Qu'a-t-on appris de l'imagerie dans la sclérose en plaques ?

Partie I – Modifications structurelles

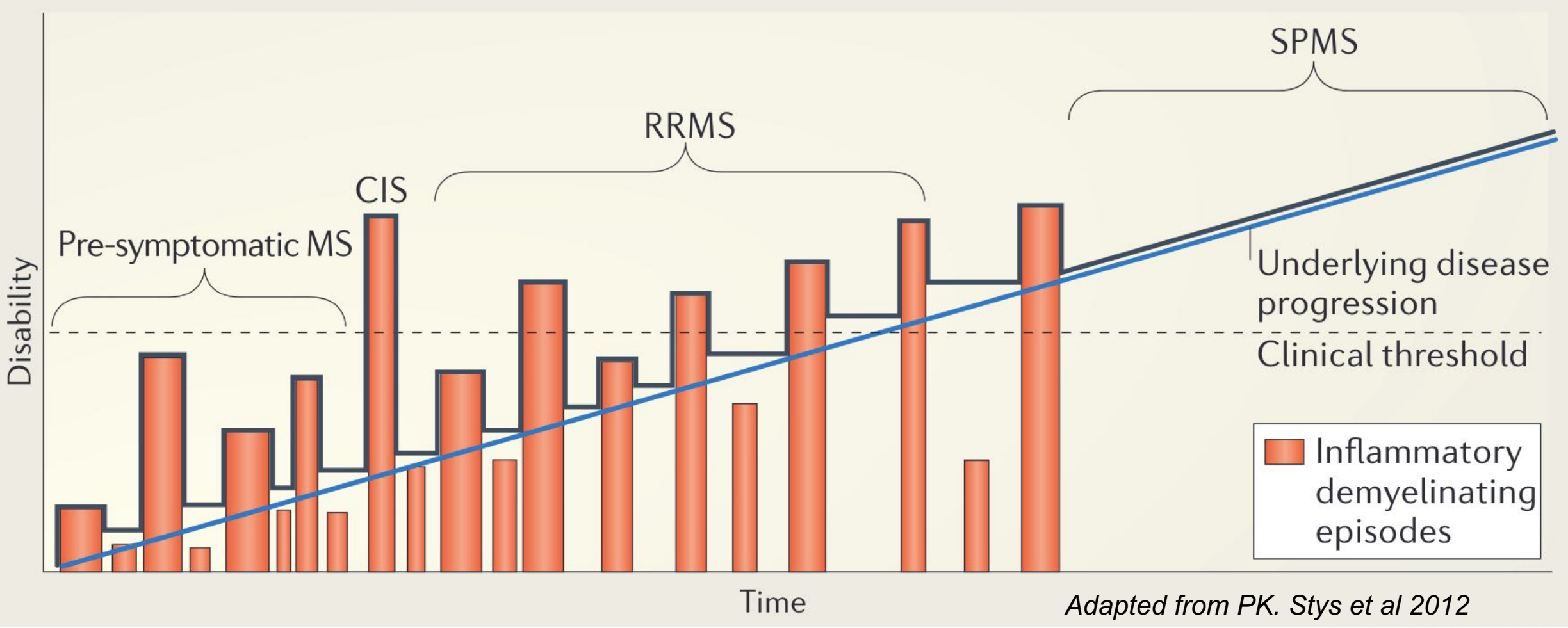
Dr Adil MAAROUF

Neurologue

Maladie Inflammatoire du Cerveau et de la Moelle Epinière (MICeME)

Assistance Publique – Hôpitaux de Marseille

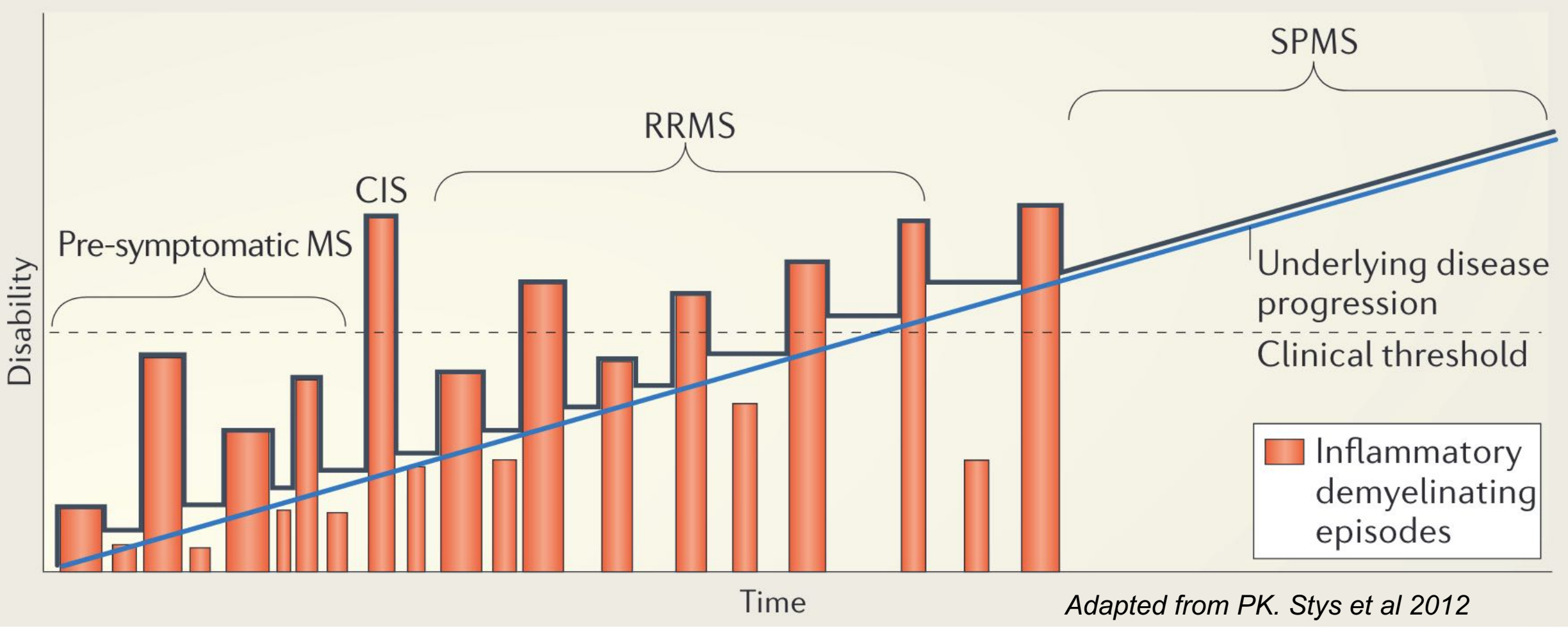
Histoire naturelle



Adapted from PK. Stys et al 2012

NATURE REVIEWS | NEUROSCIENCE

Histoire naturelle



Adapted from PK. Stys et al 2012

NATURE REVIEWS | NEUROSCIENCE

Plus de lésions que de phénomènes cliniques **(5 à 10 fois plus lésions IRM que poussées cliniques)**

NUCLEAR MAGNETIC RESONANCE IMAGING OF THE BRAIN IN MULTIPLE SCLEROSIS

I. R. YOUNG A. S. HALL

Central Research Laboratories, Thorn-EMI Ltd, Hayes, Middlesex

C. A. PALLIS N. J. LEGG
G. M. BYDDER R. E. STEINER

Departments of Medicine (Neurology) and Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 OHS

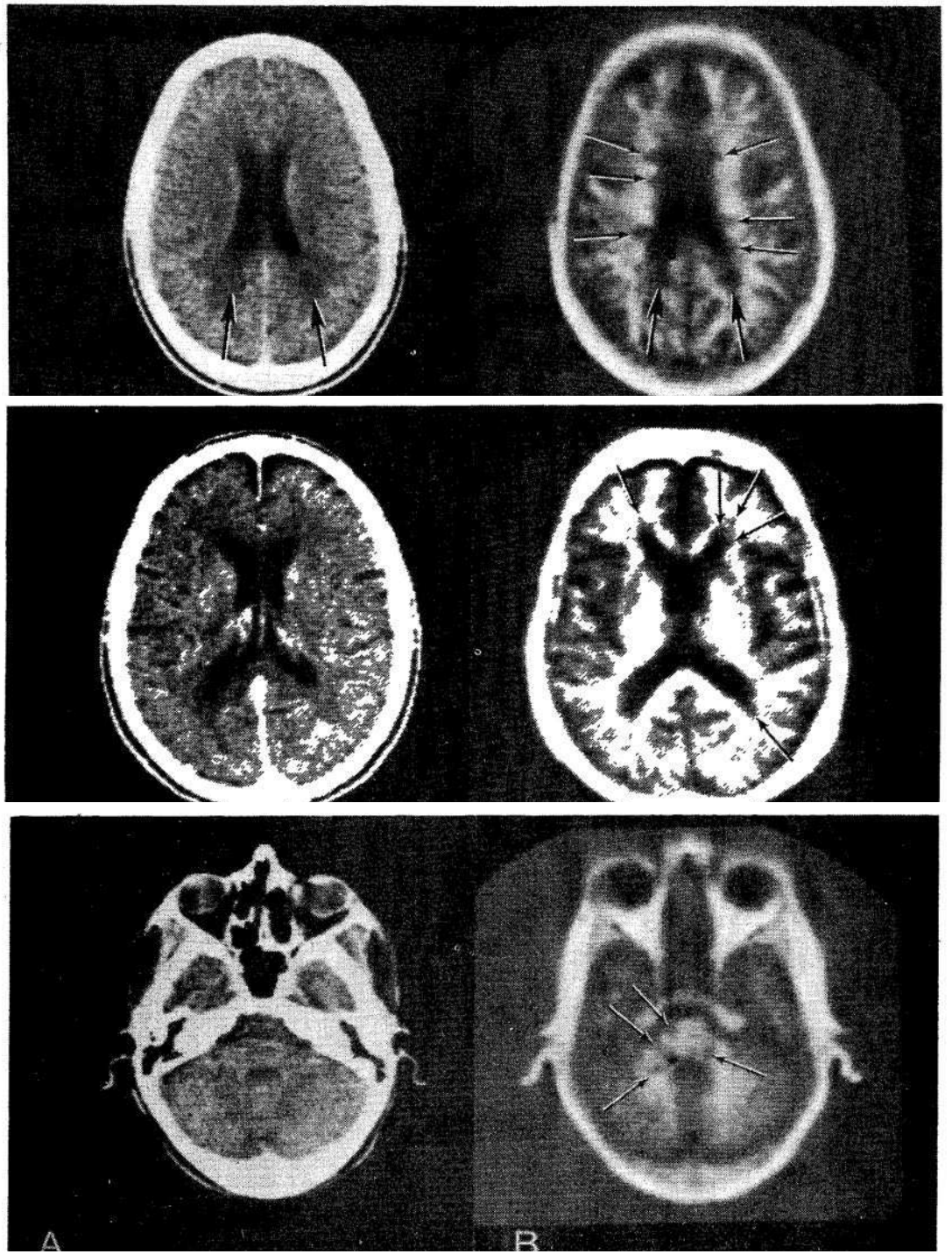
We now present the results of NMR examination of ten patients MS and compare them with those obtained with CT.

Patients and Methods

Patients

Ten patients investigated in the Department of Medicine (Neurology) at Hammersmith Hospital were chosen for evaluation. Eight (patients 1 to 8) fulfilled the criteria for a diagnosis of "clinically definite" MS suggested by McDonald and Halliday.[5] Patient 9 fell into their "progressive probable" category and patient 10 into their "early probable" group.

Level of scan	No. of slices	No. of lesions	
		CT scan	NMR scan
Supraventricular	23	3	9
High ventricular	12	2	18
Mid-ventricular	13	10	35
Low ventricular	18	4	31
Mesencephalon	16	0	17
Pons	12	0	15
Medulla	12	0	6
Total	106	19	131



The Lancet · Saturday 14 November 1981

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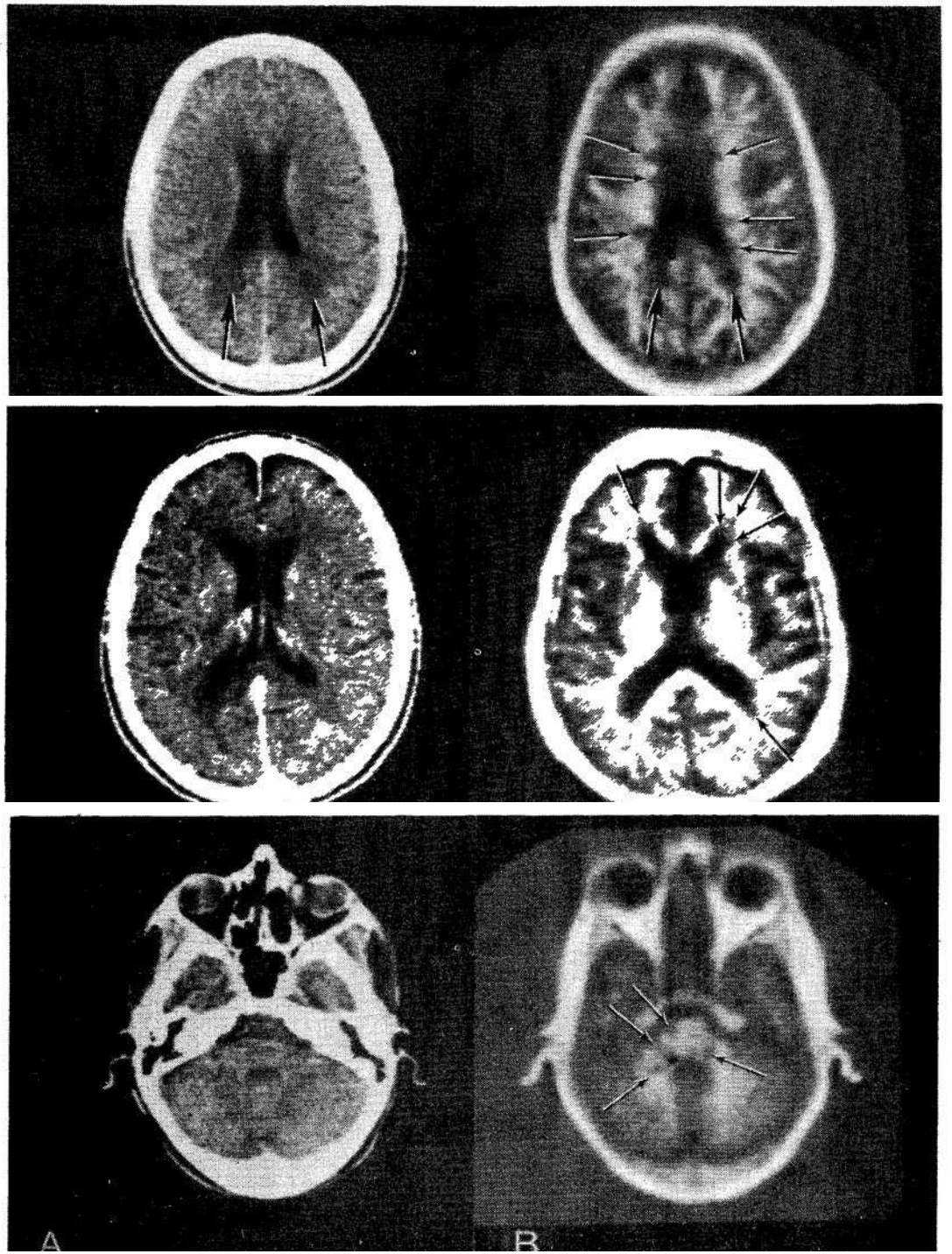
5 to 10 times more MRI lesions than clinical relapses



1999

Multiple Sclerosis (1999) 5, 283–286

http://www.stockton-press.co.uk/ms

MRI in multiple sclerosis: correlation with expanded disability status scale (EDSS)

*Frederik Barkhof**,[1]
[1]*MS-MRI centre and Department of Radiology, Vrije Universiteit Hospital Amsterdam, P.O. Box 7057, 1007 MB, Amsterdam, The Netherlands*

Table 2 Cross-sectional correlations with T2

Source	*Reference*	*Number*	*Disease course*	*Correlation*
Riahi	26	*n*=39	RR	r 0.60
Morrissey	24	*n*=89	CIS	r 0.55
Gawne-Cain	27	*n*=56	mix	r 0.49
Lycklama	11	*n*=60	RR/SP	r 0.33
Gass	28	*n*=43	mix	r 0.33
IFN-1b trial baseline	20	*n*=372	RR	r 0.22
Waesberghe	7	*n*=41	RR/SP	r 0.17
FN-1b trial 3rd year	23	*n*=712	SP	r 0.15

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Table 3 Longitudinal correlations of clinical changes with changes in T2

Source	*Reference*	*Number*	*Disease course*	*Correlation*
New T2 lesions – EDSS				
Filippi	35	213	mixed	r 0.13
IFNB-1b	23	712	SP	r 0.18
T2 lesion load – EDSS				
Walderveen	32	39	mixed	r 0.19
Truyen	29	19	SP	r 0.67
IFNB-1b	20	372	RR	r 0.23
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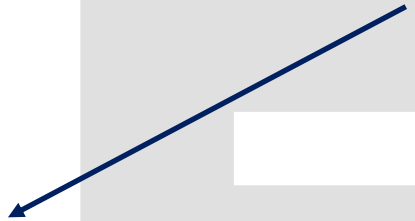
⇨ **« Clinico-radiological paradox »**

1/ les lésions ne sont pas

la source du handicap

1/ les lésions ne sont pas **la source** du handicap

2/ l'information « lésion » n'est pas suffisante pour expliquer le handicap



1. Localisation ?
2. Histologie ?
3. Cicatrisation ?
4. Temporalité ?
5. Comportement du système face à cette lésion ?
6. Exhaustivité ?

