Département d'Etudes Cognitives · Ecole normale supérieure

Neuroanatomy of developmental dyslexia

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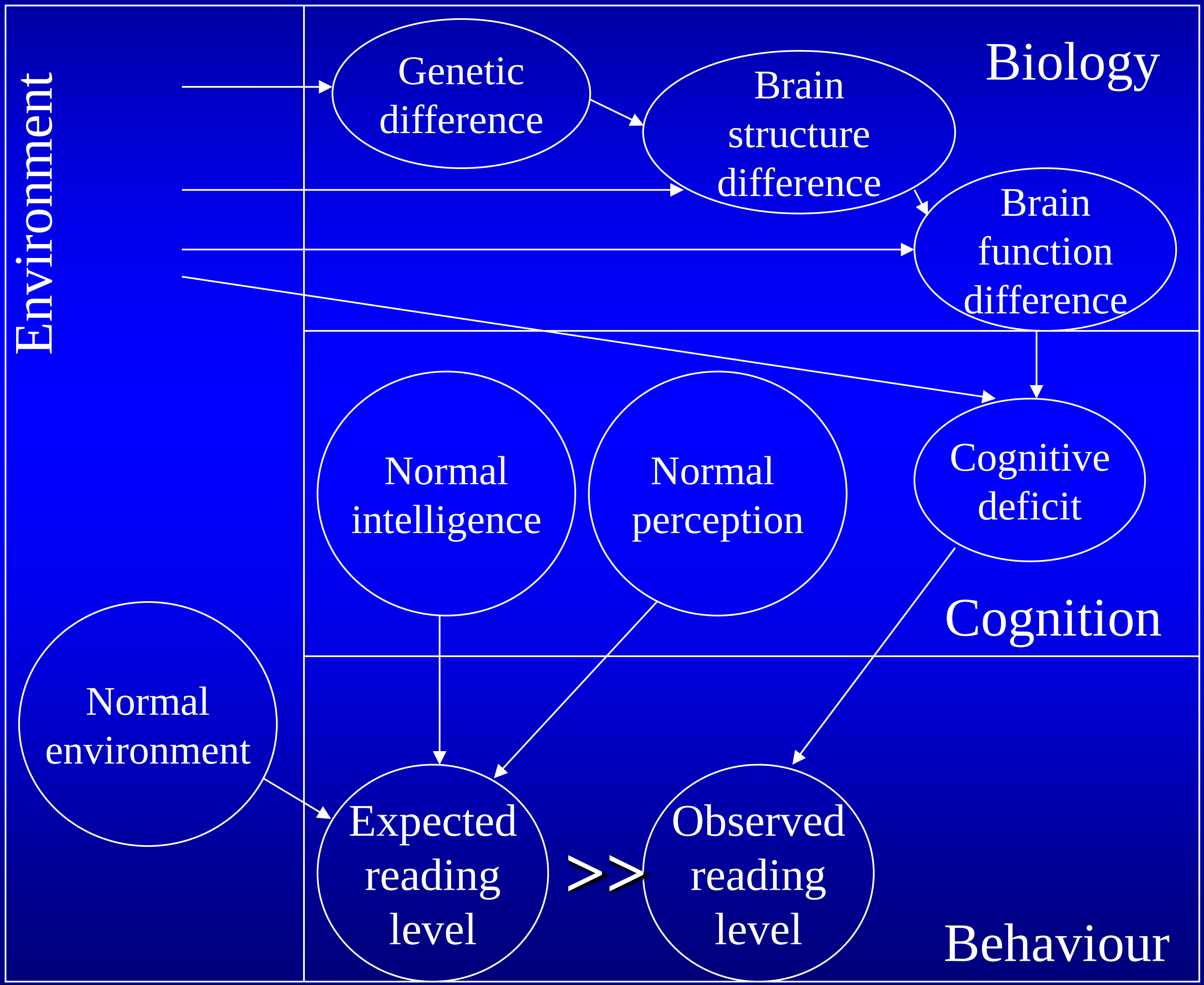
Causal modelling of dyslexia



Aims of Genedys project

- Investigate neuroanatomical correlates of dyslexia with:
- More participants (than previous studies).
- Better quality images.
- More fine-grained analyses, in each individual native space, respecting individual anatomy.
- Comprehensive behavioural battery
- DNA
- With C. Billard, G. Dehaene and the Neurospin team.

Genedys study

Å	Dyslexics	Controls
ïNumber	32	32
ïSex (M/F)	18/14	18/14
ïAge (years)	11.7 (1.3)	11.5 (1.4)

ÅSequences:

ïT1: 0.9 mm resolution 3-D

ïDTI: 1.7x1.7x1.7 mm, 60 directions, b=1400 s/mm^2.

ïT2, T2*, flairé

ïfMRI: mapping of the ventral visual pathway.

Received knowledge on the neuroanatomy of dyslexia

ÅLess grey matter in left perisylvian (language) regions

ÅLess-well connected white matter in the left arcuate fasciculus (connecting language regions).

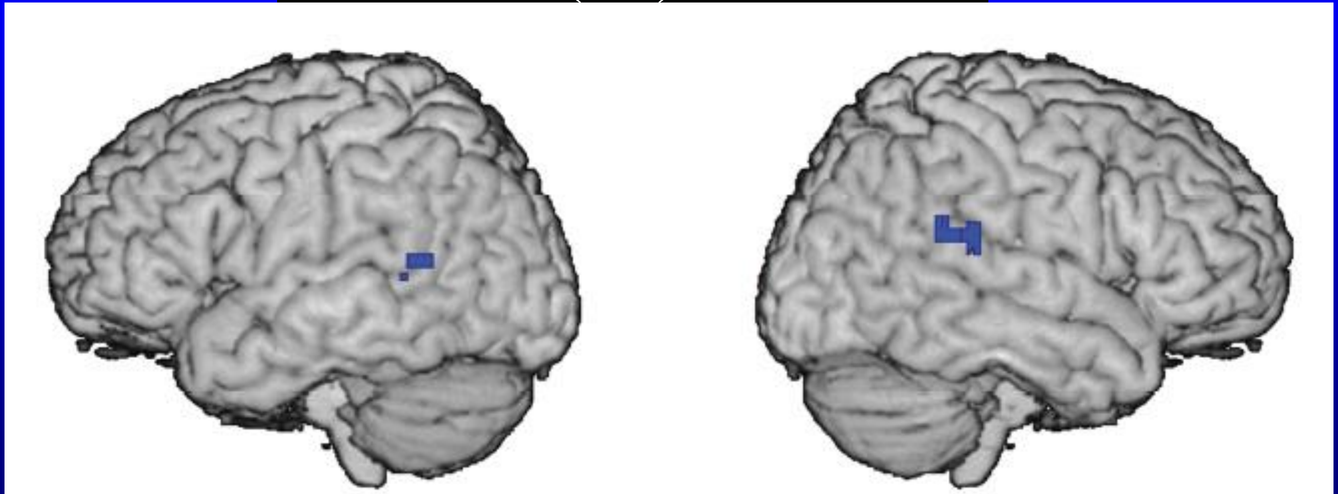
ÅLess leftward asymmetry of planum temporale?

ÅCorpus callosum?

ÅSmaller brains?

