# Trastornos del aprendizaje: nuevos aportes de las investigaciones en neurociencias

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France

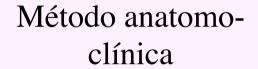
## Plan del curso

- Trastornos de aprendizaje : consideraciones clínicas basicas
  - Contribución y ventaja de un enfoque neuropsicológico
  - DSM-5 y sus nuevos conceptos
  - Proponiendo 3 perfiles de presentaciones clínicas
- Neurobiología de los trastornos de aprendizaje : el ejemplo de la dislexia
  - Datos clásicos con fMRI y MRI convencional : el modelo del trastorno fonológico
  - Algunas contribuciones recientes : nuevos modelos
- Otros trastornos : discalculia, TDAH, autismo, precocidad....
   Hasta un modelo general neurológico con foco sobre comorbilidad

## I/ Algunas consideraciones introductoras

## NEUROPSICOLOGÍA: DEFINICION Y MARCO CONCEPTUAL

Disciplina clínica et científica estudiando los vínculos entre cerebro y funciones mentales



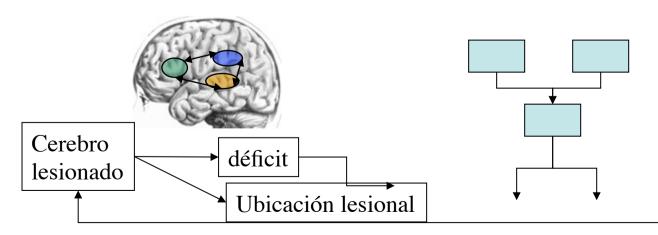
Enfoque cognitivista

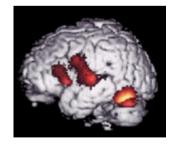
Neuro-imagería funcional

Relato estructura / función

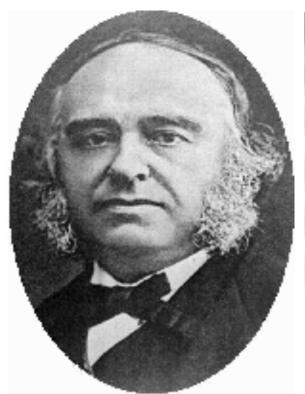
Arquitectura funcional

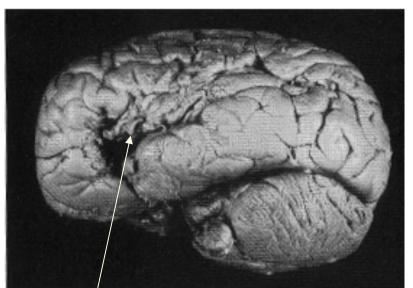
Anatomía funcional





Cerebro sano





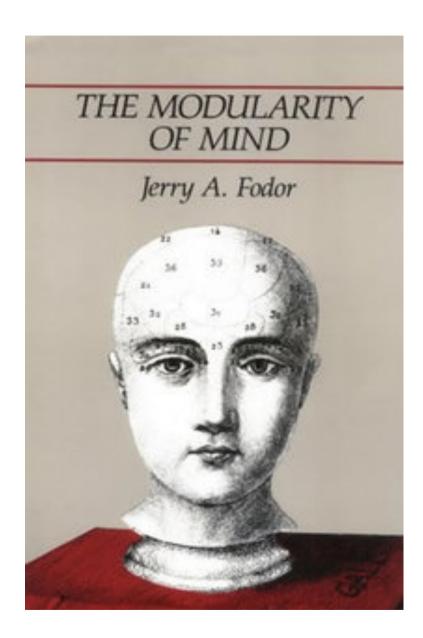
Karl Wernicke

Paul Broca





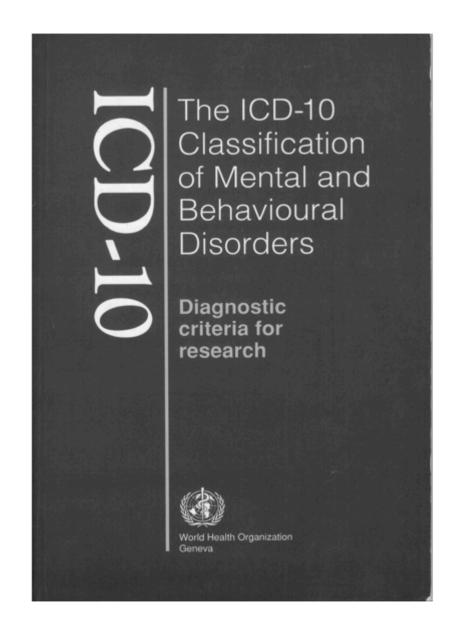
We may usefully think of the language faculty, the number faculty, and others, as "mental organs," analogous to the heart or the visual system or the system of motor coordination and planning (J.A. Fodor, 1983)

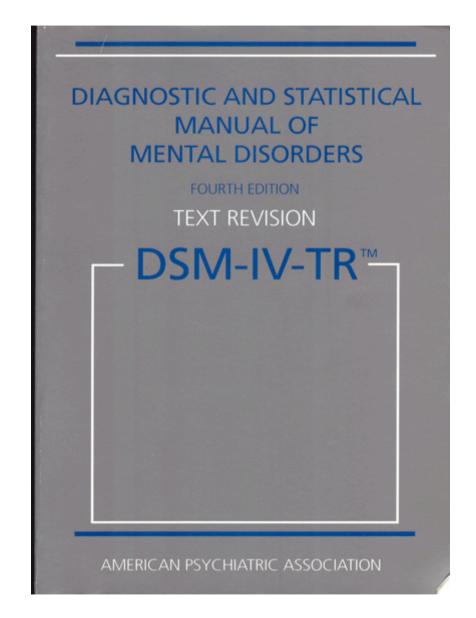


## Desde la patología lesional hasta patología desarrollal : « Neuroconstructivismo »

(A. Karmiloff-Smith, 2001; 2009)

- Concepto general: las reglas de especialización anatomo-funcional descritas en adultos no se pueden validar en niño, especialmente por lo que concierne los síndromes neurodesarrollales: rechaza considerar modulos pre-cablados existen desde el nacimiento (e.g. Williams synd.)
- En cambio, K.S. concibe especialización como emergencia de una interacción progresiva de circuitos con presiones sucesivas del medio ambiente, sean biológicas, externas, conductuales o sociales.
- Dichas presiones van a determinar la **naturaleza de las representaciones cognitivas** en el cerebro : en lugar de ser consideradas como relaciones fijas entre una estructura y una función, se trataría en cambio de representaciones parciales y evolutivas, cuya alteración, definiendo trastornos del neurodesarrollo, resultaría de una adaptación atípica a los múltiples factores de presión, mas que de un déficit innato del funcionamiento de un modulo especifico .

