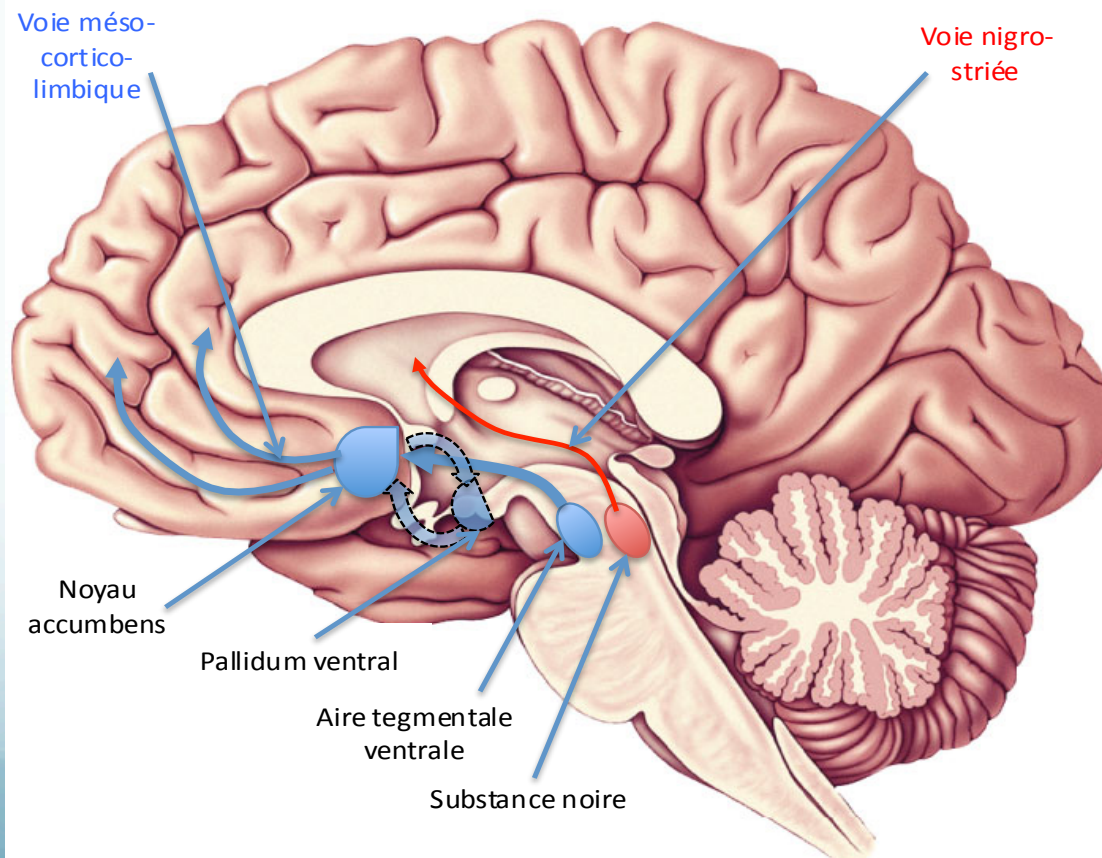
Physiopathologie du TDAH (D'après Sonuga-Barke, 2002, 2003)

Noyau accumbens
Chez l'animal : en
activité lors de
l'anticipation d'une
récompense, l'
évaluation de la
magnitude d'une
récompense
Chez l'homme
impliqué dans les
conduites à risque et
addictives

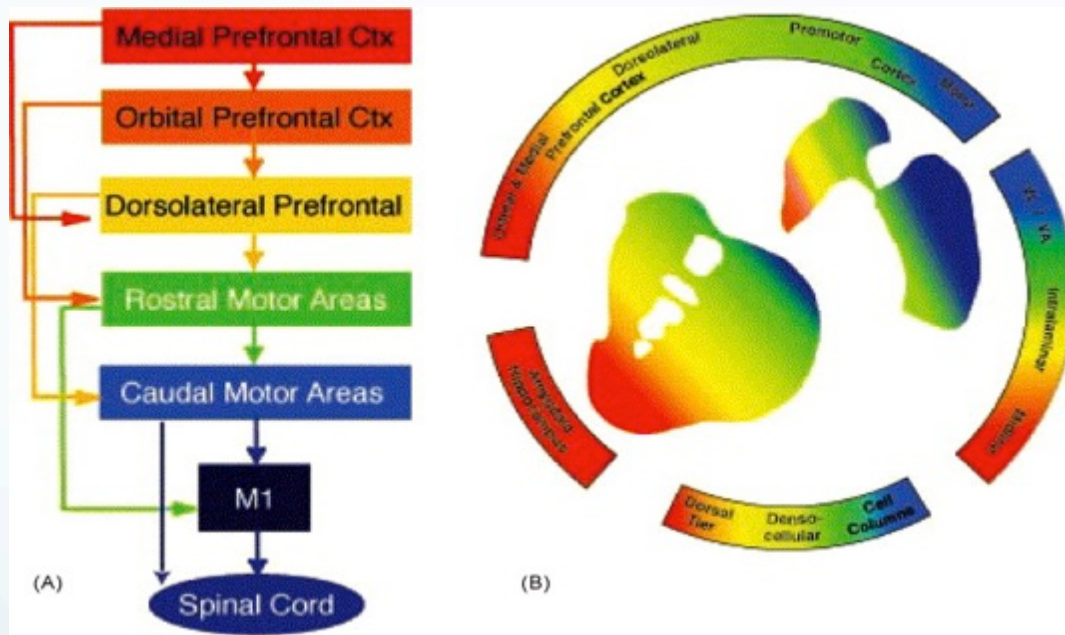




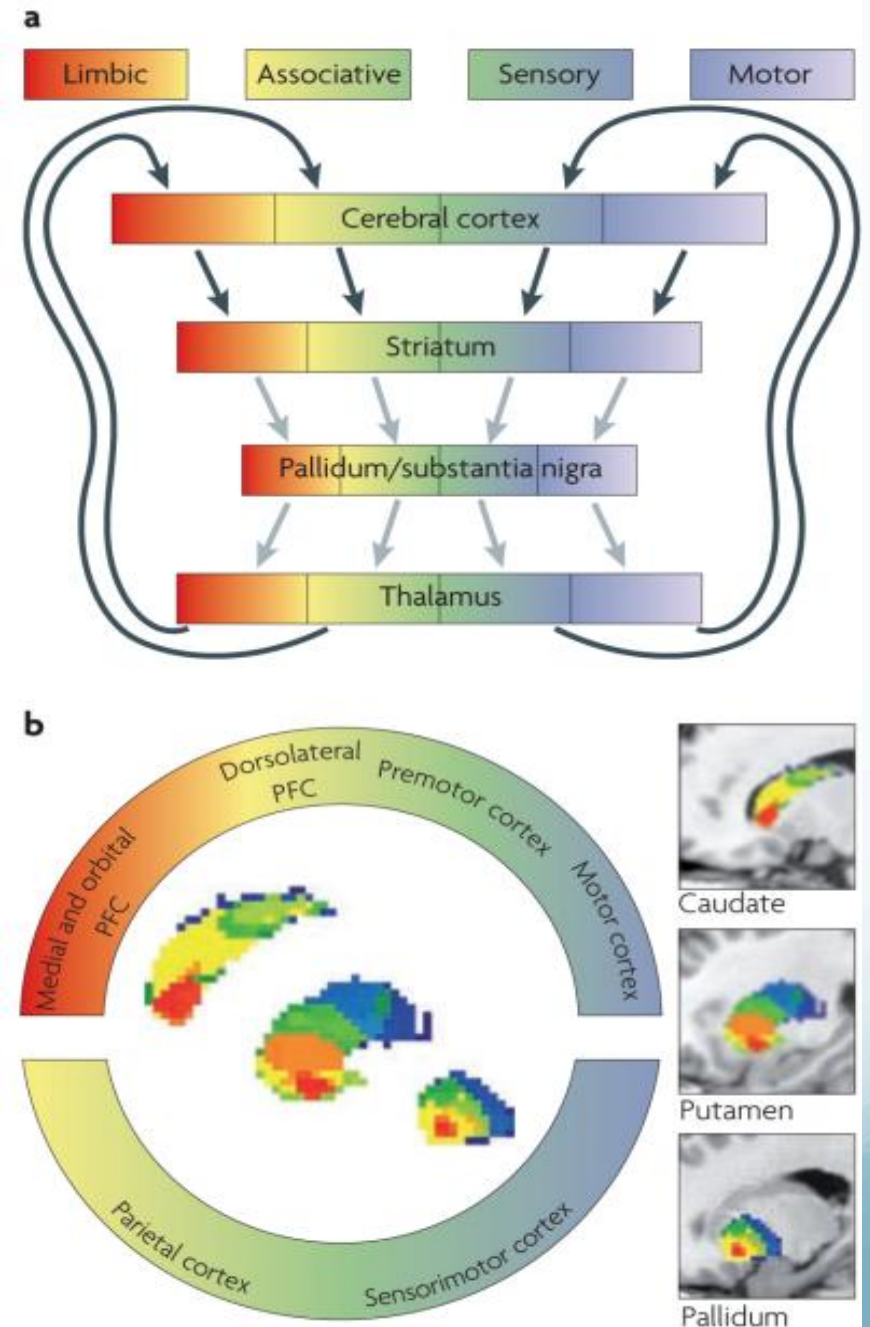
Noyau accumbens
activé lors d'une tâche
de gambling en IRM
fonctionnelle



Le « système
de la
récompense »

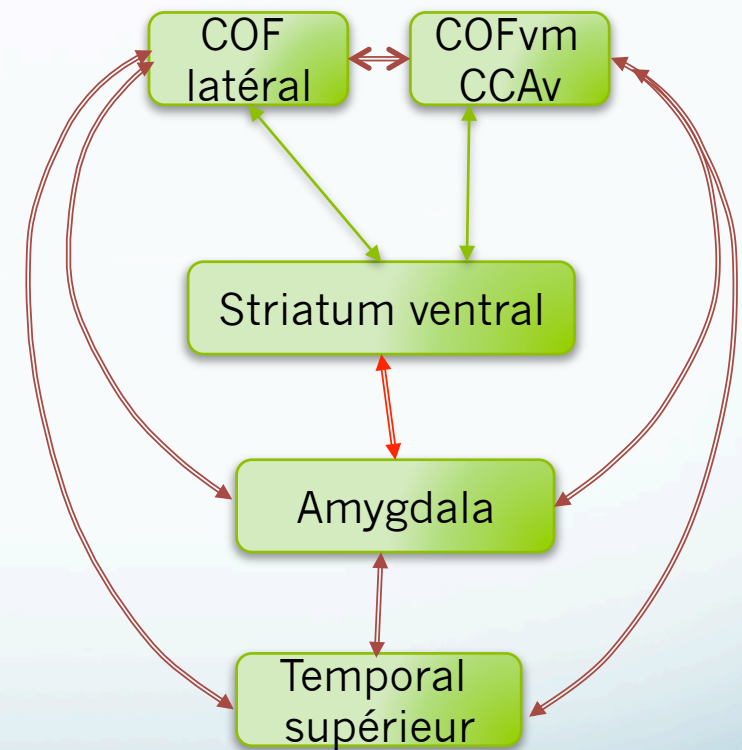
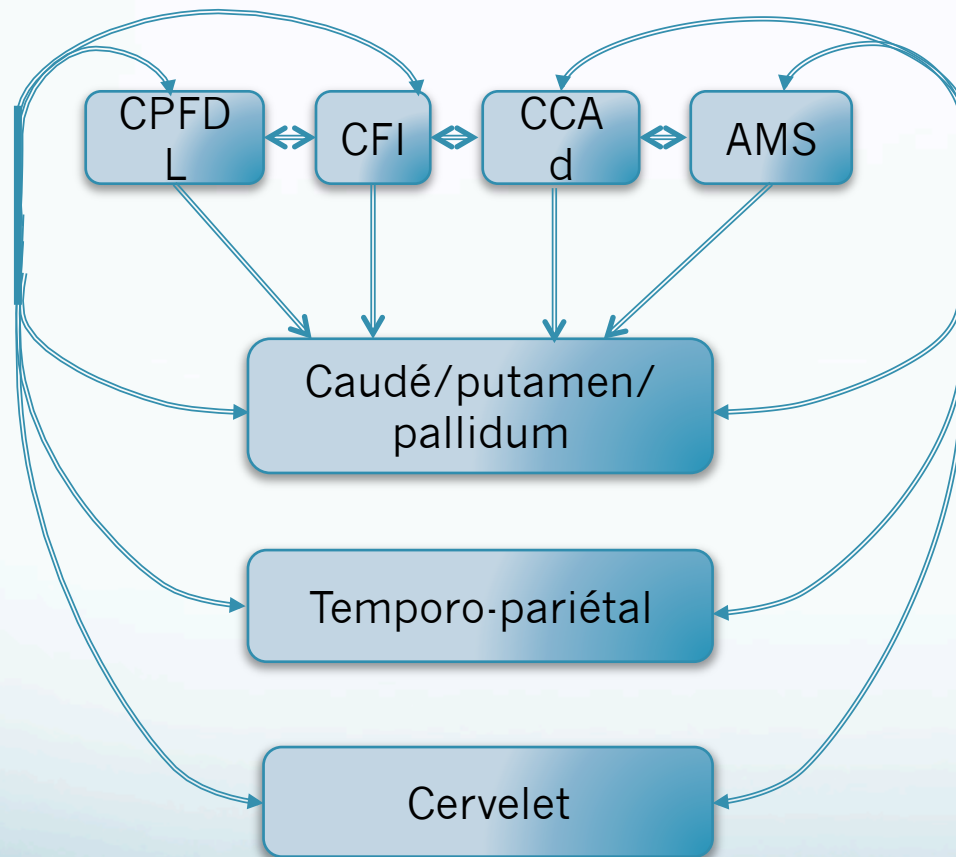


Haber, S.N. (2003) The primate basal ganglia: parallel and integrative networks. *J. Chem. Neuroanat.* 26, 317–330



Fonctions exécutives « froides »

Fonctions exécutives « chaudes »



The background features a light blue sky with a faint, pixelated sun-like shape in the upper center. The lower portion of the image is filled with stylized, layered blue waves that create a sense of depth and movement.

TDAH: apport de l'imagerie fonctionnelle

A review of fronto-striatal and fronto-cortical brain abnormalities in children and adults with Attention Deficit Hyperactivity Disorder (ADHD) and new evidence for dysfunction in adults with ADHD during motivation and attention

*Ana Cubillo, Rozmin Halari, Anna Smith, Eric Taylor and Katya Rubia**

Department of Child Psychiatry, King's College London, Institute of Psychiatry, London, UK

Comparaison adulte/enfant :
tâche d'attention soutenue :
hypoactivation fronto-pariéto-striatale (comme chez l'enfant)
Tâche récompensée :
hypoactivation ventro-médiane,
mais seulement si trouble des
conduites comorbide

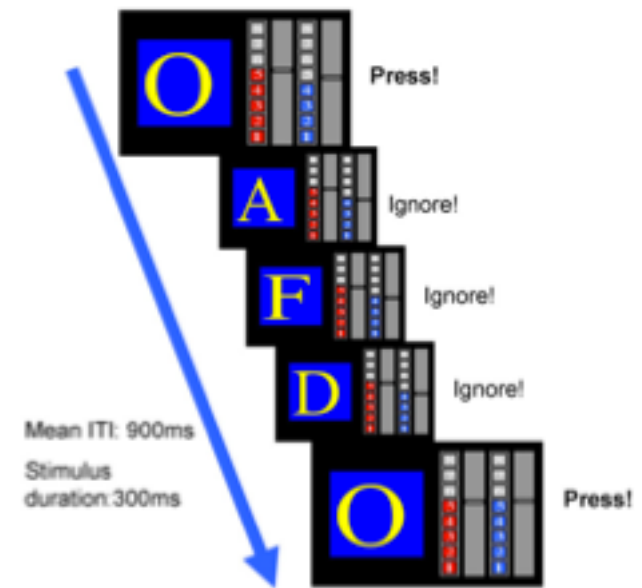
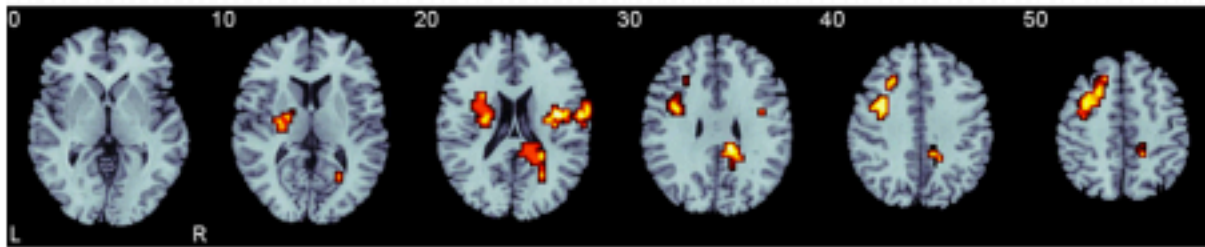


Fig. 1 – Schematic illustration of the Rewarded Continuous Performance Test. Response required to “X” or “O”, not to any other letters. Reward is given for each response to one of the two target letters (which letter was rewarded was randomised across subjects). Red/blue bars indicate correct responses to targets (X/O). Three correct responses make one score on the bar for the rewarded and non-rewarded targets, but only the rewarded target scores are remunerated with £1. Up to £8 can be won on the task.

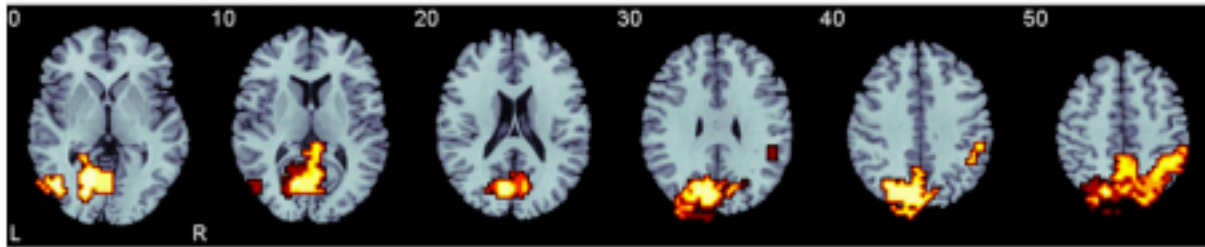
Rewarded CPT
1£ pour 3 bonnes
réponses (hits)

a Sustained attention: non-rewarded target vs non-target trials

Controls > ADHD

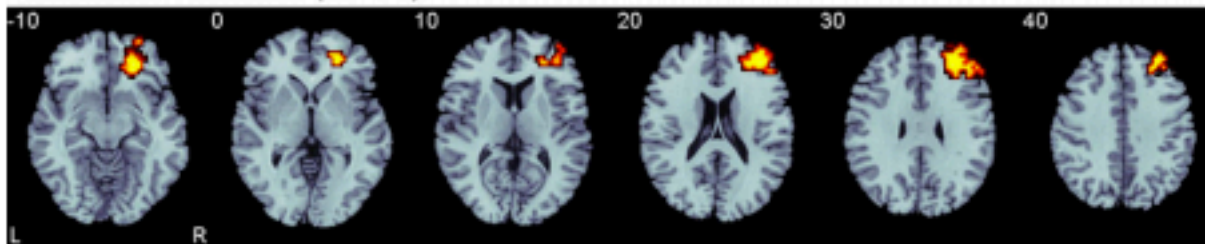


ADHD > Controls

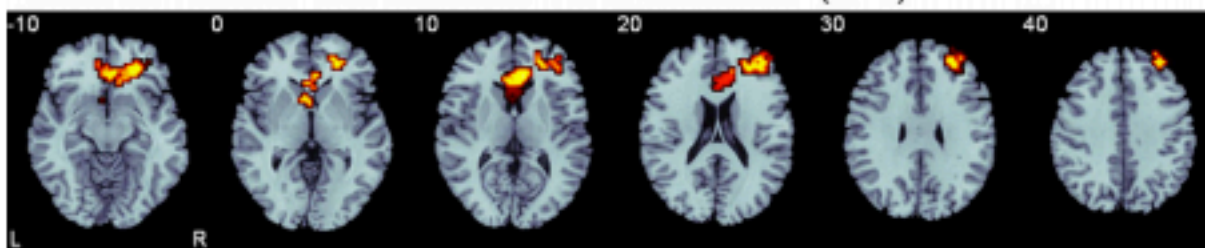


b Reward: rewarded vs non-rewarded target trials

Controls > ADHD (N=11)



Controls > ADHD with comorbid CD in childhood (N=6)