Received knowledge on gray matter volumes in dyslexia

Eckert (2004) *Neuroscientist*



Richlan, Kronbichler, & Wimmer (2012) *HBM*

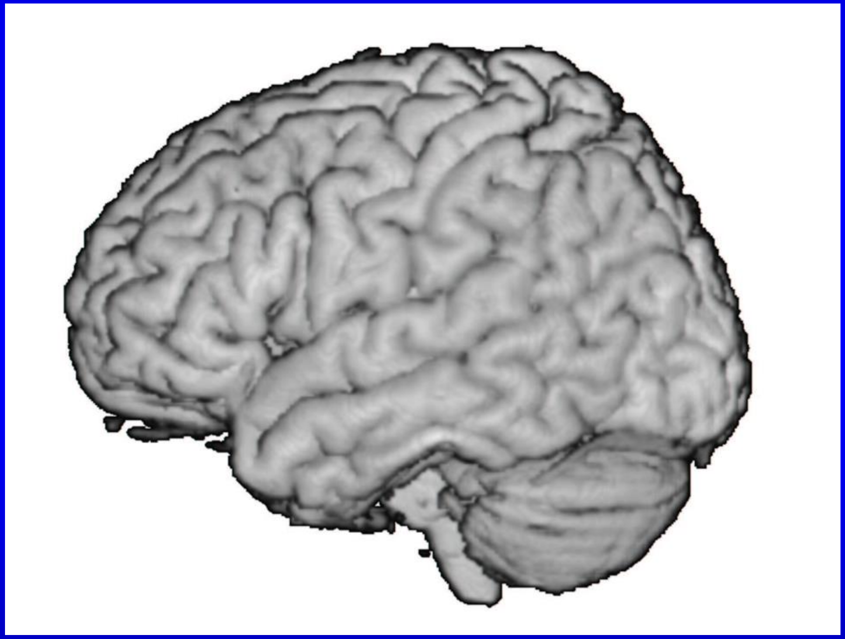
9 studies,
266 participants

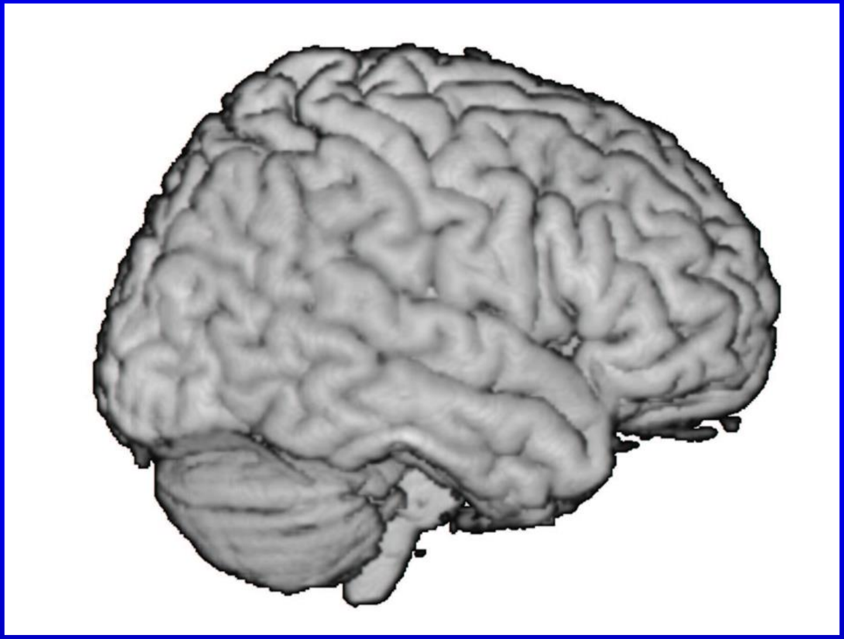
Richlan, Kronbichler, & Wimmer (2012) HBM

Table I. Main characteristics of the included studies and number of peaks used in the meta-analysis.

Year	First author	N	Dys	Con	Native language	Age mean (SD)	Modulated VBM (absolute volumes preserved)	ROI analysis	Threshold		No. of foci (reduced/ increased GM)
									Voxel-level (height) p <	Cluster-level (extent) p < or no. of voxels	
2008	Kronbichler	28	13	15	German	15.7 (0.7)	X	X	0.05 corr.	100	9/0
2008	Menghini	20	10	10	Italian	40.8 (6.9)	X	X	0.005 unc.	0.05 corr.	2/0
2008	Steinbrink	16	8	8	German	21.9 (4.1)	X	-	0.05 corr.	650	2/0
2007	Hoeft	38	19	19	English	14.4 (2.2)	X	-	0.01 corr.	0.01 corr.	6/0
2005	Eckert	26	13	13	English	11.4 (8.2)	X	-	0.00001 unc.	0.001 corr.	5/0
2005	Silani	64	32	32	English, French, Italian	25.3 (5.0)	X	X	0.05 corr.	-	1/1
2005	Vinckenbosch	23	13	10	French	range 17-30	-	-	0.01 corr.	0.05 corr.	1/1
2004	Brambati	21	10	11	Italian	29.5 (range 13-57)	X	-	0.05 corr.	25	9/0
2001	Brown	30	16	14	English	24.0 (5.0)	-	-	0.05 unc.	0.05 corr.	8/0

Our VBM results (32/32)





Complementary/replication studies

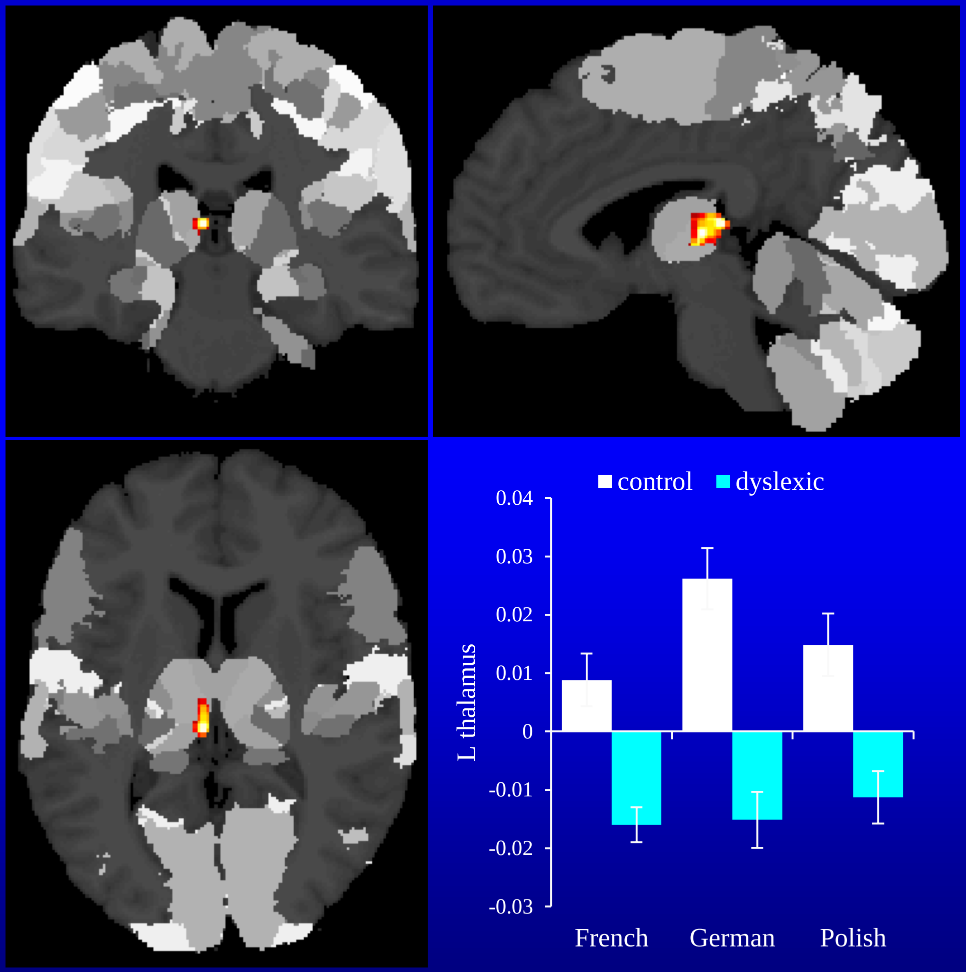
Å23 French dyslexics and 23 controls from Monzalvo et al. (2012).
+ 13 younger, reading-matched controls

Å46 Polish dyslexics and 35 controls (Jednorog et al.)