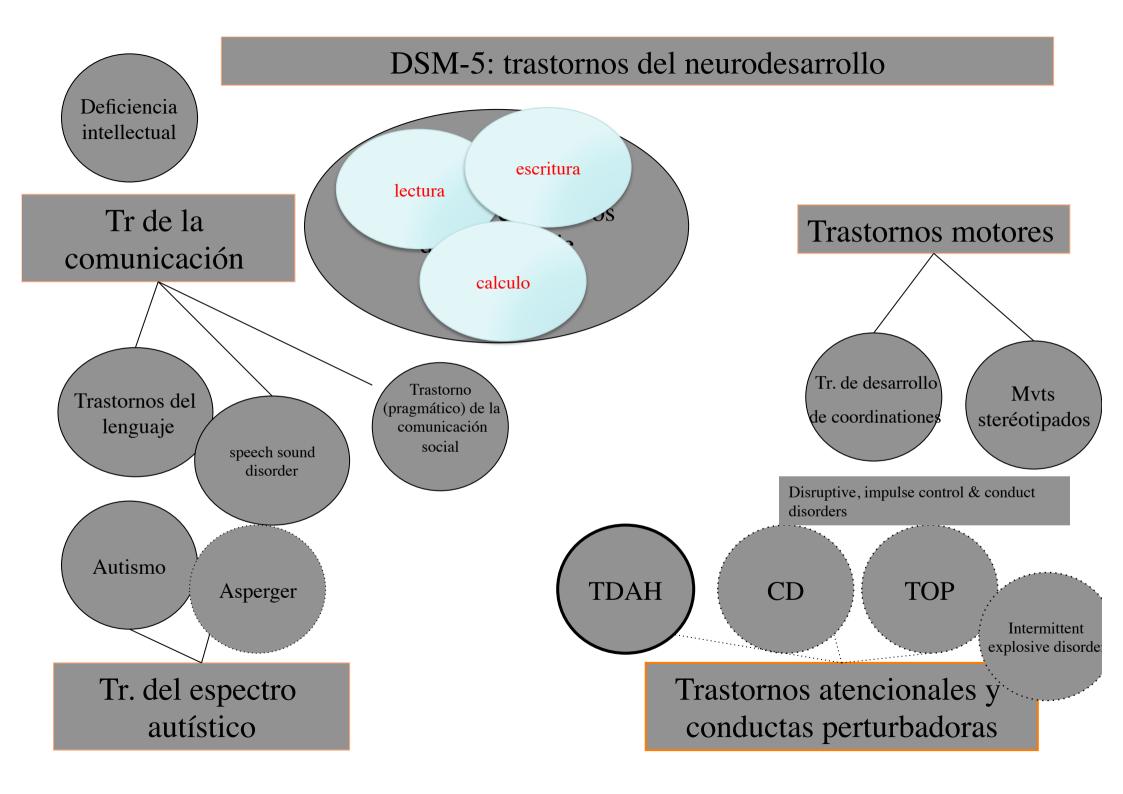




1994 : el DSM-IV



Mayo 2013 : DSM-5



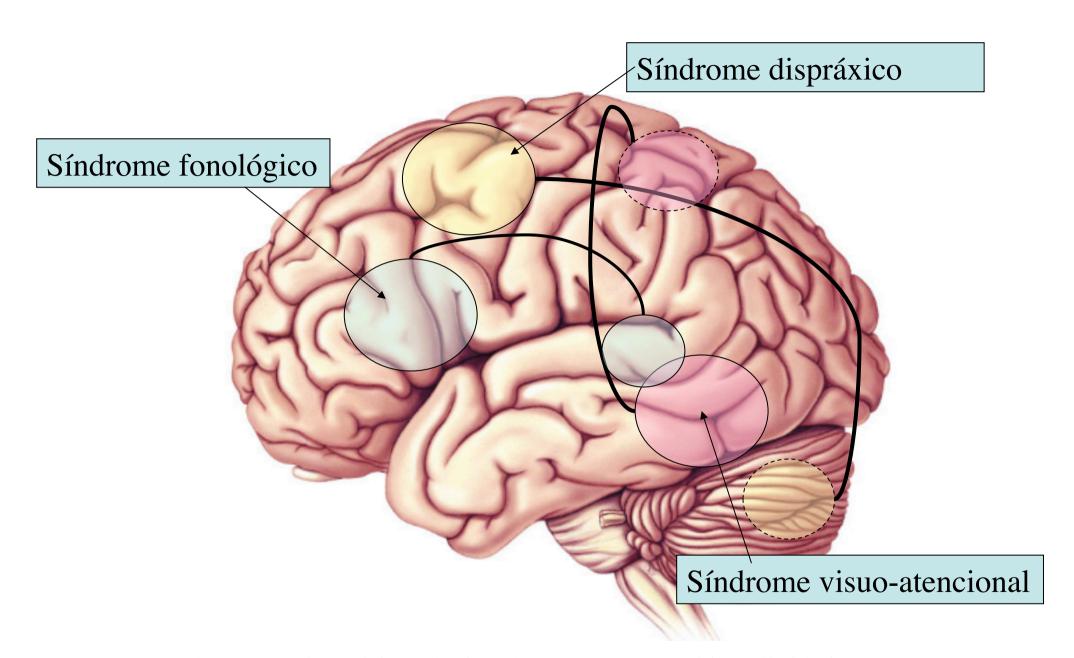
# DSM-5: trastornos específicos de aprendizaje (in: trastornos del neurodesarrollo)

A- Dificultad para aprender y utilizar las habilidades académicas, como indicado por la presencia desde al menos 6 meses de al menos uno de los síntomas siguientes:

- 1- lectura de palabras incorrecta, lenta o laboriosa
- 2- dificultad a comprender el significo de lo leído (aunque sea leído correctamente)
- 3- dificultad en ortografía (spelling)
- 4- dificultad en la expresión escrita (p.e. Errores de puntuación o gramaticales, falta de claridad de la expresión de ideas),
- 5- dificultad a dominar el sentido de los números, los hechos numéricos o el calculo
- 6- dificultad de razonamiento matemático
- B- Significativamente debajo de lo esperado por la edad y interfieren significativamente con marcas académicas o ocupaciones
- C- Empieza durante los años escolar pero puede manifestarse solamente cuando las demandas sobrepasan las capacidades limitadas del individuo
- D- no mejor explicadas por deficiencia intelectual, agudeza auditiva o visual no corregida, otros trastornos neurológicos o mentales, adversidad psico-social

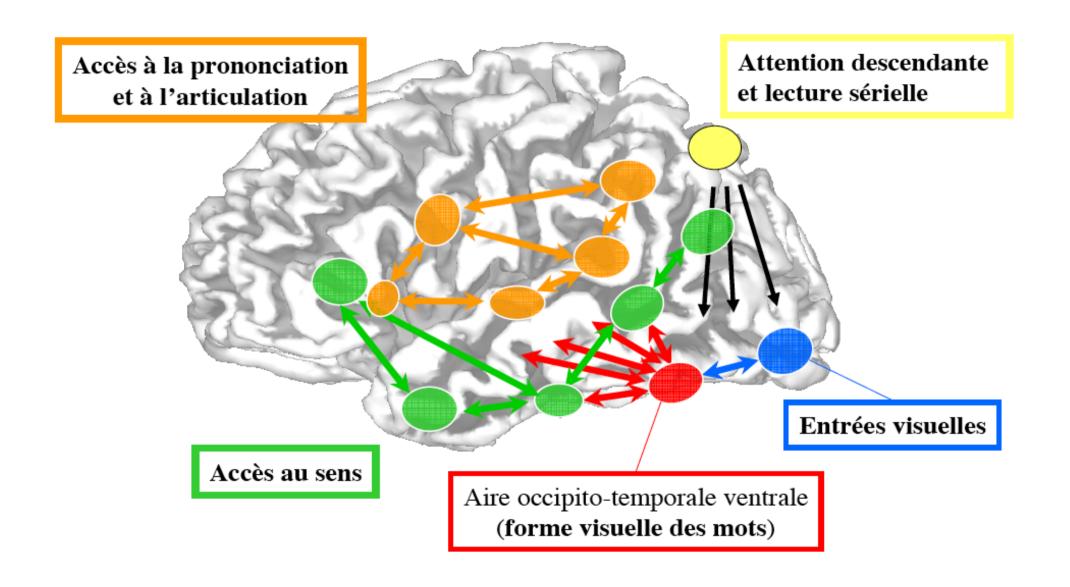
## Tres mayores presentaciones clínicas

- Síndrome fonológico: dislexia, historia de fallo del lenguaje oral, déficit mayor por decodificación, trastorno de conciencia fonológica, trastorno de memoria auditivo-verbal a corto plazo, trastorno de denominación rápida, WISC-IV: ICV<IRP
- Síndrome visuo-atencional : dislexia, decodificación correcta pero lentitud y/o paralexias de derivación o semánticas, 2 tipos :
  - ninguna historia de retraso del lenguaje oral, conciencia fonológica: normal, fallo sobre tareas atencionales, trastorno de memoria de trabajo. Forma pura: defecto en el funcionamiento de la "ventana atencional" (Valdois)
  - Dislexia "mixta", inicialmente fonológica luego con evolución hacia un perfil visuoatencional
- Síndrome dispráxico: retraso con las adquisiciones motoras respecto al lenguaje, disgrafía, instabilidad oculo-motora, + posiblemente trastorno espacial, discalculia espacial, precocidad intelectual. WISC-IV: IRP<ICV

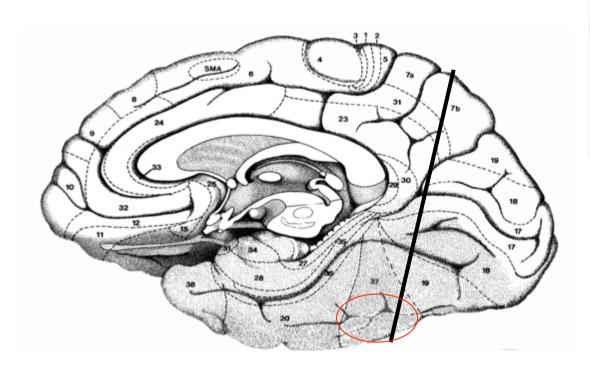


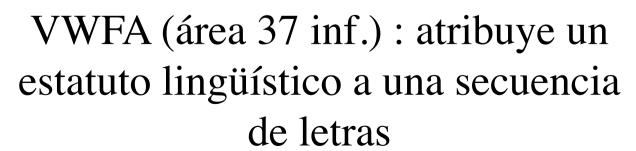
Substrato hipotético de los 3 mayores perfiles disléxicos

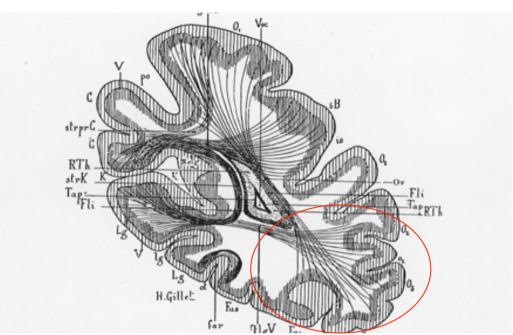
## II/ Aporte de la neuroimageria a/ datos clásicos

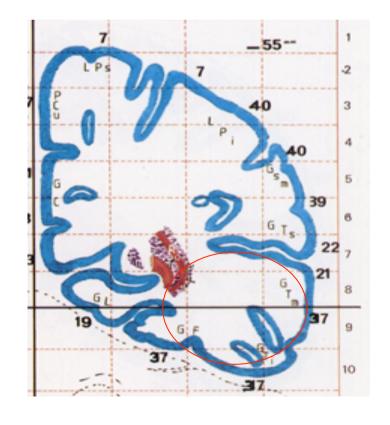


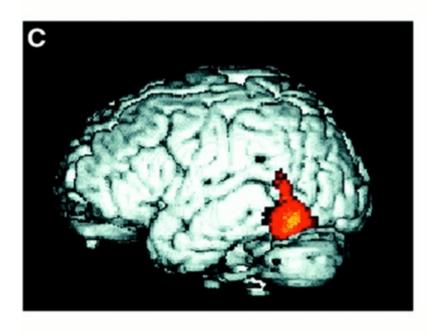
Tres principales redes de la lectura (S. Dehaene) La región occipito-temporal izquierda parece servir de vía de entrada visual al sistema en su totalidad.











Controls - dyslexics

## Dyslexia: Cultural Diversity and Biological Unity

E. Paulesu,<sup>1,2</sup>\* J.-F. Démonet,<sup>3</sup> F. Fazio,<sup>2,4</sup> E. McCrory,<sup>5</sup> V. Chanoine,<sup>3</sup> N. Brunswick,<sup>6</sup> S. F. Cappa,<sup>7</sup> G. Cossu,<sup>8</sup> M. Habib,<sup>9</sup> C. D. Frith,<sup>6</sup> U. Frith<sup>5</sup>

The recognition of dyslexia as a neurodevelopmental disorder has been hampered by the belief that it is not a specific diagnostic entity because it has variable and culture-specific manifestations. In line with this belief, we found that Italian dyslexics, using a shallow orthography which facilitates reading, performed better on reading tasks than did English and French dyslexics. However, all dyslexics were equally impaired relative to their controls on reading and phonological tasks. Positron emission tomography scans during explicit and implicit reading showed the same reduced activity in a region of the left hemisphere in dyslexics from all three countries, with the maximum peak in the middle temporal gyrus and additional peaks in the inferior and superior temporal gyri and middle occipital gyrus. We conclude that there is a universal neurocognitive basis for dyslexia and that differences in reading performance among dyslexics of different countries are due to different orthographies.