Effet de la
cible : sous-
activation
fronto-striatale

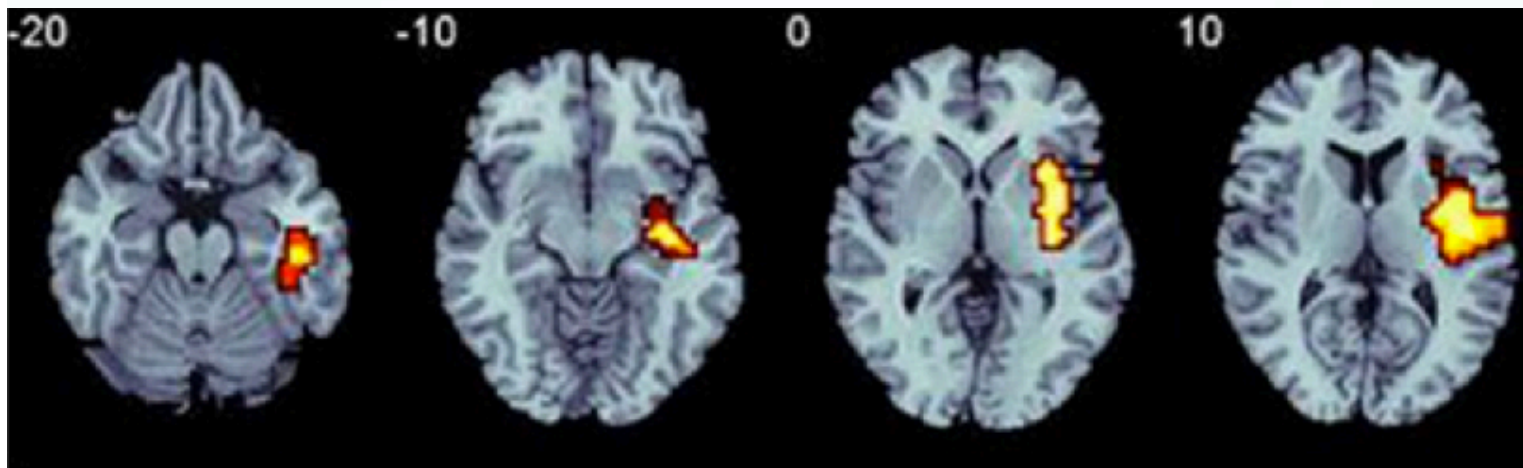
Effet de la
récompense :
sous activation
frontale
antérieure
gauche

REVIEW

“Cool” Inferior Frontostriatal Dysfunction in Attention-Deficit/Hyperactivity Disorder Versus “Hot” Ventromedial Orbitofrontal-Limbic Dysfunction in Conduct Disorder: A Review

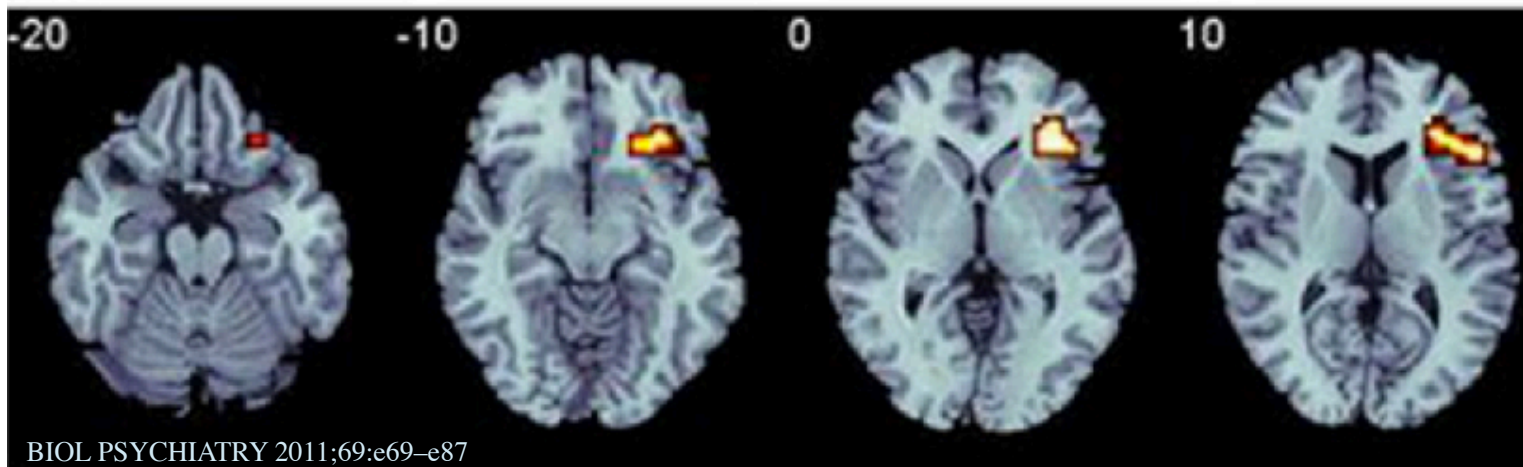
Katya Rubia

Areas of hypoactivation in CD children compared to ADHD and controls



Sustained attention

(Hippoc.+insula)



Reward

(ventro-lateral orbital)



The link between callous-unemotional traits and neural mechanisms of reward processing: An fMRI study

Kim Veroude^{a,b,*}, Daniel von Rhein^a, Roselyne J.M. Chauvin^{a,b}, Eelco V. van Dongen^{a,b}, Maarten J.J. Mennes^a, Barbara Franke^c, Dirk J. Heslenfeld^d, Jaap Oosterlaan^d, Catharina A. Hartman^e, Pieter J. Hoekstra^e, Jeffrey C. Glennon^{a,b}, Jan K. Buitelaar^{a,b,f}

^a Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen, The Netherlands

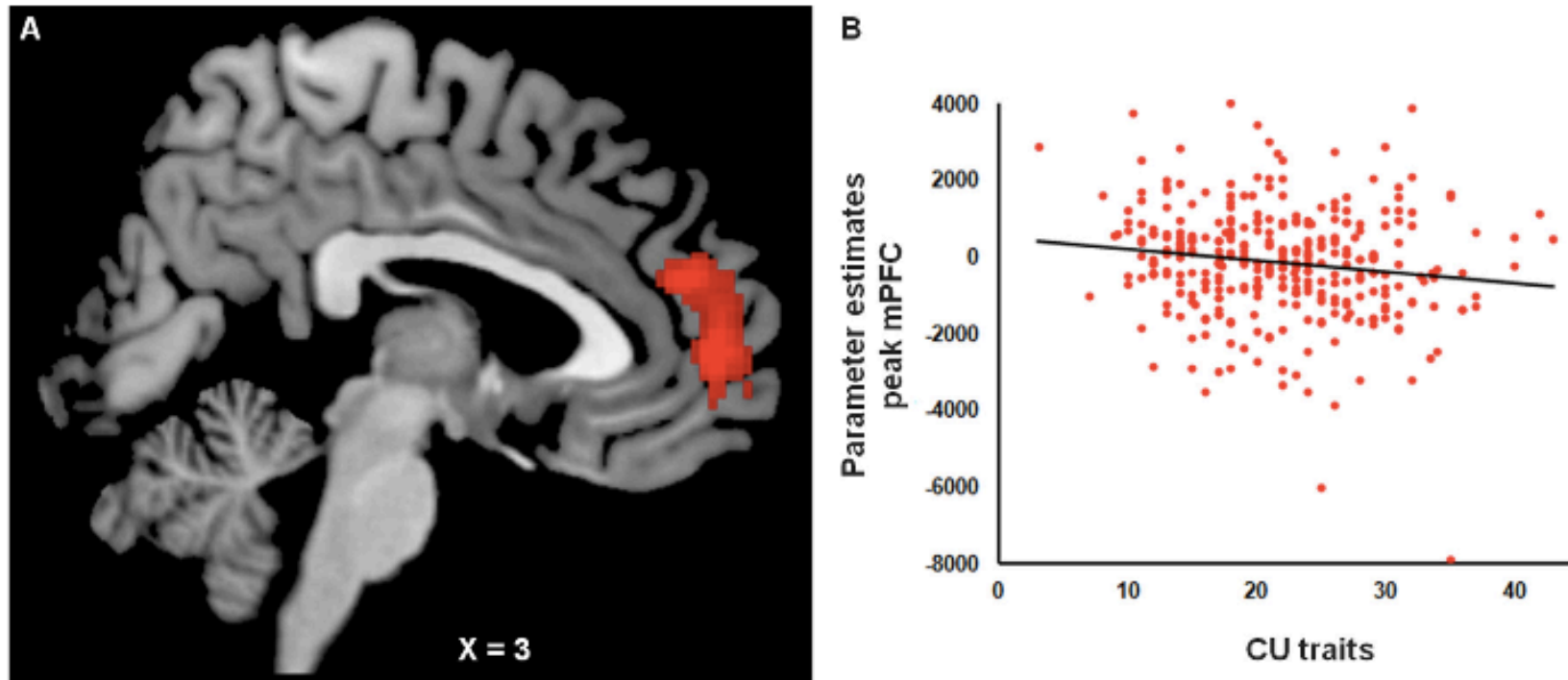
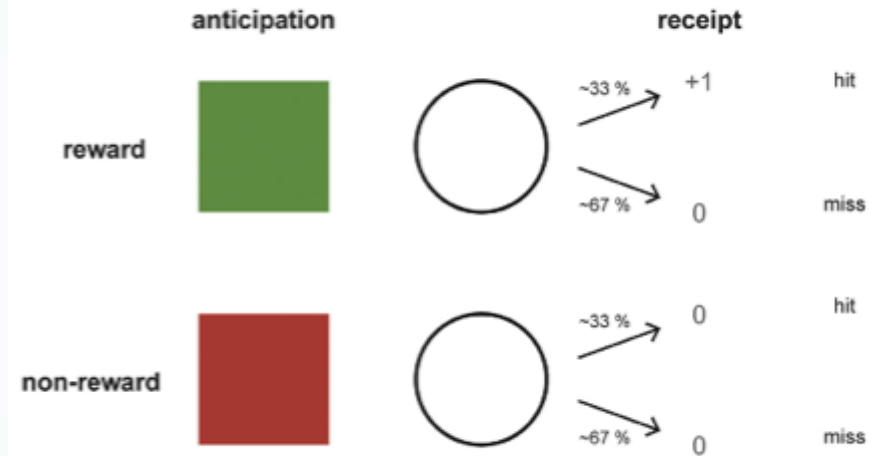


Fig. 2. Brain activity during reward anticipation related to CU traits. (A) The cluster in vmPFC/dmPFC. (B) Negative relation between CU traits and parameter estimates of the cluster peak.

BRIEF REPORTS

Ventral Striatal Hyporesponsiveness During Reward Anticipation in Attention-Deficit/Hyperactivity Disorder

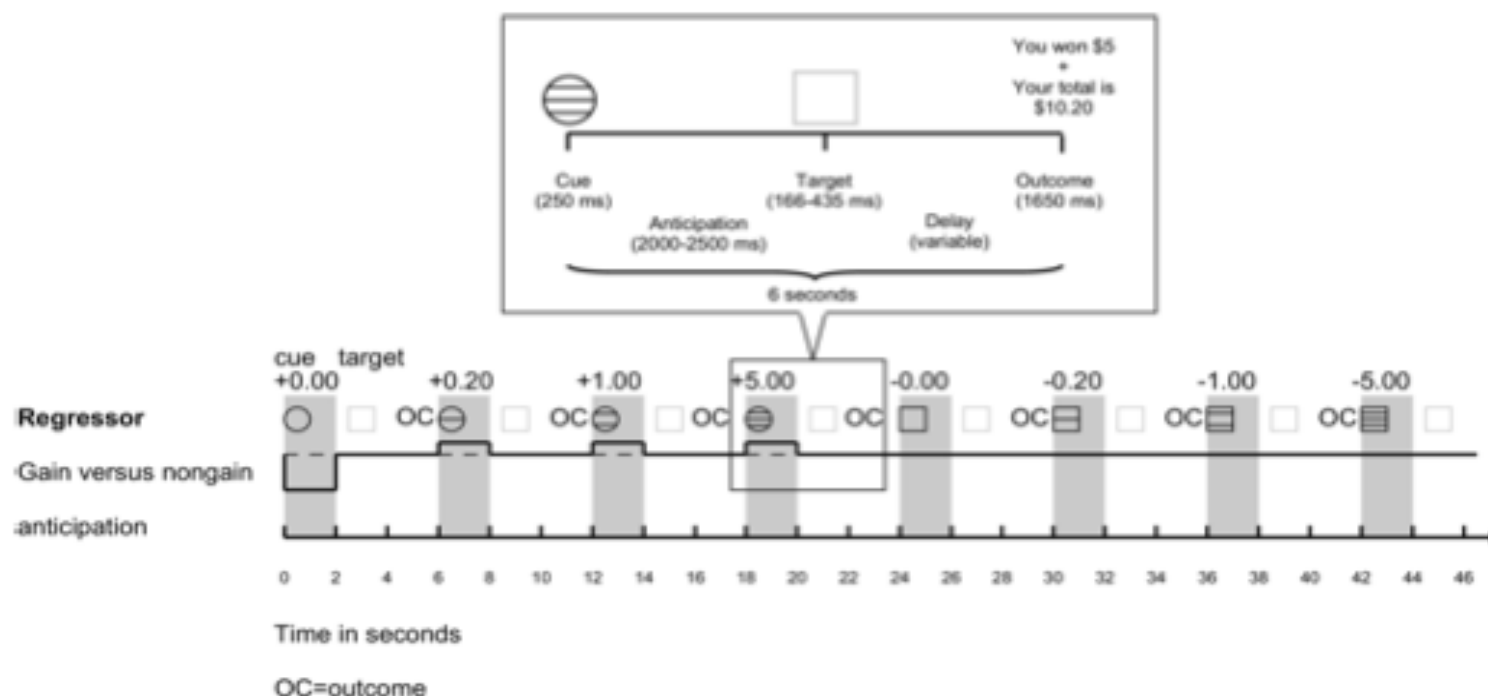
Anouk Scheres, Michael P. Milham, Brian Knutson, and Francisco Xavier Castellanos

Background: Although abnormalities in reward processing have been proposed to underlie attention-deficit/hyperactivity disorder (ADHD), this link has not been tested explicitly with neural probes.

Methods: This hypothesis was tested by using fMRI to compare neural activity within the striatum in individuals with ADHD and healthy controls during a reward-anticipation task that has been shown previously to produce reliable increases in ventral striatum activity in healthy adults and healthy adolescents. Eleven adolescents with ADHD (5 off medication and 6 medication-naïve) and 11 healthy controls (ages 12–17 y) were included. Groups were matched for age, gender, and intelligence quotient.

Results: We found reduced ventral striatal activation in adolescents with ADHD during reward anticipation, relative to healthy controls. Moreover, ventral striatal activation was negatively correlated with parent-rated hyperactive/impulsive symptoms across the entire sample.

Conclusions: These findings provide neural evidence that symptoms of ADHD, and impulsivity or hyperactivity in particular, may involve diminished reward anticipation, in addition to commonly observed executive dysfunction.



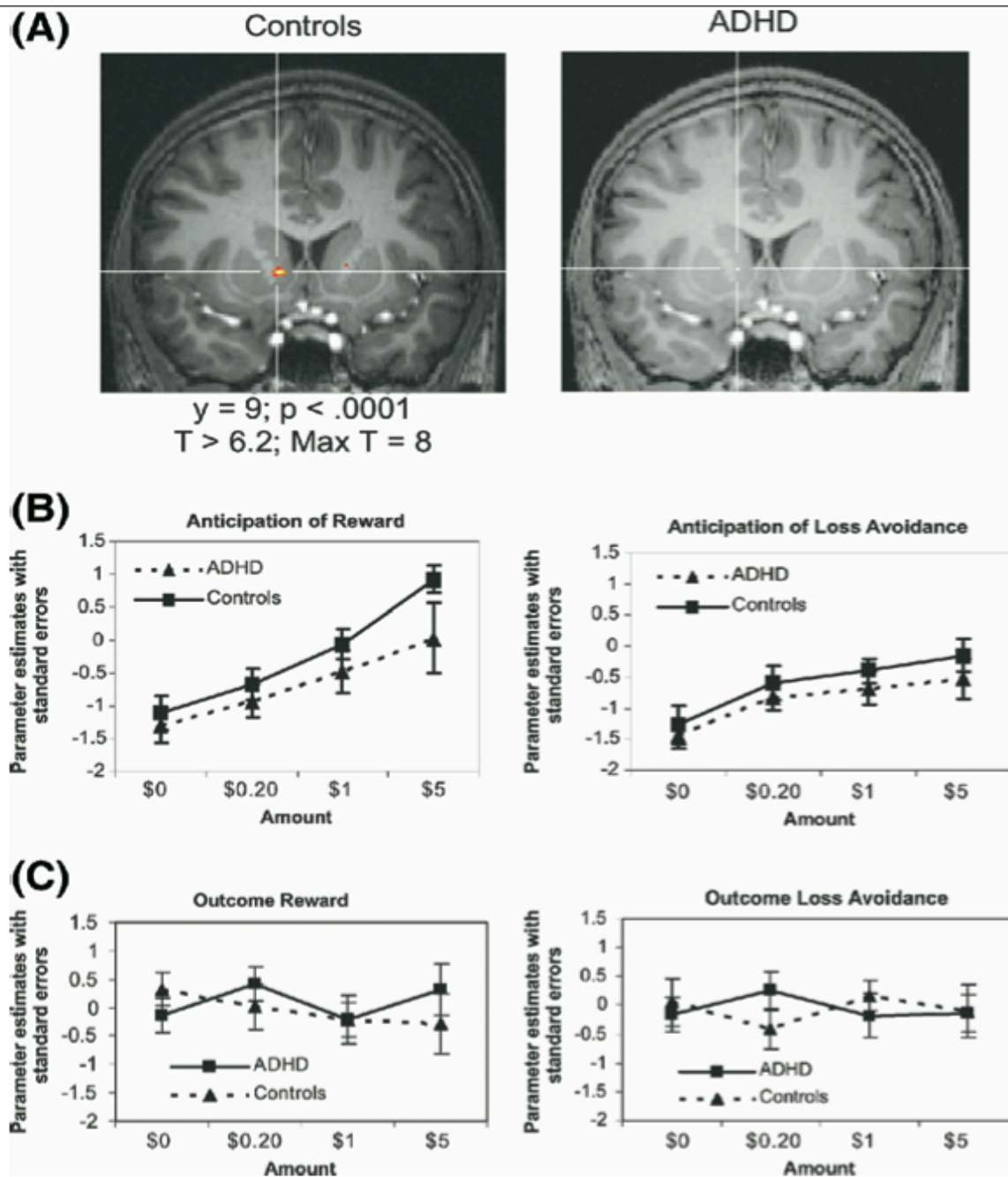


Figure 2. Impact of reward anticipation and outcome on ventral striatum (VS) activity.