1. Localisation ?

SFSEP

Brainstem lesions in clinically isolated syndromes

Tintore et al. – Neurology 2010

Figure 1 Infratentorial lesions and disability progression

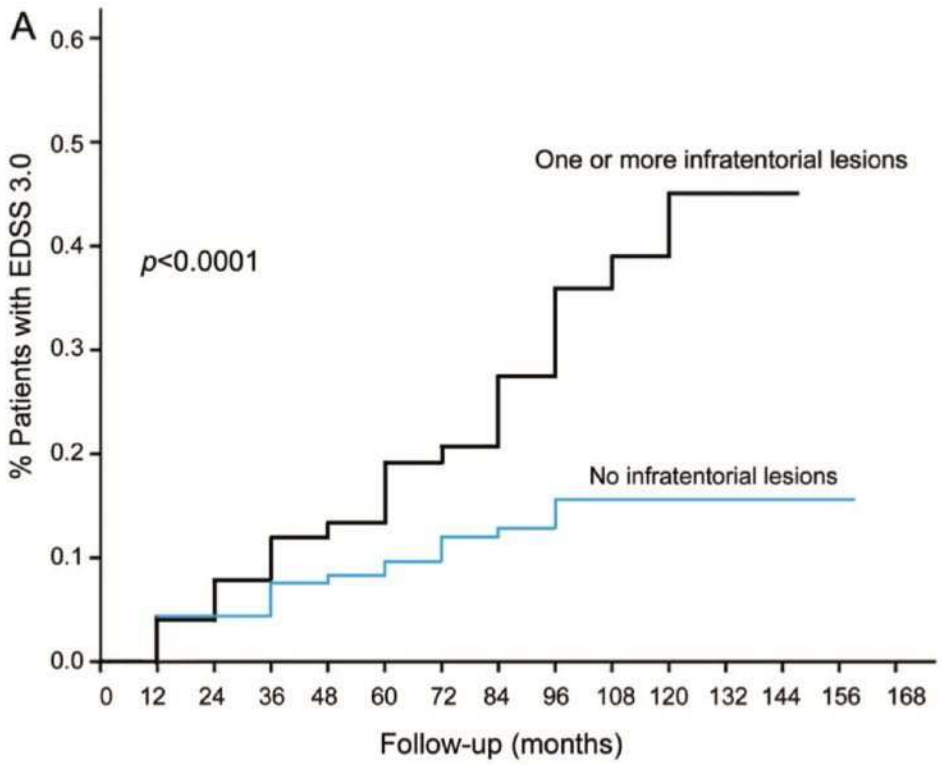


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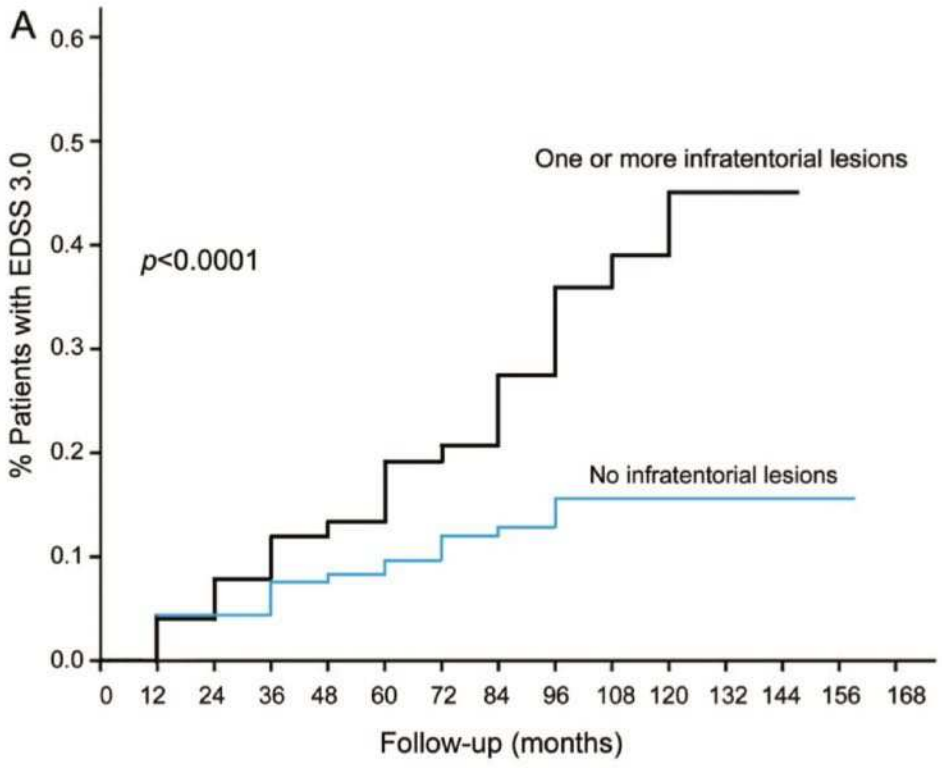
Figure 1 Infratentorial lesions and disability progression



RESEARCH ARTICLE

A 30-Year Clinical and Magnetic Resonance Imaging Observational Study of Multiple Sclerosis and Clinically Isolated Syndromes

Karen K. Chung, MBBS,[1] Daniel Altmann, DPhil,[1,2] Frederik Barkhof, MD,[1,3,4,5] Katherine Miszkiel, BM Hons,[6] Peter A. Brex, MD,[7] Jonathan O'Riordan, MD,[8] Michael Ebner, PhD,[4,9,10] Ferran Prados, PhD,[1,4,11] M. Jorge Cardoso, PhD,[10] Tom Vercauteren, PhD,[10] Sebastien Ourselin, PhD,[10] Alan Thompson, MD,[1,5] Olga Ciccarelli, PhD,[1,5] and Declan T. Chard, PhD[1,5]

TABLE 3. Best Independent Early Predictors of 30-Year EDSS >3.5 and ≤3.5. All models include EDSS 10 at or before 30 years.

Predictor	Odds Ratio (95% CI)	*p*	Predictor Combinations			
30-year EDSS >3.5, best independent predictors up to 1 year[a]						
Baseline infratentorial lesion count, ≥1 vs 0	16.8 (2.0–139.7)	0.009	0	0	≥1	≥1
1-year deep white matter lesion count, ≥1 vs 0	6.7 (1.7–26.0)	0.006	0	≥1	0	≥1
30-year EDSS >3.5, best independent predictors up to 5 years[d]						
Baseline infratentorial lesion count, ≥1 vs 0	8.0 (1.5–41.4)	0.013	0	0	≥1	≥1
5-year deep white matter lesion count, >5 vs ≤5	5.1 (1.7–15.6)	0.004	≤5	>5	≤5	>5

Lesion probability mapping to explain clinical deficits and cognitive performance in multiple sclerosis

ZT Kincses[1], S Ropele[2], M Jenkinson[3], M Khalil[2], K Petrovic[2], M Loitfelder[2], C Langkammer[2], E Aspeck[2], M Wallner-Blazek[2], S Fuchs[2], M Jehna[2], R Schmidt[2], L Vécsei[1], F Fazekas[2] and C Enzinger[2,4]

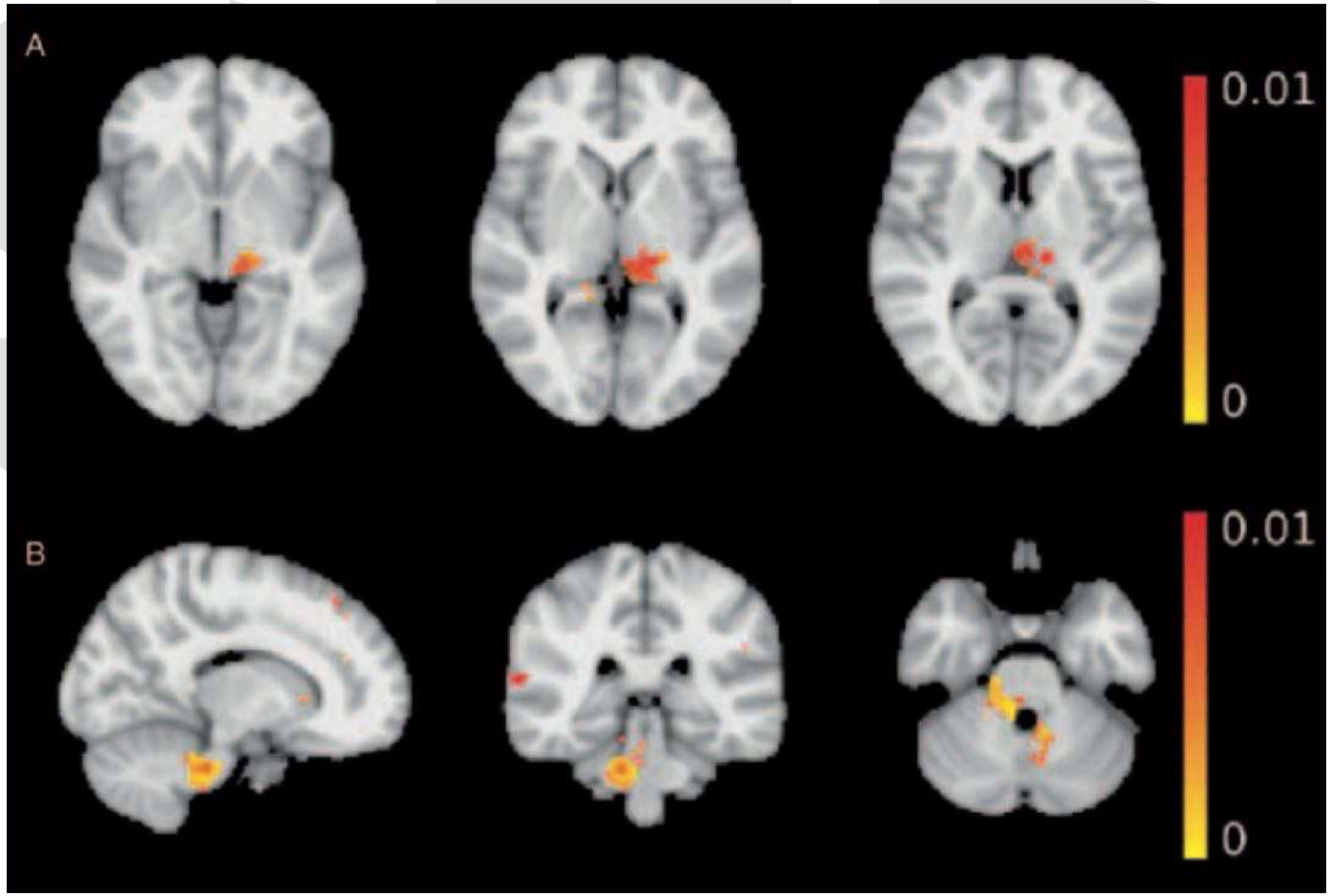
Multiple Sclerosis Journal
17(6) 681–689

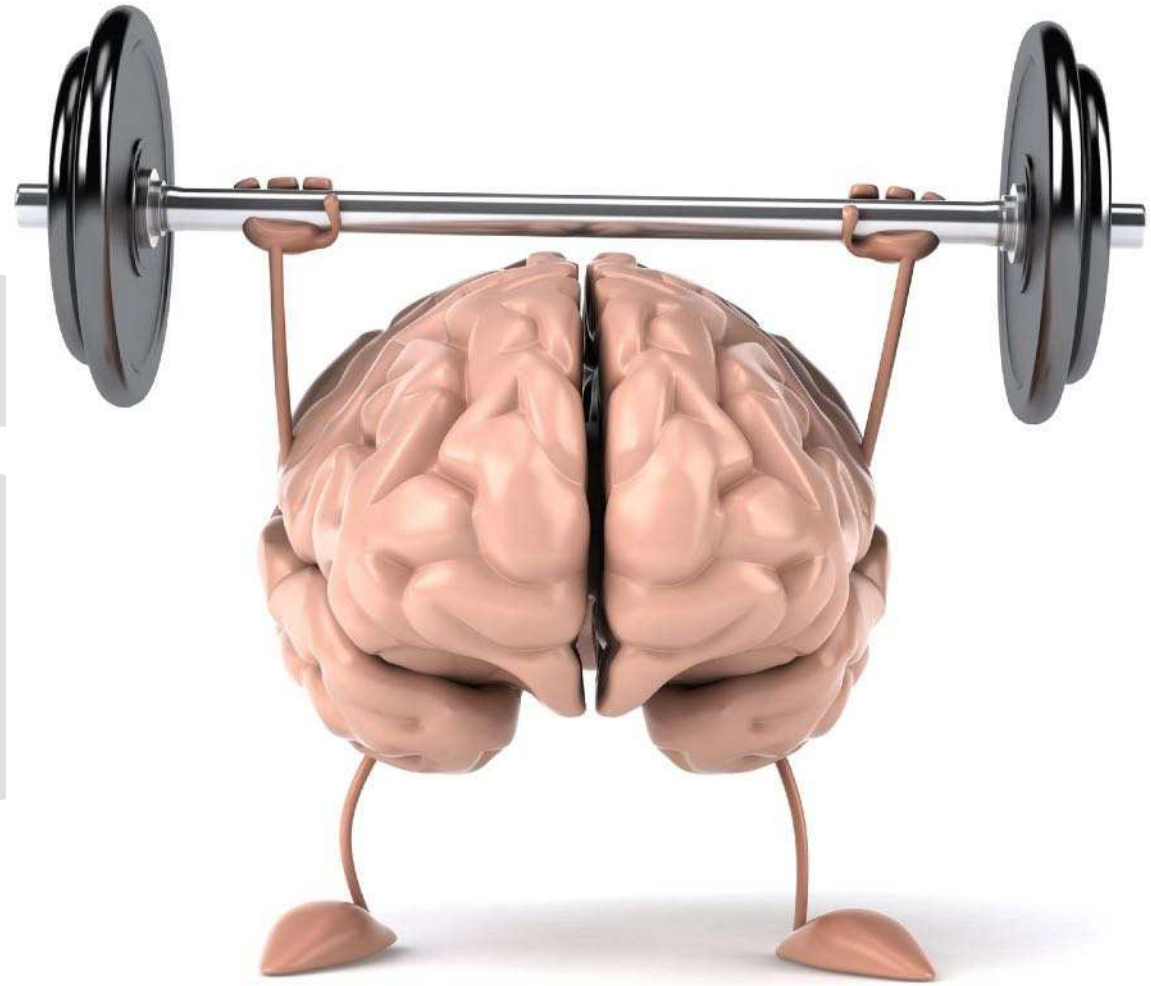
DOI: 10.1177/1352458510391342
msj.sagepub.com
SAGE