¹Psychology Department, University of Milan Bicocca, Milan, Italy. ²INB-CNR, Scientific Institute H San Raffaele, Milan, Italy. ³INSERM U455, Hôpital Purpan, Toulouse, France. ⁴Neuroscience and Biomedical Technologies Department, University of Milan Bicocca, Milan, Italy. ⁵Institute of Cognitive Neuroscience, University College London, London, UK. ⁴Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK. ²Psychology Department, University "Vita e Salute H San Raffaele", Milan, Italy. ⁴Institute of Human Physiology, University of Parma, Parma, Italy. ⁴Centre de Recherche Institut Universitaire de Gériatrie, Montréal, Quebec, Canada.

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### Seminar

### Developmental dyslexia

Jean-François Démonet, Margot J Taylor, Yves Chaix

Lancet 2004; 363: 1451-60

INSERM U455, Hôpital Purpan, IFR 96, Toulouse, France (J-F Démonet MD); CNRS UMR 5549, Faculté de Médecine de Toulouse-Rangueil, IFR 96, Toulouse, France (M J Taylor PhD); and Unité de Neuro-Pédiatrie, Hôpital des Enfants, Toulouse, France (Y Chaix MD)

Correspondence to: Dr J-F Démonet (e-mail: demonet@toulouse.inserm.fr)

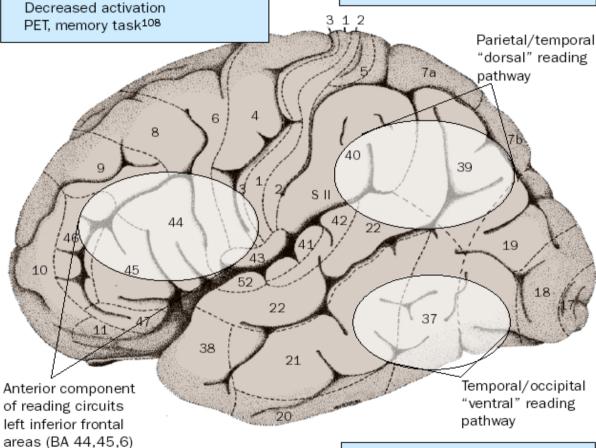
#### Dysfunction of left inferior frontal area

Increased activation: fMRI, hierarchically organised tasks with phonological process; 106 PET, implicit and explicit word and pseudoword reading 107

Decreased activation PET, memory task<sup>108</sup>

### Reduced activity in left parietal/ temporal regions

PET, rhyming task;108,109 PET, pronunciation and decision making tasks;110 fMRI, hierarchically organised tasks with phonological process106 PET, reading<sup>111</sup>



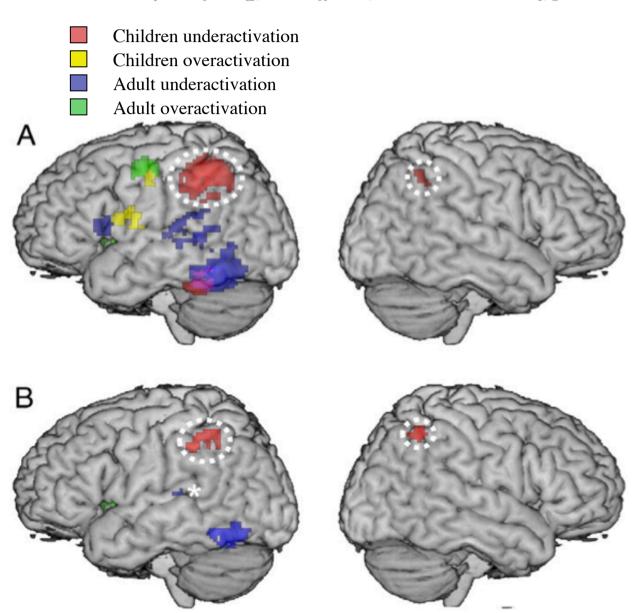
### Reduced activity in left inferior temporal/occipital area

MEG, letter perception 101 PET, implicit and explicit word and pseudoword reading107,112

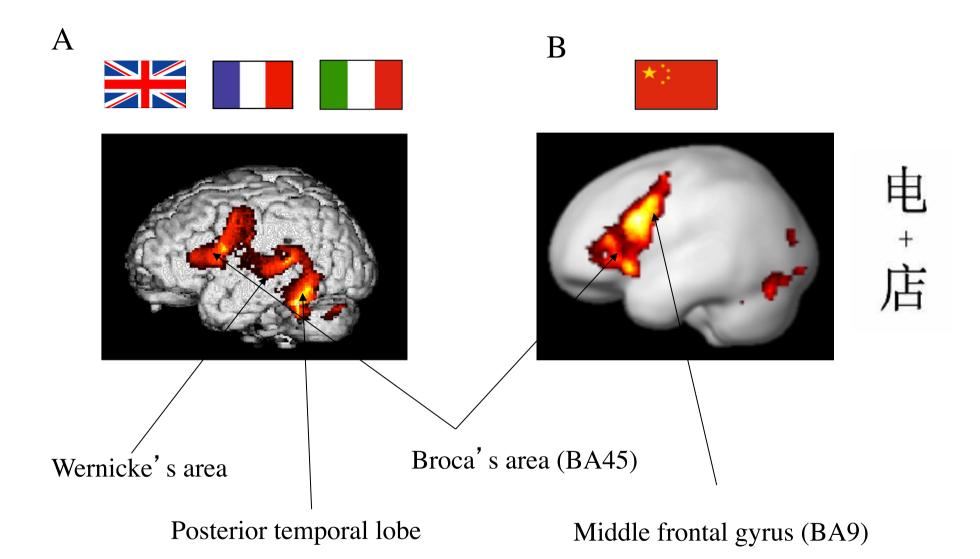
### Meta-analyzing brain dysfunctions in dyslexic children and adults

Fabio Richlan a.\*, Martin Kronbichler a.b, Heinz Wimmer a

- <sup>a</sup> Department of Psychology and Center for Neurocognitive Research, University of Salzburg, Hellbrunnerstr, 34, 5020 Salzburg, Austria
- b Neuroscience Institut and Department of Neurology, Christian Doppler Clinic, Paracelsus Private Medical University, Ignaz-Harrer-Str. 79, 5020 Salzburg, Austria



We examined the evidence from functional imaging studies for predominance of a phonological left temporo- parietal (TP) dysfunction in dyslexic children and predominance of a visual-orthographic left occipito-temporal (OT) dysfunction in dyslexic adults. Separate meta-analyses of 9 studies with children (age means: 9-11 years) and of 9 studies with adults (age means: 18-30 years) and statistical comparison of these meta-analytic maps did find support for a dysfunction of a left ventral OT region in both children and adults. The findings on a possible predominance of a left TP dysfunction in children were inconclusive. Contrary to expectation, underactivation in superior temporal regions was only found for adults, but not for children. For children, underactivation was found in bilateral inferior parietal regions, but this abnormality was no longer present when foci identified by higher dyslexic task-negative activation (i.e., deactivation in response to reading compared to baseline) were excluded. These meta-analytic results are consistent with recent findings speaking for an early engagement of left OT regions in reading development and for an early failure of such an engagement in dyslexia.



## A structural-functional basis for dyslexia in the cortex of Chinese readers

Wai Ting Siok<sup>†‡</sup>, Zhendong Niu<sup>§</sup>, Zhen Jin<sup>¶</sup>, Charles A. Perfetti<sup>I</sup>, and Li Hai Tan<sup>†‡††</sup>

<sup>†</sup>Department of Linguistics and <sup>‡</sup>State Key Laboratory of Brain and Cognitive Sciences, University of Hong Kong, Pokfulam Road, Hong Kong; <sup>§</sup>College of Computer Science and Technology, Beijing Institute of Technology, Beijing 100081, China; <sup>§</sup>Beijing 306 Hospital, Beijing 100101, China; and <sup>§</sup>Learning Research and Development Center, University of Pittsburgh, Pittsburgh, PA 15260

Communicated by Robert Desimone, Massachusetts Institute of Technology, Cambridge, MA, February 25, 2008 (received for review January 1, 2008)

### Jugement de rimes sur présentation d'idéogrammes

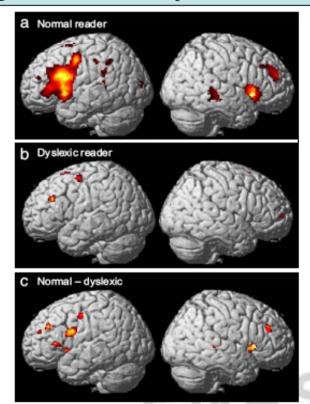


Fig. 2. Brain regions with significant activation during rhyme judgment. (a and b) Cortical activation associated with rhyme judgment contrasted with font-size decision in normal and dyslexic Chinese readers. (c) Brain regions showing group differences during rhyme judgment.

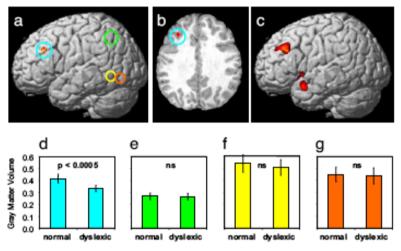


Fig. 1. Group differences in gray matter volume. (a, b, and d) A region in the left middle frontal gyrus (BA 9; x = -32, y = 31, z = 28) exhibited reduced volume in the dyslexic group, P < 0.05 corrected using the FWE correction for the whole brain. (c) At a less stringent uncorrected threshold of P < 0.001, reduced gray matter volume was seen in the left anterior temporal gyrus (BA 38/21) and the left Sylvian fissure, in addition to the left middle frontal gyrus. (e-g) ROI analysis of gray matter volume difference in the left posterior temporoparietal region (in green), the left middle temporal gyrus (in yellow), and the left inferior occipito-temporal cortex (in orange). No significant alteration was observed in these regions.