TDAH : hypoactivation du striatum ventral lors de l'anticipation de la récompense

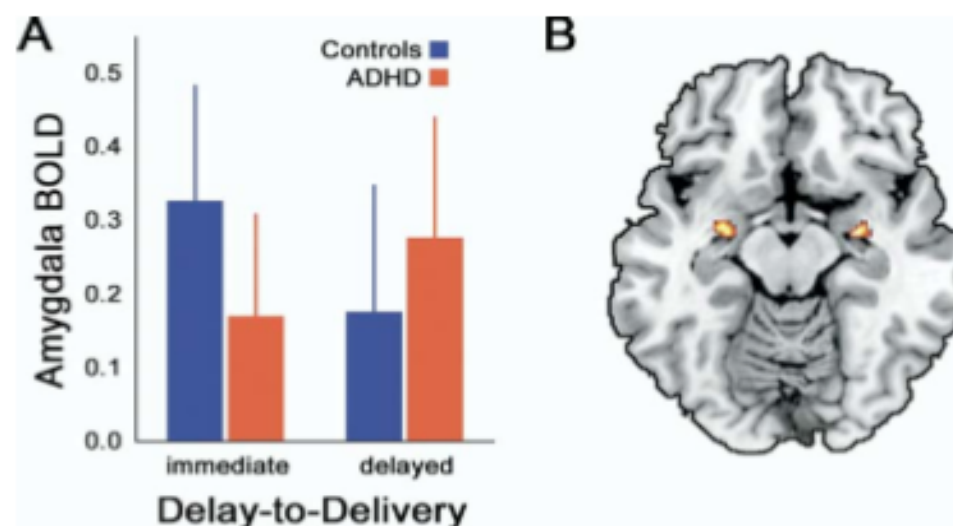
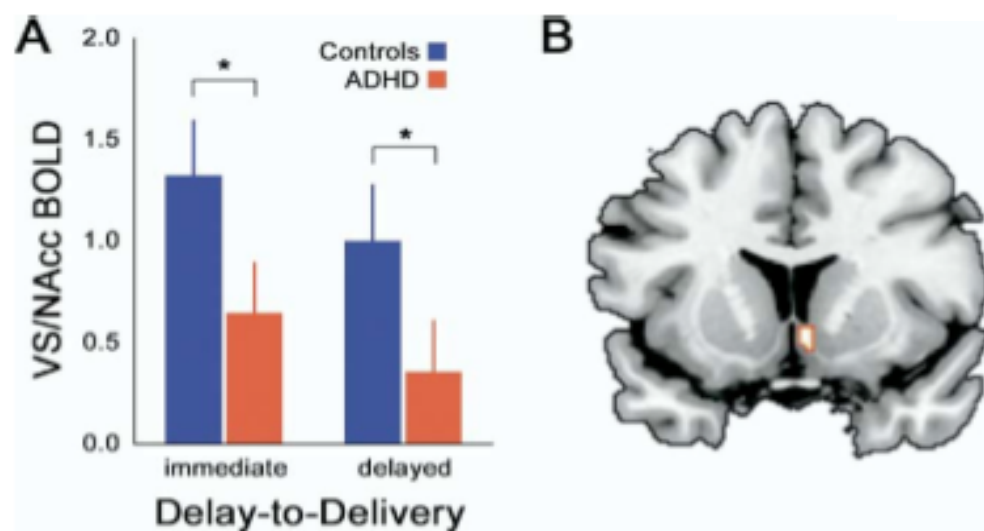
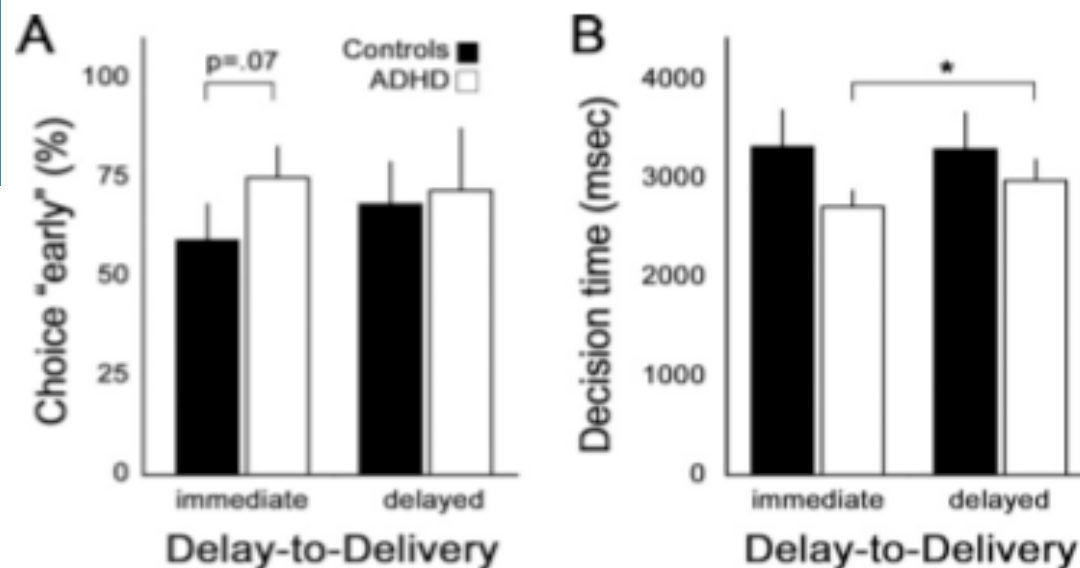
Neural Hyporesponsiveness and Hyperresponsiveness During Immediate and Delayed Reward Processing in Adult Attention-Deficit/Hyperactivity Disorder

Michael M. Plichta, Nenad Vasic, Robert Christian Wolf, Klaus-Peter Lesch, Dagmar Brummer, Christian Jacob, Andreas J. Fallgatter, and Georg Grön

BIOL PSYCHIATRY 2009;65:7-14
© 2009 Society of Biological Psychiatry

ADHD : hyporesponsiveness of the ventral-striatal reward system for both immediate and delayed rewards

delayed rewards evoked hyperactivation in dorsal caudate nucleus and amygdala of ADHD patients.



Abnormal Striatal BOLD Responses to Reward Anticipation and Reward Delivery in ADHD

Emi Furukawa^{1*}, Patricia Bado^{2,3}, Gail Tripp¹, Paulo Mattos^{2,3}, Jeff R. Wickens¹, Ivanei E. Bramati^{2,3}, Brent Alsop⁴, Fernanda Meireles Ferreira², Debora Lima², Fernanda Tovar-Moll^{2,3}, Joseph A. Sergeant⁵, Jorge Moll²

¹ Okinawa Institute of Science and Technology Graduate University (OIST), Okinawa, Japan, ² D'Or Institute for Research and Education (IDOR), Rio de Janeiro, Brazil, ³ Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, ⁴ University of Otago, Dunedin, New Zealand, ⁵ Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

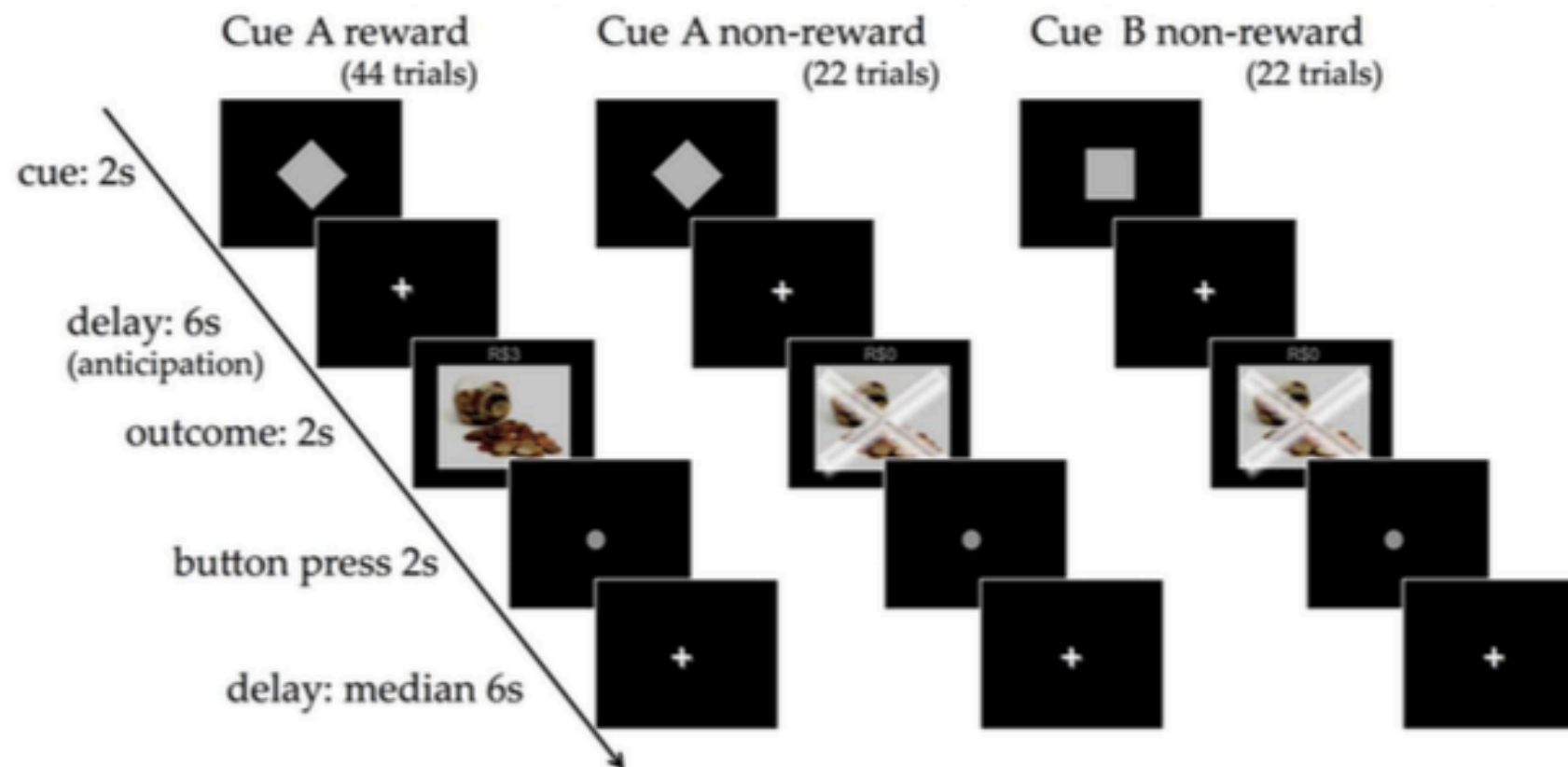
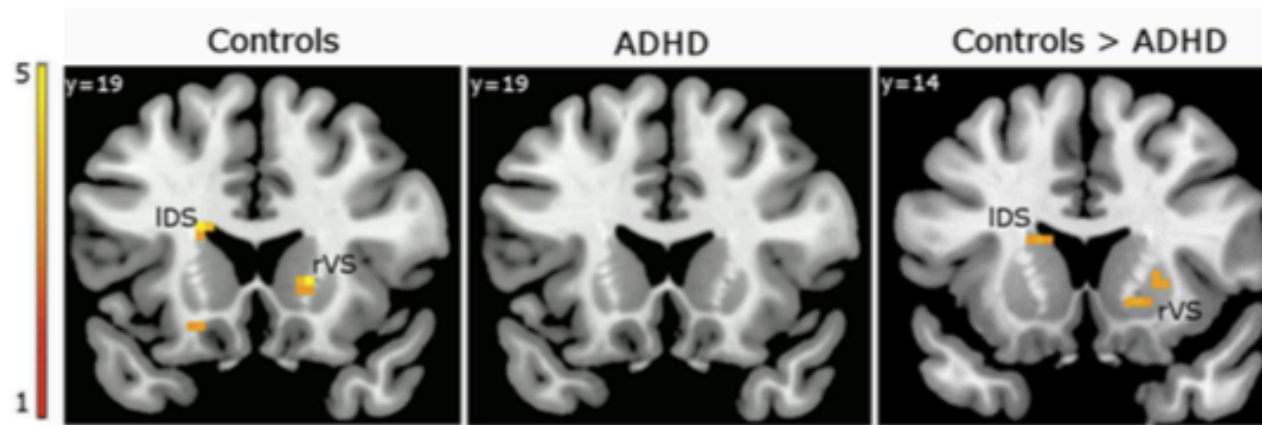
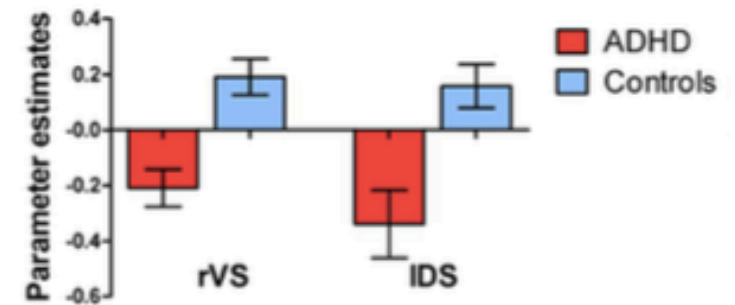


Figure 1. Classical conditioning fMRI paradigm. One of two neutral stimuli (Cue A or Cue B) was fol

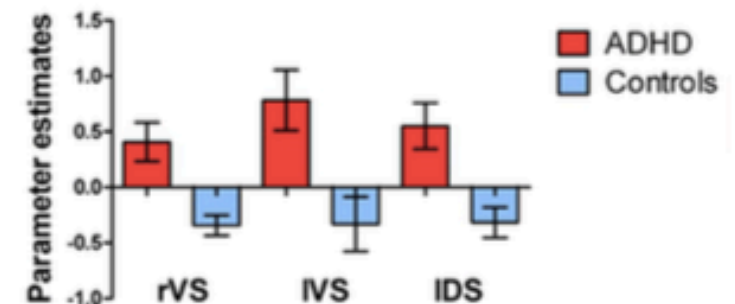
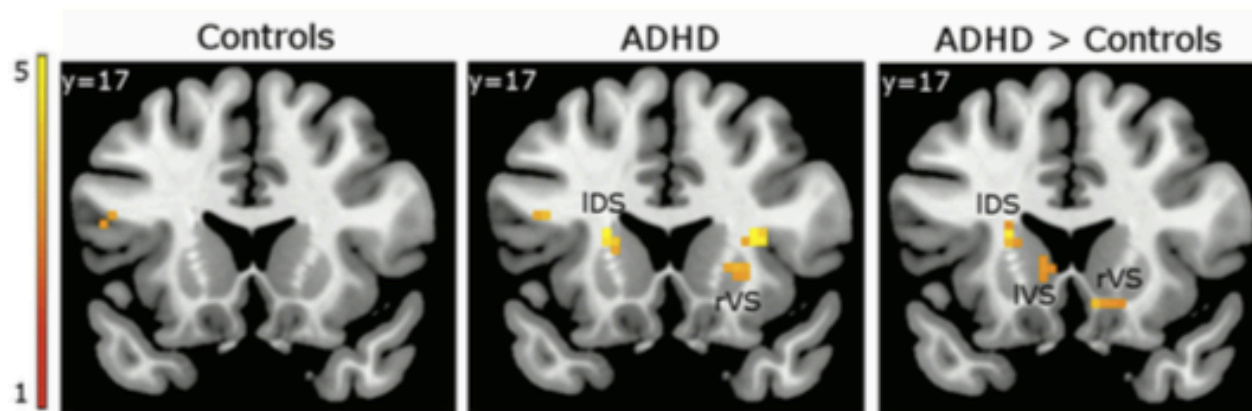
A) Striatal responses to reward anticipation in ADHD and Control groups



C) Mean parameter estimates and standard errors



B) Striatal responses to reward delivery in ADHD and Control groups



Anticipation récompense : ➤ striatum ventral droit et dorsal gauche seulement controls
 Obtention récompense : ➤ striatum ventral bilatéral et dorsal gauche seulement TDAH
 + proportionnel au nombre de symptômes d'hyperactivité/impulsivité

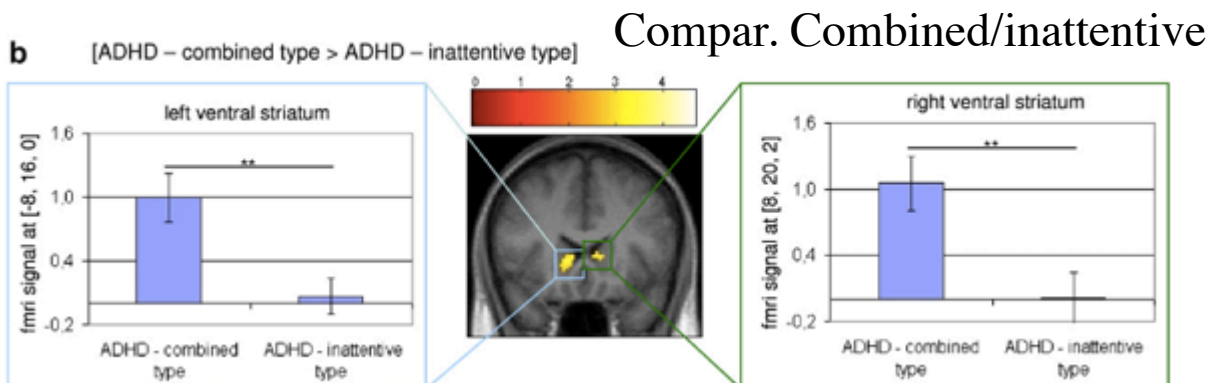
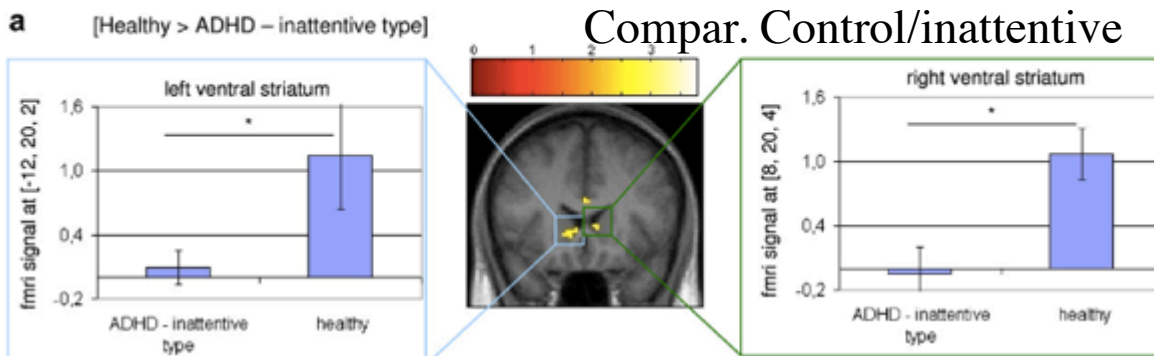


Differential reward processing in subtypes of adult attention deficit hyperactivity disorder

Marc-Andreas Edel^{a,1}, Björn Enzi^{a,*,1}, Henning Witthaus^a, Martin Tegenthoff^b, Sören Peters^c, Georg Juckel^a, Silke Lissek^b

^a Dept. of Psychiatry, Ruhr-University Bochum, LWL University Hospital, Bochum, Alexandrinenstr. 1, 44791 Bochum, Germany
^b Inst. of Neurology, Ruhr-University Bochum, RWTH Aachen University, Bochum, Germany

M.-A. Edel et al. / Journal of Psychiatric Research 47 (2013) 350–356

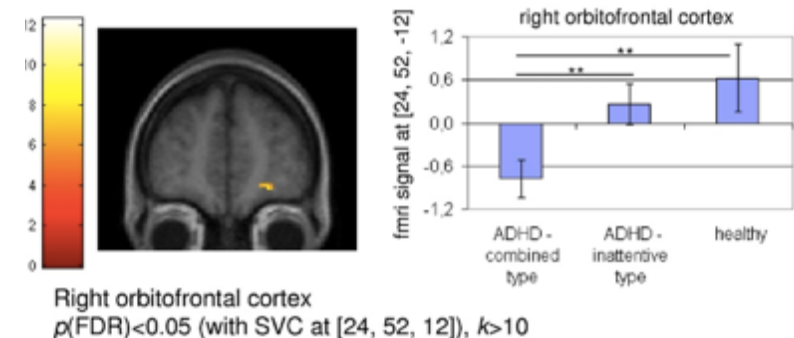


compare neural activations in the ventral striatum (VS) and prefrontal regions during reward processing in homogenous ADHD subtype groups and healthy adults, using the ‘Monetary Incentive Delay’ (MID) task.

Compared to ADHD-ct* and healthy subjects, ADHD-it** subjects showed a bilateral ventral striatal deficit during reward anticipation. In contrast, ADHD-ct subjects showed orbitofrontal hypo-responsiveness to reward feedback when compared with ADHD-it and healthy subjects.

*It = predominantly inattentive type

**ct = combined type

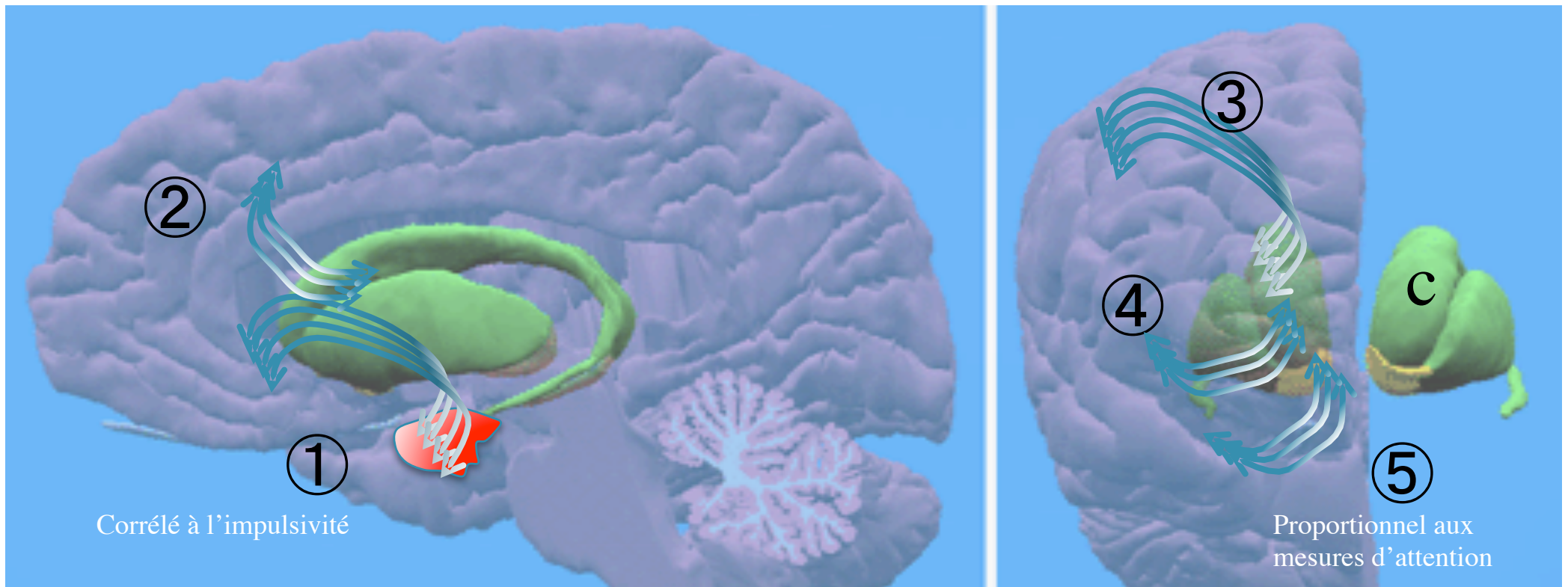


TDAH-impulsivité : imagerie fonctionnelle

- **En résumé :**
 - La distinction de déficits distincts dans deux systèmes (« chaud » et « froid ») des connexions frontales a permis de mettre en évidence une dissociation des circuits impliqués dans le TDAH par l'utilisation de tâches impliquant une récompense monétaire
 - Il y a convergence de résultats en faveur d'une sous-activation du striatum ventral dans ce type de tâches dans le TDAH, suggérant pour le moins un rôle déterminant des systèmes de la récompense dans l'impulsivité et l'aversion au délai
 - Cette dysfonction serait également présente, et peut-être encore plus nette, dans les formes inattentives pures, suggérant d'y voir une signature du phénotype TDAH, plutôt qu'une simple conséquence fonctionnelle du trouble

A faint, stylized silhouette of a human brain is visible in the background, centered behind the text.