Å45 German dyslexics and 26 controls (Heim et al.)

VBM study of dyslexia across 3 countries

Jednorog, Marchewka, Gawron, Altarelli,
Ramus, & Heim (in prep.)



84 French, 71 German, and 81 Polish children (n=236)

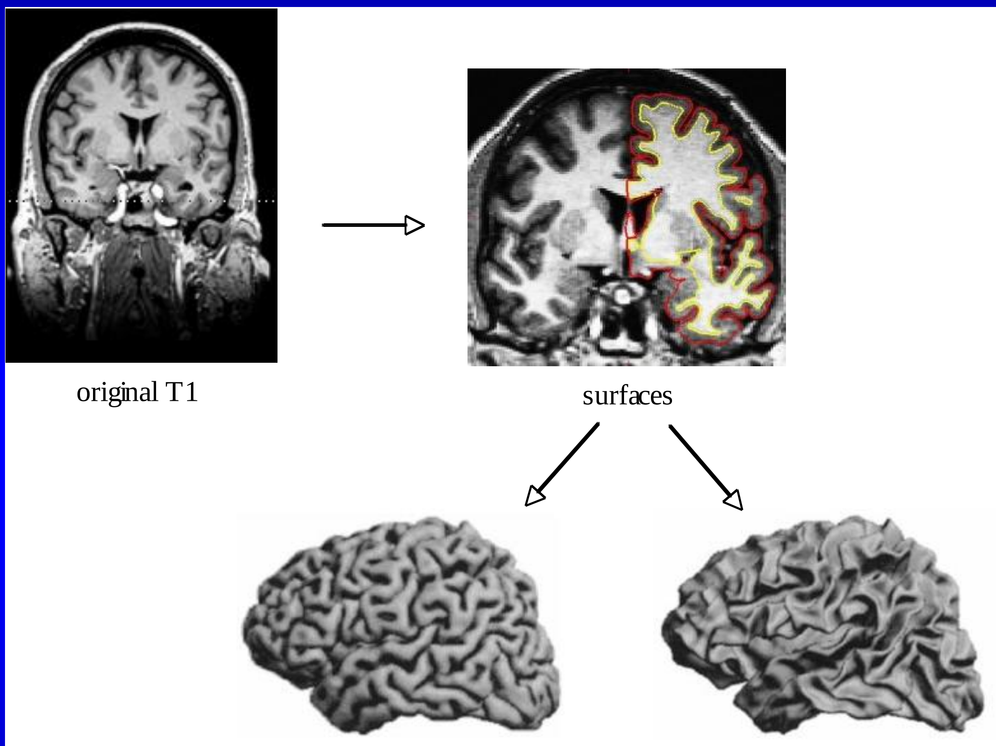
Group differences in gray matter volume overlaid on the Anatomy Atlas, Julich. Region in the left thalamus shown in red ïyellow exhibited reduced volume in the dyslexic group.

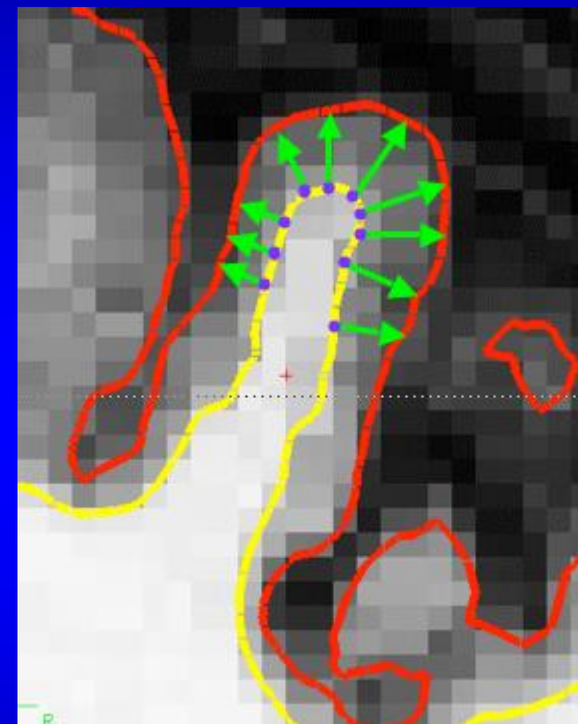
French t= 2.28; p=0.025
German t= 2.75; p=0.008
Polish t= 1.86; p=0.067

Consistent with VBM study by Brown et al. (2001), and with meta-analysis of fMRI by Maisog et al (2008).

GM volume = cortical thickness x surfac

T1 anatomical sequence processing (Freesurfer software)





Previous results on dyslexia (Frye et al. 2010 *Cereb. Cortex*):