5562 | www.pnas.org/cgi/doi/10.1073/pnas.0801750105

Slok et al.

Parmi les aires sous-activées en IRMf, une région du GFMoy Gche présente une diminution significative du volume de substance grise

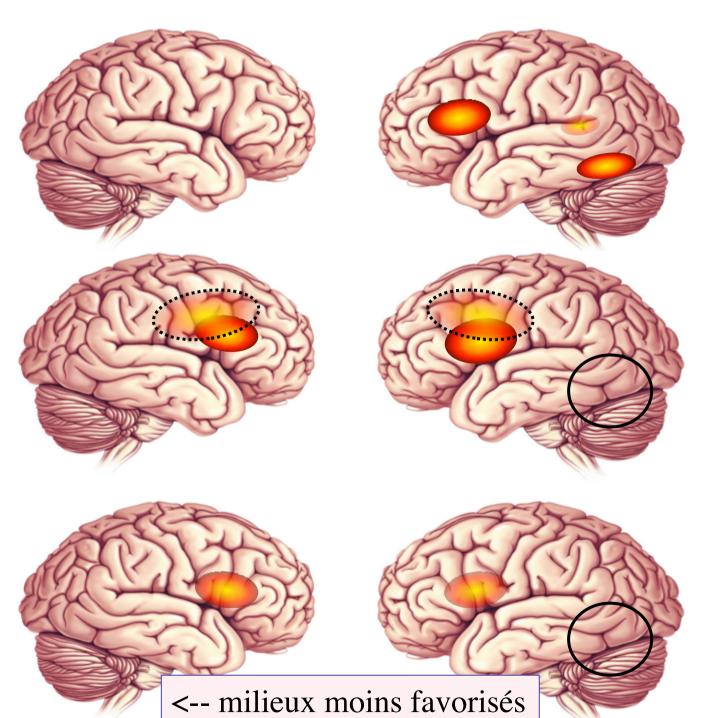
### LEAT JETE

Témoins non dys

Riment?

Dyslexiques "compensés"

Dyslexiques "persistants"



## Functional characteristics of developmental dyslexia in left-hemispheric posterior brain regions predate reading onset

Nora Maria Raschlea, Jennifer Zuka, and Nadine Gaaba, Jennifer Zuka, Jennif

<sup>a</sup>Laboratories of Cognitive Neuroscience, Division of Developmental Medicine, Department of Medicine, Children's Hospital Boston, and <sup>b</sup>Harvard Medical School, Boston, MA 02115; and <sup>c</sup>Harvard Graduate School of Education, Cambridge, MA 02138

Activation d'un réseau occipito-temporo-frontal chez des enfants pré-lecteurs (moyenne âge 5ans 8mois) avec (FHD+) ou sans (FHD-) une histoire familiale de dyslexie avérée, dans une tâche de décision de similitude du premier phonème de deux mots représentés sur des dessins

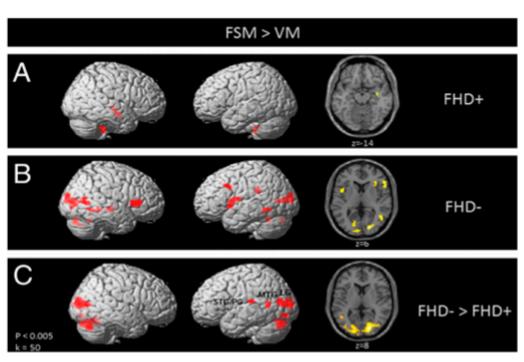


Fig. 1. Statistical parametric maps showing brain activation during phonological processing (FSM > VM) for children with (A) and without (B) a familial risk for DD, as well as group differences between children with compared to without (FHD<sup>-</sup> > FHD<sup>+</sup>) a familial risk for DD (C). FHD<sup>-</sup> show significantly greater activation compared to FHD<sup>+</sup> children in bilateral occipitotemporal and left temporoparietal brain regions, as well as left and right cerebellar regions.

## Neuroanatomia funcional de la dislexia : sintesis de los datos clásicos

- El cerebro disléxico es caracterizado por una hipoactivación durante pruebas de lectura y de consciencia phonológica de una red hemisférica izquierda incluyendo : la WVFA, junción temporo-occipital, ± area de Broca
- Este patrón de activación atípica parece modificable por al menos tres factores del medio ambiente : lengua maternal, nivel socioeconómico y remediación
- Sin embargo, tales diferencias parecen preexistir a el aprendizaje de la lectura, por tanto serían parcialmente genéticamente determinadas

## II/ Aporte de la neuroimageria b/ hallazgos recientes



McGurk effect: an auditory /ba/ presented with a visual /ga/ is typically "heard" as /da/ (the reverse, i.e., auditory /ga/ and visual /ba/, tends to yield /bga/).

## Effecto McGurk en adultos disléxicos y no-disléxicos

- 9 adultos con dislexia de desarrollo (4 M, 5 F; edad media: 38, range: 34-52) y 10 adultos no-dyslexics (5 M, 5 F; edad media: 30, range: 20-40)
- 81 presentaciones separadas por intervalos de 10 sec.
- 3 estímulos auditivos (/aba/, /ada/, o /aga/) asociados con pasajes video, bajo dos condiciones : congruente o incongruente.
- Previa validación del material : /aba/-/aga/, --> /ada/; /ada/-/aba/, --> /abga/ (Cathiard et al., 2001).

# Effecto McGurk en adultos disléxicos y no-disléxicos

	COHE	COHERENT AUDIO-VISUAL : ABA								
	ABA	ADA	AGA	ABDA	ABGA	ADBA	ADGA	AGBA	Autres	
Non-dyslexic	93	1	0	3	0	2	0	0	0	
Dyslexic	<mark>100</mark>	0	0	0	0	0	0	0	0	

	COH	COHERENT AUDIO-VISUAL : ADA								
	ABA	ADA .	AGA	ABDA	ABGA	ADBA	ADGA	AGBA	Autres	
Non-dyslexic	0	80	0	9	0	0	1	0	10	
Dyslexic	0	77	0	20	0	0	1	0	2	

	COH	COHERENT AUDIO-VISUAL : AGA								
	ABA	ADA	<mark>AGA</mark>	ABDA	ABGA	ADBA	ADGA	AGBA	Autres	
Non-dyslexic	0	0	94	0	0	0	6	0	0	
Dyslexic	0	1	91	0	4	0	4	0	0	

Las tres condiciones coherentes

# Effecto McGurk en adultos disléxicos y no-disléxicos

#### Audio ADA / Visual ABA

	AUDIO	VISUAL	FUSION	COMB*	OTHER
Non-dyslexics	17 (19.1)	0	0	83 (19.1)	0
Dyslexics	38 <i>(41.5)</i>	0	0	57 (38.2)	6 <i>(8.4)</i>

#### Audio AGA / Visual ABA

	AUDIO	VISUAL	FUSION	COMB	OTHER
Non-dyslexics	14 (21.0)	0	0	84 (23.0)	1 <i>(3.5)</i>
Dyslexics	31 <i>(35.5)</i>	0	0	65 <i>(34.3)</i>	4 (8.3)

#### Audio ABA / Visual AGA

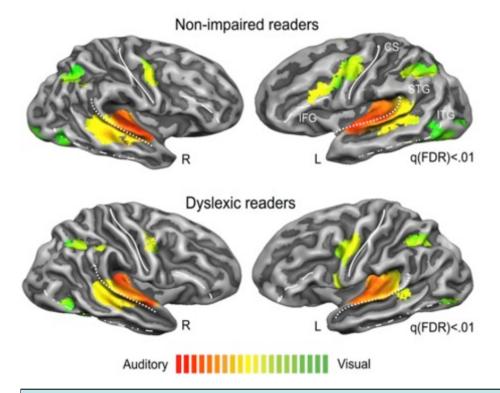
	AUDIO	VISUAL	FUSION	COMB	OTHER
Non-dyslexics	44 <i>(46.3)</i>	3 (7.5)	50 (43.0)	0	2 (4.7)
Dyslexics	67 <i>(34.6)</i>	3 (5.1)	25 (31.3)	3 (5.1)	3 (5.1)

- Condiciones incongruentes : menos combinación o fusión en disléxicos;
- <-- déficit de integración intermodal
- preferencia general por estímulos auditivos

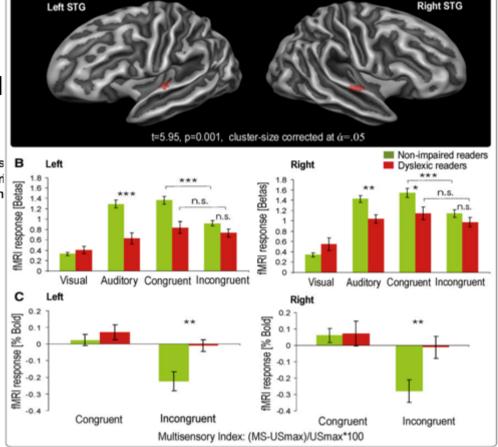
## Reduced Neural Integration of Letters and Speech Sounds Links Phonological and Reading Deficits in Adult Dyslexia

Vera Blau,<sup>1,2,\*</sup> Nienke van Atteveldt,<sup>1,2</sup> Michel Ekkebus,<sup>3</sup> Rainer Goebel,<sup>1,2</sup> and Leo Blomert<sup>1,2</sup>
<sup>1</sup>University of Maastricht

for letters and speech s dyslexia have been pradequately representin



Zonas activadas por estímulos unimodales (habla=rojo, letras=verde, común=amarillo)