TDAH : apport des études de connectivité (en particulier morphométriques)



- TDAH : schématisation des principaux faisceaux d'association issus du cortex frontal tels qu'ils peuvent être individualisés en tractographie IRM.
- **anomalie d'anisotropie en tractographie** proportionnelle à diverses mesures des fonctions exécutives (mémoire de travail, attention soutenue, flexibilité...)

4, 5 : fronto-strié ventro-latéral et orbito-caudé : corrélés au déficit attentionnel

1 : unciné : corrélé à l'impulsivité

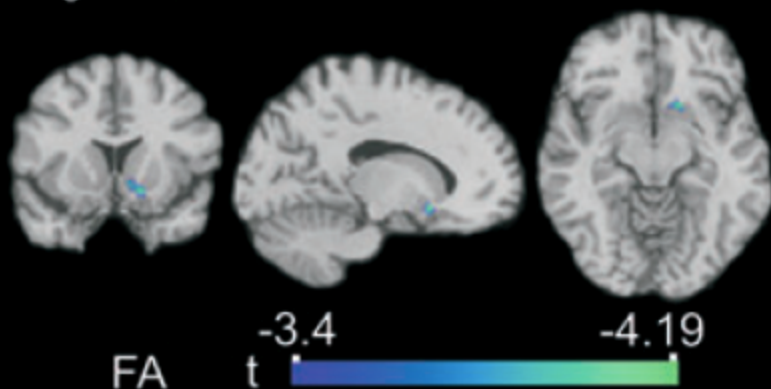
D'après Chang et al. (2012); Wu et al. (2012)

Disturbed structural connectivity is related to inattention and impulsivity in adult attention deficit hyperactivity disorder

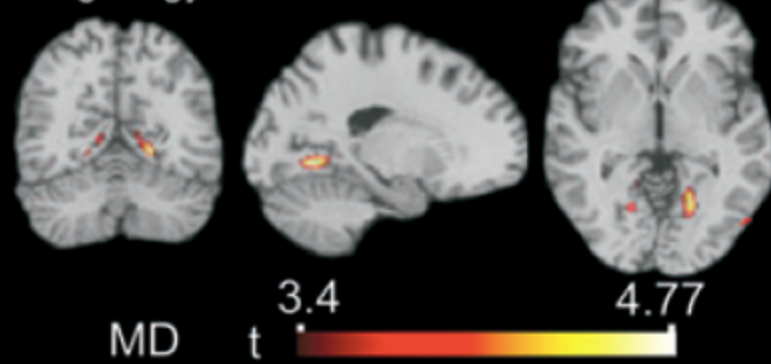
Andreas Konrad,¹ Thomas F. Dierker, ^{1,2} Dschamil El Masri,¹ Martin Bayerl,^{1,3} Christoph Fehr,¹ Thomas Gesier
Goran Vucurevic,⁴ Peter Stoeter⁴ and Georg Winterer⁵
¹Department of Psychiatry and Psychotherapy, University Medical Centre of the Johannes Gutenberg-University, Mainz, Ger



Right orbitofrontal white matter

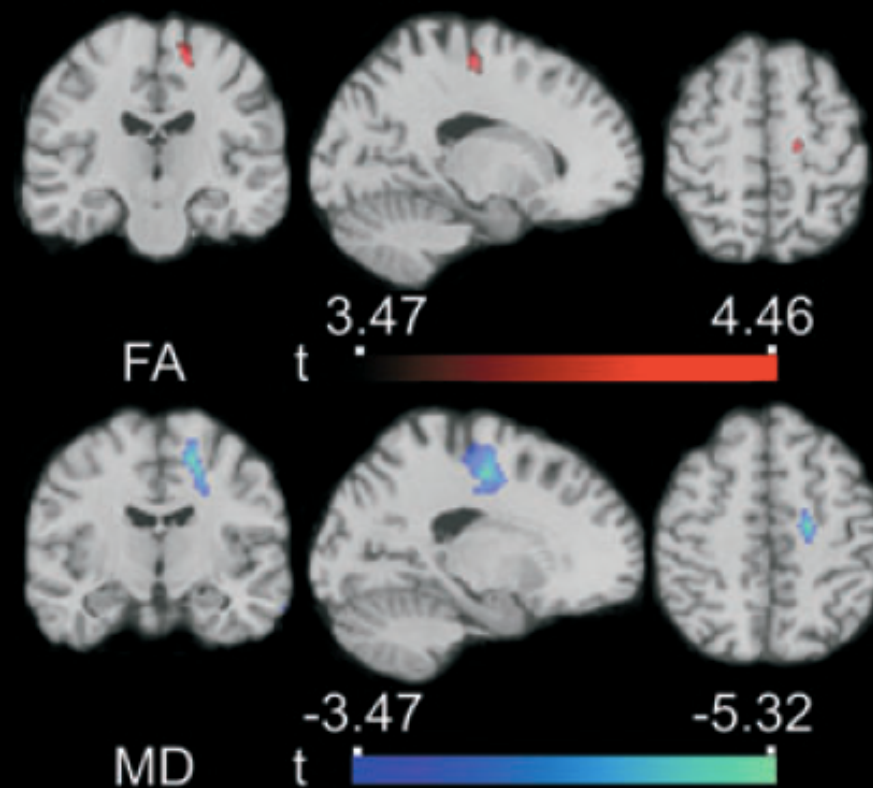


Lingual gyrus



Corrélacion
négative FA
et impulsivité :
Orbito-frontal et
VS

Right superior longitudinal fasciculus



Corrélacion entre les mesures
tractographiques
(anisotropie=FA; diffusivité
moyenne = MD) et

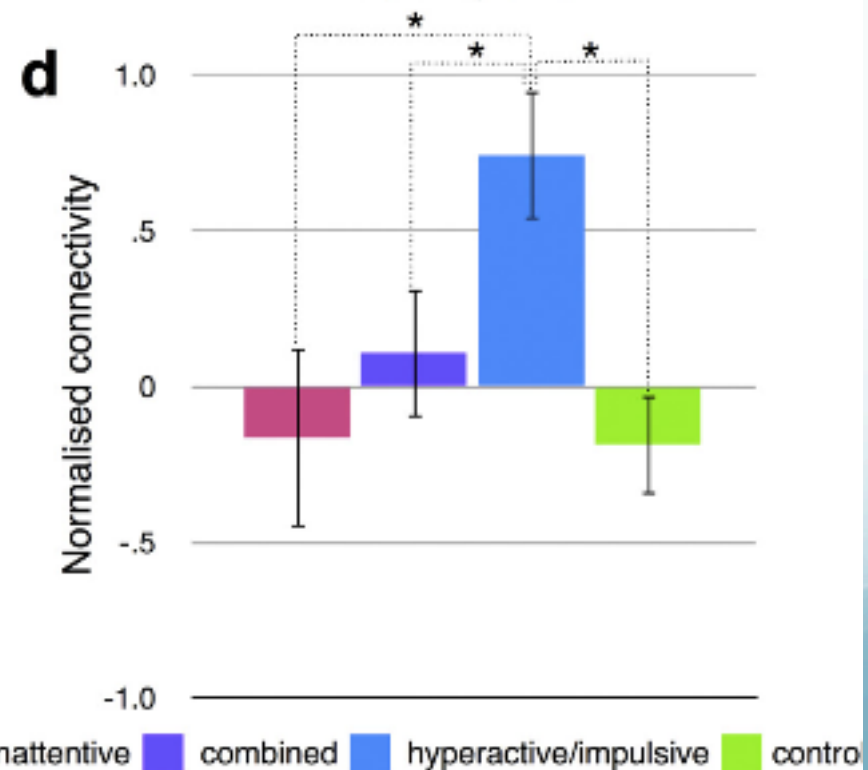
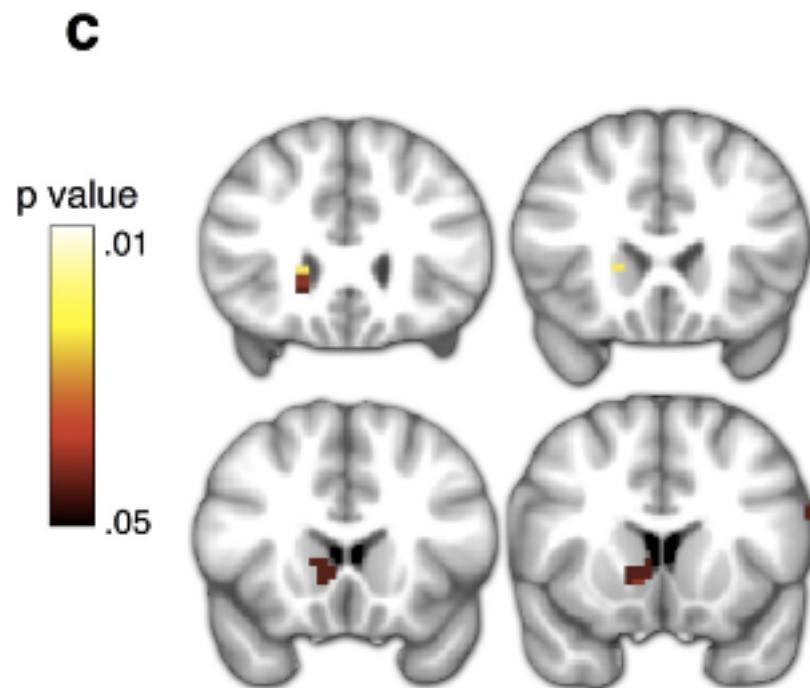
- le score d'inattention,
- le degré d'impulsivité

Double-dissociation between the mechanism leading to impulsivity and inattention in Attention Deficit Hyperactivity Disorder: A resting-state functional connectivity study

Masafumi Sanefuji ^{a,b,1}, Michael Craig ^{a,b,f,1}, Valeria Parlatini ^{a,b}, Mitul A. Mehta ^c, Declan G. Murphy ^{a,b}, Marco Catani ^{a,b,c}, Leonardo Cerliani ^{d,e} and Michel Thiebaut de Schotten ^{a,b,c,d,e,*}

^a Natbrainlab, Department of Forensic and Neurodevelopmental Science (FANS), Institute of Psychiatry, King's College London, UK

The right striatum shows an increased functional connectivity in the group 'hyperactive/impulsive when compared to the group 'inattentive for the cortico-striatal network



<http://dx.doi.org/10.1016/j.cortex.2016.06.005>

Particularly, the hyperactive / impulsive subtype was associated with increased connectivity in cortico-striatal network, whereas the inattentive subtype was associated with increased connectivity in the right ventral attention network.

Average functional connectivity in the cluster reported as significant in the striatum.



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Reward circuit connectivity relates to delay discounting in children with attention-deficit/hyperactivity disorder

Taciana G. Costa Dias^{a,b,*}, Vanessa B. Wilson^a, Deepti R. Bathula^c, Swathi P. Iyer^a, Kathryn L. Mills^{d,e}, Bria L. Thurlow^{a,b}, Corinne A. Stevens^{a,b}, Erica D. Musser^b, Samuel D. Carpenter^{a,b}, David S. Grayson^{a,b}, Suzanne H. Mitchell^{a,b}, Joel T. Nigg^{a,b}, Damien A. Fair^{a,b,f,g,h}

^aDepartment of Behavioral Neuroscience, Oregon Health & Science University, Portland, OR, USA

Reward circuit connectivity in ADHD

39

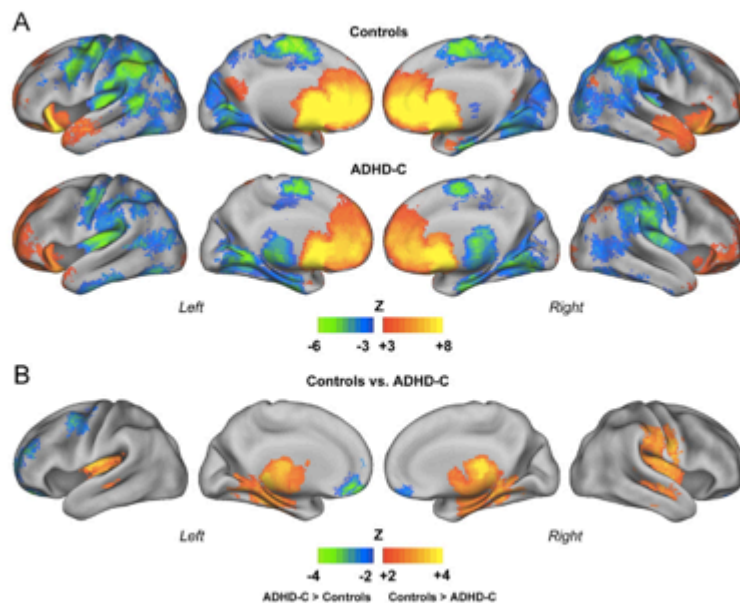
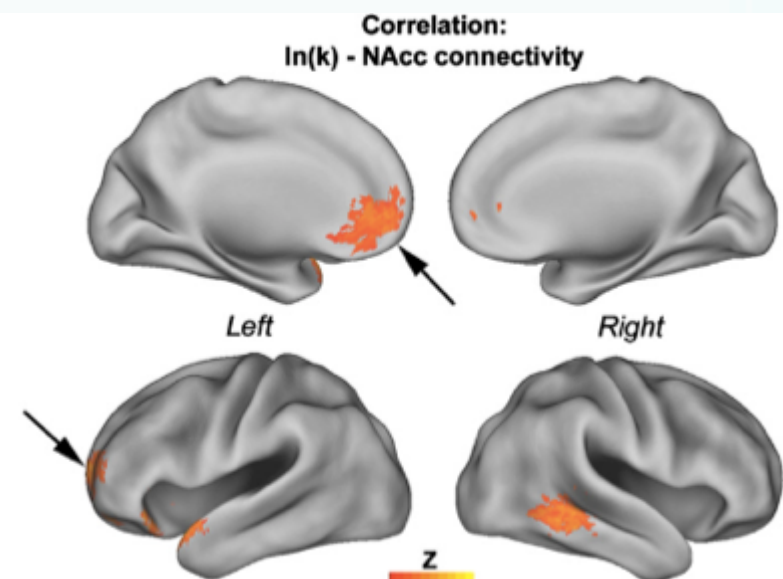


Figure 1 Voxelwise resting state functional connectivity maps for the nucleus accumbens (NAcc). Results for control children and children with combined type ADHD (ADHD-C) (A); and direct comparison between groups (B). Results show atypical functional connectivity of the NAcc in children with ADHD-C. For all analyses Monte Carlo simulation was applied to correct for multiple comparisons (minimum $Z > 2.25$, $p < 0.05$, corrected).

133 Children were presented a computerized task (Wilson et al. (2011): 91 questions for which children had to choose between smaller amounts of hypothetical money now and hypothetical \$10.00 after a varying delay. K values indicate greater preference for immediate rewards

We found that functional connectivity of NAcc was atypical in children with ADHD and the ADHD-related increased connectivity between NAcc and the prefrontal cortex was associated with greater impulsivity (steeper delayed-reward discounting).

These findings are consistent with the hypothesis that atypical signaling of the NAcc to the prefrontal cortex in ADHD may lead to excessive approach and failure in estimating future consequences; thus, leading to impulsive behavior.



White Matter Microstructure and the Variable Adult Outcome of Childhood Attention Deficit Hyperactivity Disorder

Philip Shaw^{1,2,4}, Gustavo Sudre^{1,4}, Amy Wharton¹, Daniel Weingart¹, Wendy Sharp² and Joelle Sarlls³

¹Section on Neurobehavioral Clinical Research, Social and Behavioral Research Branch, National Human Genome Research Institute, Bethesda, MD, USA; ²Intramural Program of the National Institute of Mental Health, Bethesda, MD, USA; ³NIH MRI Research Facility/National Institute of Neurological Diseases and Stroke/National Institutes of Health, Bethesda, MD, USA

Table 1 Demographic and Clinical Characteristics of the Participants

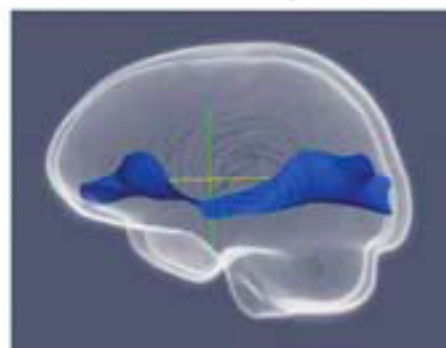
	Persistent ADHD N = 32	Remitted ADHD N = 43	Never-affected comparison N = 74	
Age (years) at assessment: mean (SD)	23.3 (3.7)	24.1 (3.9)	24 (3.3)	F(2,146) = 0.51, p = 0.61
IQ: mean (SD)	111 (12)	114 (14)	113 (11)	F(2,127) = 0.89, p = 0.41
Sex: males/females	13/19	26/17	44/30	χ ² (2) = 3.77, p = 0.15
Symptoms, mean number (SD)				
Inattention	5.7 (1.9)	1.8 (1.4)	NA	t(73) = 10.5, p < 0.0001
Hyperactivity-impulsivity	4.3 (2.5)	1.5 (1.4)	NA	t(73) = 6.0, p < 0.0001
Comorbidity				
Any comorbidity	9 (28%)	5 (11%)	N/A	Any comorbidity vs none, Fisher's exact test p = 0.08
Depression	4	1		
Dysthymia	1	1		
GAD/panic disorder	2	2		
Anxiety NOS	2	2		
Psychostimulant treatment				
Taking psychostimulant medication	16 (50%)	2 (5%)	N/A	Fisher's exact test p < 0.0001

Abbreviations: GAD, Generalized anxiety disorder; NOS, not otherwise specified. Missing data are indicated in the degrees of freedom.