Å Greater overall GMV and cortical surface in dyslexics

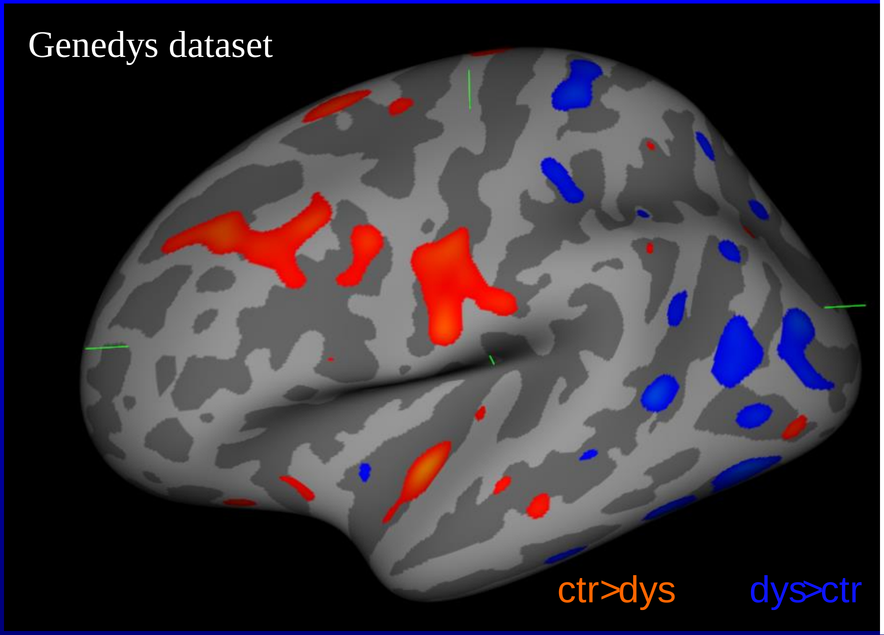
Å Greater surface in rSMG in dyslexics

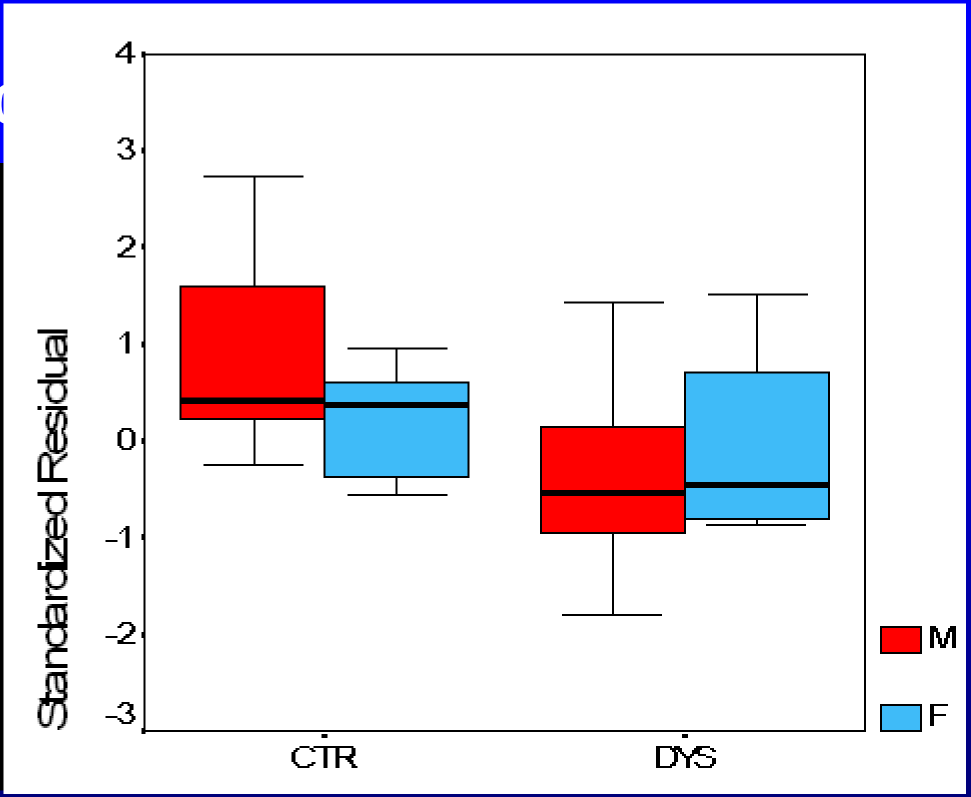
Å Lower surface in IFG and fusiform gyrus in dyslexics

Our results on cortical thickness and surface (Altarelli + Monzalvo)

Å*Lower* whole brain volume and surface in dyslexics.