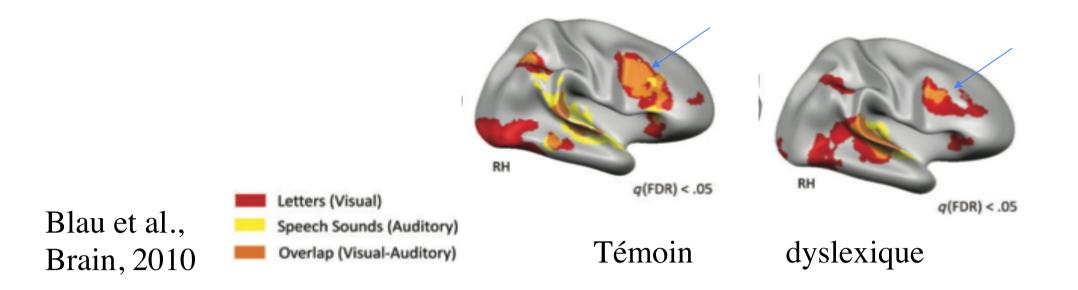


4 condiciones : unimodal visual, unimodal auditivo, multimodal congruente y multimodal incongruente

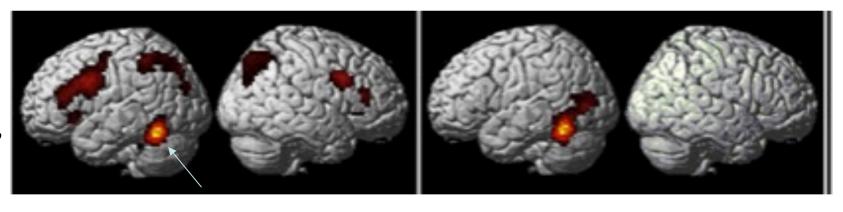
A/ la interacción grupo x condición es significativa en ambas regiones auditivas medias

B/ disléxicos activan menos por unimodal como por multimodal

C/ controles tienen menos fuerte activación por pares congruentes, pero no es el caso por disléxicos

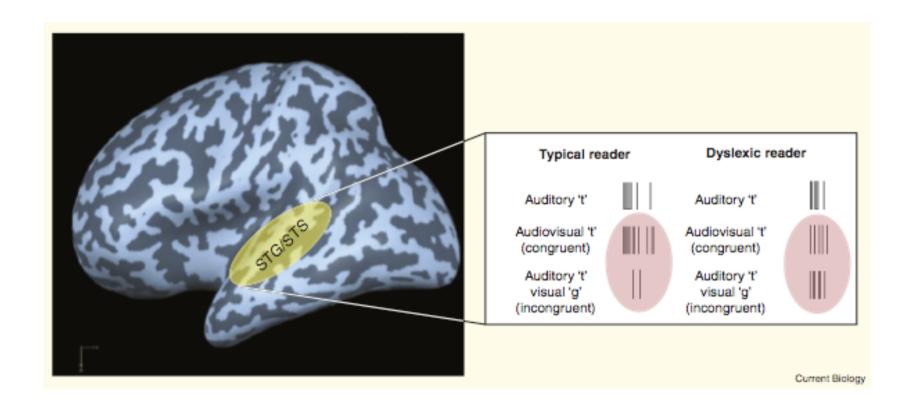


Van den Mark, Neuroimage, 2011



Témoin dyslexique

Étude de connectivité en fMRI (18 dyslexiques, ~9.3 ans lecture de pseudo-homophones "mézon", "sourri")



Cuando el estímulo esta congruente (escucha 't' et ve la letra T), la descarga ("firing") neuronal es menos organizada que en controles; además, ésa es mucho más importante que debería ser por estímulos incongruentes (le escucha 't' et ve la letra G).

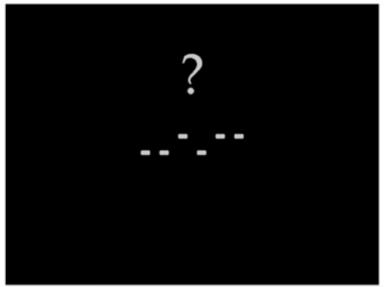
### --> problema de integración intermodal

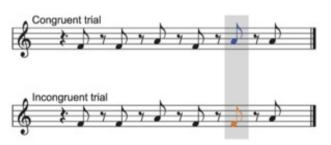


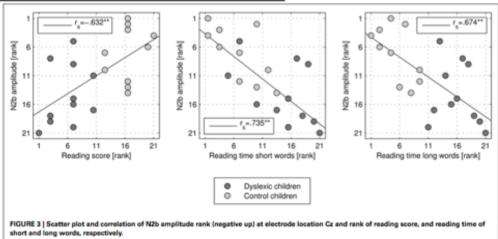
## Mapping symbols to sounds: electrophysiological correlates of the impaired reading process in dyslexia

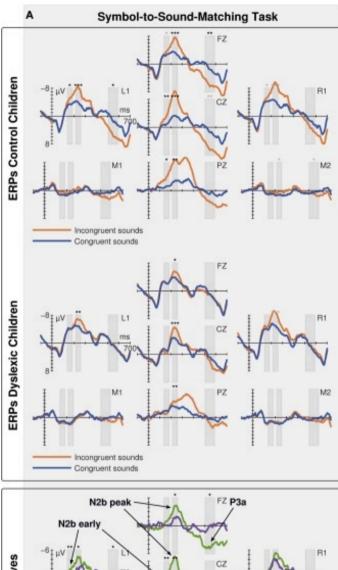
Andreas Widmann<sup>1</sup>\*, Erich Schröger<sup>1</sup>, Mari Tervaniemi<sup>2,3</sup>, Satu Pakarinen<sup>2</sup> and Teija Kujala<sup>2,4</sup>

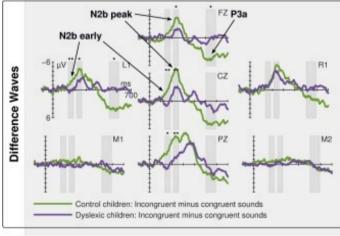
- 1 Institute of Psychology, University of Leipzig, Leipzig, Germany
- Cognitive Brain Research Unit, Cognitive Science, Institute of Behavioural Sciences, University of Helsinki, Helsinki, Finland
- <sup>2</sup> Center of Excellence in Interdisciplinary Music Research, University of Jyväskylä, Jyväskylä, Finland
- 4 Cicero Learning, University of Helsinki, Helsinki, Finland











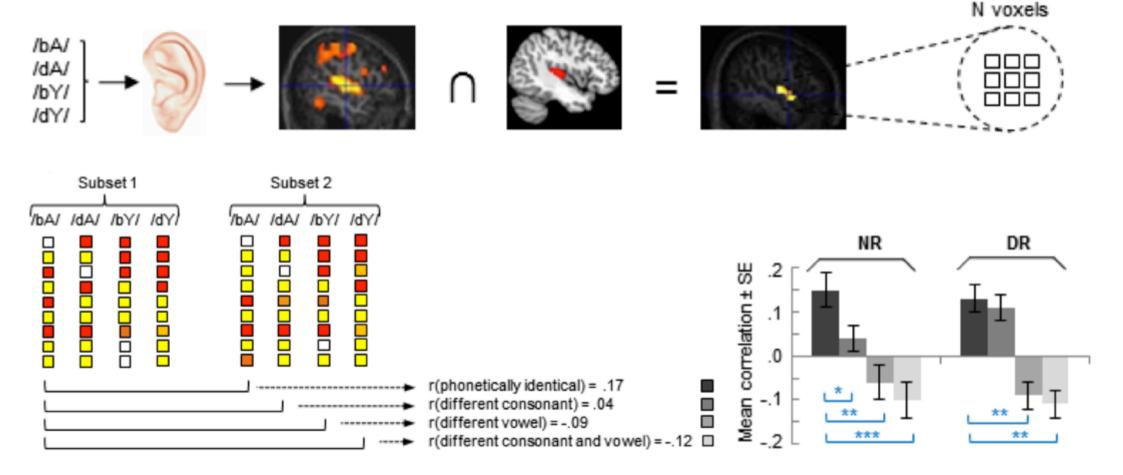




### Intact But Less Accessible Phonetic Representations in Adults with **Dyslexia**

Bart Boets et al.

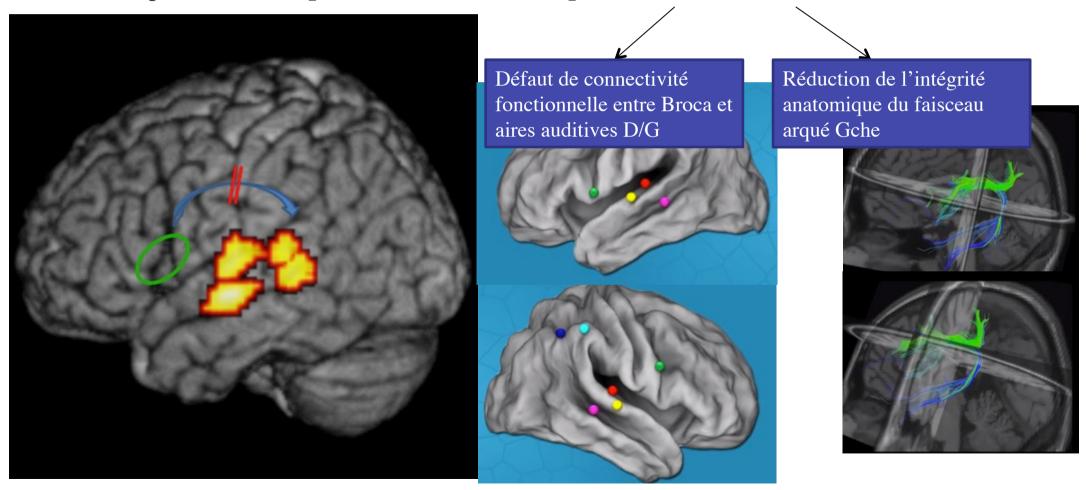
Science 342, 1251 (2013); DOI: 10.1126/science.1244333