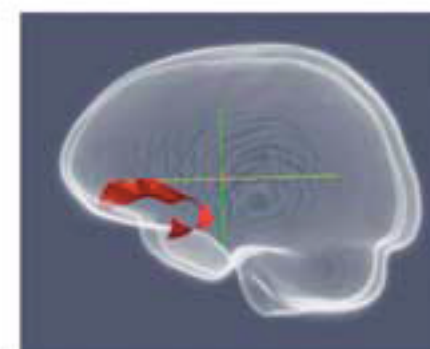
All tracts



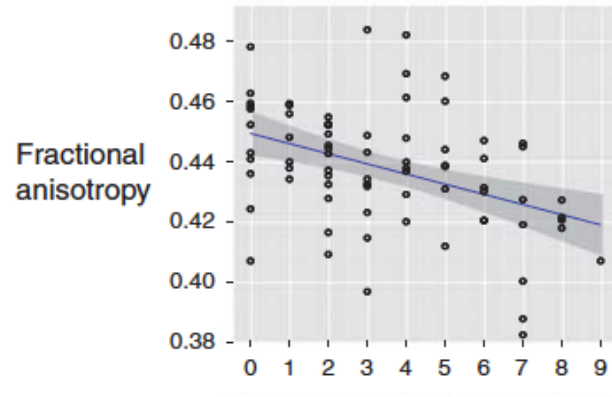
Inferior fronto-occipital fasciculus



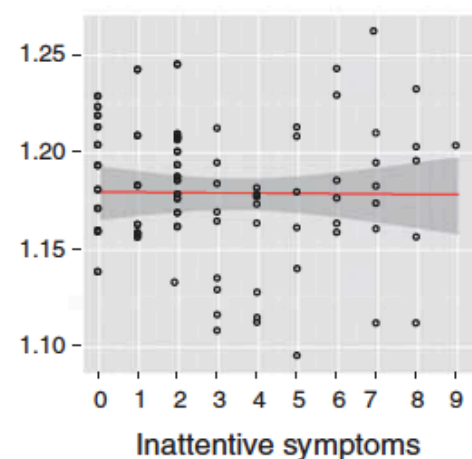
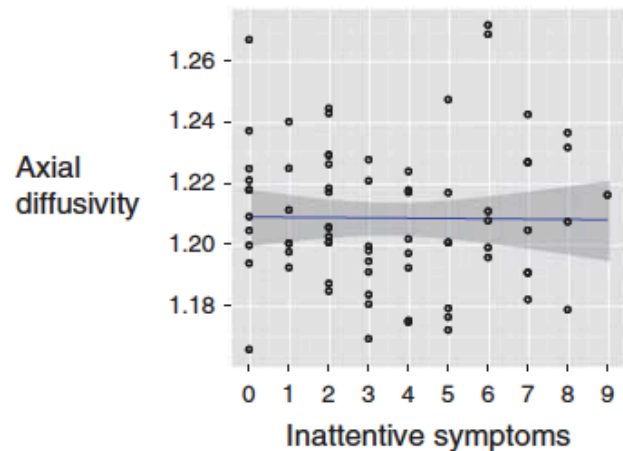
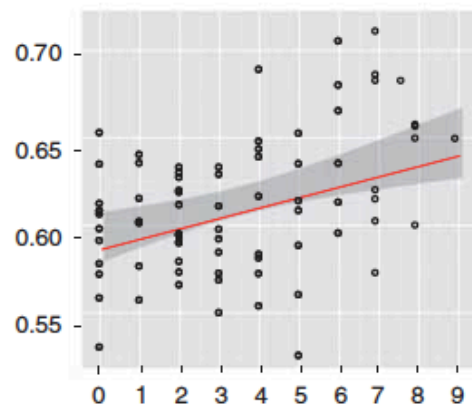
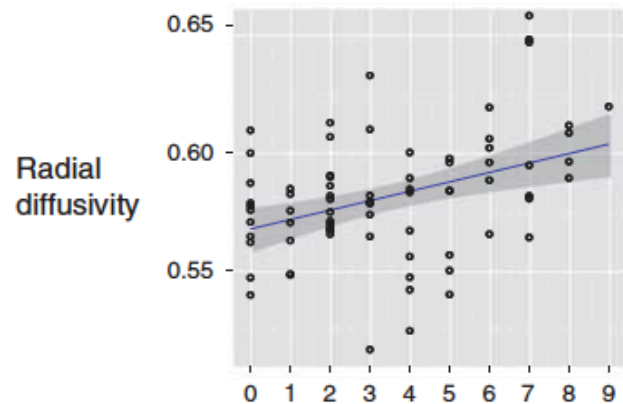
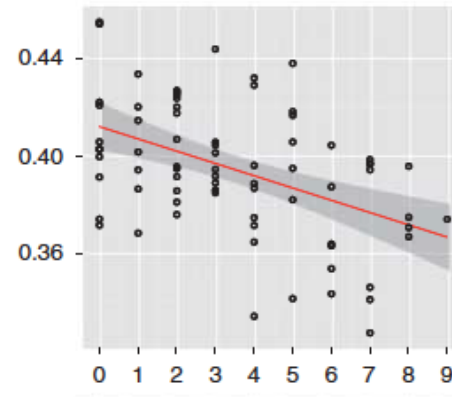
Uncinate fasciculus



Uncinate



IFOF



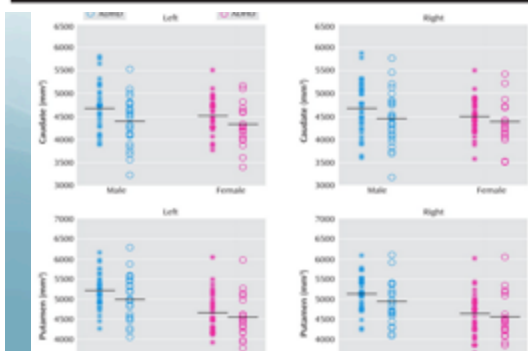
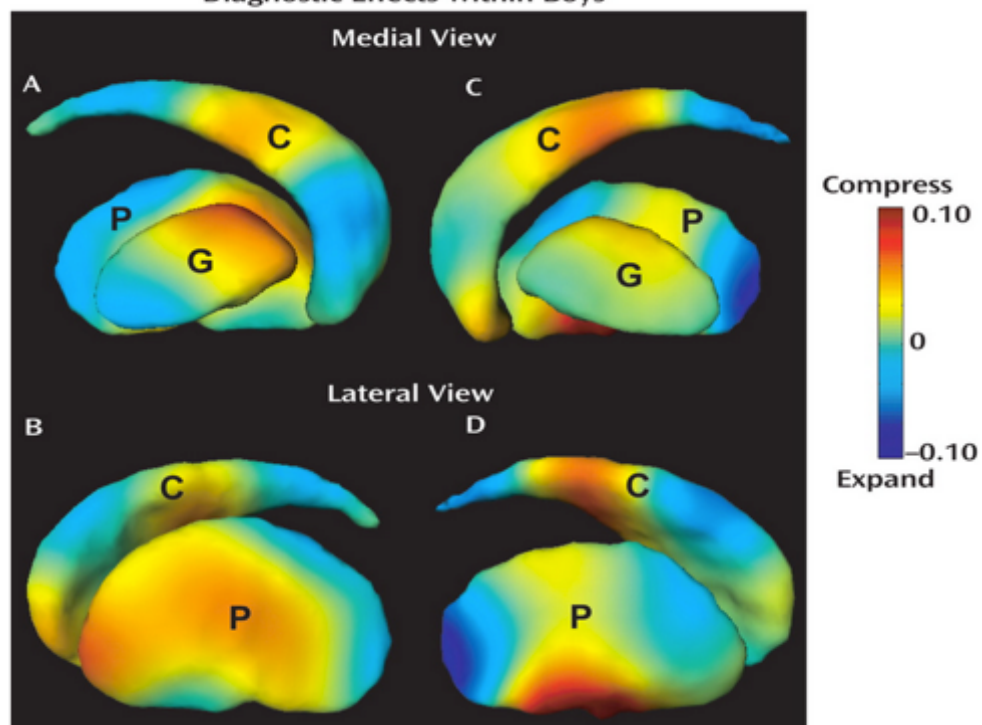
- Tract-based analyses showed that greater adult inattention, but not hyperactivity–impulsivity, was associated with significantly lower fractional anisotropy in the left uncinate (standardized b . 0.37, t .3.28, p . 0.002) and inferior fronto-occipital fasciculi (standardized b . 0.37, t .3.29, p .0.002).

- The ADHD group with symptoms persisting into adulthood had significantly lower fractional anisotropy than the never-affected controls in these tracts, differences associated with medium to large effect sizes. By contrast, the ADHD group that remitted by adulthood did not differ significantly from controls. The anomalies were found in tracts that connect components of neural systems pertinent to ADHD, such as attention control (inferior fronto-occipital fasciculus) and emotion regulation and the processing of reward (the uncinate fasciculus).

- Change in radial rather than axial diffusivity was the primary driver of this effect, suggesting pathophysiological processes including altered myelination as future targets for pharmacological and behavioral interventions.



Diagnostic Effects Within Boys



New research

Mapping the Development of the Basal Ganglia in Children With Attention-Deficit/Hyperactivity Disorder

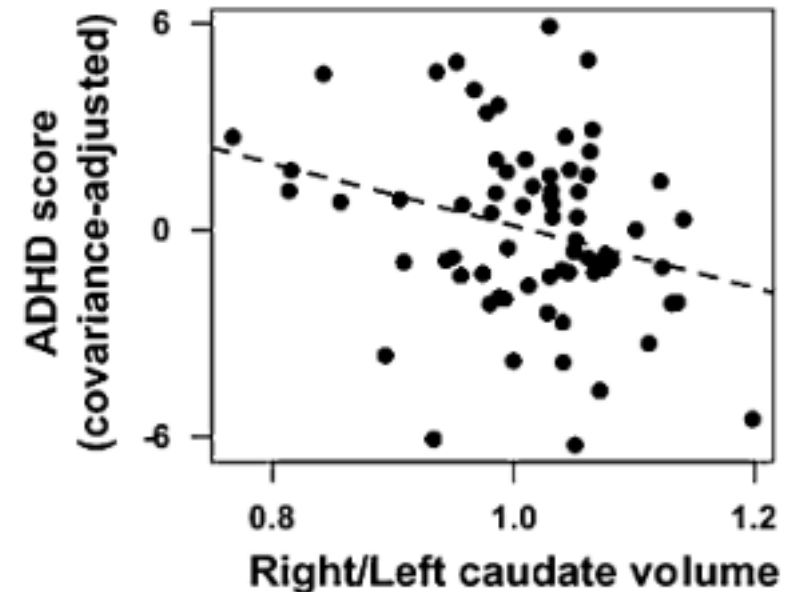
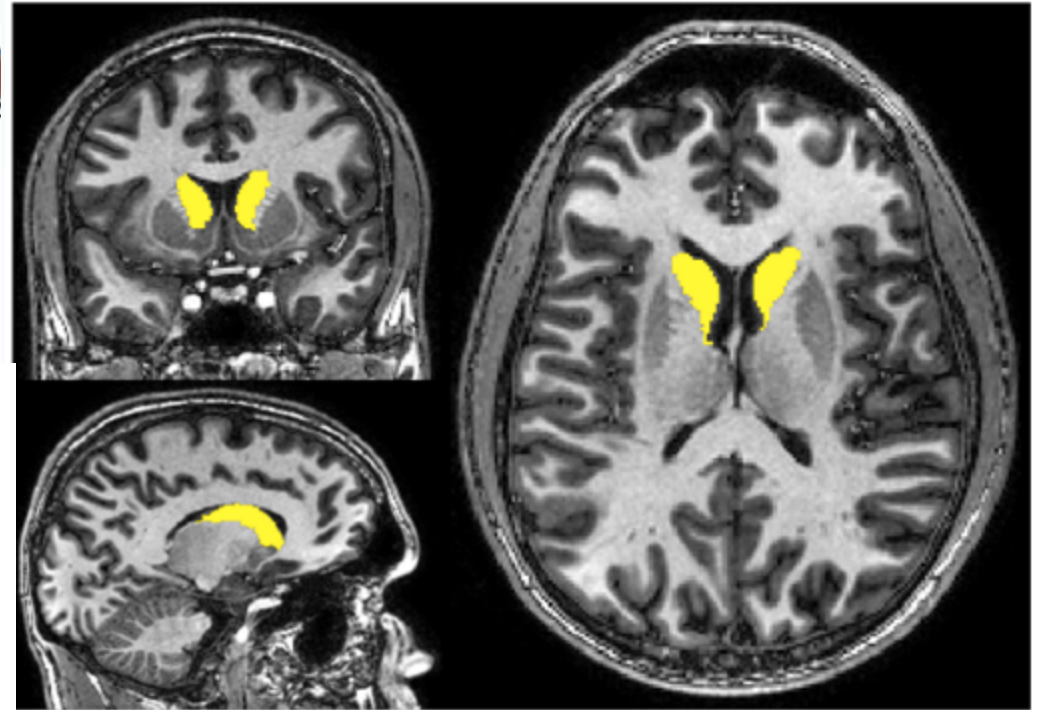
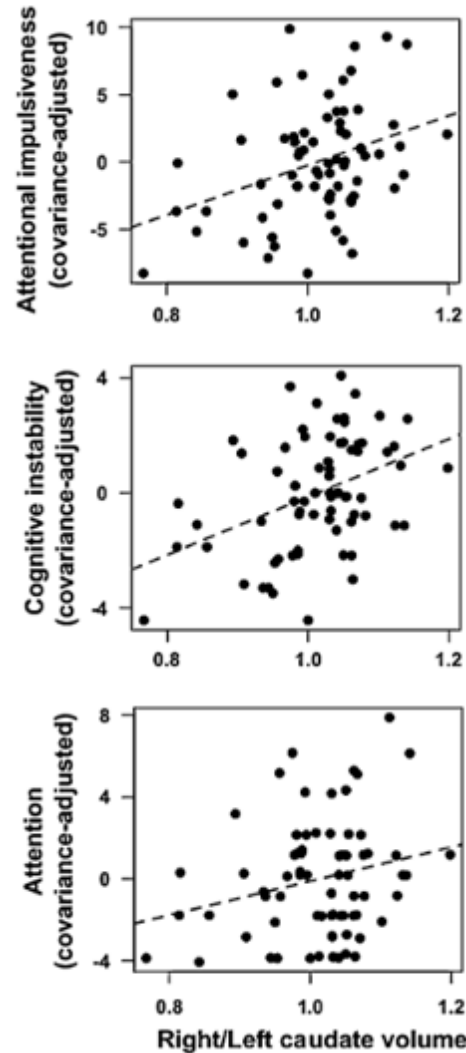
Philip Shaw, MD, PhD^a, Pietro De Rossi, MD^b, Bethany Watson, BA^a, Amy Wharton, BA^a, Deanna Greenstein, PhD^c, Armin Raznahan, MD, PhD^c, Wendy Sharp, MSW^a, Jason P. Lerch, PhD^a, M. Mallar Chakravarty, PhD^d

In the **ventral striatal surfaces**, there was a diagnostic difference in developmental trajectories ($t = 5.6, p < .0001$). Here, the typically developing group showed **surface area expansion with age** (estimated rate of increase of 0.54 mm^2 per year, standard error [SE] 0.29 mm^2 per year), whereas **the ADHD group showed progressive contraction** (decrease of 1.75 mm^2 per year, SE 0.28 mm^2 per year). The ADHD group also showed significant, **fixed surface area reductions in dorsal striatal regions**, which were detected in childhood at study entry and persisted into adolescence.

Caudate asymmetry is related to attentional impulsivity and an objective measure of ADHD-like attentional problems in healthy adults

Linh C. Dang · Gregory R. Samanez-Lark
Jacob S. Young · Ronald L. Cowan ·

We found that larger right relative to left caudate volumes correlated with both higher attentional impulsiveness and worse ADHD scores on the TOVA. Increased stimulus-driven signals reaching the right hemisphere may result in unnecessary updating of current cortical representations, leading to instability in attentional processing.

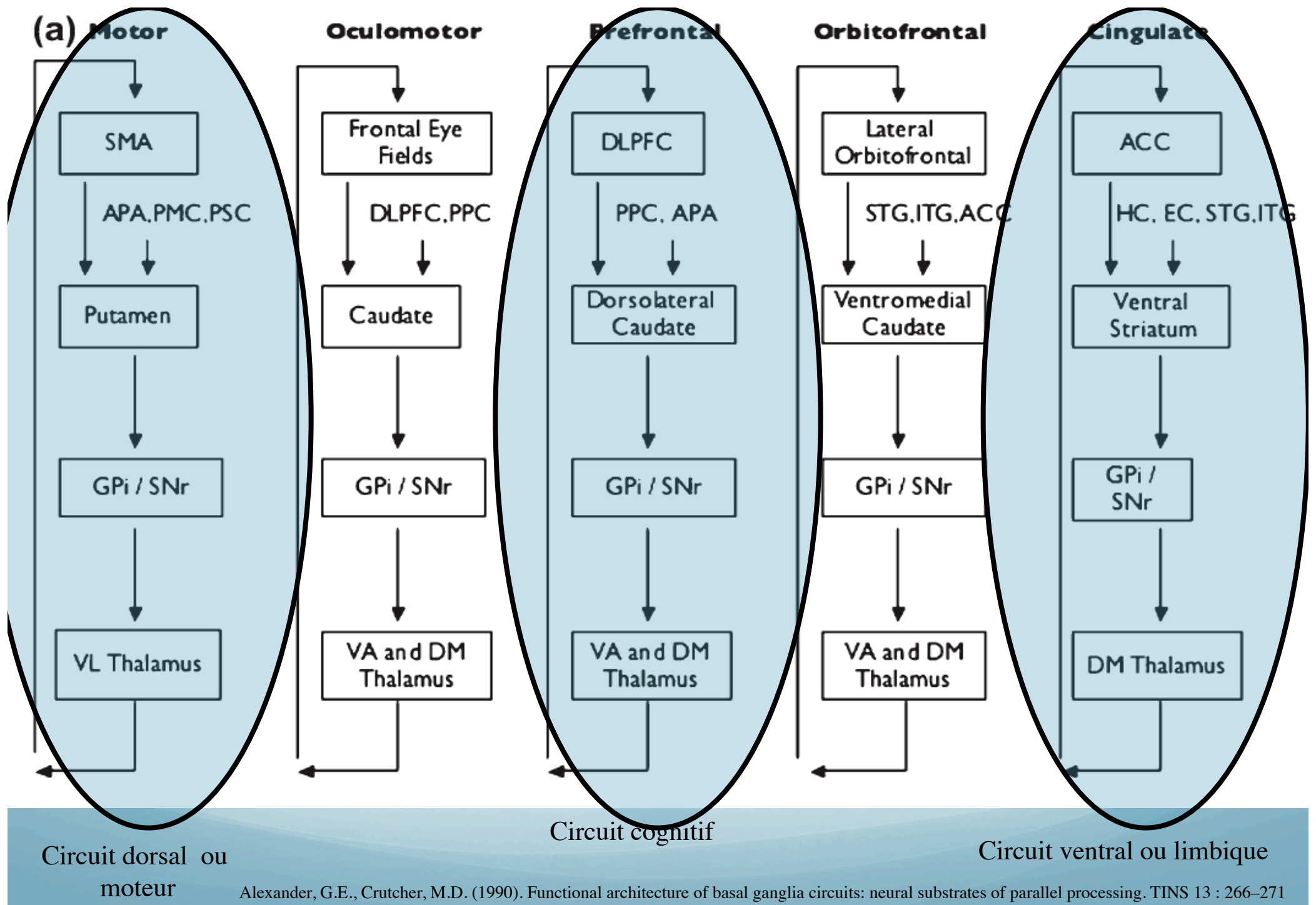


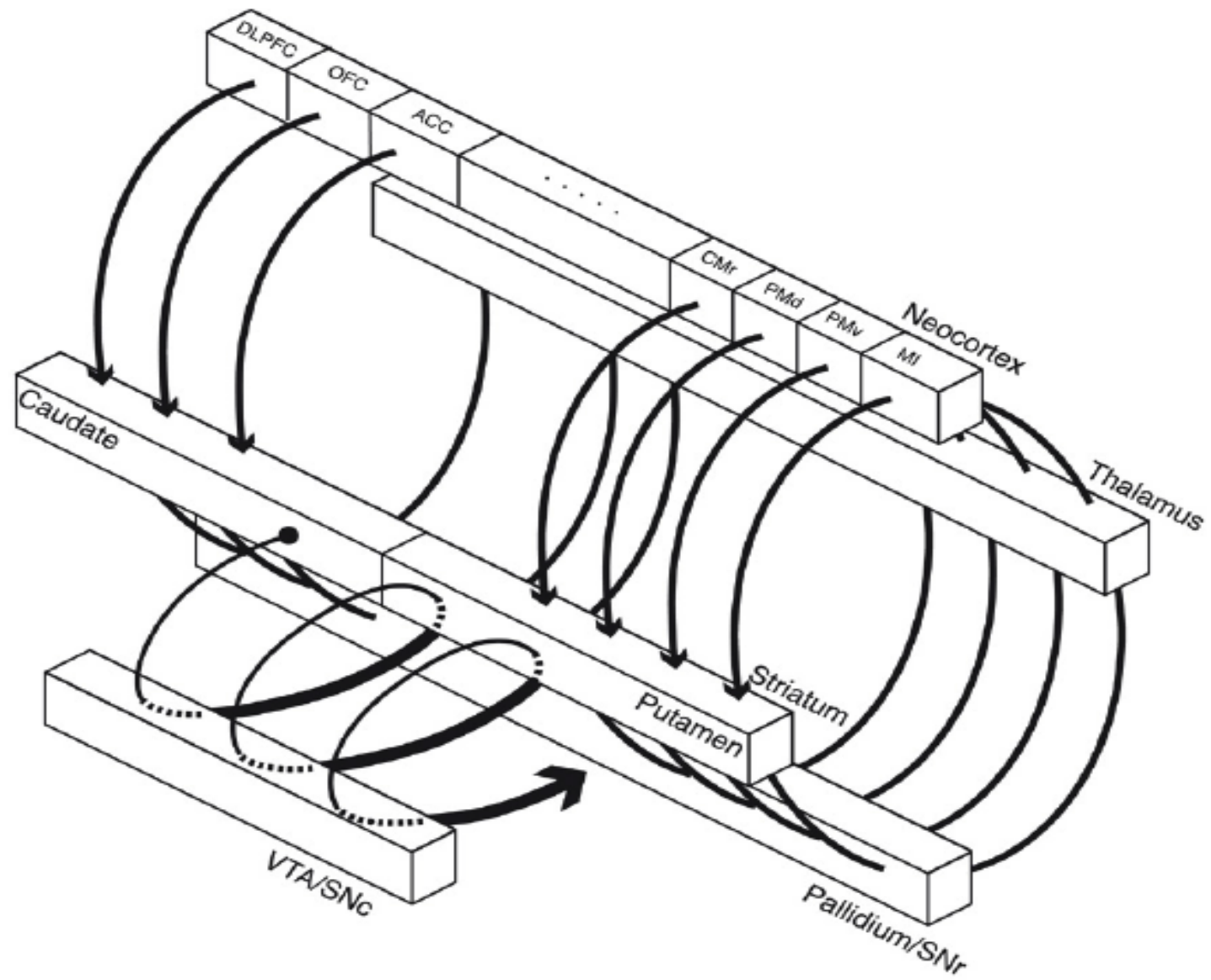
Conclusion (1)

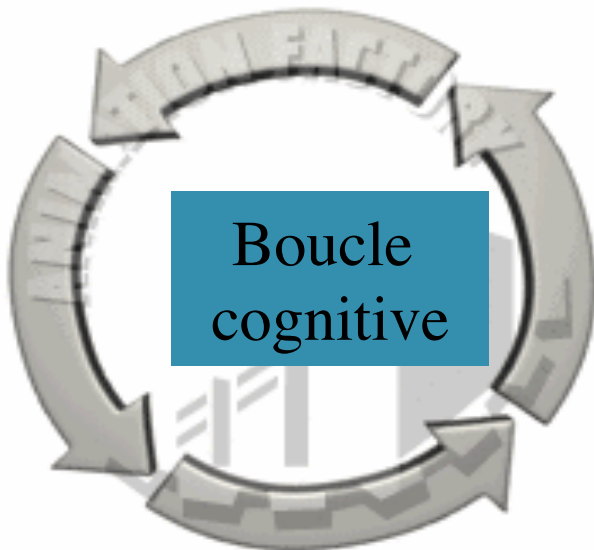
- La dysfonction des systèmes exécutifs « froids », sous-tendus par le cortex frontal latéral, reste une explication valide de la limitation des capacités attentionnelles, en particulier l'attention soutenue
- L'impulsivité et l'aversion au délai (« hot-executive »), sous-tendus par les circuits à origine orbito-frontale, seraient plutôt liés à un défaut d'ajustement des systèmes de la récompense, en particulier lors de comorbidité avec des troubles des conduites
- En définitive, tout se passe comme si dans le TDAH il y avait une altération de la capacité d'anticiper la valeur récompensante des stimuli, entraînant un comportement d'approche excessif et une hyperconnectivité de ces mêmes structures avec le cortex préfrontal (médian et orbitaire principalement), pouvant contribuer au trouble de l'attention.