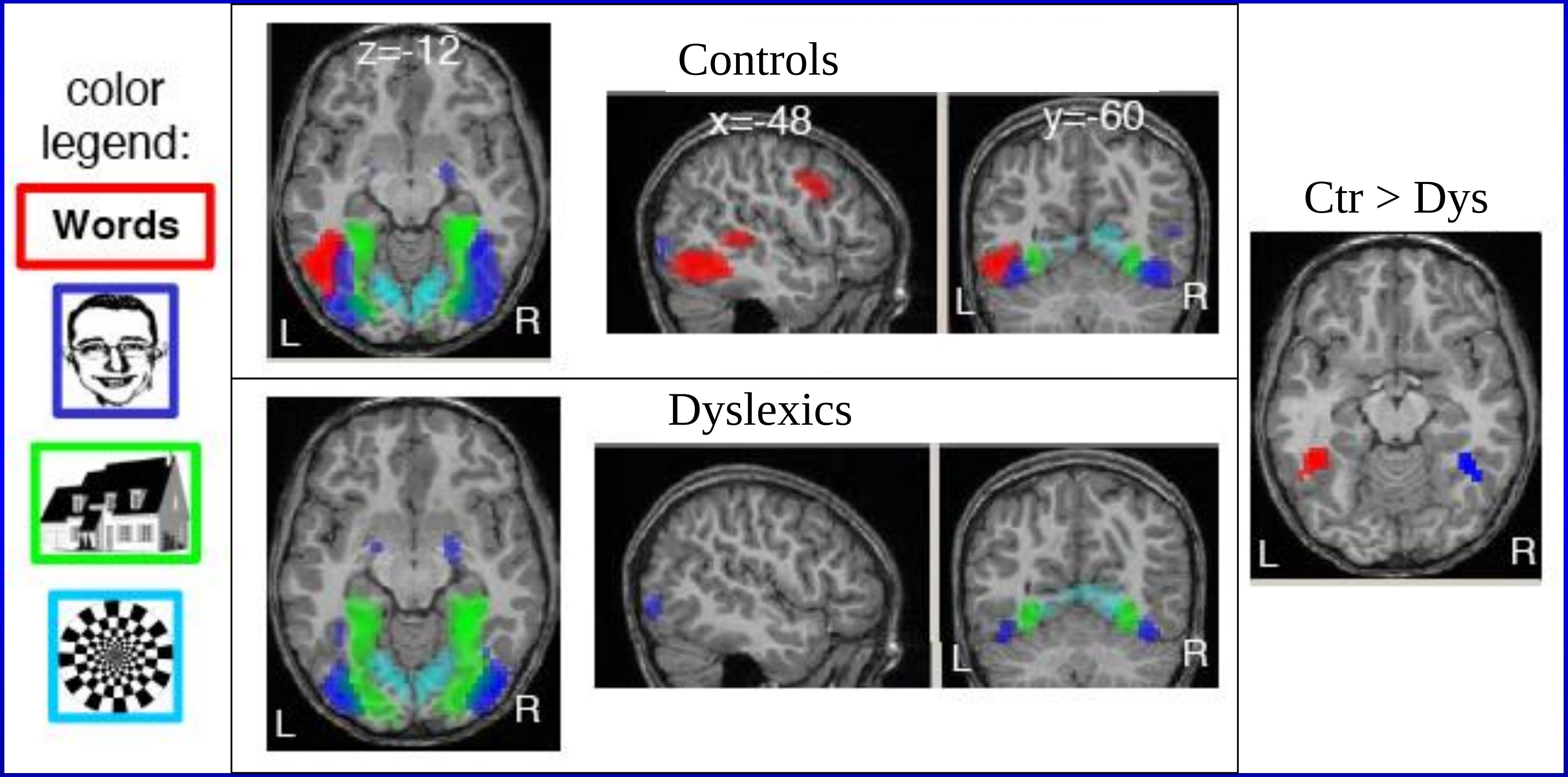
ÅNo consistent local d





Functional sequence

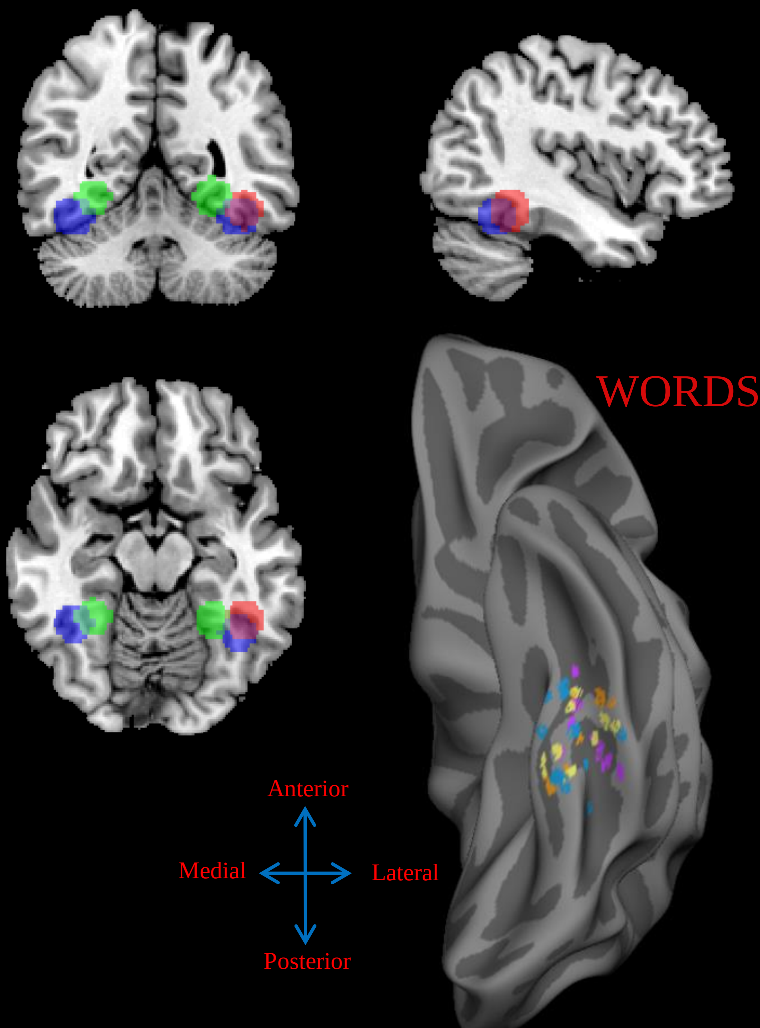
9.7 years old

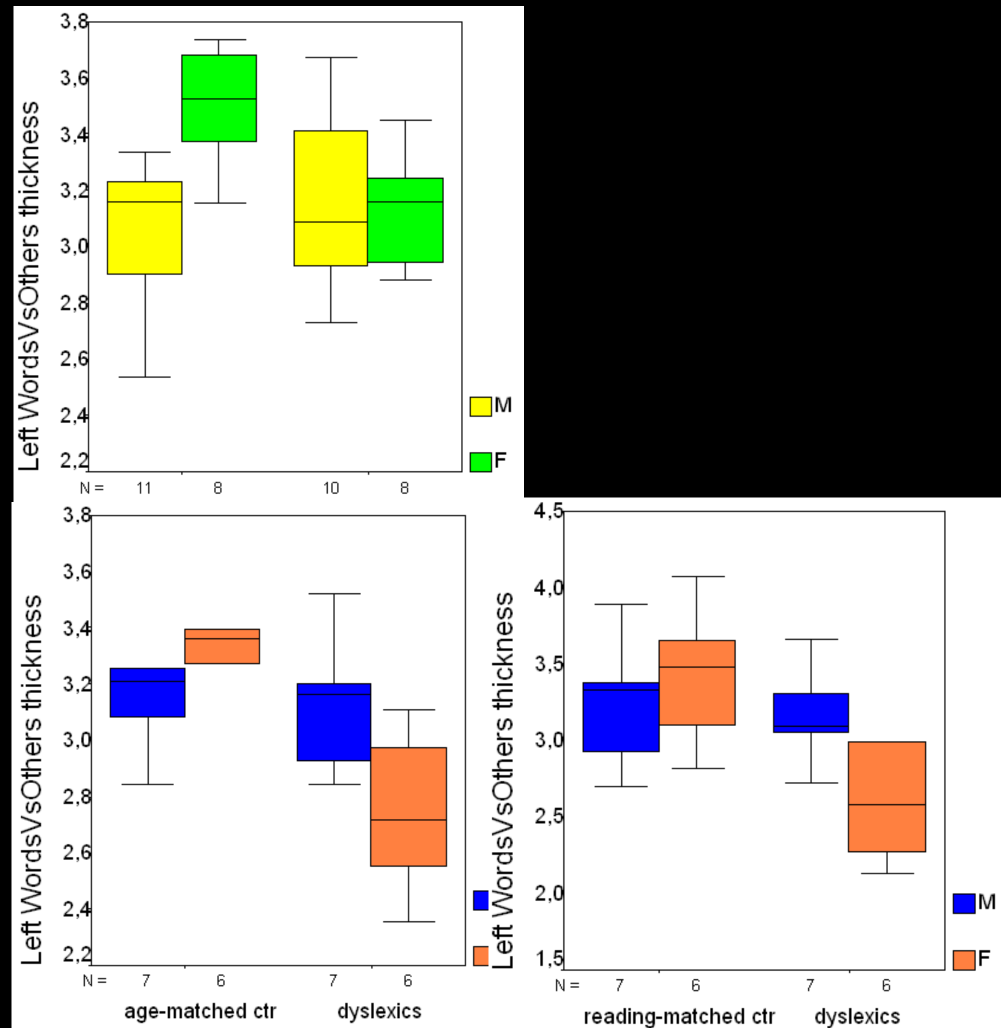


Monzalvo et al., 2012 *Neuroimage*

Cortical thickness of VWFA in dyslexic children

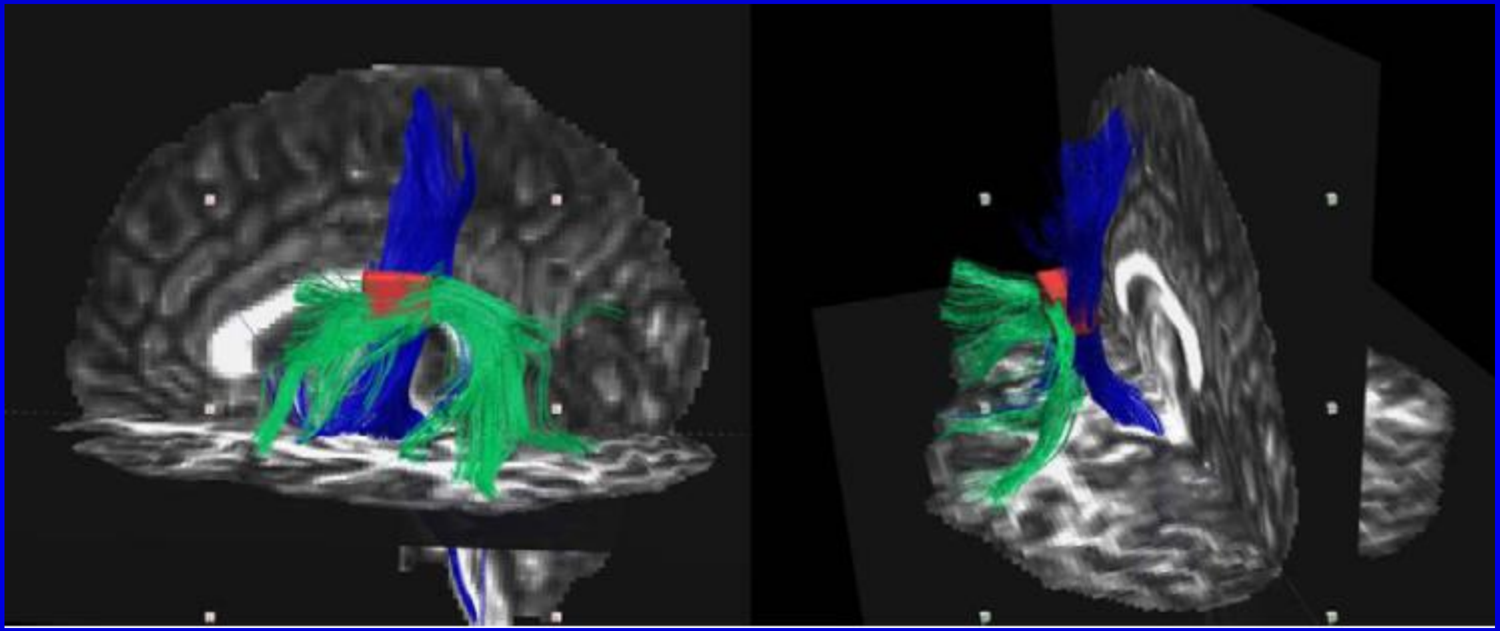
Altarelli, I., Monzalvo, K., Iannuzzi, S., Fluss, J., Billard, C., Ramus, F., & Dehaene-Lambertz, G. (2013) *J. of Neuroscience*