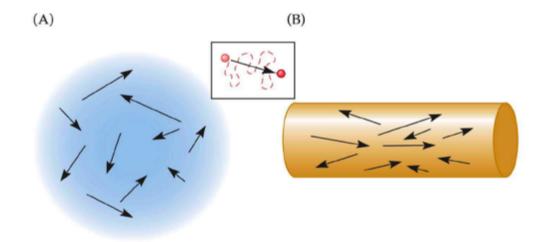
### Boets et al.: conclusiones

- corelaciones mas fuertes dentro una categoría que entre categorias, lo que firma la solidez de las representaciones
- ++ las representaciones estan tan robustas en DIS como en los NL : representaciones no deben ser degradadas o alteradas en los DIS

→ Los DIS padecen de un problema de aceso a representaciones intactas

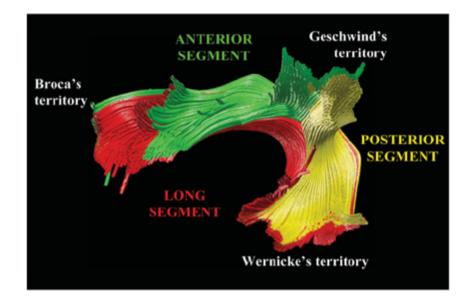


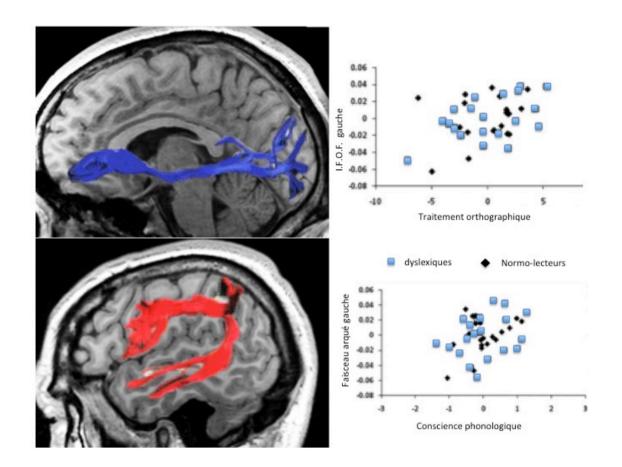
#### 5.18 Isotropic and anisotropic diffusion.



FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 5.18 © 2004 Strauer Association

Diffusion tensor imaging (D.T.I.)

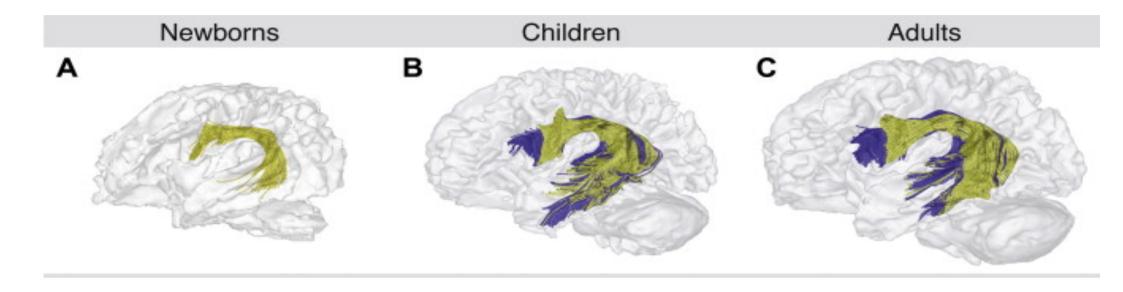




Estudio en Tractografía de déficit fono-auditivos ortográficos y en la dislexia: la disociación entre una ruta inferior (fascículo fronto-occipital inferior o IFOF) y superior (fascículo arcuato) en la sustancia blanca del hemisferio izquierdo.

La ruta superior y inferior están respectivamente correlacionadas con eficiencia en una tarea de conciencia fonológica y una tarea de procesamiento ortográfico en lectura.

Según Vandermosten et al., 2012.



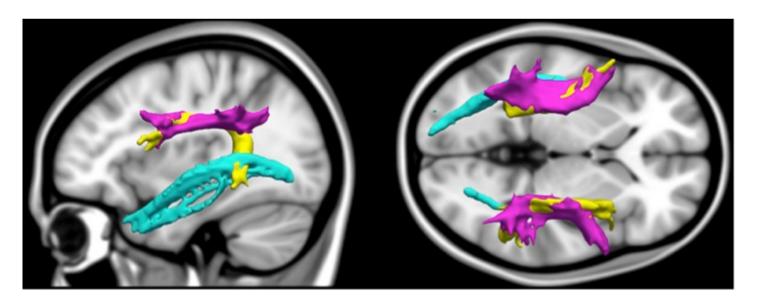
El fascículo arqueado (o arcuato), que conecta areas de Broca y Wernicke (22) tiene dos contingentes: uno ventral, presente al nacer, que sería responsable del desarrollo del lenguaje inicial (funciona como extractor de reglas de invariancia en fonología y sintaxis). El otro dorsal, apareciendo sólo a 7 años, responsable de las funciones lingüísticas más complejas (bajo la influencia de la lectura?).

#### Behavioral/Cognitive

#### Tracking the Roots of Reading Ability: White Matter Volume and Integrity Correlate with Phonological Awareness in Prereading and Early-Reading Kindergarten Children

Zeynep M. Saygin,<sup>1\*</sup> Elizabeth S. Norton,<sup>1\*</sup> David E. Osher,<sup>1</sup> Sara D. Beach,<sup>1</sup> Abigail B. Cyr,<sup>1</sup> Ola Ozernov-Palchik,<sup>3</sup> Anastasia Yendiki,<sup>4</sup> Bruce Fischl,<sup>2,4</sup> Nadine Gaab,<sup>3</sup> and John D.E. Gabrieli<sup>1</sup>

1McGovern Institute for Brain Research and Department of Brain and Cognitive Sciences and 2Computer Science and Artificial Intelligence Laboratory



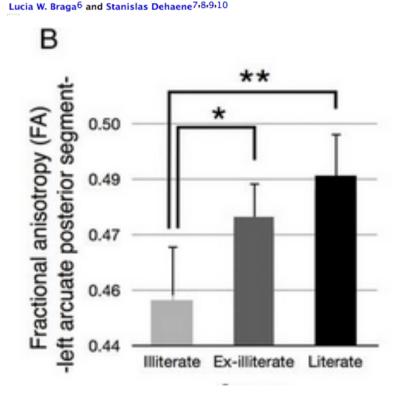
In kindergarten children, we found a correlation between phonological awareness for spoken language and indices of white matter organization of the left arcuate fasciculus, specifically volume and FA. This relationship was both anatomically and behaviorally specific; it was not observed in other tracts (left ILF, left SLFp, or right hemisphere homologs) or for other behavioral predictors of dyslexia. These results were observed in the whole group of 40 children with varied reading abilities in the first half of kindergarten and also in the subset of 18 children who were prereaders. The specific relation between phonological awareness and the left arcuate fasciculus was corroborated by an independent whole-brain analysis. The discovery that such a relation between white matter organization and one of the strongest behavioral predictors of dyslexia, poor phonological awareness, exists before formal reading instruction and substantial reading experience favors the view that differences in white matter organization are not only the consequence of dyslexia, but also may be a cause of dyslexia.

#### Cerebral CORTEX CONTACT THIS JOURNAL Institution: INIST-CNRS Sign In as Personal Subscriber

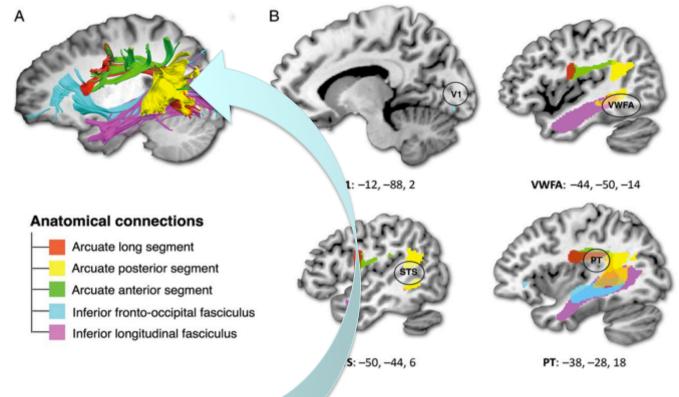
Oxford Journals > Life Sciences & Medicine > Cerebral Cortex > Advance Access > 10.10

#### Learning to Read Improves the Structure of the Arcuate Fasciculus

- Michel Thiebaut de Schotten 1,2,3 \$\psi\$. Laurent Cohen 3,4,5. Eduardo Amemiva 6.



- Illettrés (n= 10): proviennent de la région rurale (5) ou urbaine (5) des environs de Brasilia
- « Participants were illiterates for social reasons, with no history of special difficulty other than the lack of access to schools. »
- Ex-illettrés (n= 10) : parcours similaire à celui des illettrés (parents illettrés de secteur rural) mais ont reçu un enseignement à l'âge adulte.
- Non-illettrés : (n= 11) proviennent de la même communauté sociale que les illettrés mais ont appris à lire pendant l'enfance.