Conclusion (2)

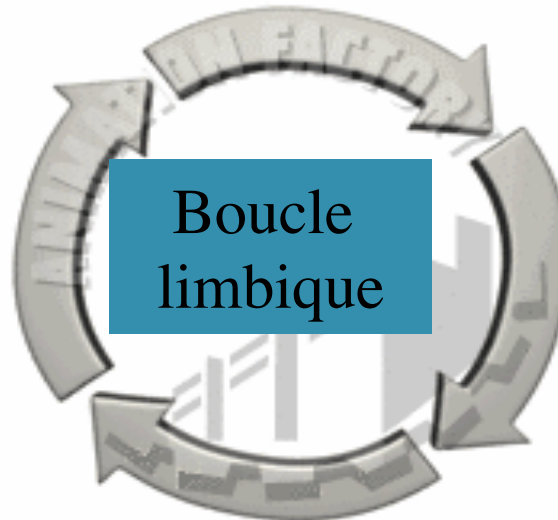
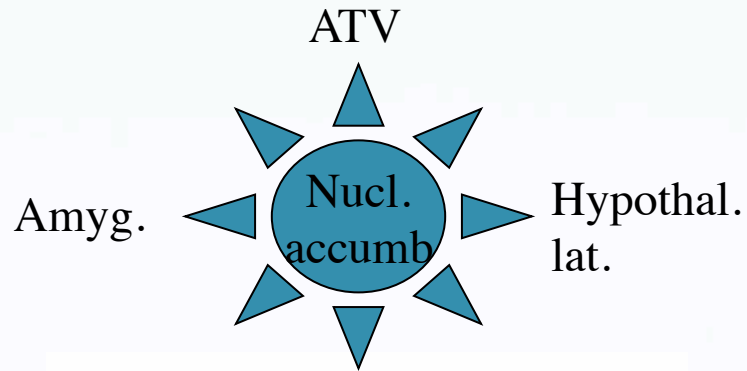
- On relève des différences de résultats entre les différents travaux disponibles à ce jour, peut-être liées à des différences méthodologiques (dans la technique IRM ou selon l'approche catégorielle ou dimensionnelle du problème)
- Malgré ce, il y a convergence de la majorité des travaux pour lier l'impulsivité à une connectivité accrue dans les circuits cortico-striataux sous-tendant les fonctions exécutives « chaudes », circuits centrés sur le striatum ventral ou limbique, élément crucial du système de la récompense.
- Ainsi, il existe de plus en plus d'arguments, en particulier anatomiques, pour présumer que le primum movens dans le TDAH est une dysfonction au niveau des circuits de la récompense et que les autres systèmes sont secondairement dysfonctionnels.



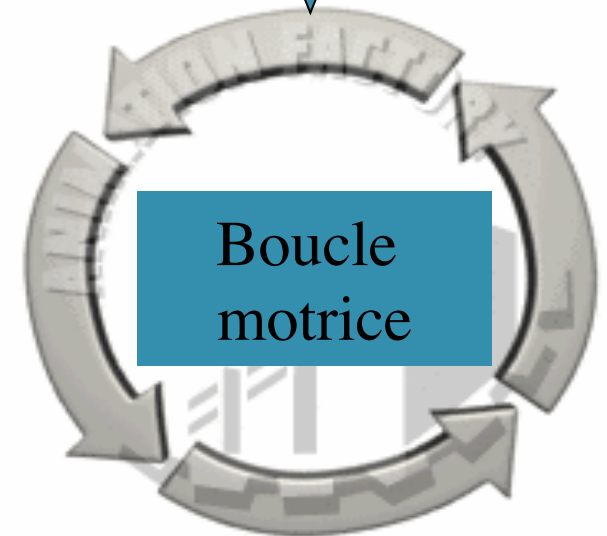




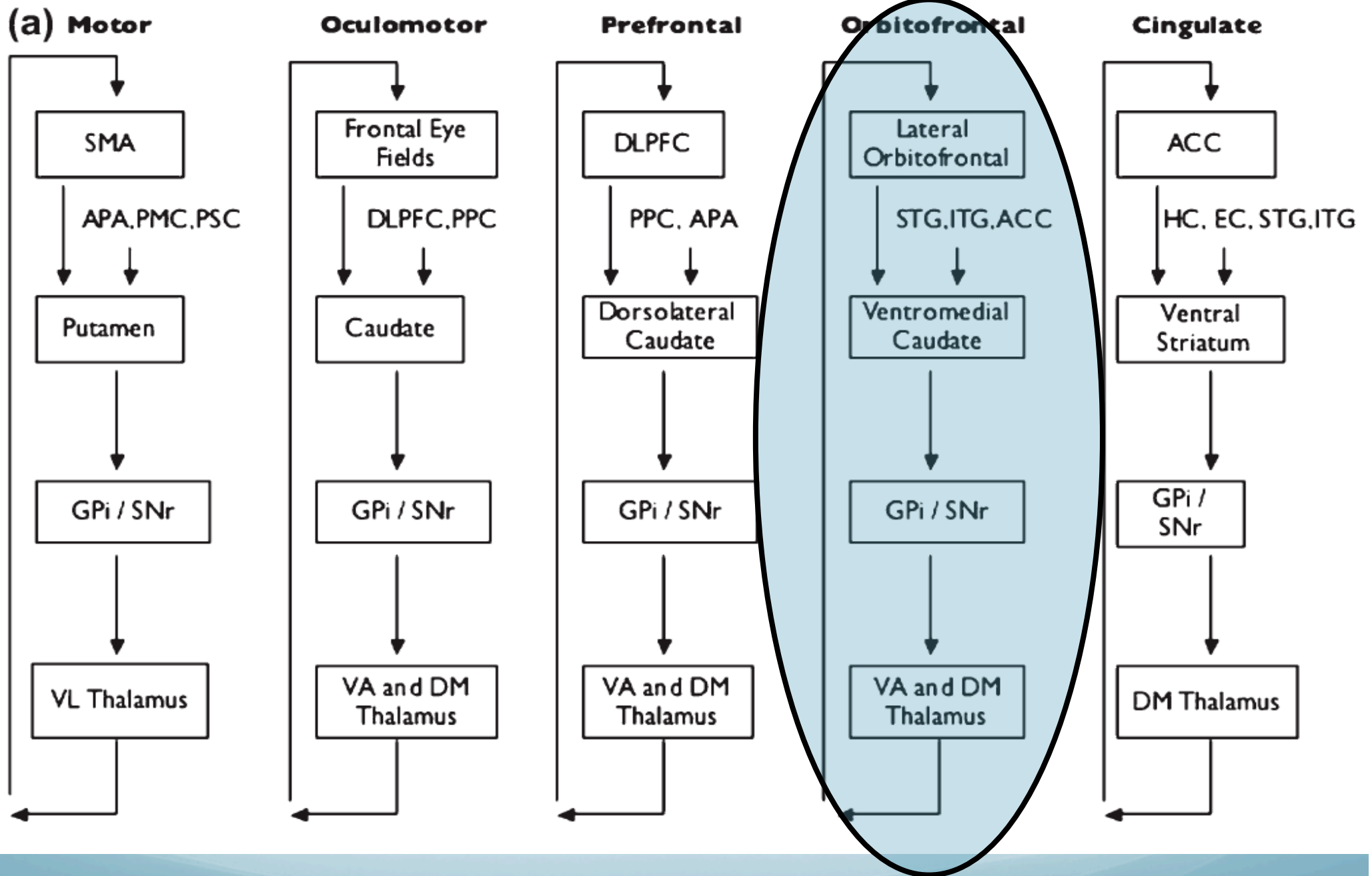
Inattention, sensibilité interférence,
mémoire de travail , fct exé froides
←hyperactivité mentale?



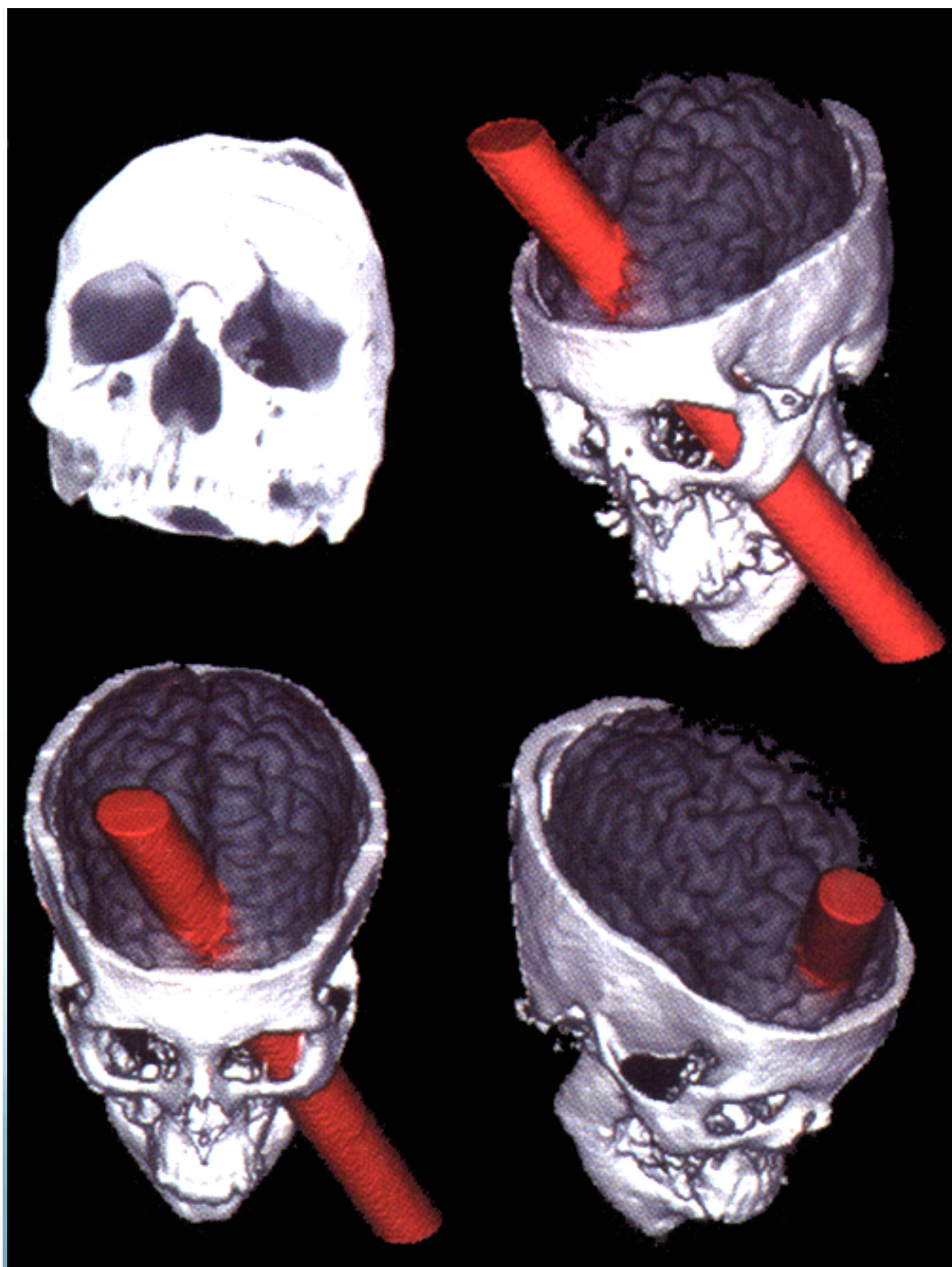
Impulsivité, « delay
aversion », fct exé
'chaudes' défaut
renforcement, tendance
aux addictions



Agitation motrice
Troubles coordination et procédures



Circuit ventral latéral : ajustement social, conduites à risques, prises de décision...



ASYMMETRIC FUNCTIONAL ROLES OF RIGHT AND LEFT VENTROMEDIAL PREFRONTAL CORTICES IN SOCIAL CONDUCT, DECISION-MAKING, AND EMOTIONAL PROCESSING

Daniel Tranel, Antoine Bechara and Natalie I. Denburg

(Department of Neurology, Division of Cognitive Neuroscience, University of Iowa
College of Medicine)

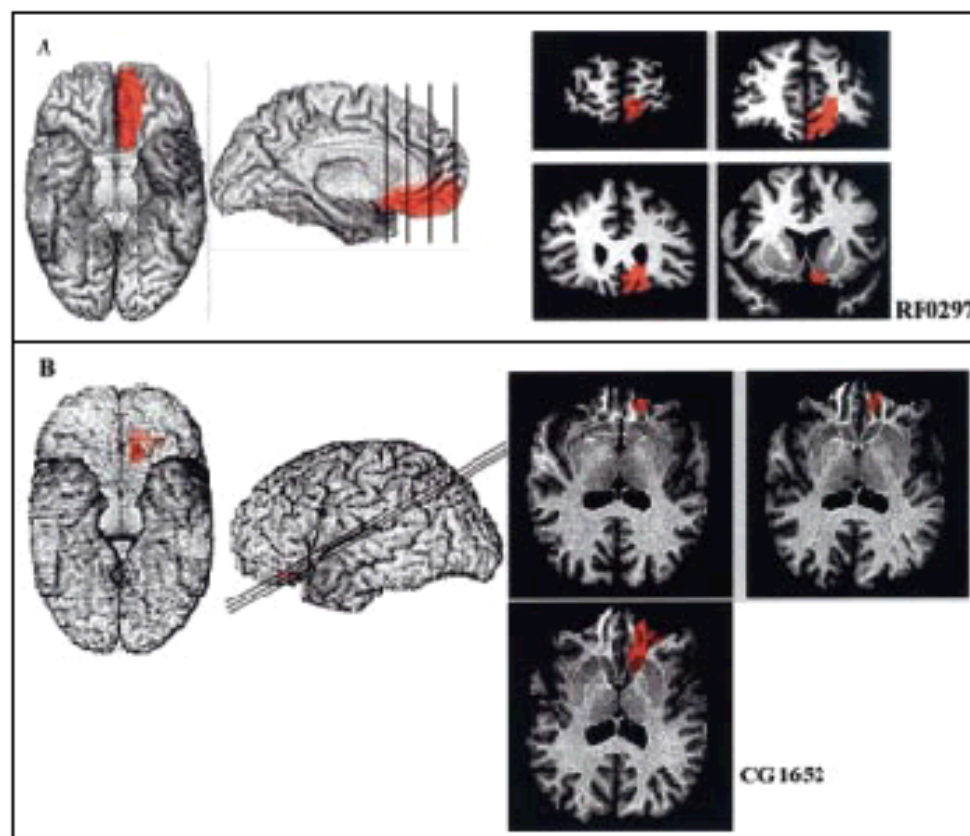


Fig. 1 – Brain sections depicting the extent of the prefrontal lesions in the 7 subjects who participated in this study. Each panel depicts the lesion from one subject. The identification number of the subject is shown in the lower right corner of each panel.

La prise de décision

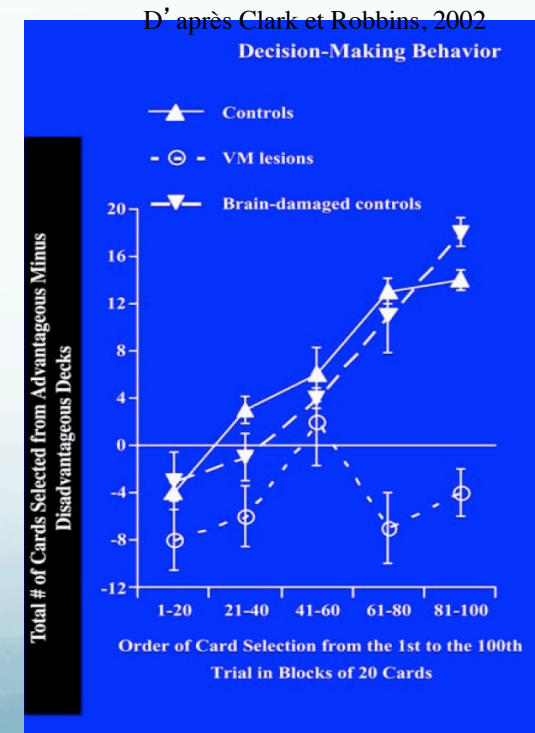
- Tâche de prise de décision: tâche de casino (Iowa gambling test)
- Déficits en marqueurs somatiques
 - VM: choix désavantageux > avantageux (Bechara, 2004)
 - Psychopathie: controversé
 - Absent (Blair et Cipolotti, 2000 ; Schmitt et al., 1999)
 - Présent (Blair et al., 2001 ; Mitchell et al., 2002 ; Van Honk et al., 2002)



insensibilité aux punitions
ou hypersensibilité aux récompenses

	Decks A and B	Decks C and D
Original task	High reward (\$100 per go). Intermittent high losses. Net loss.	Lower reward (\$50 per go). Intermittent low losses. Net profit.
Variant task	High loss (\$100 per go). Intermittent high reward. Net profit.	Lower loss (\$50 per go). Intermittent low reward. Net loss.