2010

A) PF Sensitif

B) PF Cérébelleux





2011

Short Report

MULTIPLE SCLEROSIS JOURNAL | MSJ

Multiple Sclerosis Journal
0(00) 1–4

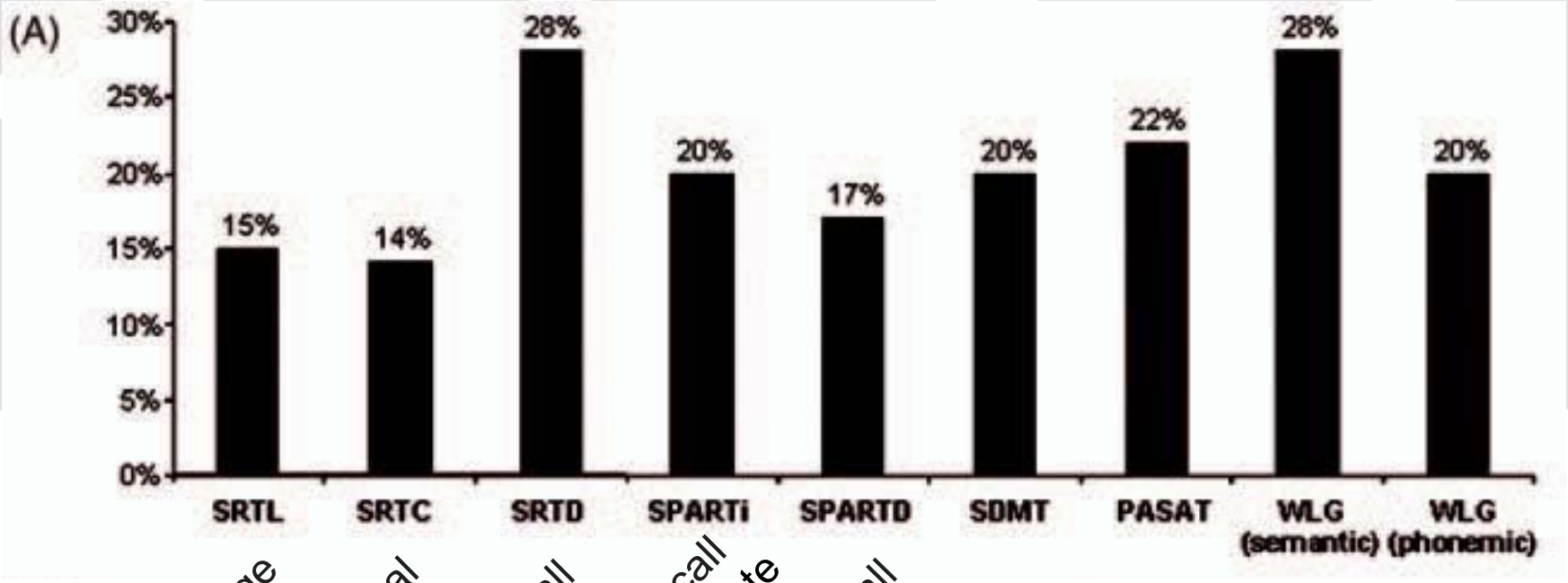
DOI: 10.1177/1352458511398265
msj.sagepub.com
SAGE

Cognitive impairment at the onset of multiple sclerosis: relationship to lesion location

Françoise Reuter[1,2], Wafaa Zaaraoui[2], Lydie Crespy[2], Anthony Faivre[2], Audrey Rico[1,2], Irina Malikova[1,2], Sylviane Confort-Gouny[2], Patrick J Cozzone[2], Jean-Philippe Ranjeva[2], Jean Pelletier[1,2] and Bertrand Audoin[1,2]

Table 1. Demographic and clinical characteristics of the sample

	CIS patients $n = 97$	Controls $n = 55$	*t*-test
Gender (male/female)	20/77	15/40	
Age, years (mean ± SD)	31 ± 8	28 ± 8	n.s.
Education, years (mean ± SD)	13 ± 3	13 ± 2	n.s.
Disease duration, months (median, range)	5 (1–17)	n.a.	
EDSS (median, range)	1 (0–2)	n.a.	



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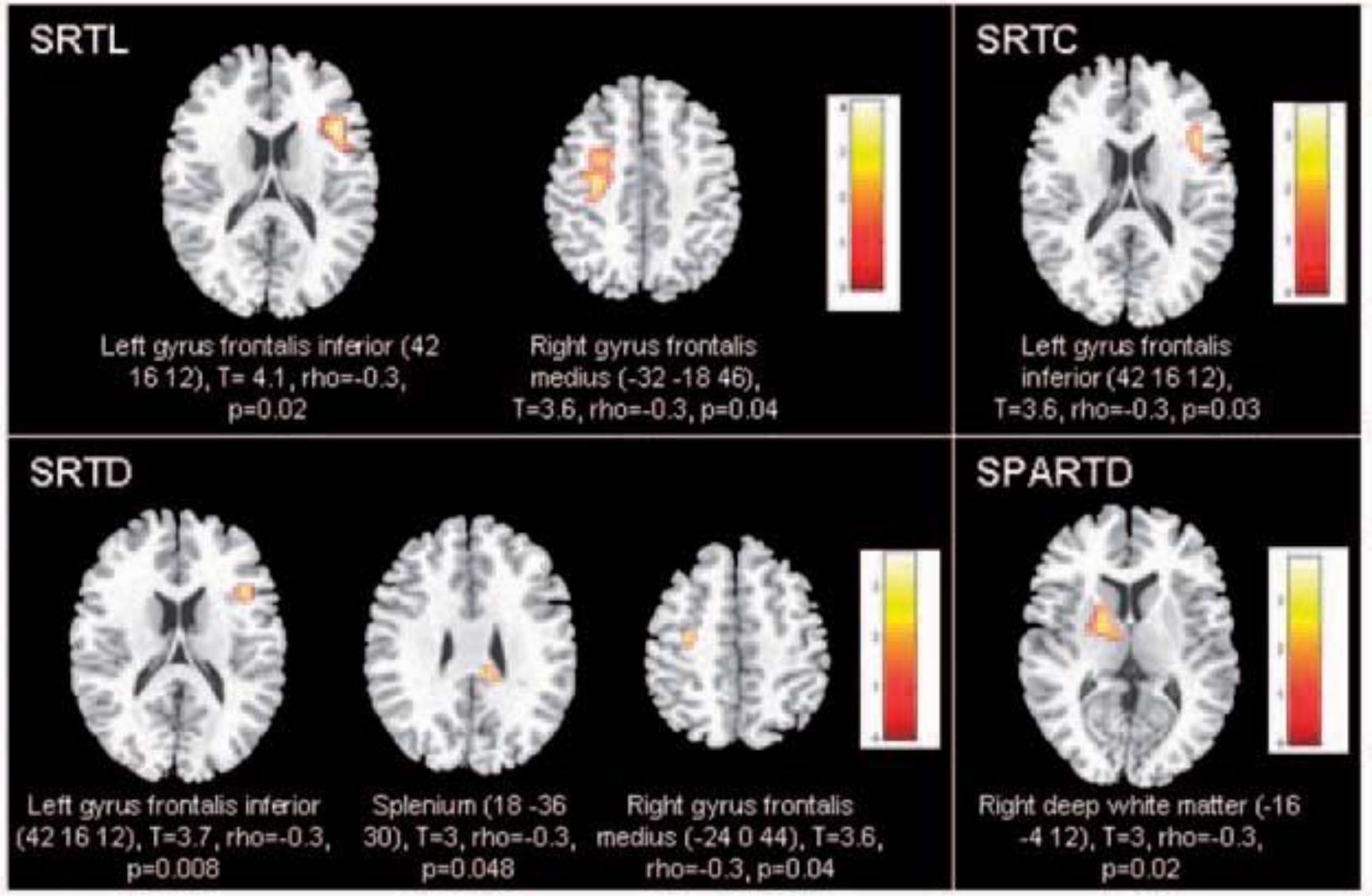
No correlation between total lesion & cognitive performances

Verbal learning performance:
- Broca's area
- Right frontal lobe
- Splenium

Spatial learning performance:
- Deep white matter



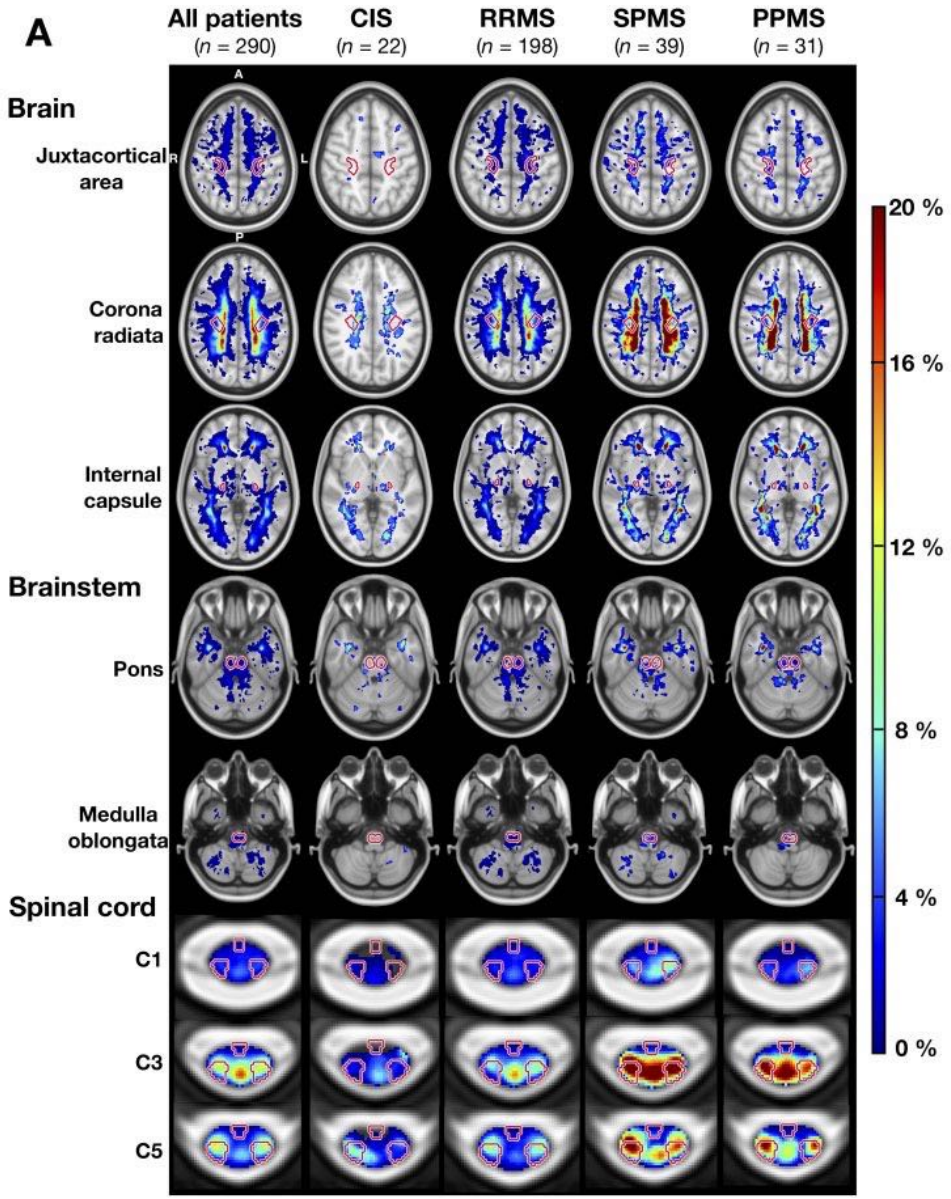
Moelle épinière

- Lésions et atrophie principalement au niveau de la moelle cervicale
- Existence de lésions médullaires asymptomatiques
  (Okuda DT et al, Neurology 2011)
- Rare dans les autres pathologies

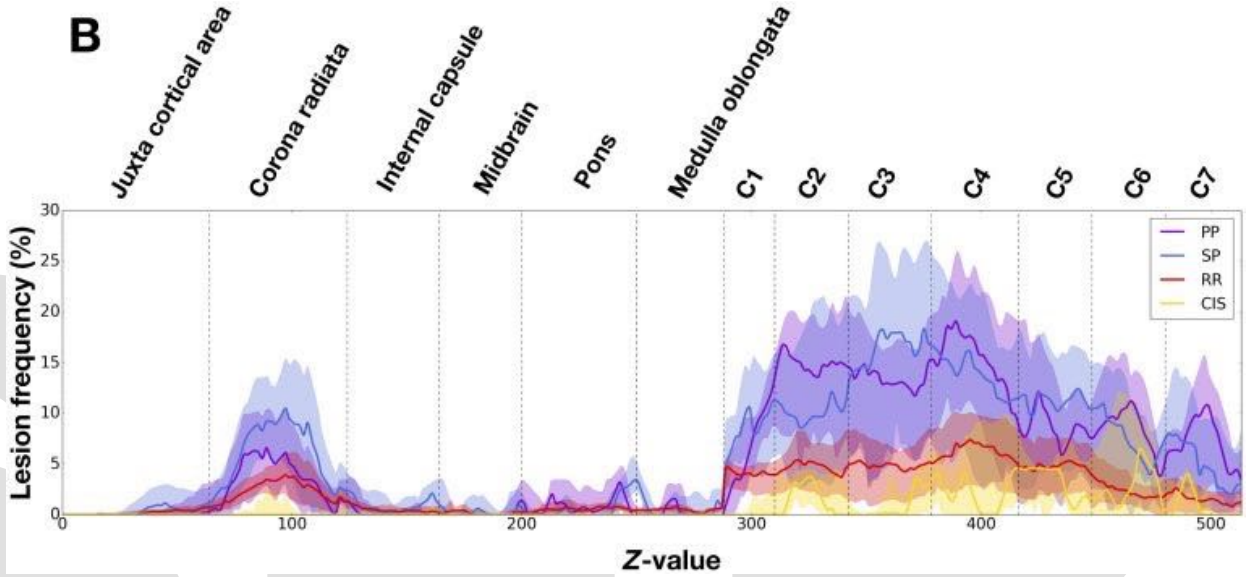
doi:10.1093/brain/awaa162 Kerbrat et al BRAIN 2020: 143; 2089–2105 | 2089

BRAIN
A JOURNAL OF NEUROLOGY

Multiple sclerosis lesions in motor tracts from brain to cervical cord: spatial distribution and correlation with disability



Lesion volume fraction in the CST is higher in SP and PPMS



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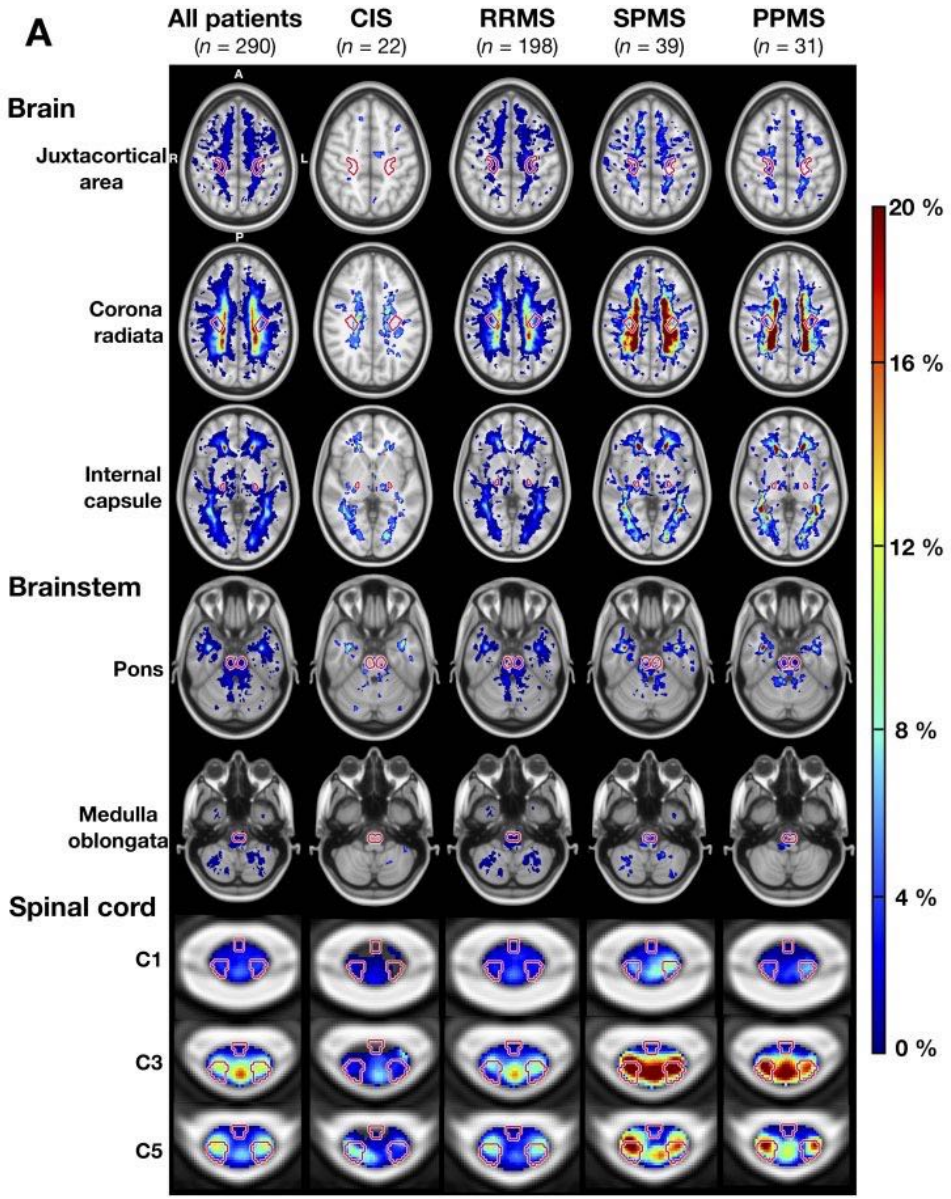