Región posterior del fascículo arqueaco: El volumen es inversamente proporcional al grado de iletrismo

## Three Dyslexia Susceptibility Genes, *DYX1C1*, *DCDC2*, and *KIAA0319*, Affect Temporo-Parietal White Matter Structure

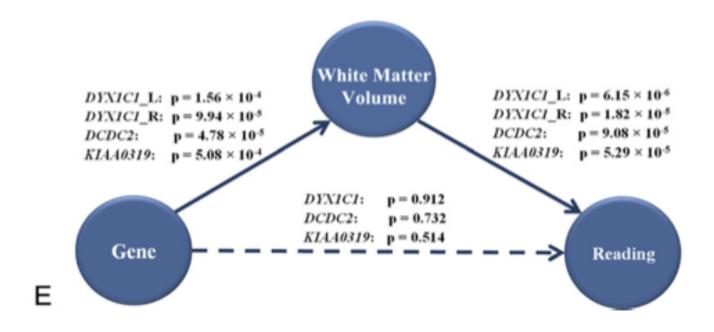
Fahimeh Darki, Myriam Peyrard-Janvid, Hans Matsson, Juha Kere, and Torkel Klingberg

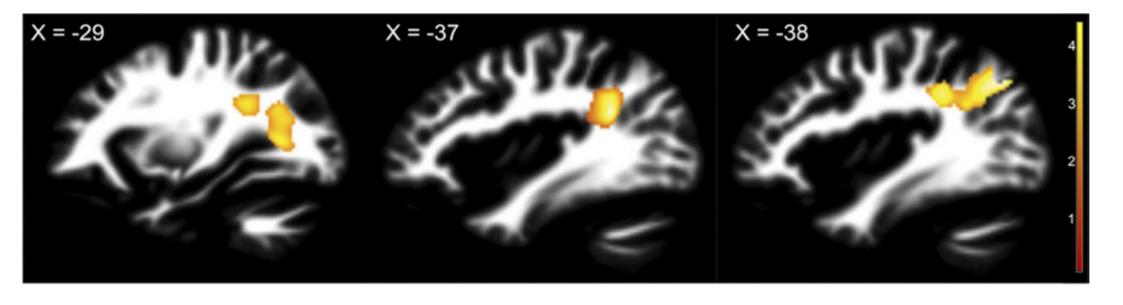
**Background:** Volume and integrity of white matter correlate with reading ability, but the underlying factors contributing to this variability are unknown.

**Methods:** We investigated single nucleotide polymorphisms in three genes previously associated with dyslexia and implicated in neuronal migration (*DYX1C1*, *DCDC2*, *KIAA0319*) and white matter volume in a cohort of 76 children and young adults from the general population.

**Results:** We found that all three genes contained polymorphisms that were significantly associated with white matter volume in the left temporo-parietal region and that white matter volume influenced reading ability.

**Conclusions:** The identified region contained white matter pathways connecting the middle temporal gyrus with the inferior parietal lobe. The finding links previous neuroimaging and genetic results and proposes a mechanism underlying variability in reading ability in both normal and impaired readers.





DYX1C1 DCDC2 KIAA0319

3 genes involucrados en el proceso de migración neuronal y relacionados a la eficiencia en lectura

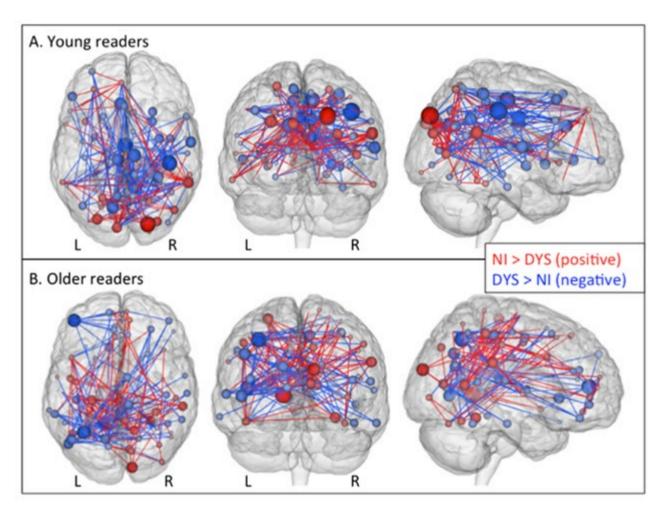
**Results:** «We found that all three genes contained polymorphisms that were significantly associated with white matter volume in the left temporo-parietal region and that white matter volume influenced reading ability ».

#### **ARCHIVAL REPORT**

## Disruption of Functional Networks in Dyslexia: A Whole-Brain, Data-Driven Analysis of Connectivity

Emily S. Finn, Xilin Shen, John M. Holahan, Dustin Scheinost, Cheryl Lacadie, Xenophon Papademetris, Sally E. Shaywitz, Bennett A. Shaywitz, and R. Todd Constable

4 BIOL PSYCHIATRY 2013; II: IIII-



Etude de connectivité fonctionnelle comparée entre dyslexiques et normolecteurs, chez 75 enfants (43 NI, 32 DYS) et 104 adultes (64 NI, 40 DYS).

Résultats: enfants DYS: moindre connectivité entre régions postérieures et frontales; plus forte connectivité entre zones à courte distance. Adulte DYS: persistance anormale de connexions de l'aire de Broca

### Topological properties of large-scale structural brain networks in children with familial risk for reading difficulties

S.M. Hadi Hosseini<sup>a,\*</sup>, Jessica M. Black<sup>a,c</sup>, Teresa Soriano<sup>a</sup>, Nicolle Bugescu<sup>a,b</sup>, Rociel Martinez<sup>a,b</sup>, Mira M. Raman<sup>a</sup>, Shelli R. Kesler<sup>a</sup>, and Fumiko Hoeft<sup>a,d</sup>

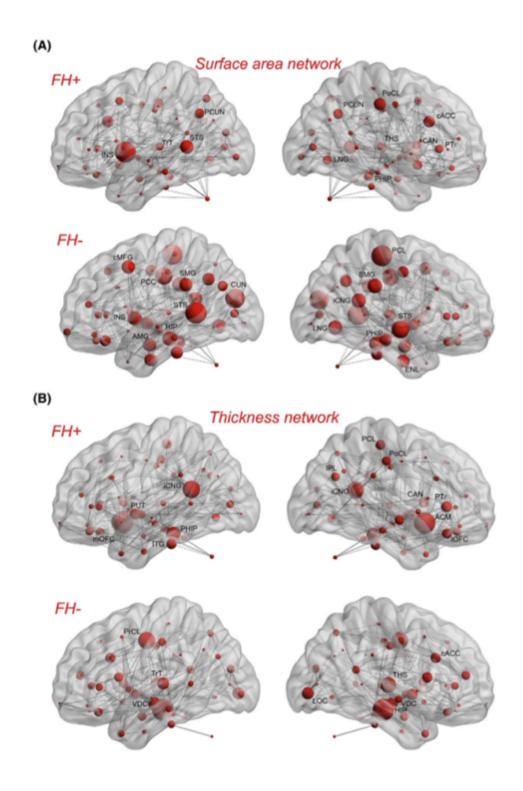
<sup>a</sup>Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Rd., Stanford, CA 94305-5795, USA

42 enfants de 5-6 ans, non lecteurs, présence d'antécédents familiaux (FH+ = 22) ou absence (FH-=20) déterminée par un questionnaire standardisé destiné aux parents.

Mesure en IRM de la connectivité de deux variables :

- surface
- épaisseur

Résultat: « altered topological properties of structural correlation networks in children at risk for reading difficulties. »