TRENDS in Cognitive Sciences



D'après Bechara, 2004

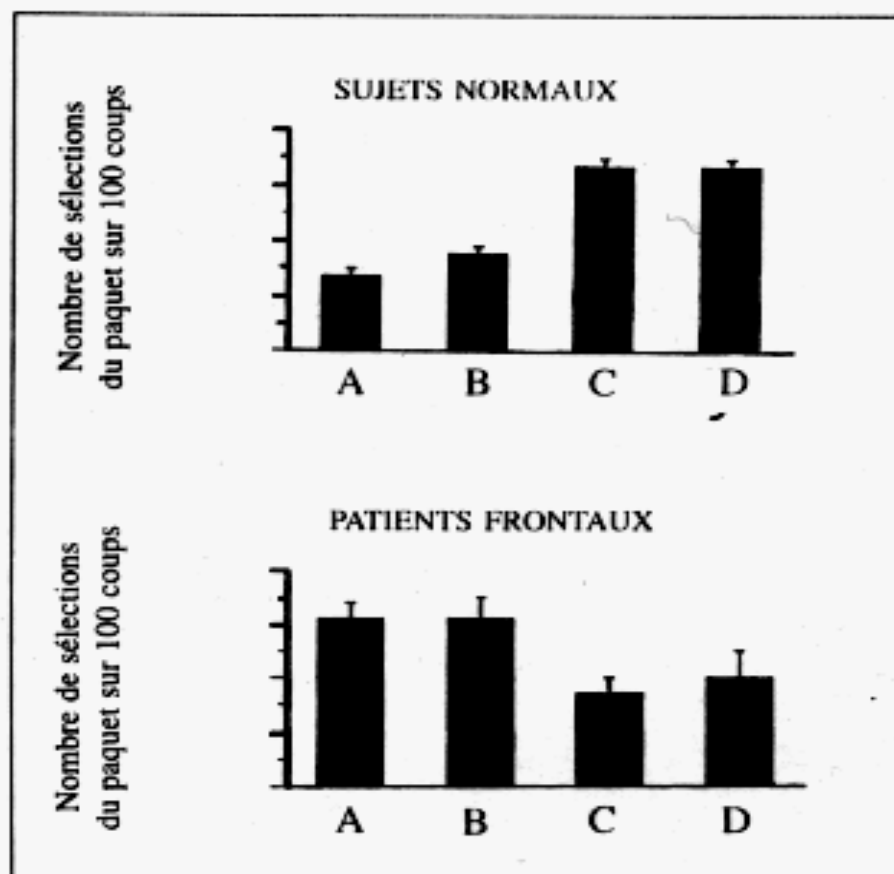
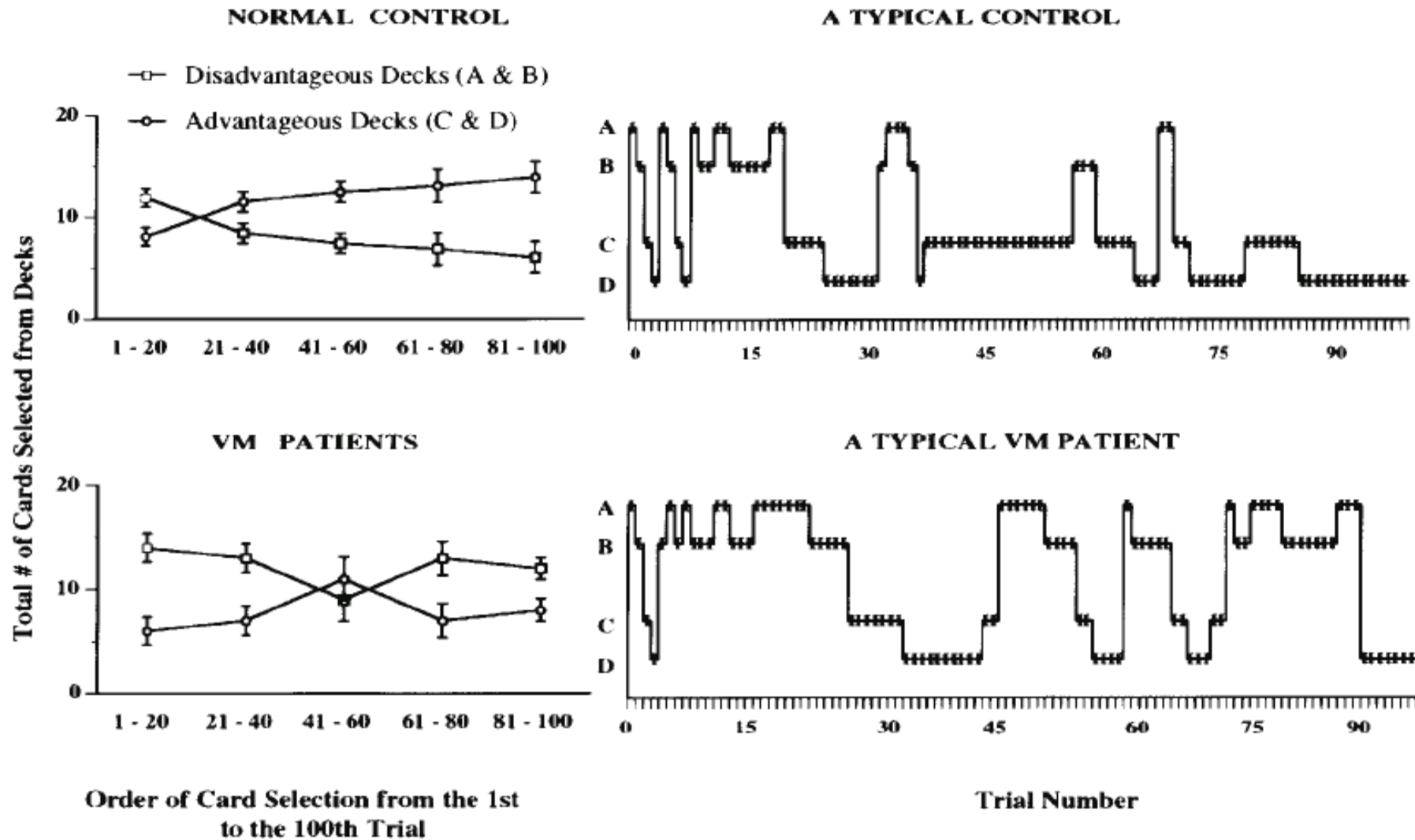


Figure 9-2. Diagramme montrant les résultats des différents types de sujets au « test du jeu de poker », en termes de fréquence de choix des paquets respectifs. Les sujets normaux préfèrent globalement retourner les cartes des paquets C et D, tandis que les patients souffrant de lésions frontales font les choix opposés. Cette différence de comportement est statistiquement significative.

Normaux : diminution progressive des " tirages à risque"

RED : moins d'activation au fur et à mesure des blocs



Orbito-front : pas de diminution des tirages à risque ni de l'activité RED

DSM-IV : critères de troubles des conduites

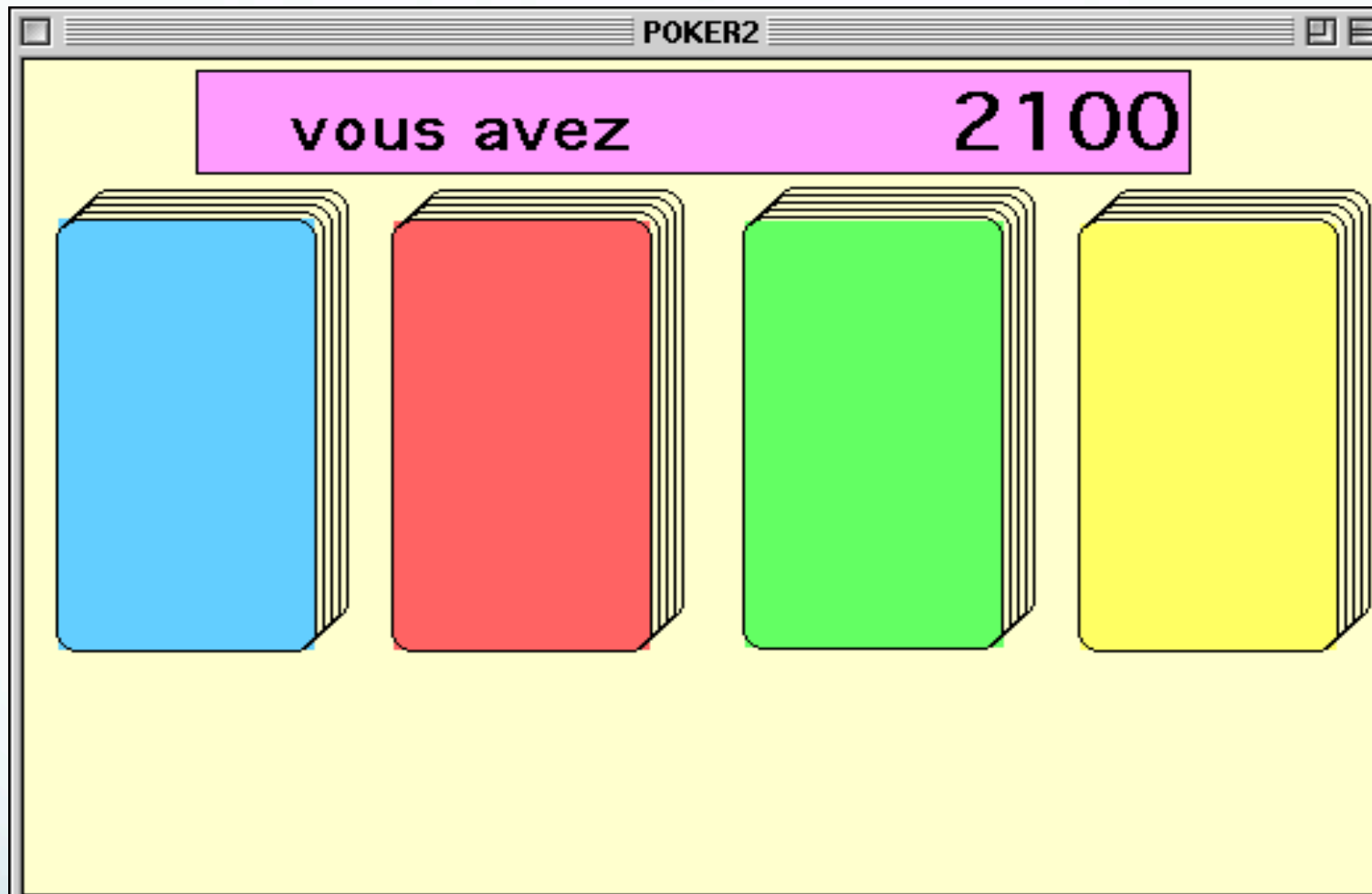
A. Pattern comportemental répétitif et persistant de violation des droits et normes sociales se manifestant par la présence de trois ou plus des critères suivants sur les derniers 12 mois, avec au moins un critère présent dans les 6 derniers mois

➤ Agression portée à autrui (personnes et animaux)

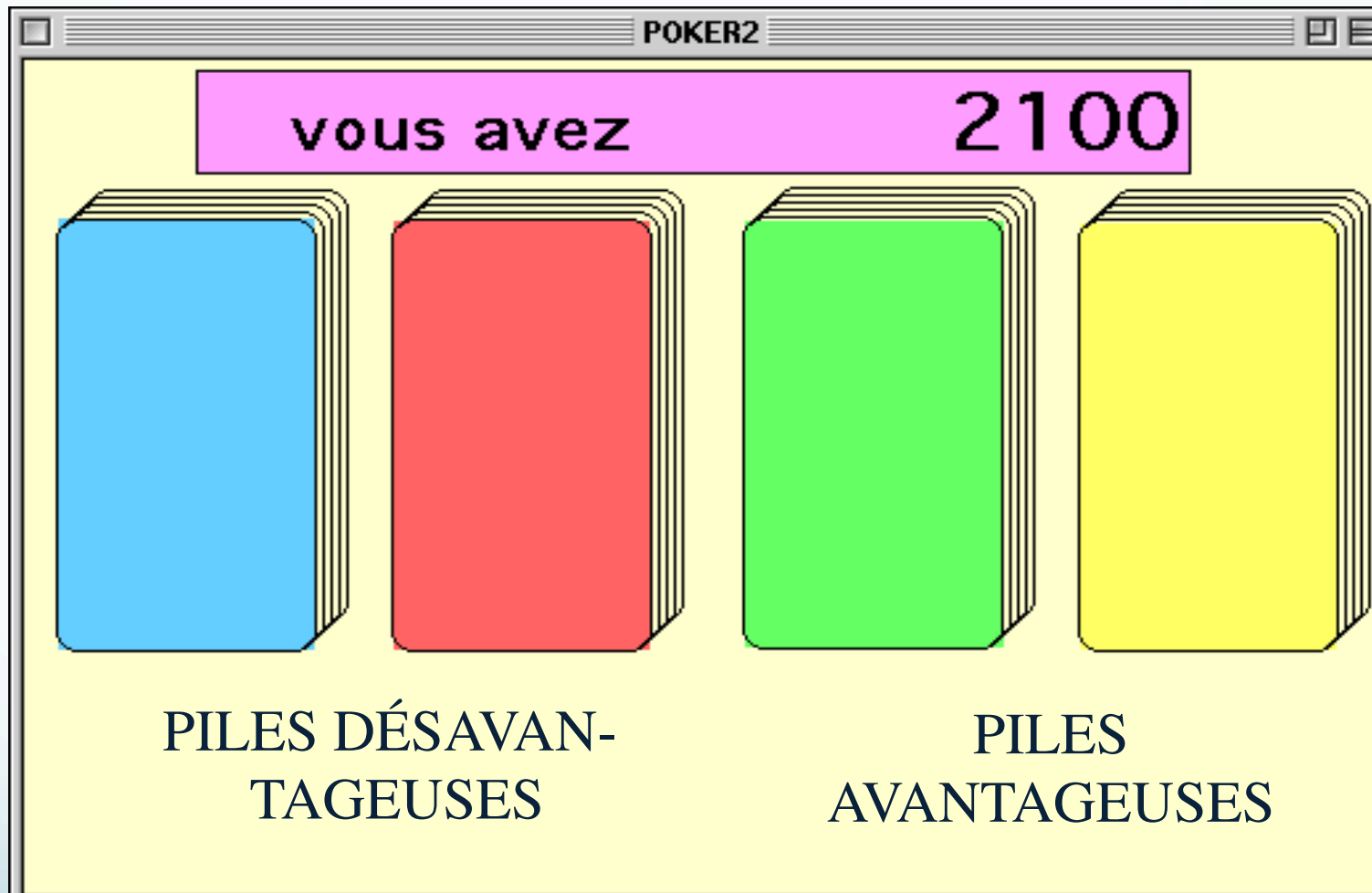
- (1) intimidation fréquente à l'égard d'autrui
- (2) souvent à l'origine de combats physiques
- (3) a utilisé une arme pouvant causer du mal à autrui (couteau, pistolet...)
- (4) a été physiquement cruel envers autrui
- (5) a été physiquement cruel envers des animaux
- (6) a volé une victime
- (7) a forcé autrui à une pratique sexuelle

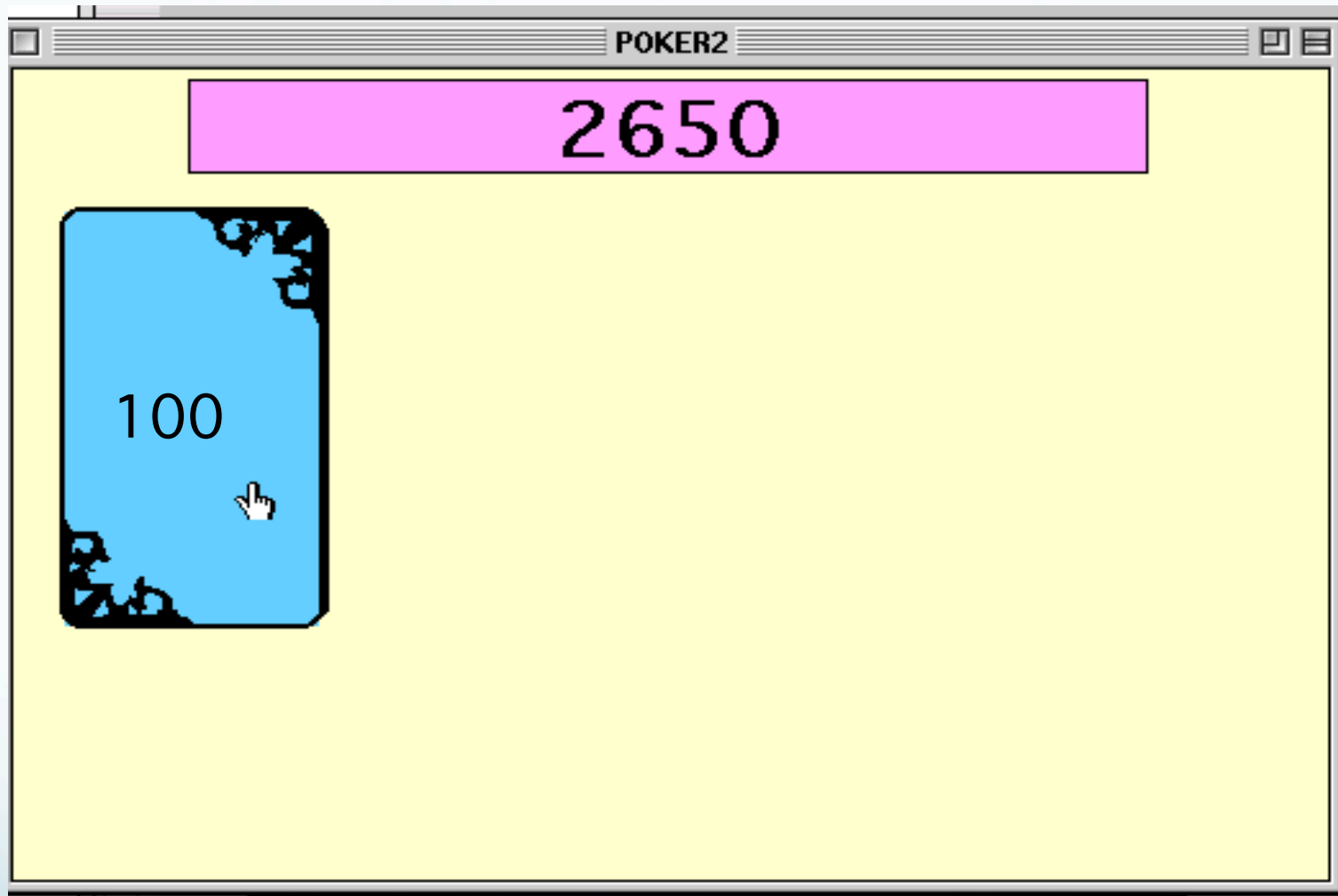
➤ Destruction de biens

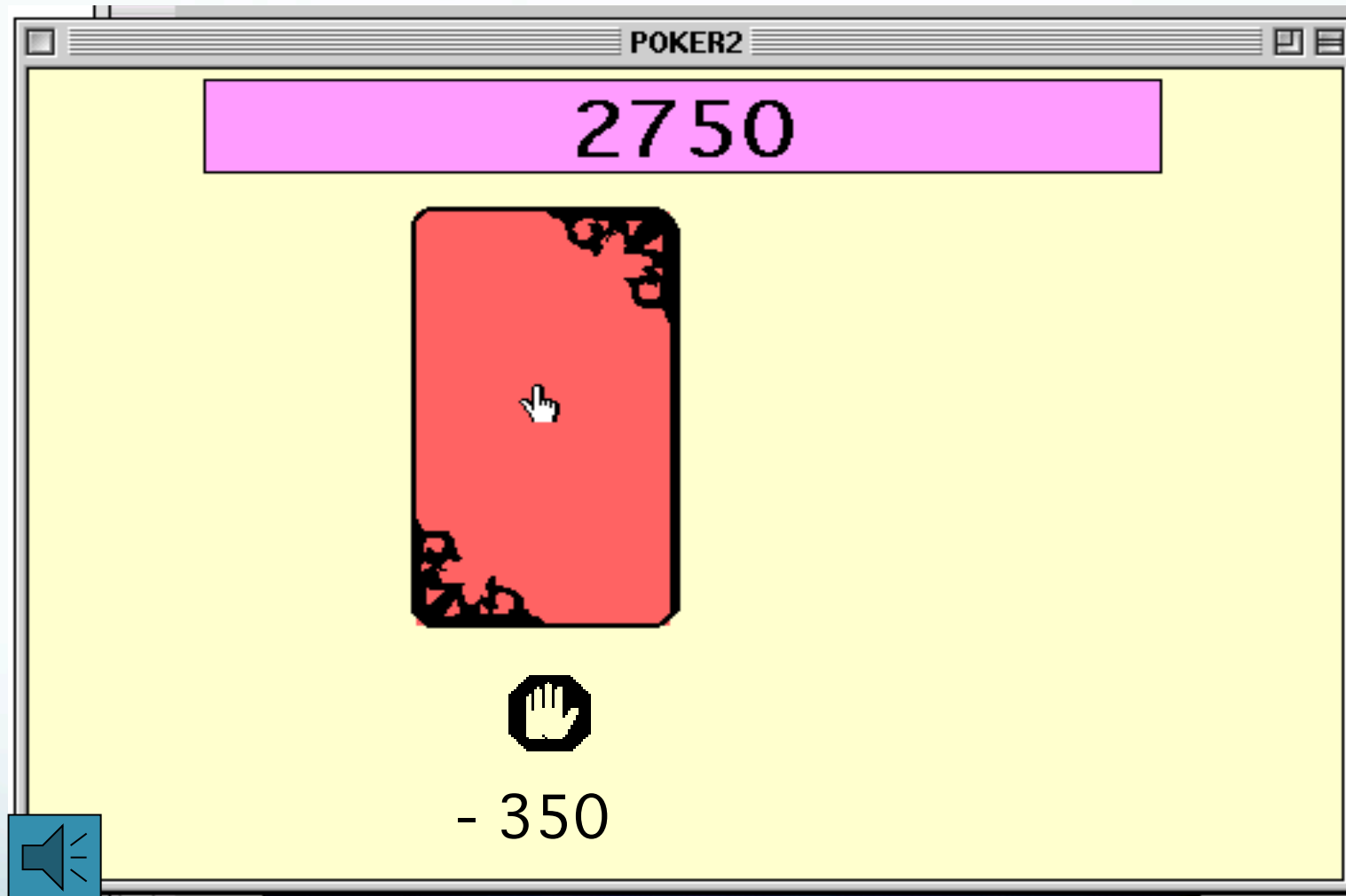
- (8) a volontairement initié un incendie avec l'intention de causer des dommages
- (9) a volontairement détruit les biens d'autrui



ADAPTATION du TEST DU « JEU DE POKER »
(GAMBLING TEST DE BECHARA ET DAMASIO)







Méthodes (2)

- Diagnostic de troubles des conduites :
 - critères du DSM-IV : 12/22 TDAH, 0/15 témoins
 - Quantification : critères spécifiques du questionnaire de Conners et Achenbach
- Exploration du système de récompense : adaptation de l'Iowa Gambling Test (IGT)
 - Deux passations à 1 heure d'intervalle
 - Mesure du « biais de désavantage » par blocs de 20 essais