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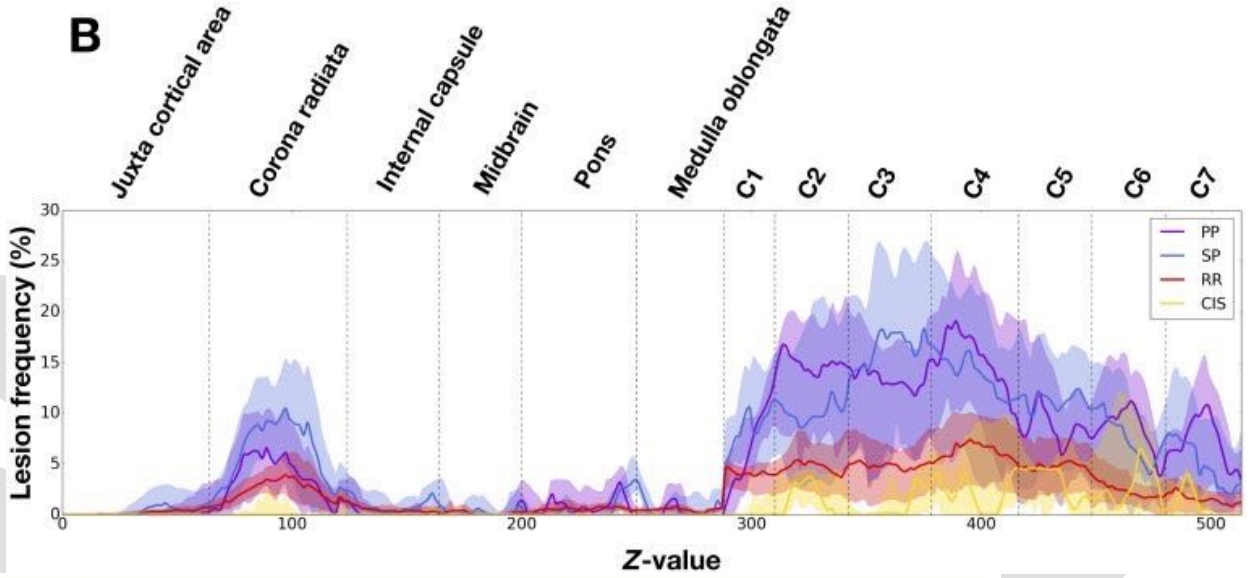

	Standardized β coefficient[a]	*P*-value
EDSS score (R^2 = 0.60)		
Age, years	0.28	<0.0001
Disease duration, years	0.18	0.007
Normalized brain CST lesion volume	0.11	0.02
Normalized brainstem CST lesion volume	0.09	0.02
Normalized cervical cord CST lesion volume	0.31	<0.0001
Spinal cord cross sectional area, mm^2	–0.12	0.02

The spinal cord corticospinal tracts lesion volume remained the strongest factor in the regression model, independently from cord atrophy

doi:10.1093/brain/awaa162 **Kerbrat et al** BRAIN 2020: 143; 2089–2105 | 2089

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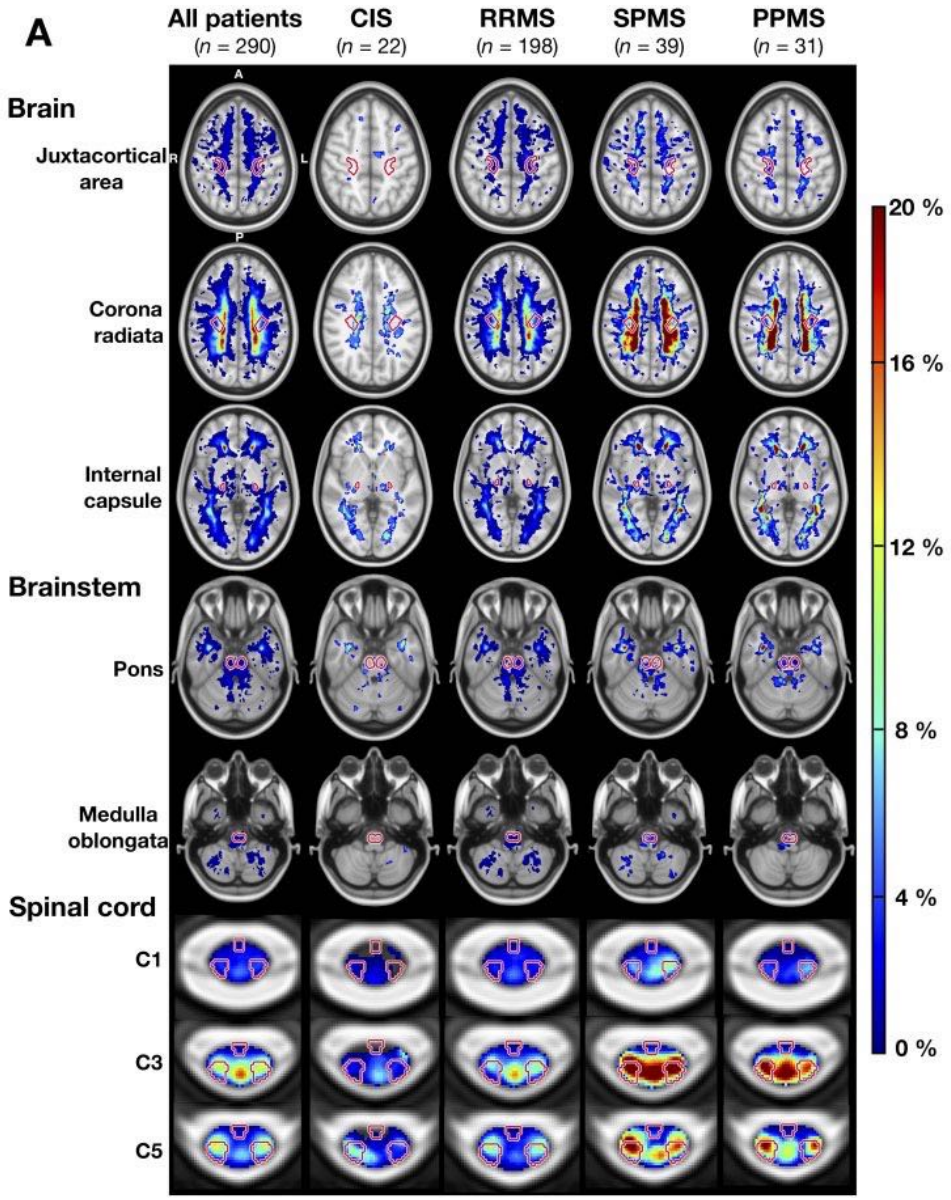

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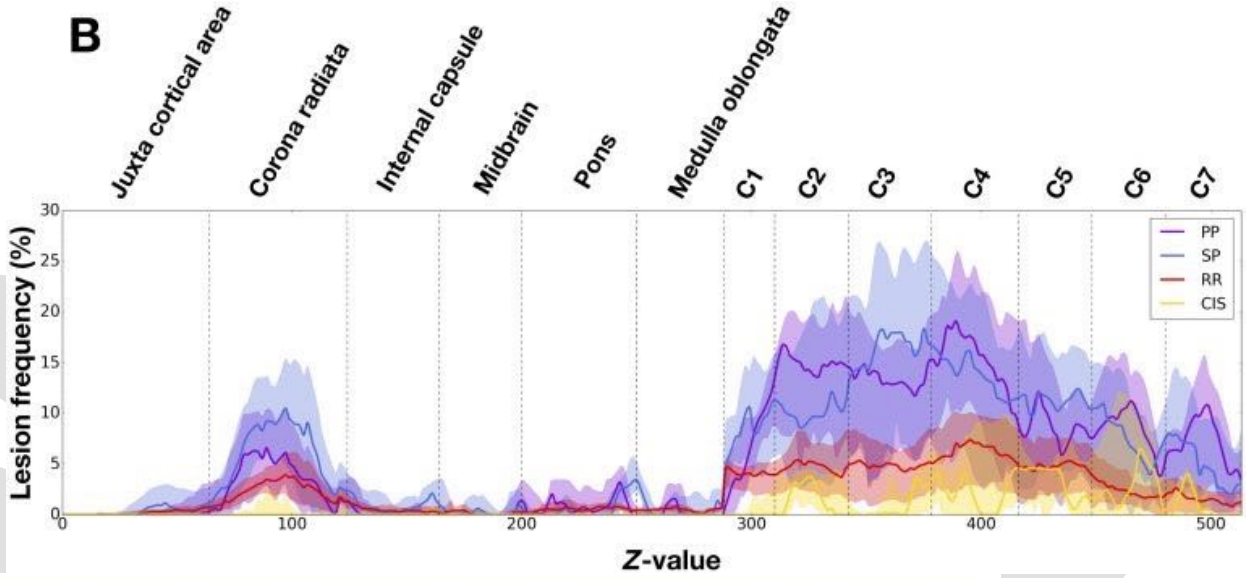

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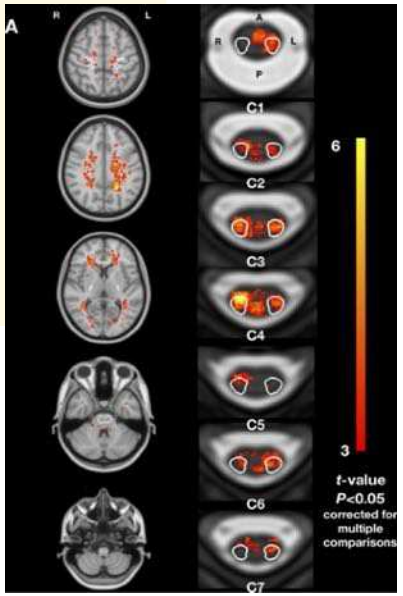

2. Histologie ?

Hétérogénéité des lésions

Kuhlmann et al, Acta Neuropathol 2017

Table 1 Histological characteristics of active, mixed active/inactive, and inactive MS lesions

	Macrophages/microglia throughout lesion	Only macrophages/microglia at lesion border	LFB+ or MBP+ or PLP+ degradation products within macrophages/microglia	CNP+ or MAG+ or MOG+ degradation products within macrophages/microglia
Active	+	−	±	±
Active and early demyelinating	+	−	+	+
Active and late demyelinating	+	−	+	−
Active and post-demyelinating	+	−	−	−
Mixed active/inactive	−	+	±	±
Mixed active/inactive and demyelinating	−	+	+	±
Mixed active/inactive and post-demyelinating	−	+	−	−
Inactive	−	−	−	−

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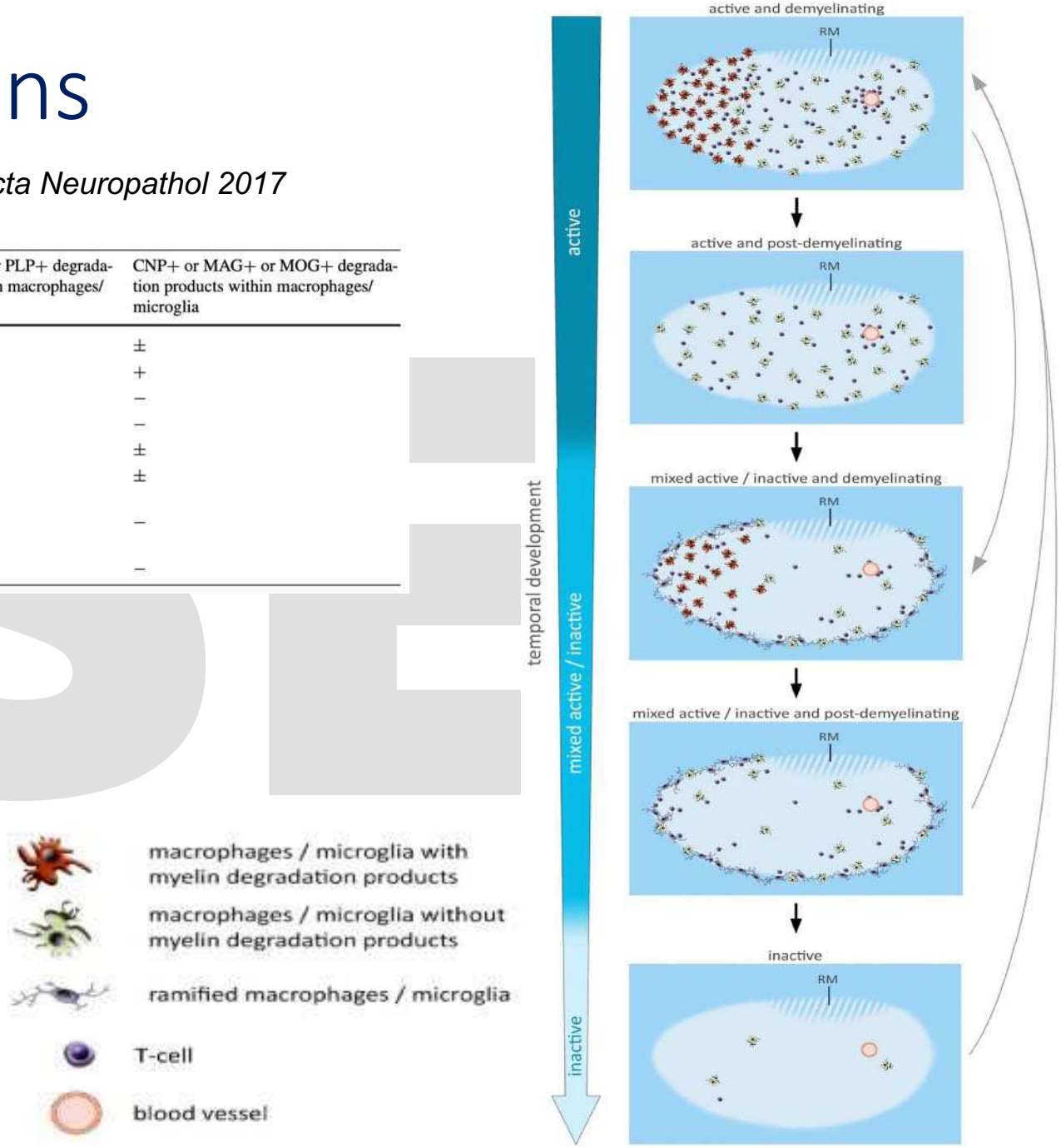
Active and post-demyelinating	+	−	−	−
Mixed active/inactive	−	+	±	±
Mixed active/inactive and demyelinating	−	+	+	±
Mixed active/inactive and post-demyelinating	−	+	−	−
Inactive	−	−	−	−



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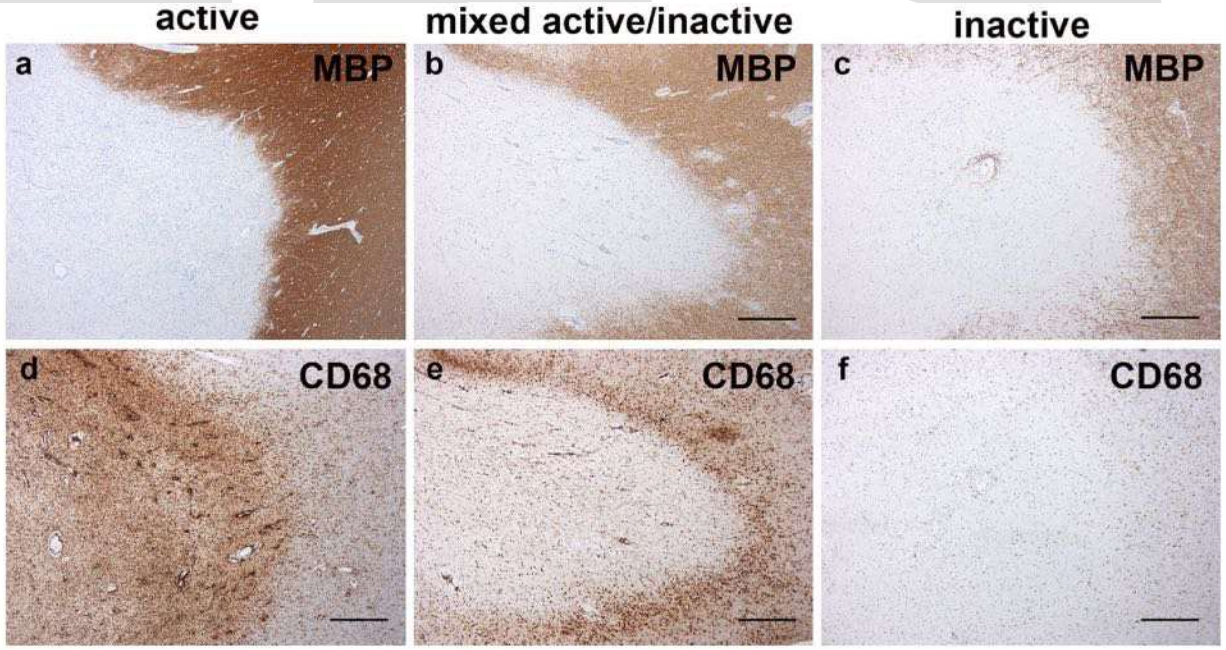