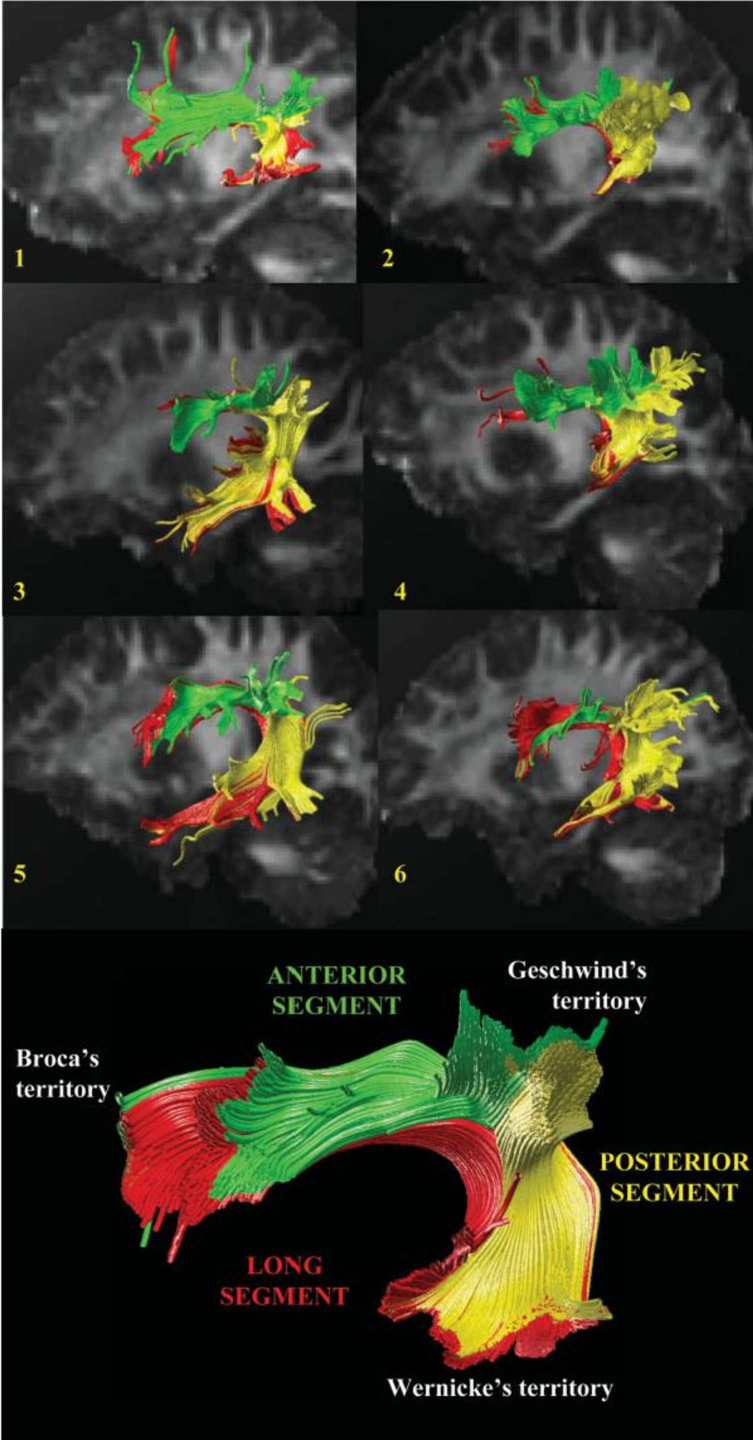


Diffusion Tensor Imaging

Meta-analysis (Vandermosten et al. 2012)

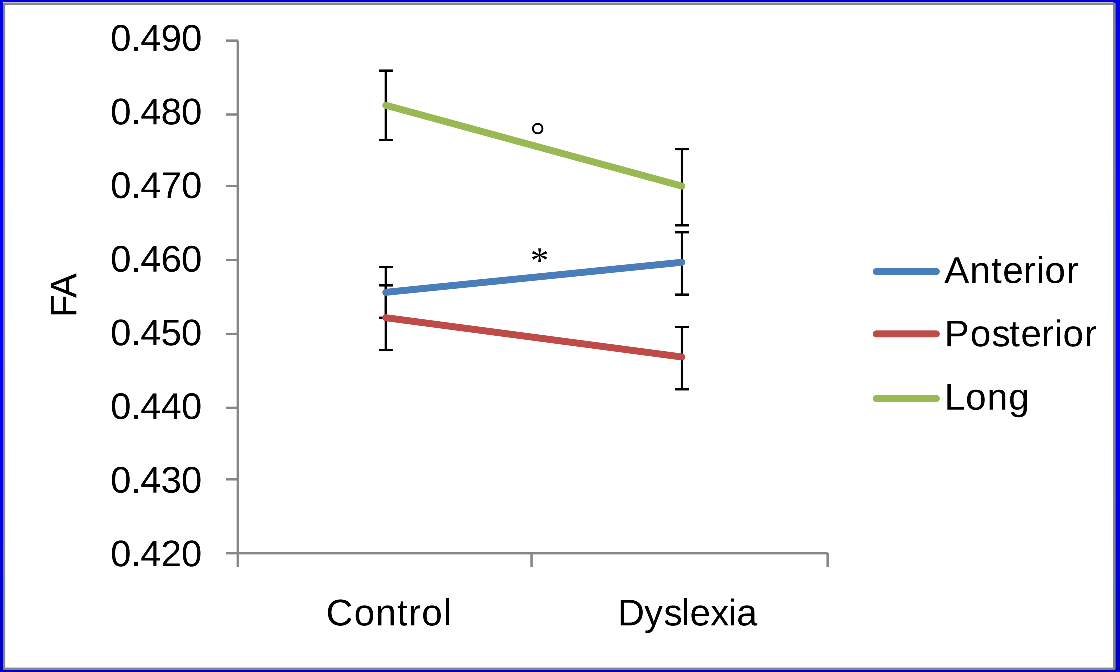


Dyslexics: lower FA in left long segment of arcuate fasciculus



Dissection of the arcuate fasciculus (32/31)

Zhao, Thiebaut de Schotten, Altarelli, Dubois, & Ramus (in prep)



- Å Group X Segment: $F(2, 82)=3.446$, $p=0.037$
- Å We find the same trend in both hemispheres
- Å And the opposite effect in the anterior segment
- Å And no correlation with behavioural measures

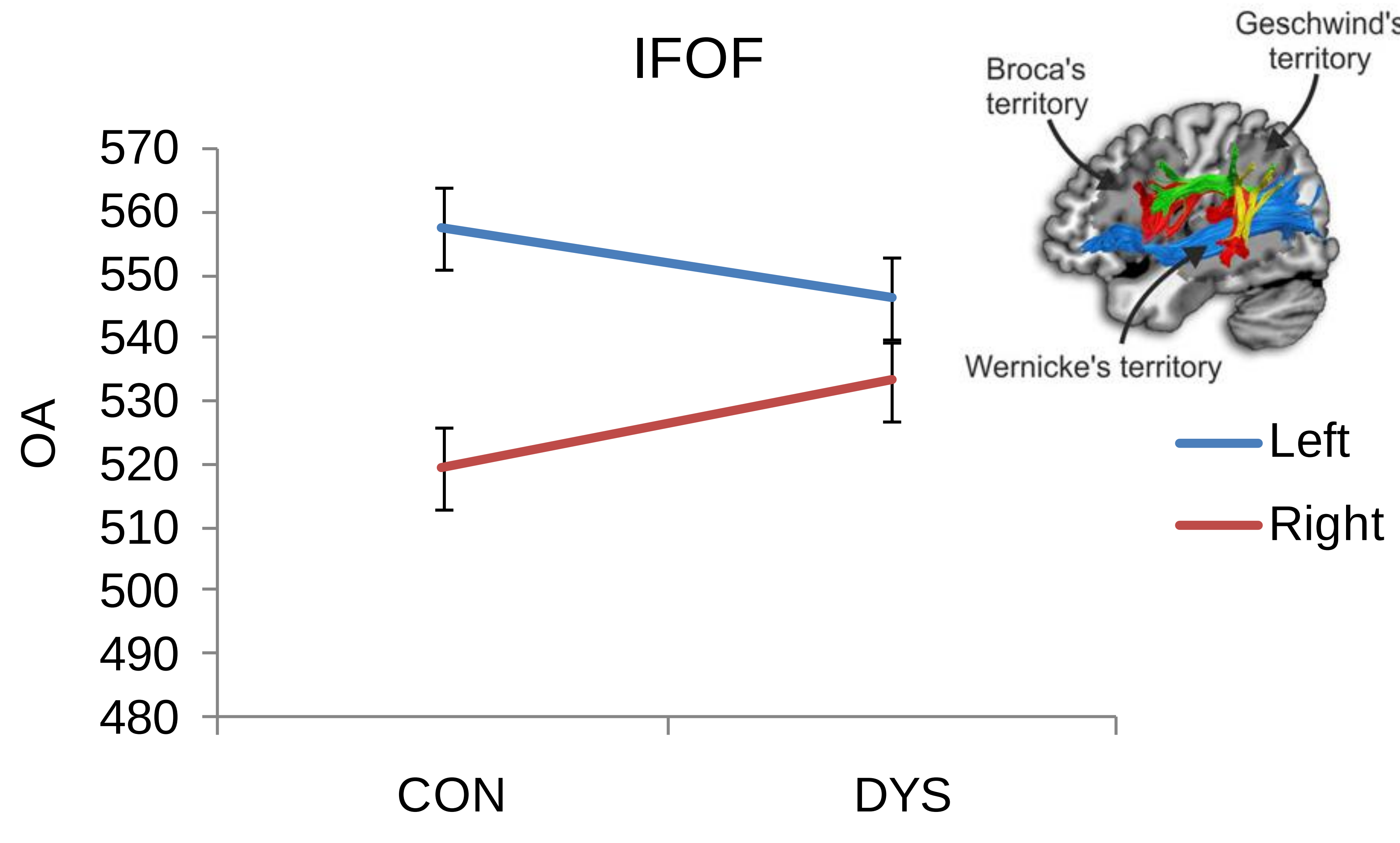
Problems with standard DTI analysis methods