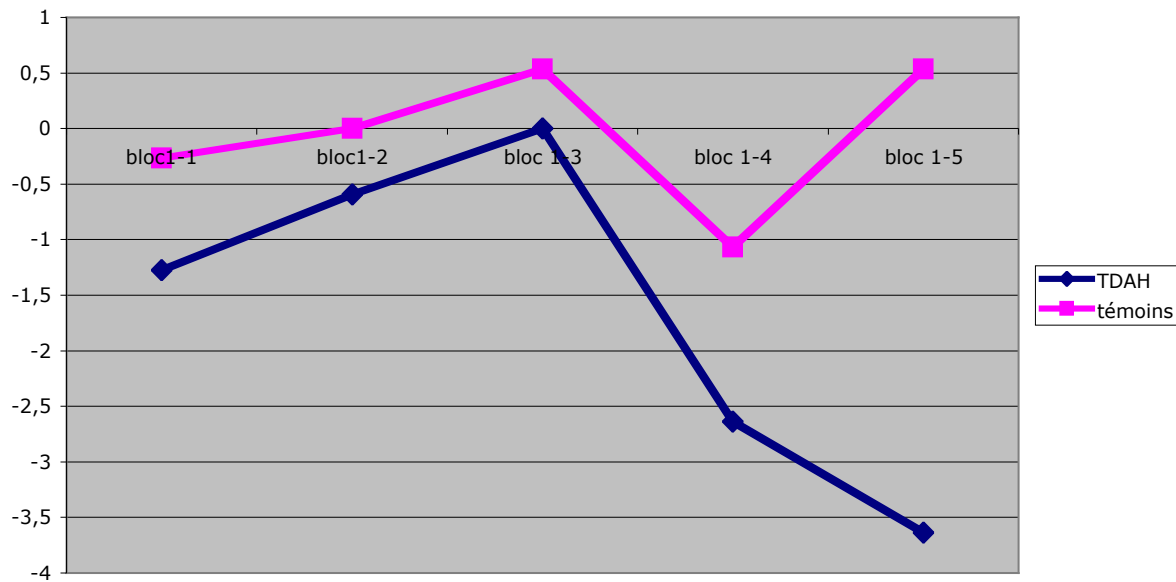
Gambling test (d' après Bechara)

Nb de tirages piles
avantageuses -
désavantageuses

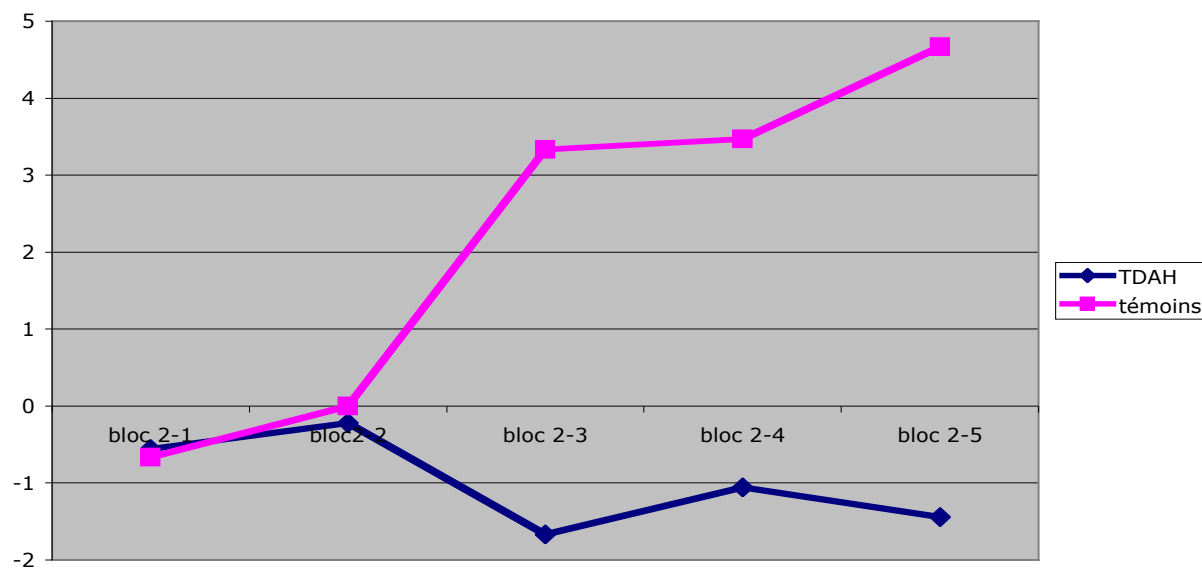
TDAH (N=22)

Témoins (N=15)

gambling session 1



gambling session 2



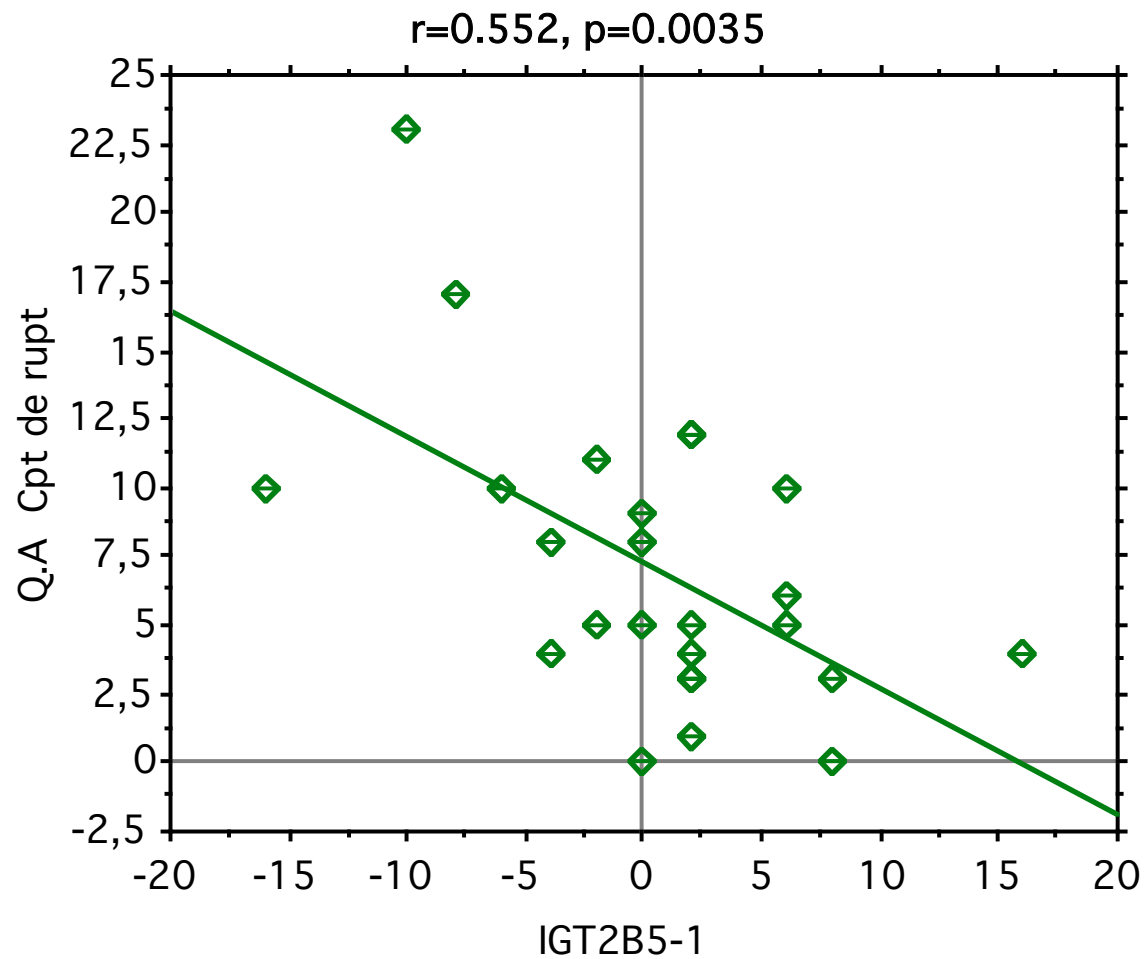
ANOVA à mesures répétées

1ere session:

- effet du groupe $p=0.066$
- interaction répétition $p=0.083$

2me session:

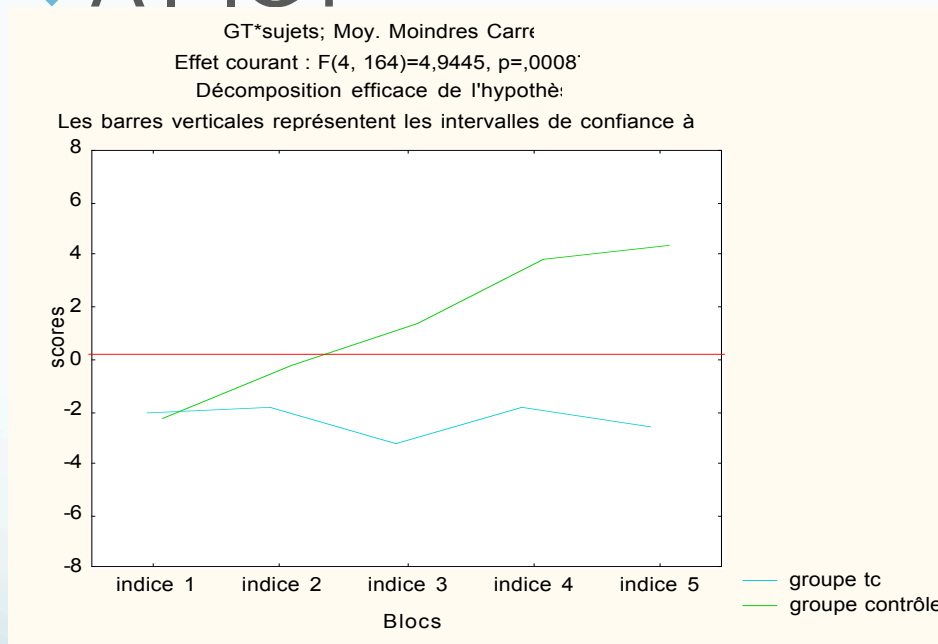
- effet du groupe $p=0.0508$
- interaction répétition $p=0.0011$



Corrélation entre l'indice de choix désavantageux (5^e-1^{er} blocs) lors de la deuxième passation et le score de "comportement de rupture" au questionnaire d'Achenbach (TDAH seuls)

Etude de 13 enfants TDAH avec TC vs 30 témoins appariés

❖ A l'IGT



Les enfants TC prennent plus de risques tout au long du test et ne semblent pas sensibles aux pertes qu'occasionnent les tirages désavantageux.

❖ Mesure de perception émotionnelle

Mesure d' Identification des Emotions de Base

(Ekman & Friesen, 1978)

→ 3 étapes

❖ Discrimination des visages

→ Etape perceptive

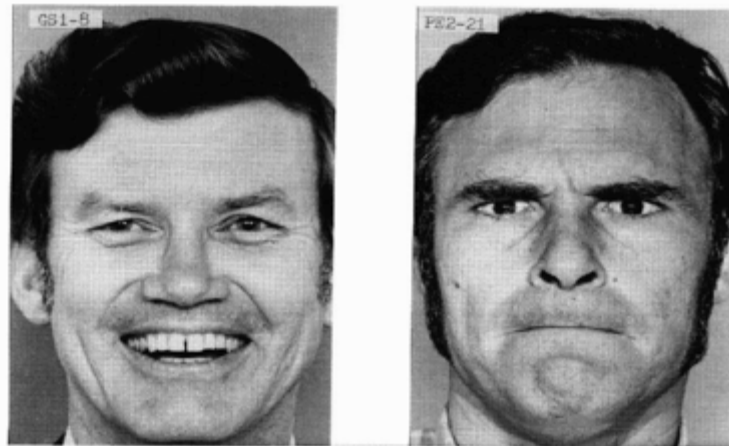


La réponse correcte est « oui »

Mesure d'IEB *(Ekman & Friesen, 1978)*

❖ Discrimination d'émotions

→ Etape de comparaison



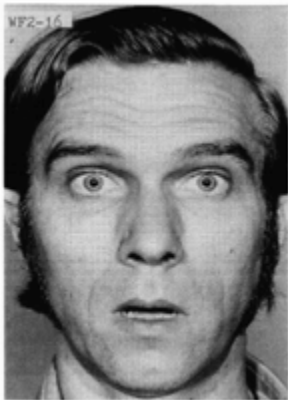
La réponse correcte est « non » (joie et colère)

Mesure d' Identification des Emotions de Base

(Ekman & Friesen, 1978)

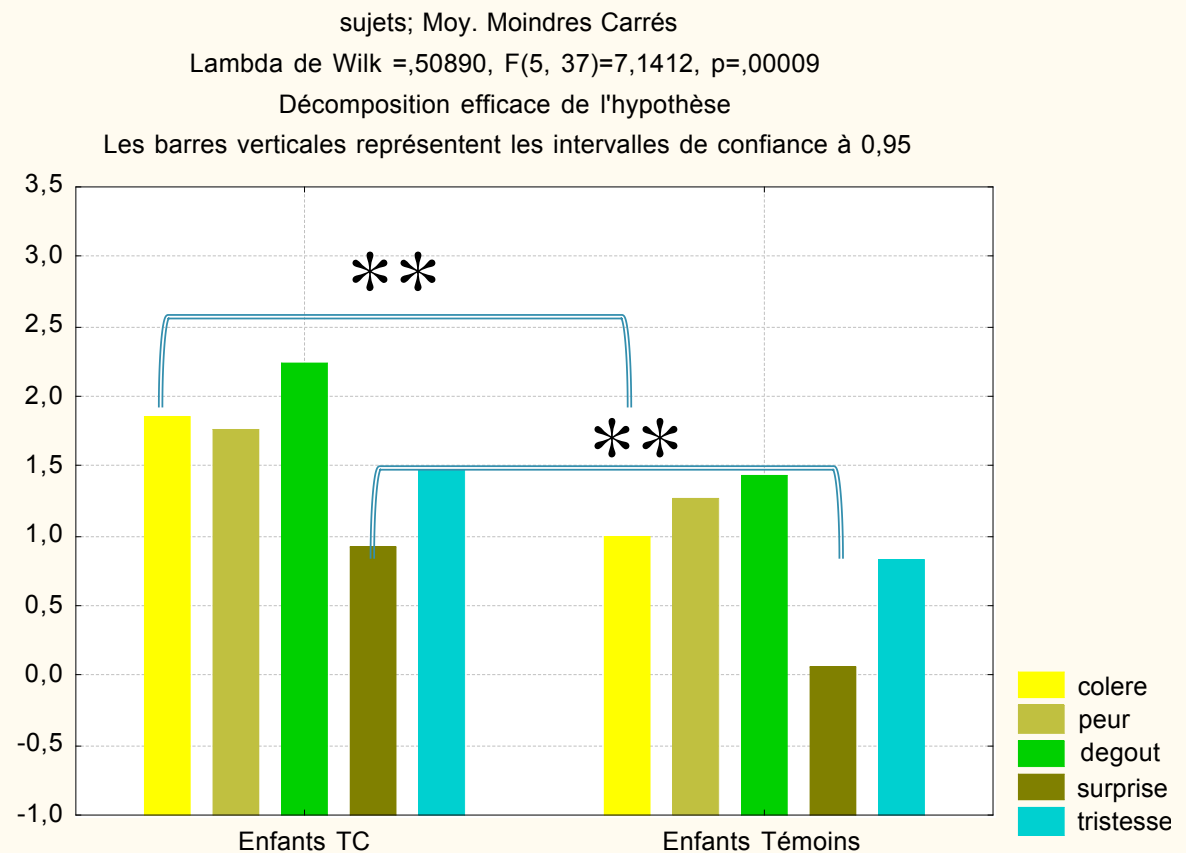
❖ IEB à choix multiples

→ Etape d' identification



Colère
Joie
Surprise
Dégout
Tristesse
Peur

La réponse correcte est « surprise »

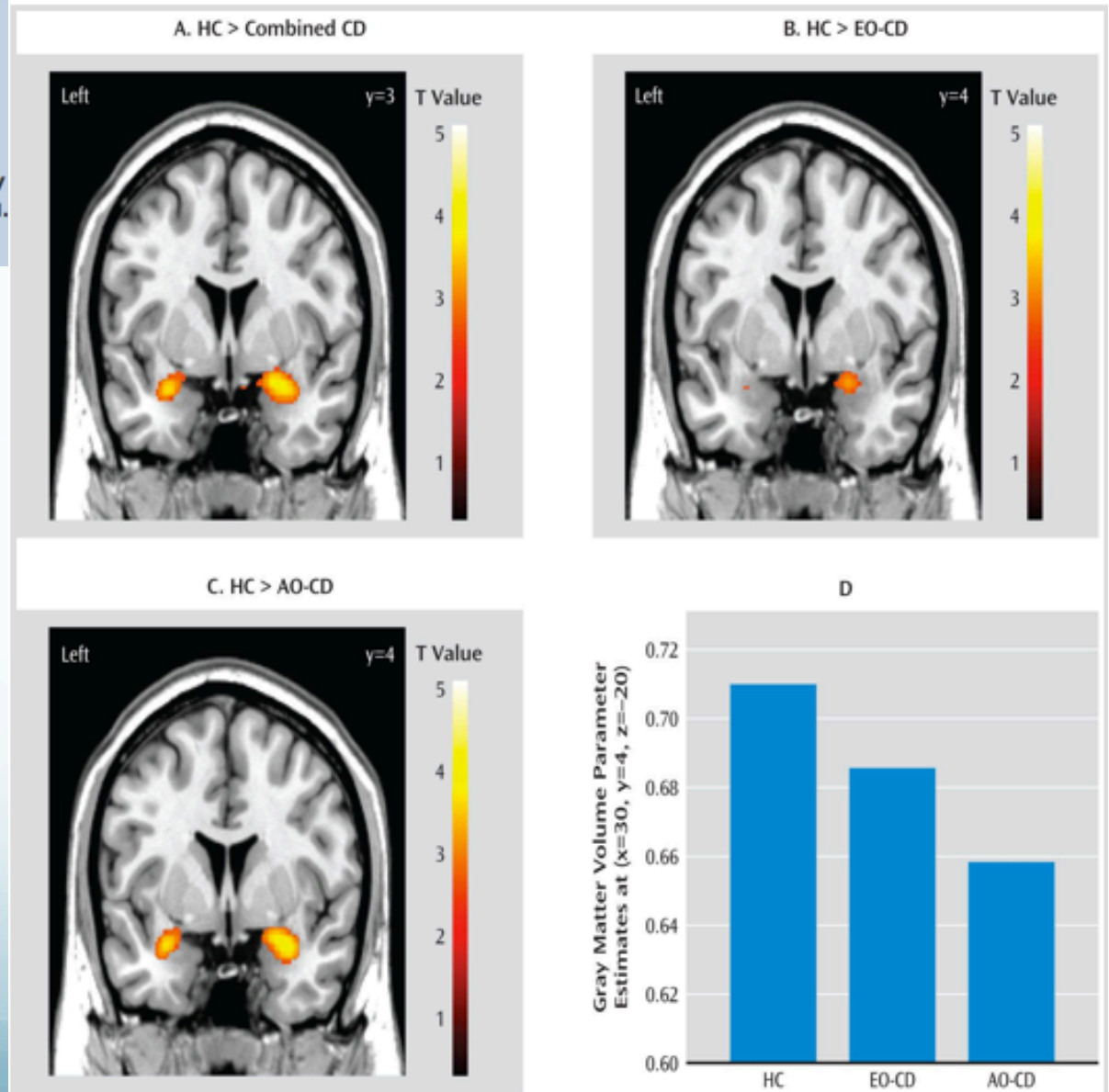


NEW RESEARCH | June 01, 2011

Brain Structure Abnormalities in Early-Onset and Adolescent-Onset Conduct Disorder

Graeme Fairchild, Ph.D.; Luca Passamonti, M.D.; Georgina Hurford, B.Sc.; Cindy Elisabeth A.H. von dem Hagen, Ph.D.; Stephanie H.M. van Goozen, Ph.D.; Ian M. Andrew J. Calder, Ph.D.

gray matter volume reductions in brain regions involved in processing socioemotional stimuli are associated with conduct disorder, regardless of age of onset. Brain structural abnormalities may contribute to the emergence of adolescent-onset as well as early-onset conduct disorder.



En conclusion

- Les études d'imagerie dans le TDAH ont clairement évolué depuis une position « cortico-centrique » faisant du TDAH une pathologie des systèmes neurocognitifs les plus sophistiqués et « récents » de la cognition humaine, vers une conception clairement « limbique », impliquant des circuits bien plus basiques voire archaïques de notre cerveau
- Parmi ces circuits, celui de la récompense, basé sur la portion limbique des boucles sous-cortico frontales, pourrait être impliqué de manière prioritaire, entraînant dans sa dysfonction les systèmes moteurs et cognitifs
- Paradoxalement, la dysfonction de ce circuit serait encore mieux corrélée au trouble de l'attention qu'aux troubles d'agitation et d'impulsivité
- Une mention particulière pour le circuit impliquant l'amygdala et le cortex orbital médian qui seraient impliqués dans la comorbidité avec des troubles des conduites