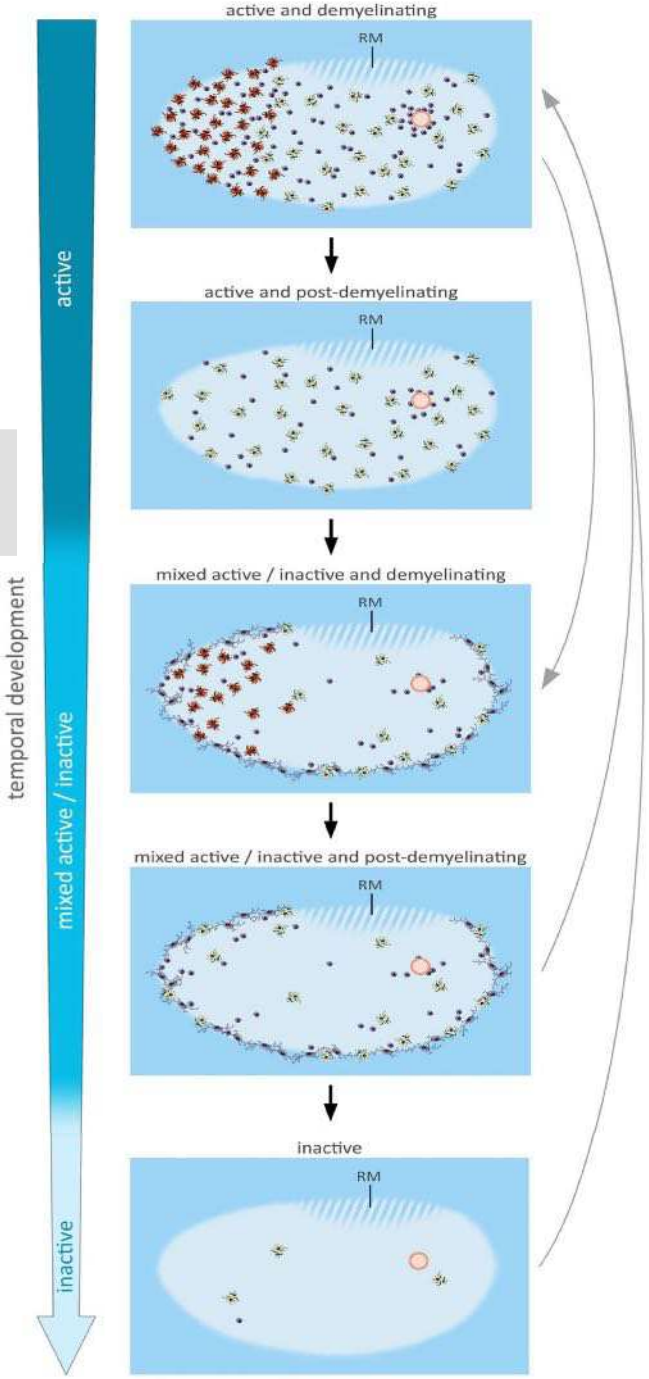

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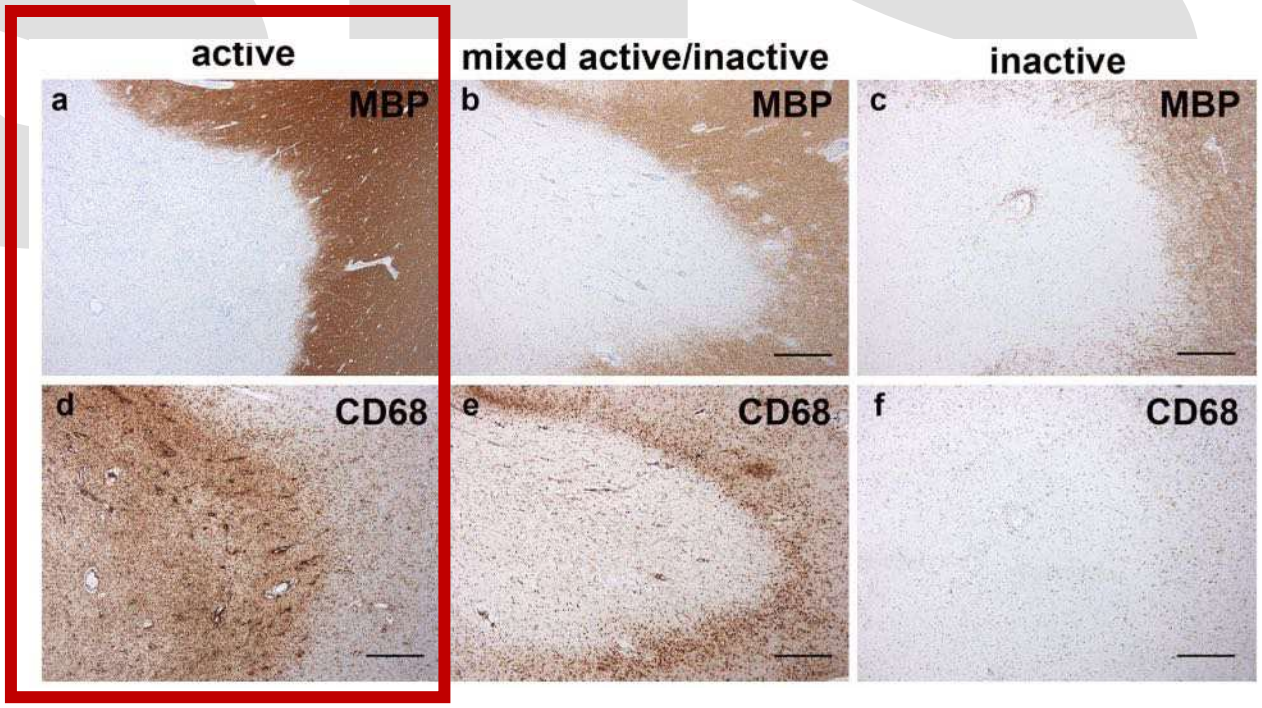
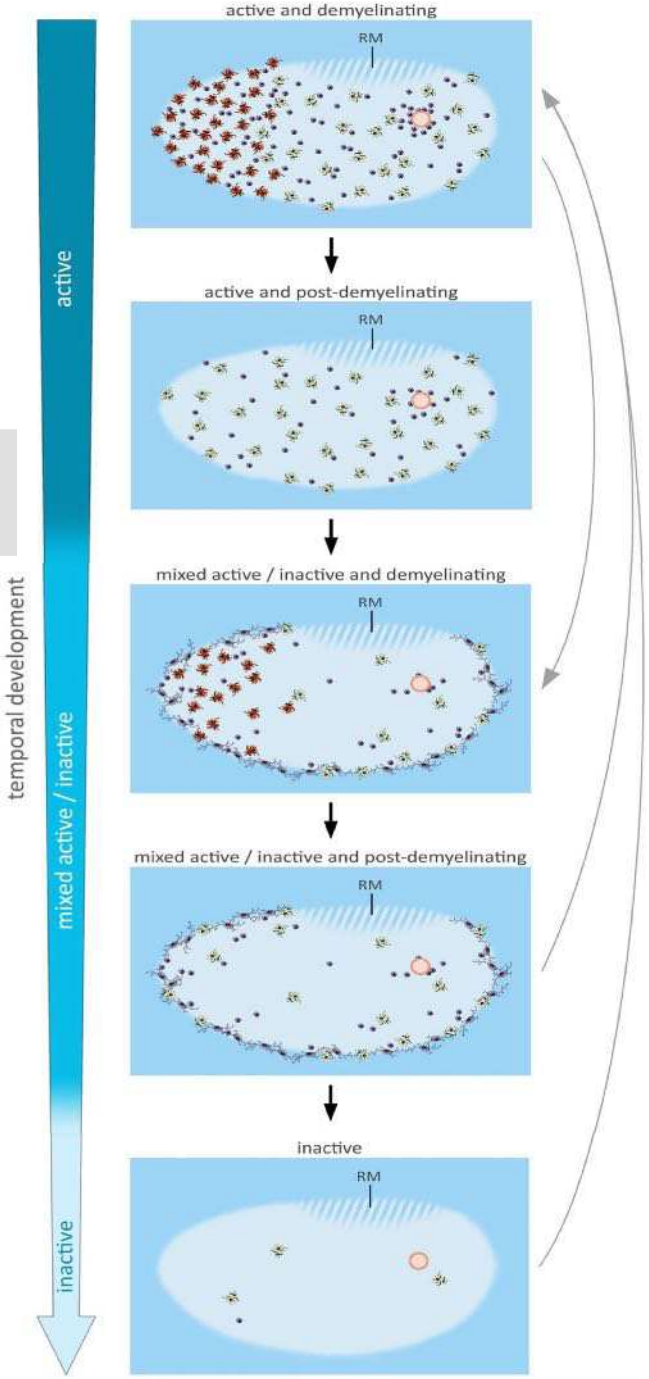
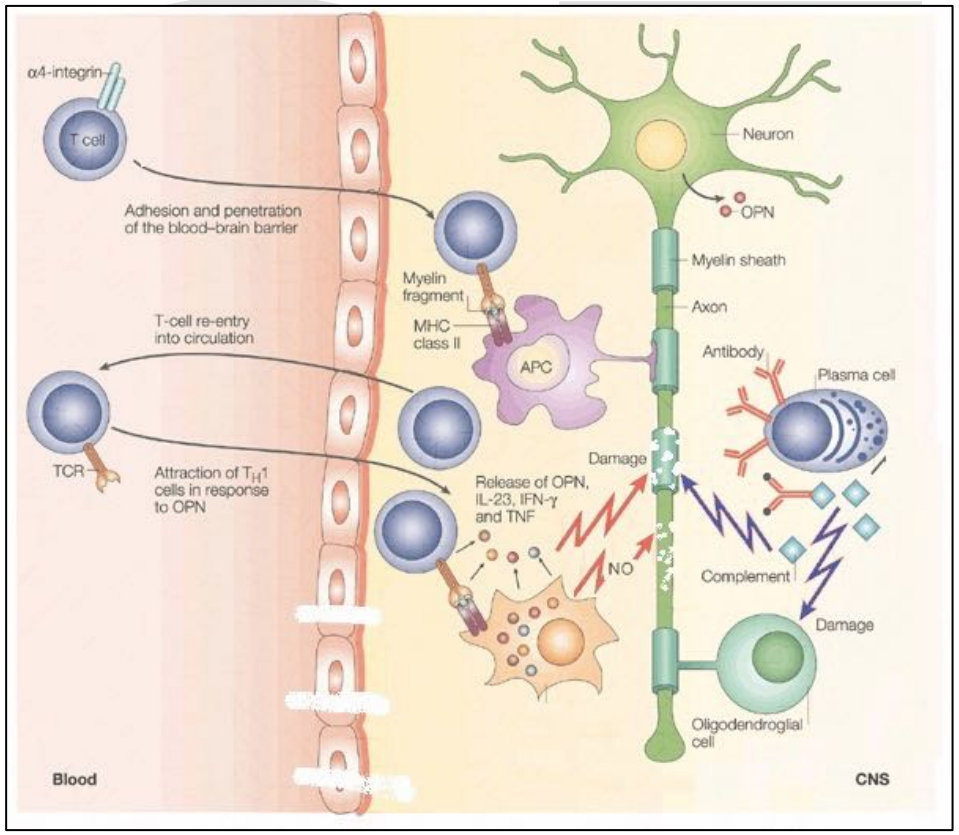
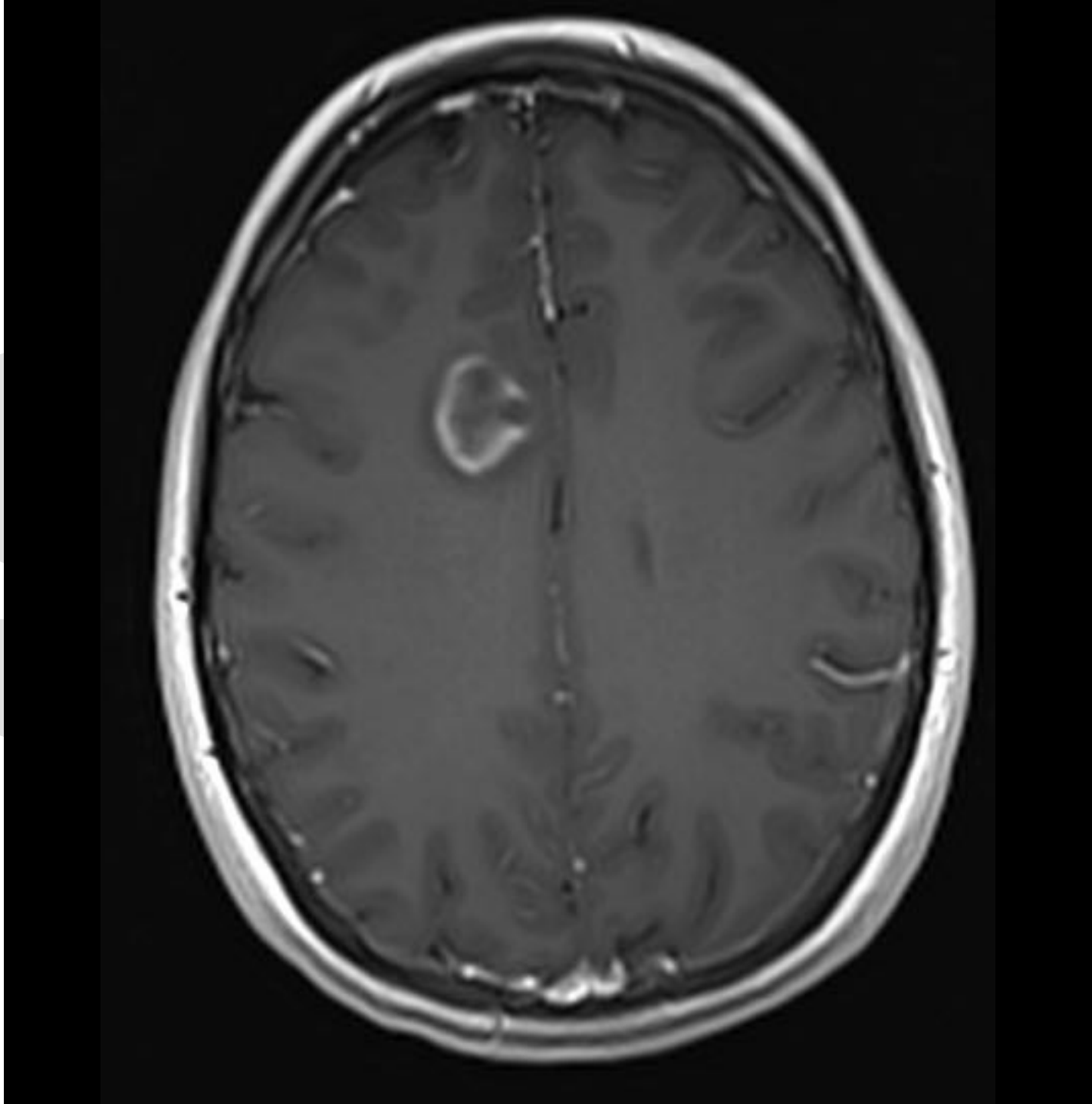
Active and late demyelinating	+	−	+	−
Active and post-demyelinating	+	−	−	−
Mixed active/inactive	−	+	±	±
Mixed active/inactive and demyelinating	−	+	+	±
Mixed active/inactive and post-demyelinating	−	+	−	−
Inactive	−	−	−	−