ÅFiber-crossing regions not well handled

ÅArcuate fasciculus confounded with superior longitudinal fasciculus.

ÅOur sequence parameters (1.7x1.7x1.7 mm, 60 non-collinear directions, b=1400 s/mm^2) allow us to try and do better.

ÅNew measure: Hindrance modulated orientational anisotropy (HMOA or OA).



ÅInferior frontal-occipital fasciculus

ïGroup X Hemisphere F(1, 56)=6.805, p=0.012

Summary of tractography results

ÅUsing standard DTI analysis of arcuate fasciculus:

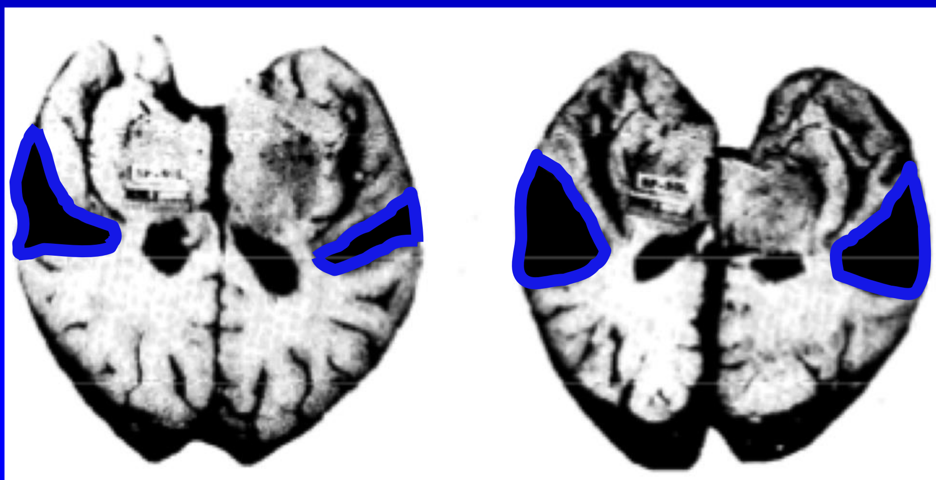
- ï Partial replication of disruption (lower FA) of the long segment of arcuate.
- ï But bilateral
- ï Seems compensated (?) by higher FA in anterior segment (consistent with greater frontal involvement)

ÅUsing spherical deconvolution tractography:

- ï No difference in arcuate.
- ï Higher OA in right SLF II in dyslexics (greater involvement of attentional networks?)
- ï More symmetrical IFOF (less specialised direct reading route?)

Asymmetry of the planum temporale

A long, sad s t o r y é



L>R
63% of cases

L Ò R
37% of cases

Geschwind & Levitsky 1968
Galaburda et al. 1987

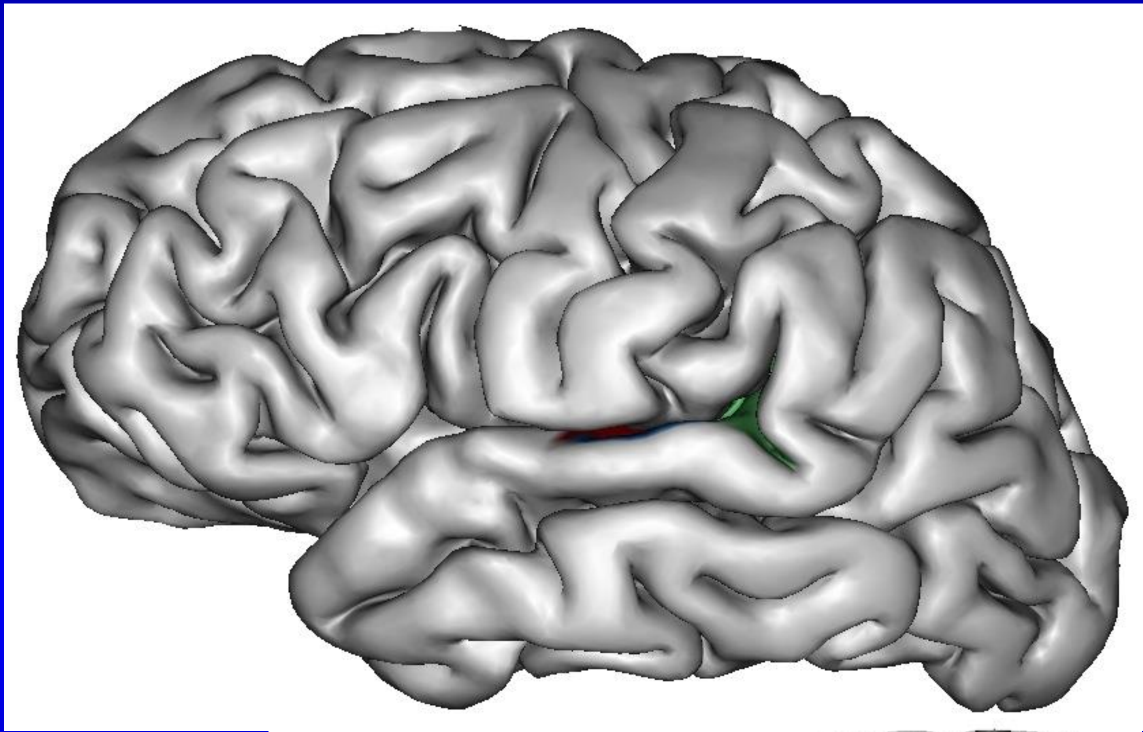
L ÒR in 5 out 5 male dyslexic brains dissected by Galaburda et al. 1985