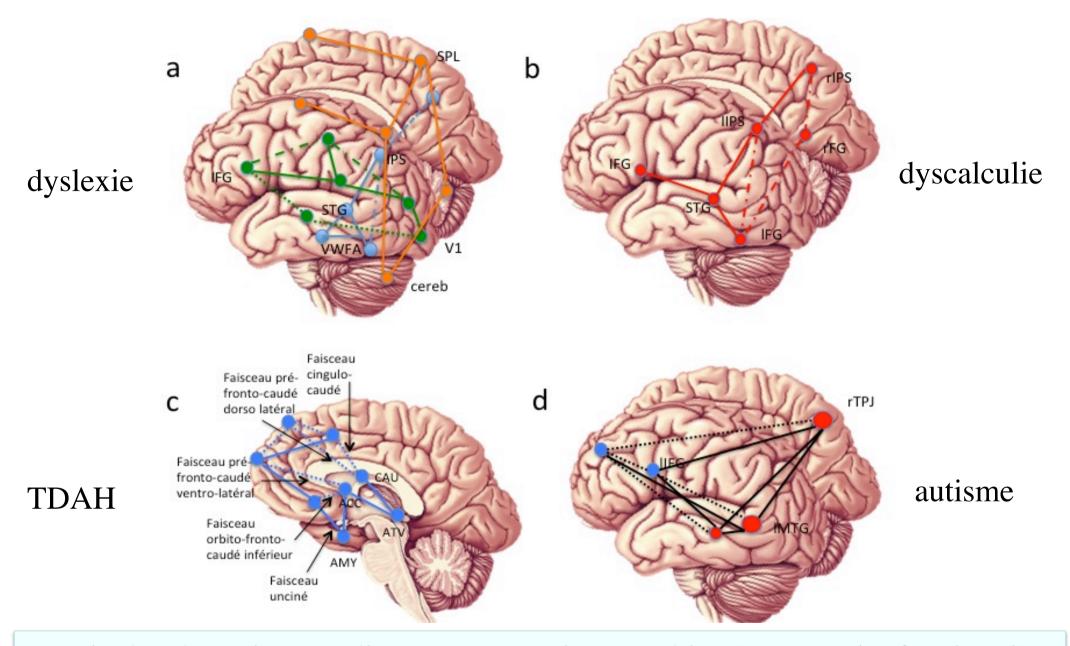


# Neurobiologia de la dislexia : estado actual de conocimiento

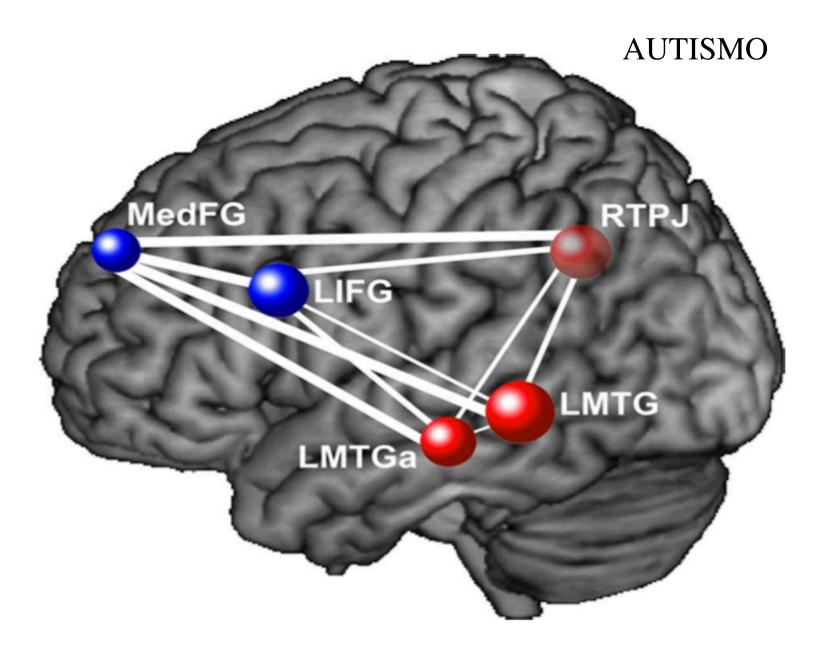
- La dislexia es caracterizada por una inaptitud fundamental a poner en relación las características visuales, sonoras y motoras de los elementos constitutivos del lenguaje, cada uno siendo representado (en forma correcta) en partes diferentes del cerebro.
- La anomalía crucial sería un defecto de organización y/o integridad de un haz de materia blanca, llamado fascículo arcuato, uniendo las regiones auditivas a la área de Broca, la cual sería un nodo, o centro neurálgico (« hub ») a la intersección entre aferencias sensoriales y producción lingüística, oral y escrita.
- Este fascículo, ya se halla anormal antes del aprendizaje de la lectura, y su constitución recibe influencias de (al menos) 3 genes conocidos por su asociación con defectos de adquisición lectora.
- De modo mas general, el cerebro disléxico sería marcado por una organización atípica del desarrollo de conexiones entre zonas criticas por aprender a leer, y este atipia parece preexistir al initio de la lectura

## Mas alla de la dislexia...

- Además de las evidencias de un defecto de integración entre los códigos visual y auditivo-lingüístico a la origen del déficit de lectura, hay pruebas crecentes de defecto de mecanismos basados sobre la asociación entre percepción auditiva y repuesta motora, especialmente en el contexto de actividad rítmica (por ejemplo datos clásicos con la tarea de Mira-Stambak)
- Estas observaciones, que pueden relacionar con las nociones previas de defecto de conectividad, pueden servir en modos originales de rehabilitación, por ejemplo usando música
- También tal podría ser el mecanismo, casi universal, a la origen de trastornos varios : lenguaje oral y escrito, calculo, cognición social...



Resultados de varios estudios en resonancia magnética (structural y funcional) sobre 4 diferentes trastornos del neurodesarrollo : hipo o dis- conectividad.



Representación esquematica de la hipo-connectividad funcional entre areas corticales frontales y posteriores . Mason et al., 2008



#### Convergent Findings of Altered Functional and Structural Brain Connectivity in Individuals with High Functioning Autism: A Multimodal MRI Study

Sophia Mueller<sup>1</sup>\*<sup>9</sup>, Daniel Keeser<sup>1,2,9</sup>, Andrea C. Samson<sup>3</sup>, Valerie Kirsch<sup>4,5</sup>, Janusch Blautzik<sup>1</sup>, Michel Grothe<sup>6</sup>, Okan Erat<sup>1</sup>, Michael Hegenloh<sup>2,7</sup>, Ute Coates<sup>1</sup>, Maximilian F. Reiser<sup>1</sup>, Kristina Hennig-Fast<sup>2</sup>, Thomas Meindl<sup>1</sup>

1 Institute of Clinical Radiology, Ludwig-Maximilians University Munich, Munich, Germany, 2 Department of Psychiatry and Psychotherapy, Ludwig-Maximilians University Munich, Munich, Germany, 3 Department of Psychology, Stanford University, Stanford, California, United States of America, 4 Department of Neurology, Ludwig-Maximilians University Munich, Munich, Germany, 5 German, 5 Germany, 6 Department of Psychiatry, University of Rostock, Rostock, Germany, 7 Department of Psychology, Ludwig-Maximilians University Munich, Munich, Germany

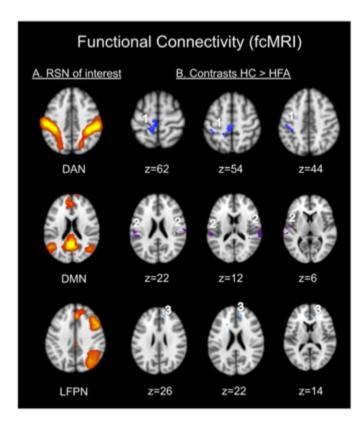


Figure 2. Functional connectivity between group differences. (A) Resting state networks (RSN) of interest, identified by group-ICA of resting state fMRI data and subjected to analysis of functional connectivity differences between high functioning autism (HFA) participants and healthy controls (HC). Three RSNs, namely the DAN (dorsal attention network), the DMN (default mode network) and the LFPN (left-lateralized fronto-parietal network) exhibited clusters of decreased functional connectivity in HFA as compared to HC (B). Indices

« our results indicate common sites of structural and functional alterations in higher order association cortex areas and may therefore provide multimodal imaging support to the long-standing hypothesis of autism as a disorder of impaired higherorder multisensory integration. »

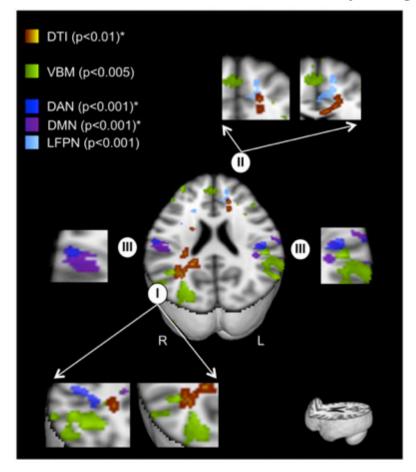


Figure 3. Localization of common sites of structural and functional alterations in high functioning autism. (I) indicates

### Traitement analogique (IPS):

- appréciation des magnitudes
- comparaisons de quantités
- soustraction

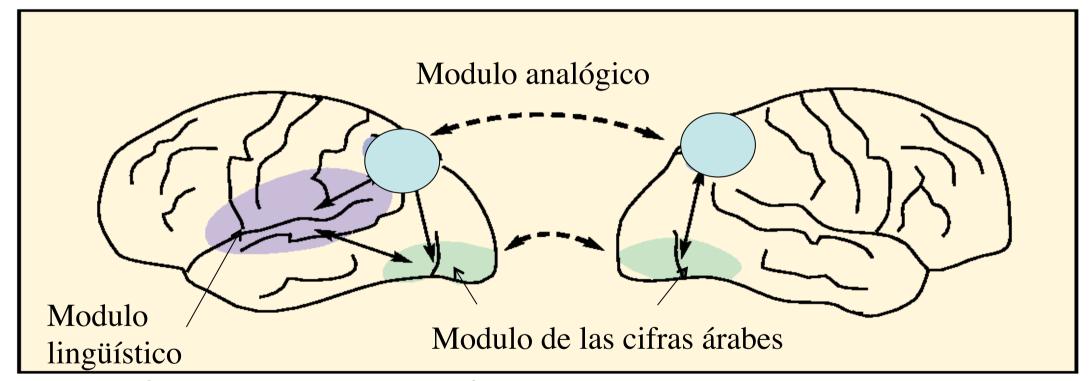


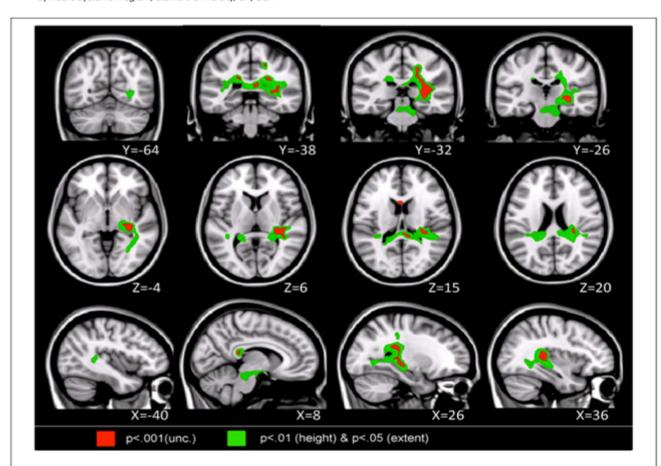
Figure 3 - Implémentation anatomique du triple code (traitement visuel arabe en vert, traitement analogique en bleu et traitement langagier en violet).

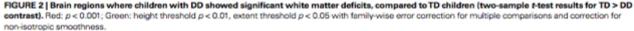


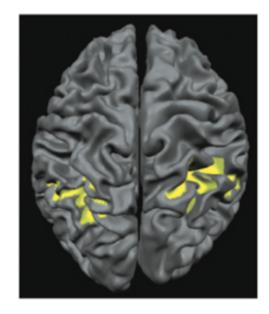
## Neuroanatomical correlates of developmental dyscalculia: combined evidence from morphometry and tractography

Elena Rykhlevskaia<sup>1,2</sup>, Lucina Q. Uddin<sup>1</sup>, Leeza Kondos<sup>1</sup> and Vinod Menon<sup>1,3,4</sup>\*

- <sup>1</sup> Department of Psychiatry and Behavioral Sciences, Stanford University, CA, USA
- <sup>2</sup> Department of Psychology, Stanford University, CA, USA
- 3 Program in Neuroscience, Stanford University, CA, USA
- <sup>4</sup> Symbolic Systems Program, Stanford University, CA, USA







DTI tractography suggests that long-range WM projection fibers linking the right fusiform gyrus with temporal-parietal WM are a specific source of vulnerability in DD

# Trastornos de aprendizaje : un modelo general tentativo con enfase sobre comorbilidad