Gadolinium

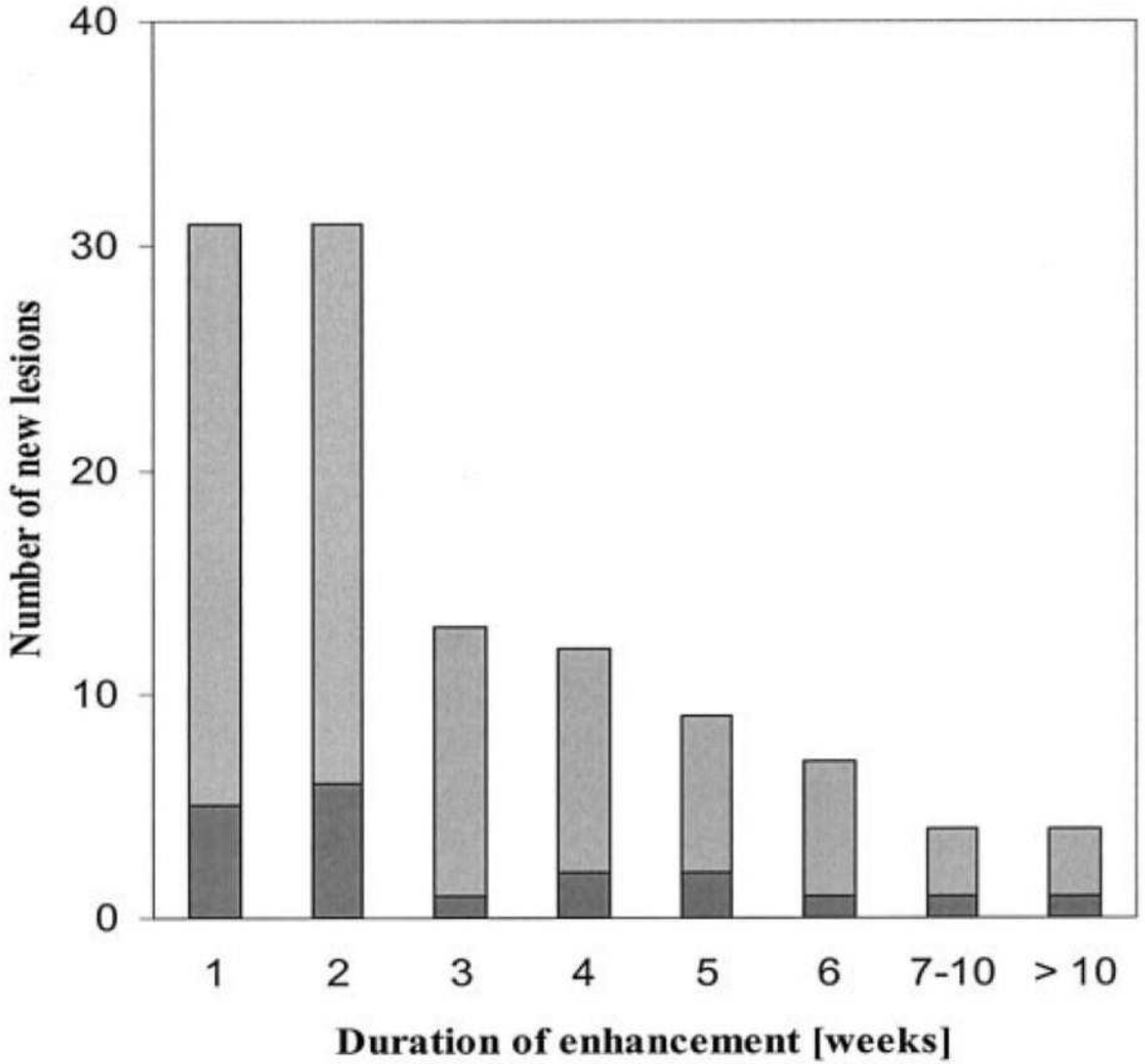

α4-integrin
T cell
Adhesion and penetration of the blood–brain barrier
T-cell re-entry into circulation
TCR
Attraction of T_H1 cells in response to OPN
Myelin fragment
MHC class II
APC
Neuron
OPN
Myelin sheath
Axon
Antibody
Plasma cell
Damage
Release of OPN, IL-23, IFN-γ and TNF
NO
Complement
Damage
Oligodendroglial cell
Blood
CNS



MRI contrast uptake in new lesions in relapsing-remitting MS followed at weekly intervals

2003

Francois Cotton, MD; Howard L. Weiner, MD; Ferenc A. Jolesz, MD; and Charles R.G. Guttmann, MD



Dark gray: corticotherapy (n 21); light gray: natural history lesions (n 92)

MRI contrast uptake in new lesions in relapsing-remitting MS followed at weekly intervals

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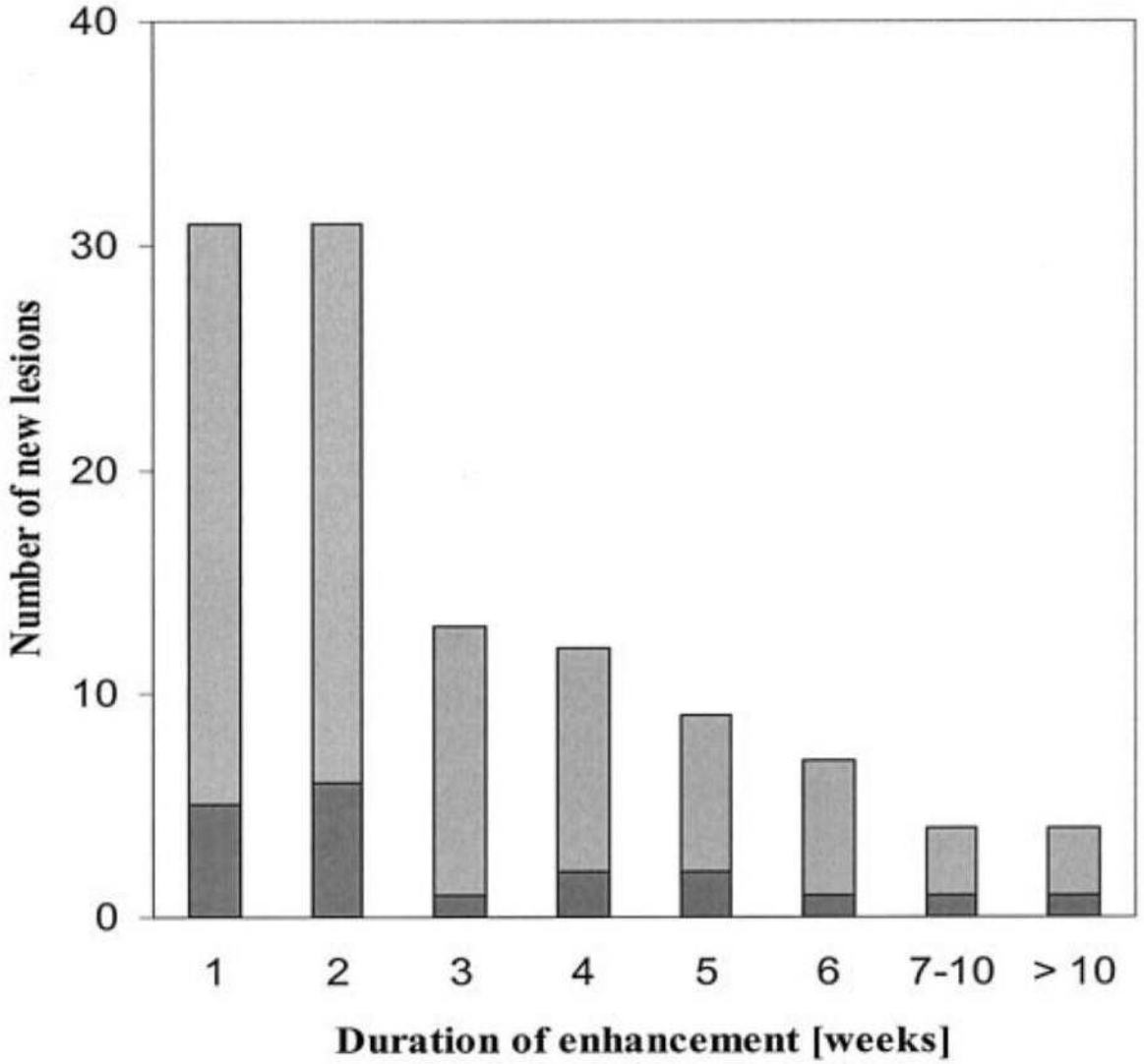

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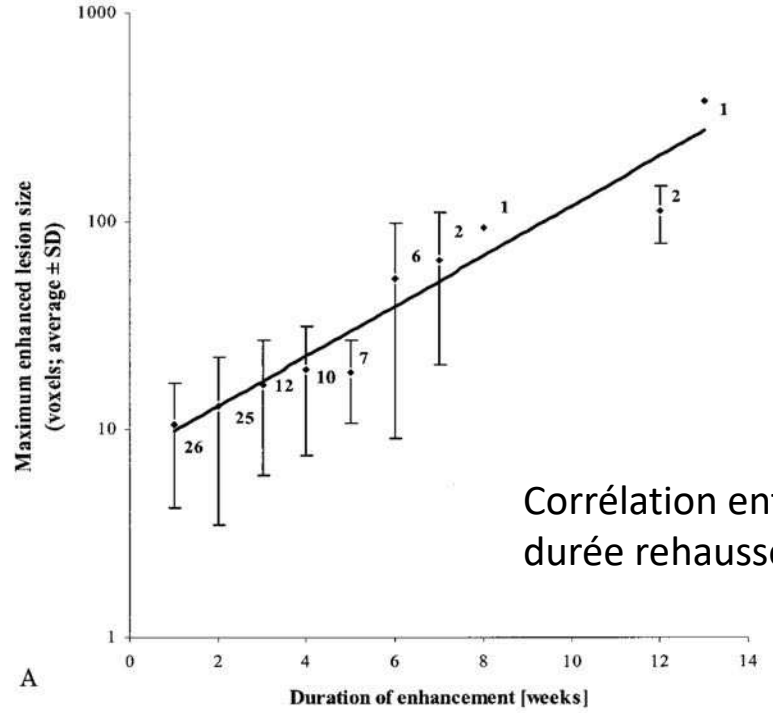
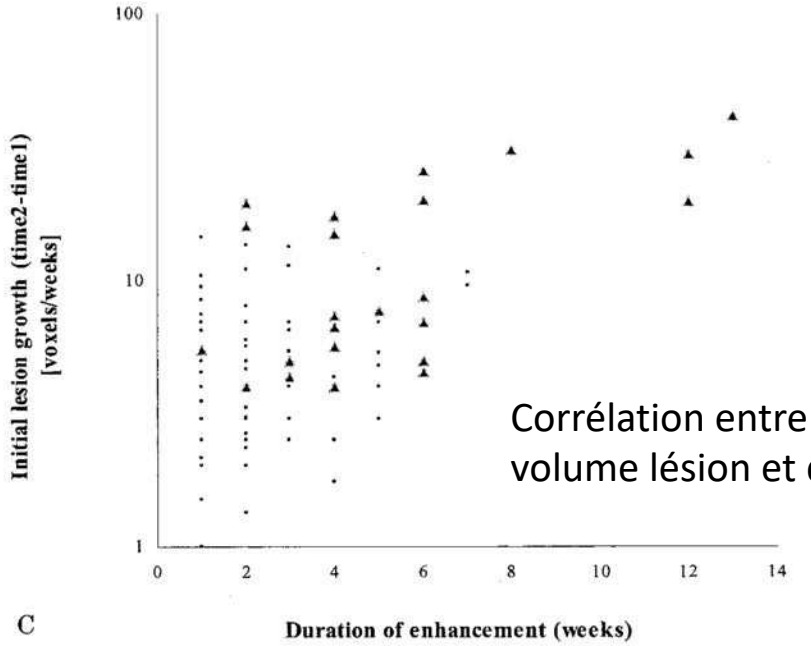


A

Corrélation entre taille lésion et durée rehaussement



C

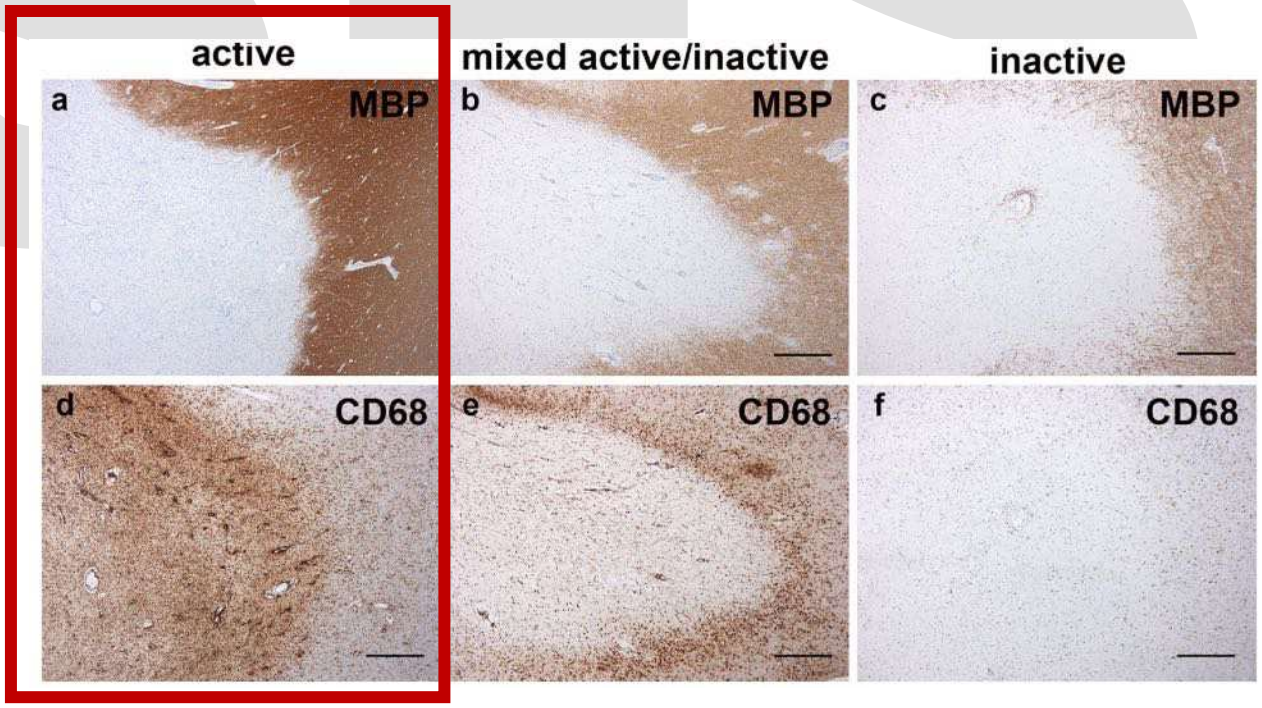
Corrélation entre augmentation volume lésion et durée rehaussement