Authors	N	Anatomical criteria	Ctr asymm	Group difference
Green 1999	16	Heschl's sulcus (excluding H2) to end of PAR	no	larger PT+ area overall in dys; no diff in asymm
Leonard 2002 (study 1)	14	Heschl's sulcus (excluding H2??) to intersection		Leftward PT asymm in dys, symm in SLI (but comparison ns)
Leonard 2006	22	Heschl's sulcus (excluding H2??) to intersection		marked leftward asymm
Schulz 1994	31	Heschl's sulcus (or end of insula) to end of syl fis. Excluding H2?	yes	No diff between groups, trend for dys girls symm but not signif, age correlated with struct size/area
Hynd 1990	20	ridge of Heschl's gyrus (excluding H2) to end of syl fis	yes	
Larsen 1990	36	ridge of Heschl's gyrus (excluding H2) to end of syl fis	yes	Dyslexic symm
Semrud-Clikeman 1991	20	ridge of Heschl's gyrus (excluding H2) to end of syl fis	yes	Dyslexic symm or rightward length, left PT smaller
Semrud-Clikeman 1996	20	ridge of Heschl's gyrus (excluding H2) to end of syl fis	yes	
Best and Demb 1999	10	Heschl's sulcus to end of desc branch	yes	No diff in PT asymm, regardless of method
Heiervang 2000	40	Heschl's sulcus to end of desc branch	yes	all leftward asymm, smaller left PT in dys
Hugdahl 1998	50	Heschl's sulcus to end of desc branch	yes	Trend for smaller left PT in dys; reduced leftward asymm in dys
Hugdahl 2003	46	Heschl's sulcus to end of desc branch	yes	No diff in asymm, smaller left PT in dys
Preis 1998	42	Heschl's sulcus to end of desc branch	yes	No diff in PT or PP asymm
Robichon 2000	30	Heschl's sulcus to end of syl fis	yes	No diff in PT asymm, more leftward asymm in PO in dys
Eckert 2003	50	Heschl's sulcus to intersection		No group nor group*gender effect
Foster 2002	31	Heschl's sulcus to intersection	?	Larger right PT in dys
Kibby 2004	17	Heschl's sulcus to intersection; desc branch excluded	yes?	No diff in PT or pars triang asymm
Leonard 1993	21	Heschl's sulcus to intersection; desc branch excluded	yes	More marked leftward in dys but signif not reported; rightward asymm PP; greater par than temp tissue in the right hemi in dys
Rumsey 1997	30	Heschl's sulcus to intersection; desc branch excluded	yes	No diff in PT or PP asymm
Leonard 2001	28	Heschl's sulcus to intersection; desc branch excluded; right: if no planum, asc branch instead		Tendency towards more marked leftward but not signif; leftward asymm PT+ in all; no diff in ratio of PT to asc branch

Asymmetry of the planum temporale

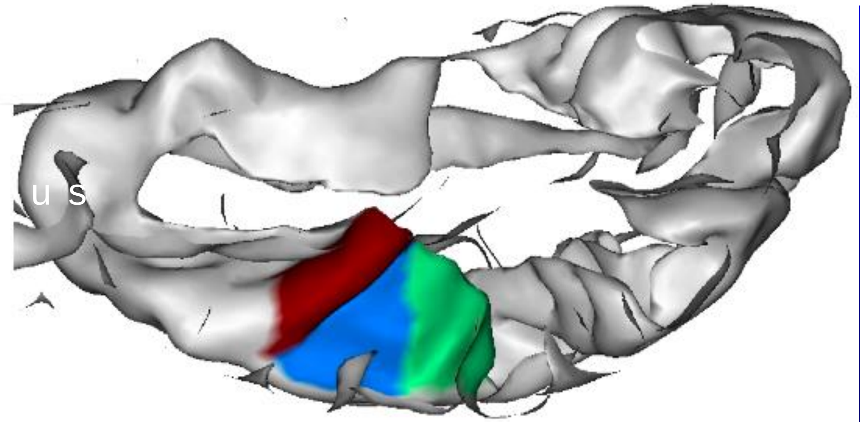
Altarelli, Leroy, Dehaene-Lambertz, & Ramus (in prep)

Under guidance of Al Galaburda



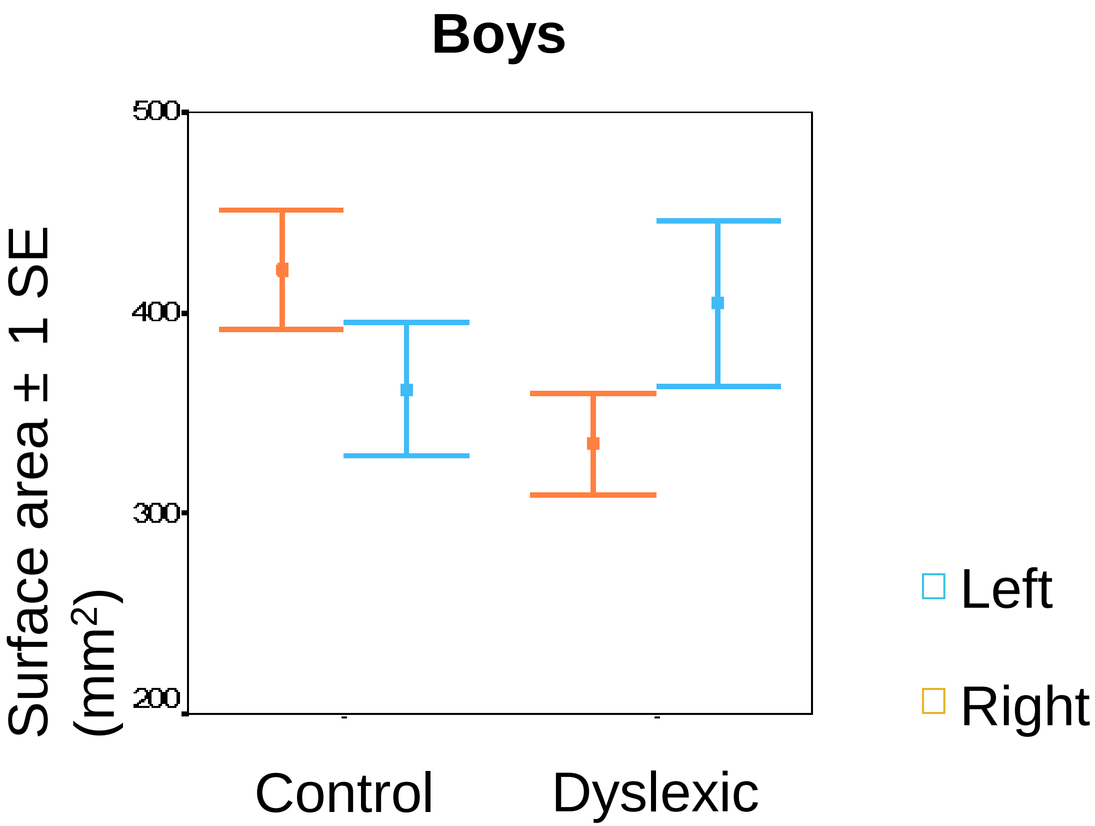
81 subjects, all right-handed

25 control M	20 dyslexic M
21 control F	15 dyslexic F



- Heschlôs gyrus
- Planum Temporale
- Posterior ramus

PT Hemi*gender*diagnosis $F_{(1,71)}$=4.2 p=0.04



Boys
Hemi*diagnosis $F_{(1,39)}$=6.1 p=0.02

Nature Reviews Neuroscience | AOP, published online 10 April 2013; doi:10.1038/nrn3475

ANALYSIS

Power failure: why small sample size undermines the reliability of neuroscience

Katherine S. Button[1,2], John P. A. Ioannidis[3], Claire Mokrysz[1], Brian A. Nosek[4], Jonathan Flint[5], Emma S. J. Robinson[6] and Marcus R. Munafò[1]

Abstract | A study with low statistical power has a reduced chance of detecting a true effect, but it is less well appreciated that low power also reduces the likelihood that a statistically significant result reflects a true effect. Here, we show that the average statistical power of studies in the neurosciences is very low. The consequences of this include overestimates of effect size and low reproducibility of results. There are also ethical dimensions to this problem, as unreliable research is inefficient and wasteful. Improving reproducibility in neuroscience is a key priority and requires attention to well-established but often ignored methodological principles.

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- Neurospin: G. Dehaene-Lambertz, K. Monzalvo, J. Dubois, F. Leroy, nurses and radiographers
- Bicêtre: C. Billard, F. Delteil-Pinton, J. Fluss

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