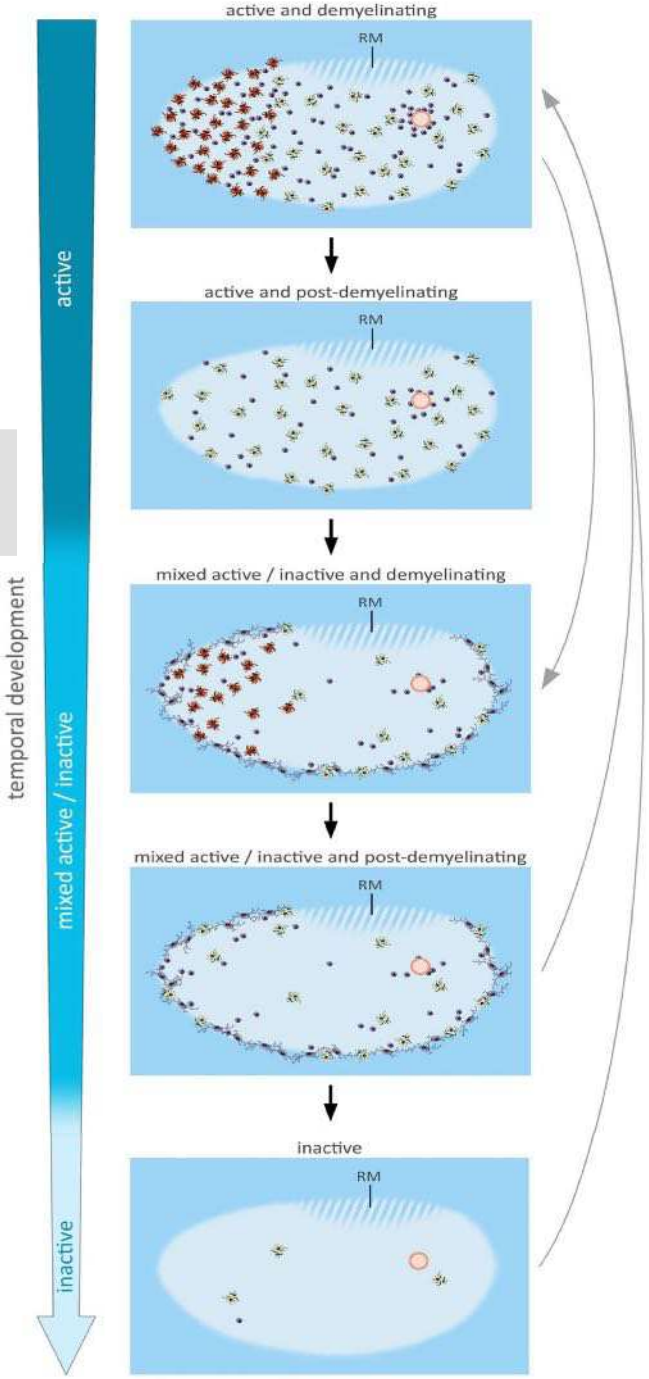
Hétérogénéité des lésions

Kuhlmann et al, Acta Neuropathol 2017

Table 1 Histological characteristics of active, mixed active/inactive, and inactive MS lesions

	Macrophages/microglia throughout lesion	Only macrophages/microglia at lesion border	LFB+ or MBP+ or PLP+ degradation products within macrophages/microglia	CNP+ or MAG+ or MOG+ degradation products within macrophages/microglia
Active	+	−	±	±
Active and early demyelinating	+	−	+	+
Active and late demyelinating	+	−	+	−
Active and post-demyelinating	+	−	−	−
Mixed active/inactive	−	+	±	±
Mixed active/inactive and demyelinating	−	+	+	±
Mixed active/inactive and post-demyelinating	−	+	−	−
Inactive	−	−	−	−



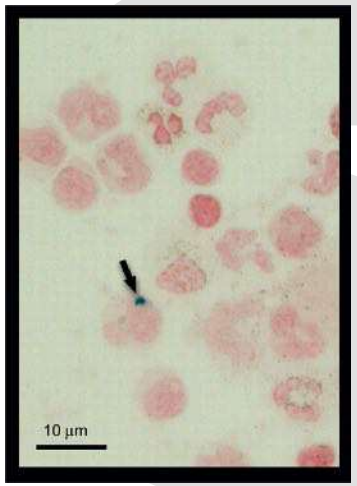


2008

doi:10.1093/brain/awn009 *Brain* (2008), **131**, 800–807

Pluriformity of inflammation in multiple sclerosis shown by ultra-small iron oxide particle enhancement

Machteld M. Vellinga,[1] Raoul D. Oude Engberink,[2,3] Alexandra Seewann,[1] Petra J. W. Pouwels,[4] Mike P. Wattjes,[5] Susanne M. A. van der Pol,[2] Christiane Pering,[6] Chris H. Polman,[1] Helga E. de Vries,[2] Jeroen J. G. Geurts[5,7] and Frederik Barkhof[5]



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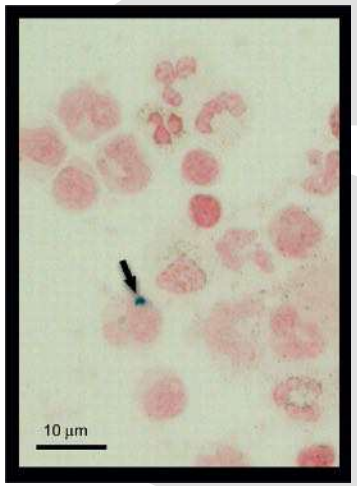
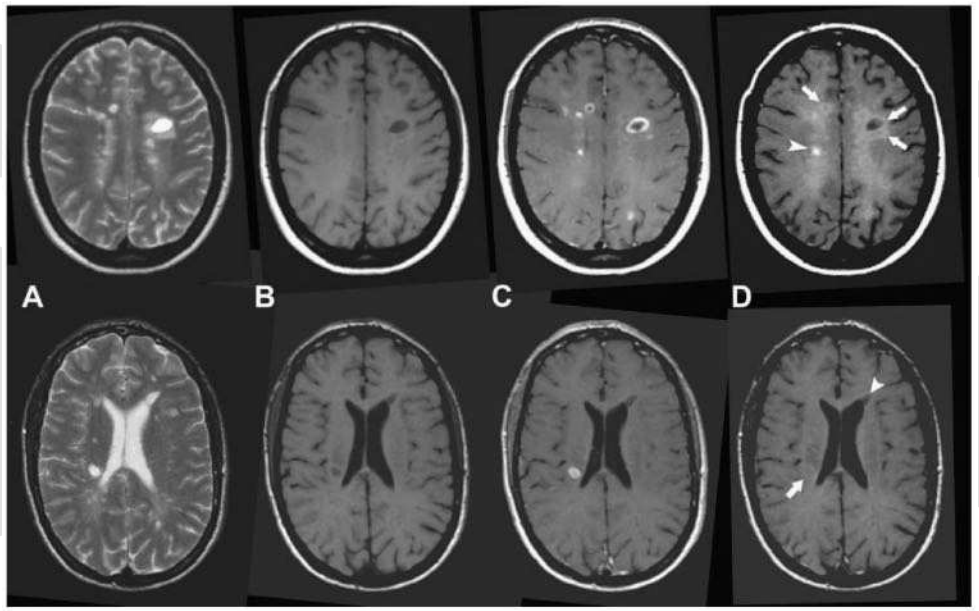




A) M0 Post-Gd B) M0 Post USPIO C) M1 post Gd

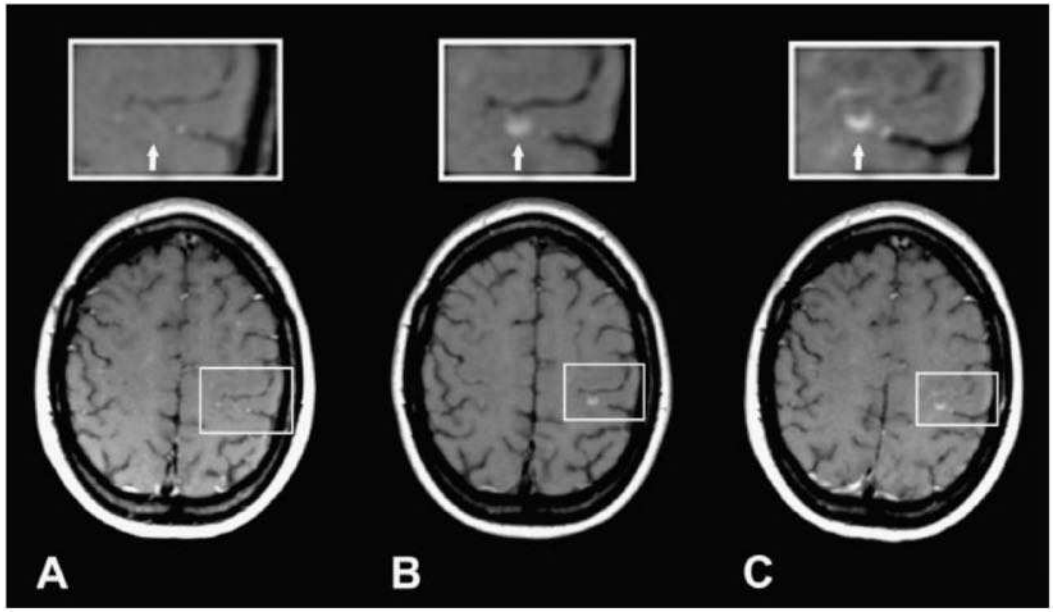


Table 2 Longitudinal TI patterns (rows) of the 200 identified hypointense lesions around USPIO injection, related to patterns of USPIO-enhancement (columns) of these lesions

TI pattern	Pattern of USPIO-enhancement				
	Return to isointensity	Focal	Ring-like	No USPIO-enhancement	Total
Chronic	8 (6%)	0	8 (6%)	111 (88%)	127
Acute and persistent	4 (13%)	0	1 (3%)	27 (84%)	32
Transient	27 (66%)	0	1 (2%)	13 (32%)	41
Total	39 (19%)	0	10 (5%)	151 (76%)	200

« return to isointensity » most frequently for lesions that turned out to be transiently hypointense

ring-enhancing lesions were less likely to evolve into black holes

MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

2015

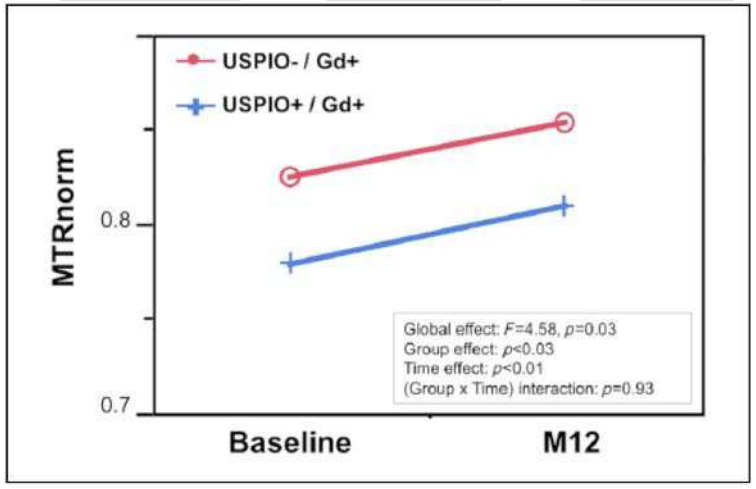
Ultra-small superparamagnetic iron oxide enhancement is associated with higher loss of brain tissue structure in clinically isolated syndrome

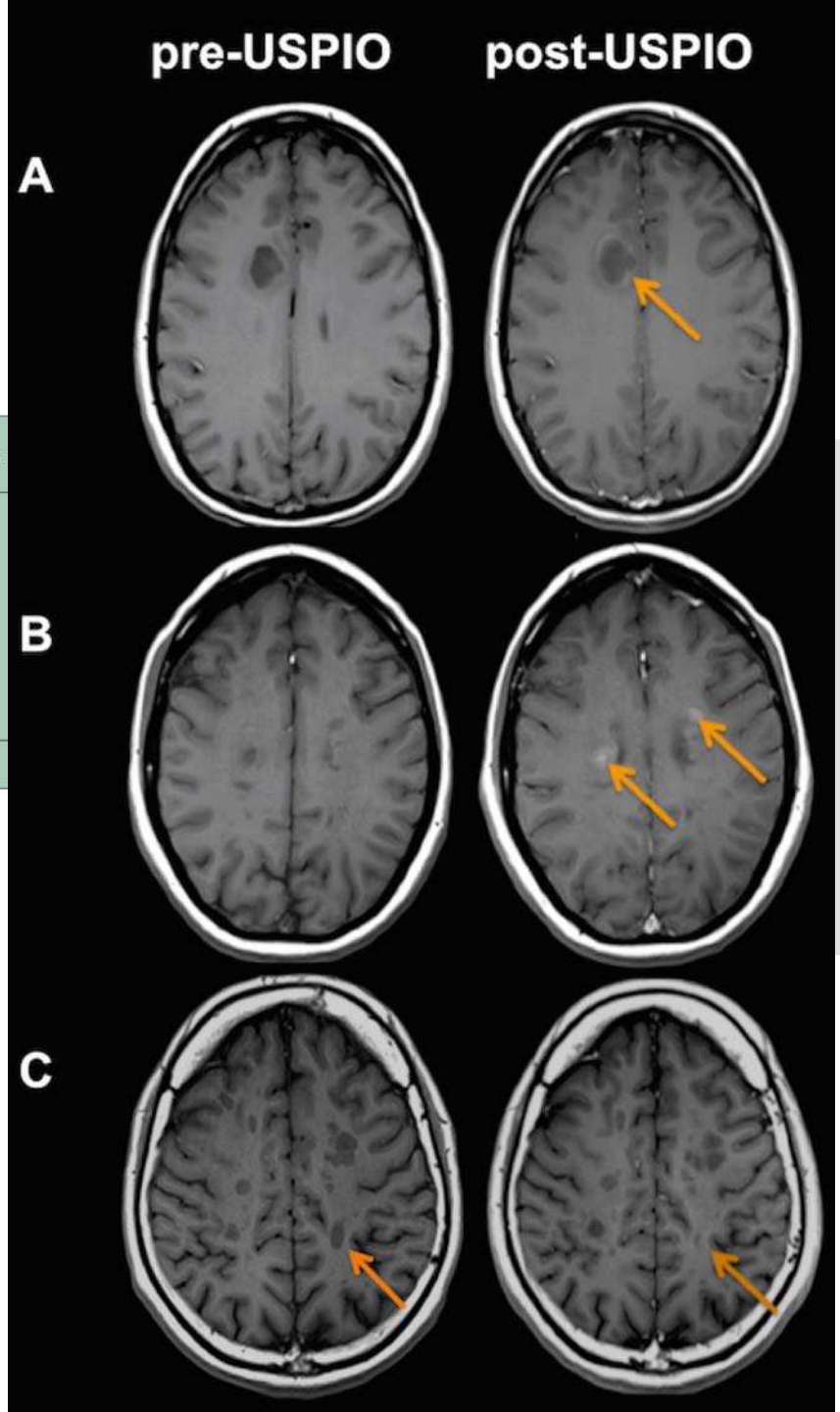
Multiple Sclerosis Journal
1–8
DOI: 10.1177/1352458515607649

Adil Maarouf, Jean-Christophe Ferré, Wafaa Zaaraoui, Arnaud Le Troter, Elise Bannier, Isabelle Berry, Maxime Guye, Laurent Pierot, Christian Barillot, Jean Pelletier, Ayman Tourbah, Gilles Edan, Bertrand Audoin and Jean-Philippe Ranjeva

	Patients with at least one USPIO-enhanced lesion (n=9)	Patients with only gadolinium-enhanced lesion(s) (n=7)
Age (years) Mean (±SD)	31 ±9	33 ±9
Gender	5F / 4M	6F / 1M
Delay 1st event – 1st MRI (days) Mean (±SD)	60 ±21	69 ±32
Treatment at baseline	None	None
Treatment introduced during the first year	66%	57%
EDSS at baseline Mean (±SD)	1.33 ±0.87	0.85 ±0.90
EDSS at M12 Mean (±SD)	1.05 ±1.05	1.5 ±1.05
Conversion to MS according to McDonald criteria*	100%	100%
Conversion to clinically definite MS	77%	14%
Relapse rate	1.88	1.14

M12: month-12 follow-up; EDSS: Expanded Disability Status Scale; MRI: magnetic resonance imaging; SD: standard deviation; F: Female; M: Male. * according to Polman et al.[21]





MULTIPLE SCLEROSIS JOURNAL | MSJ

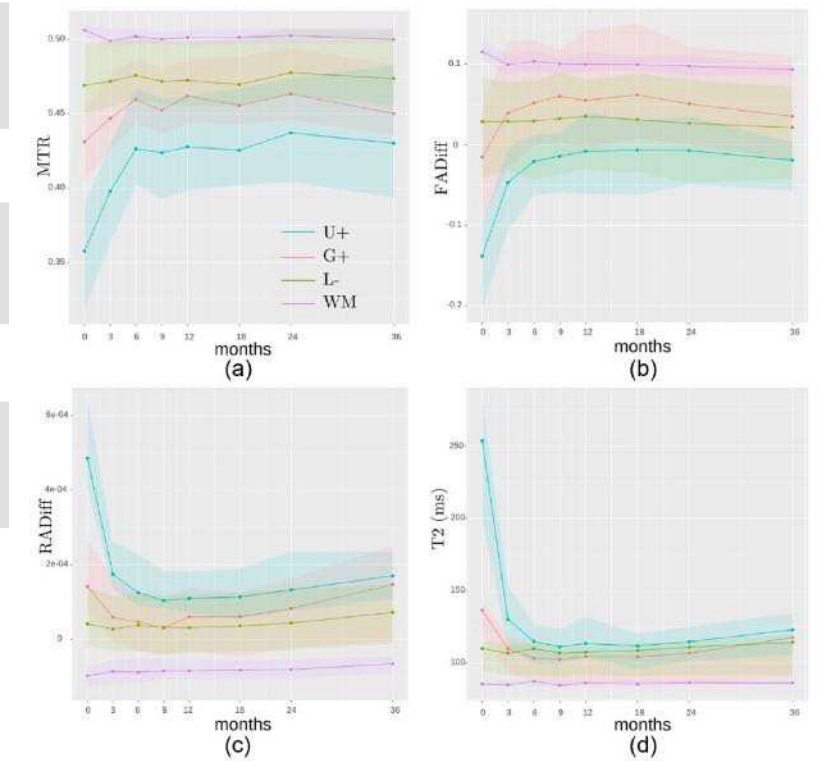
Original Research Paper

2017

USPIO-positive MS lesions are associated with greater tissue damage than gadolinium-positive-only lesions during 3-year follow-up

Multiple Sclerosis Journal
1–10
DOI: 10.1177/1352458517736148

Anne Kerbrat, Benoit Combès, Olivier Commowick, Adil Maarouf, Elise Bannier, Jean Christophe Ferré, Ayman Tourbah, Jean-Philippe Ranjeva, Christian Barillot and Gilles Edan



Hétérogénéité des lésions

Kuhlmann et al, Acta Neuropathol 2017

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Active and late demyelinating	+	−	+	−
Active and post-demyelinating	+	−	−	−
Mixed active/inactive	−	+	±	±
Mixed active/inactive and demyelinating	−	+	+	±
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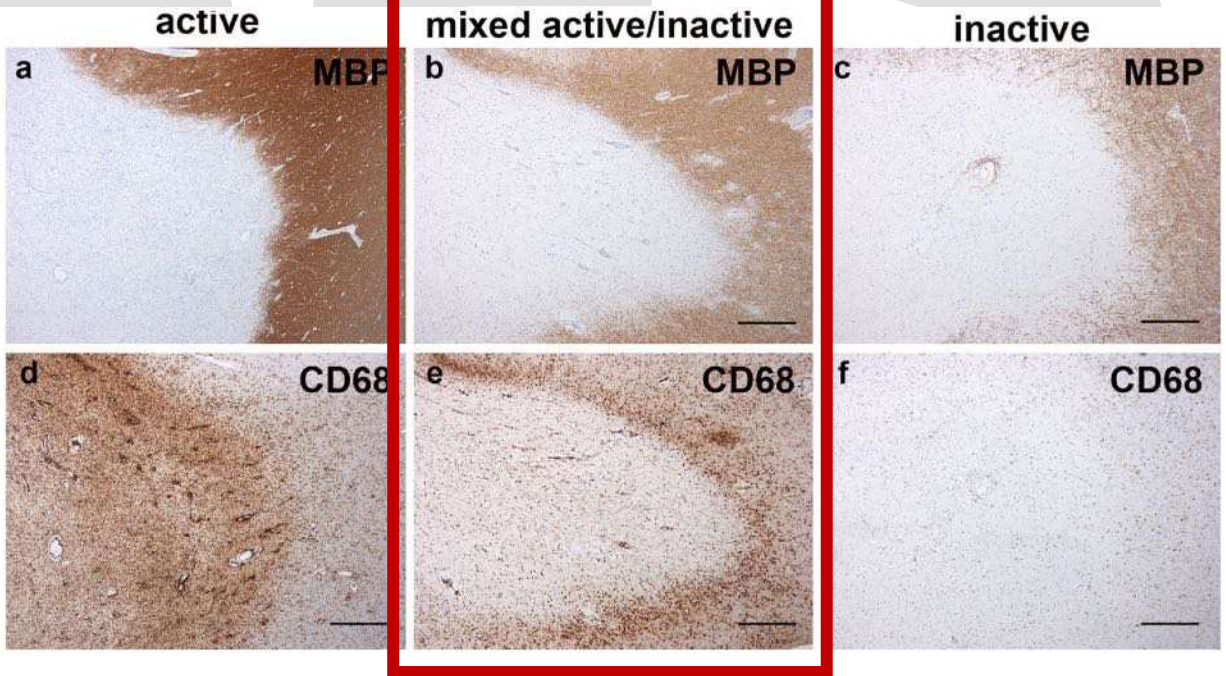
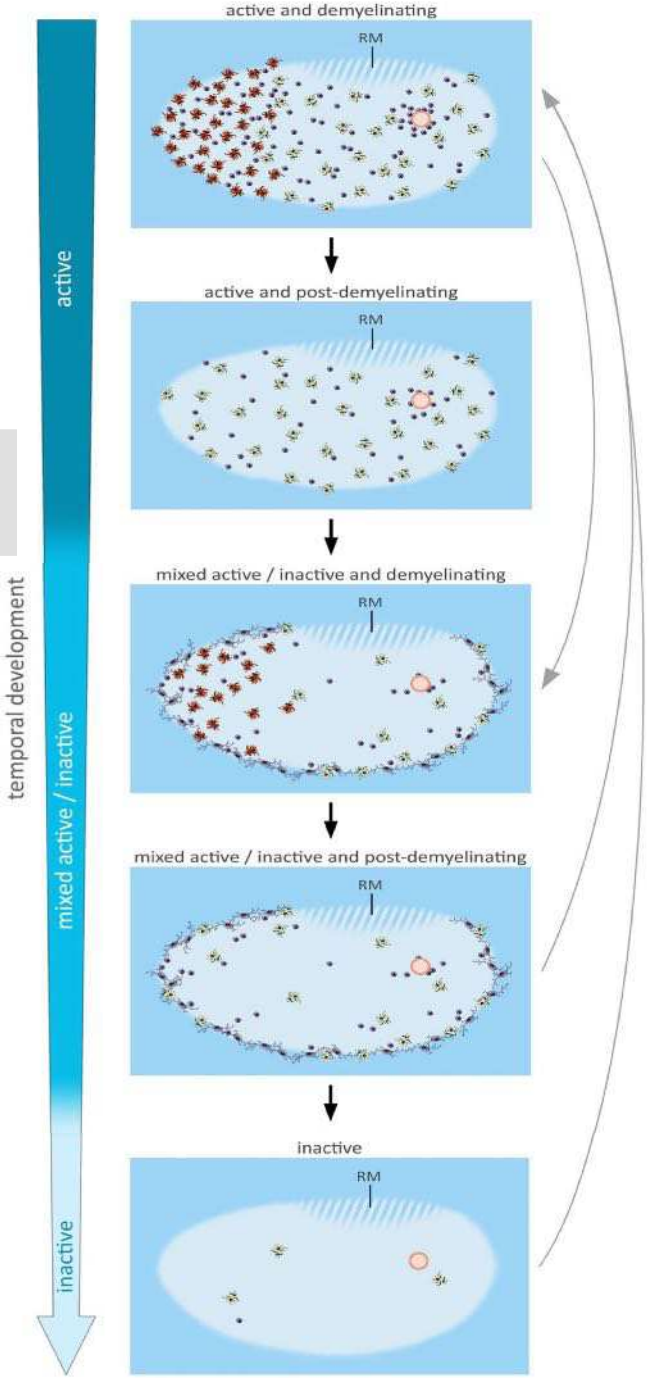
Inactive	−	−	−	−





Iron Deposits Surrounding Multiple Sclerosis Plaques

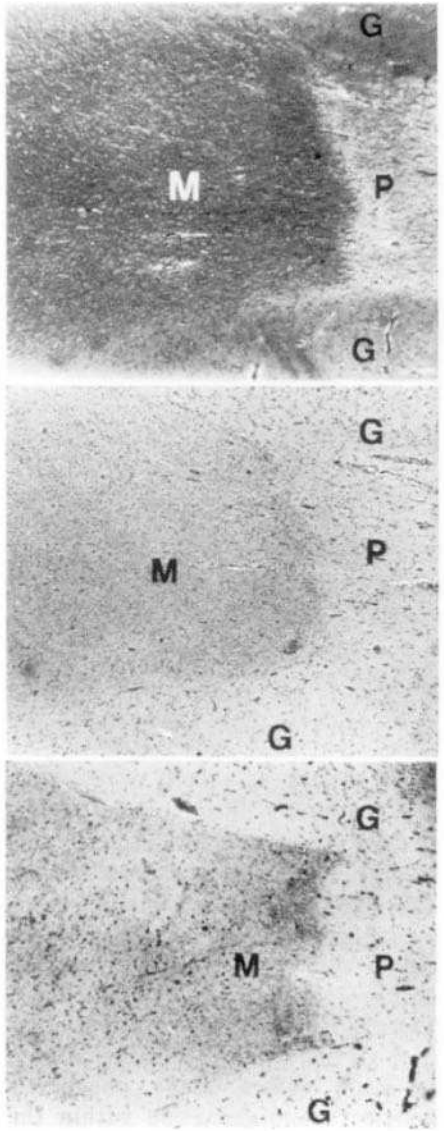
William Craelius, PhD; Michael W. Migdal; Christian P. Luessenhop; Arnon Sugar; Isidore Mihalakis, MD

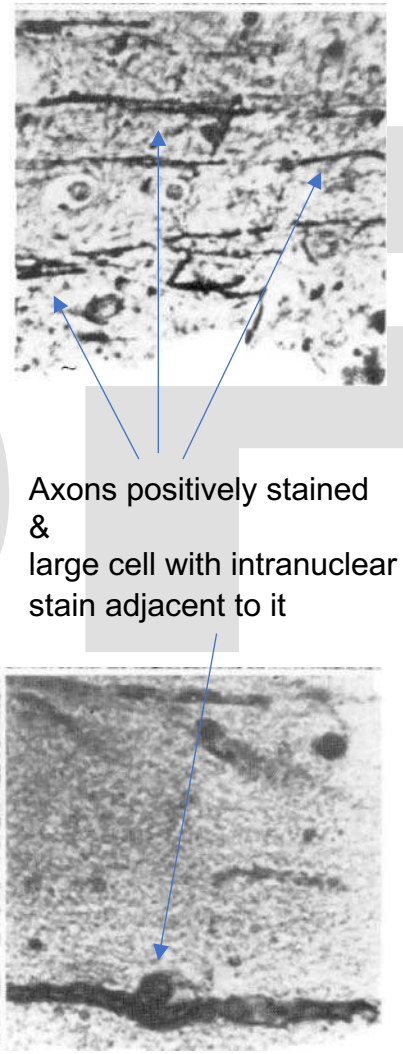
Arch Pathol Lab Med-Vol 106, Aug 1982

Myéline

Cellules

Fer





Axons positively stained
&
large cell with intranuclear stain adjacent to it

ELSEVIER

Brain Research 760 (1997) 298–303

BRAIN RESEARCH

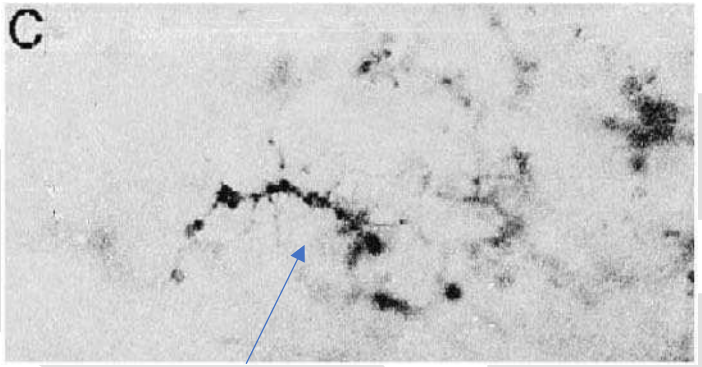
Short communication

Iron deposits in multiple sclerosis and Alzheimer's disease brains

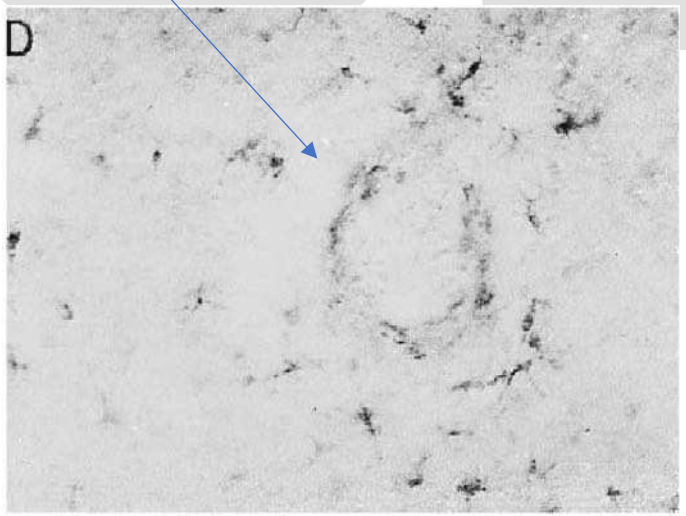
Steven M. LeVine *

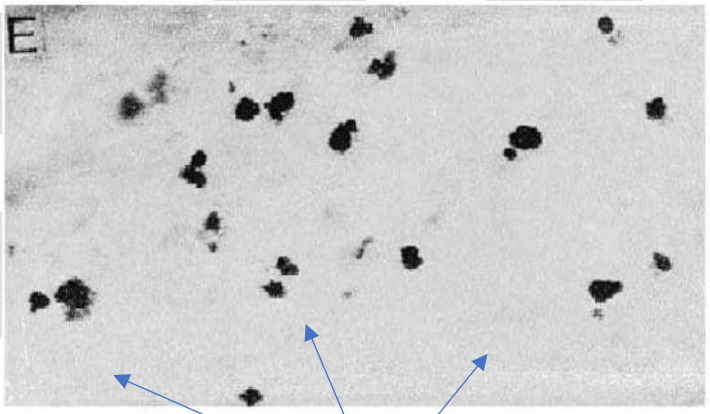
Department of Physiology and the Smith Mental Retardation Research Center, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160, USA

Accepted 25 March 1997



reactive microglial cell at the edge of a region with high reactive microglia concentration
&
around blood vessel





round macrophages are intensely labeled

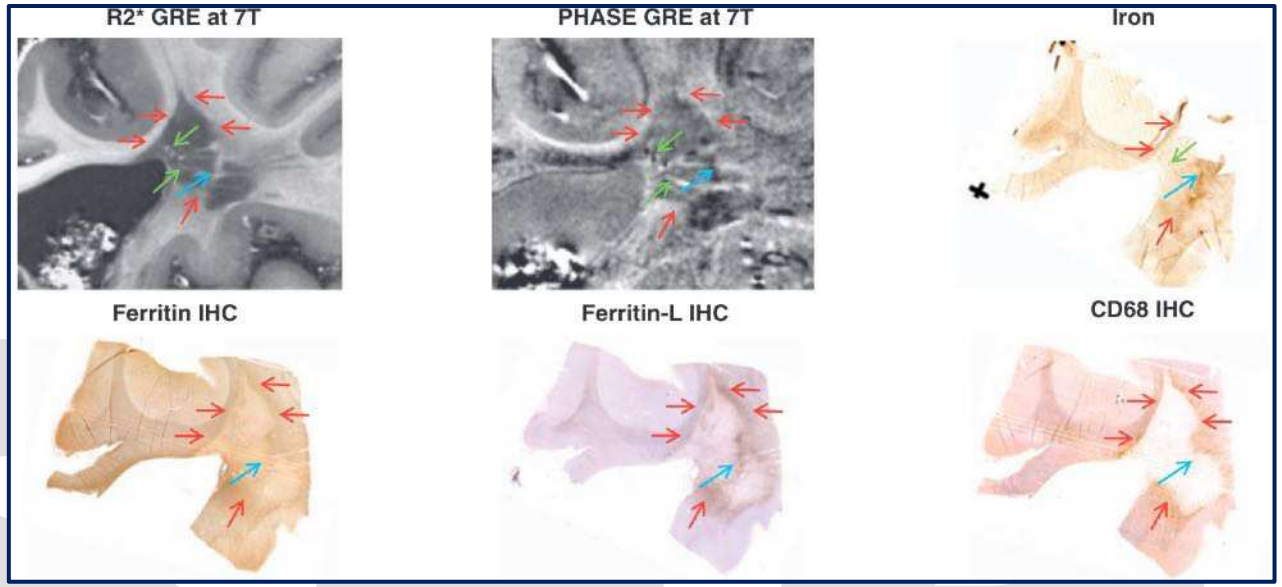
doi:10.1093/brain/awr278 Brain 2011: 134; 3599–3612 | 3599

BRAIN
A JOURNAL OF NEUROLOGY

Tracking iron in multiple sclerosis: a combined imaging and histopathological study at 7 Tesla

Francesca Bagnato,[1,*] Simon Hametner,[2,*] Bing Yao,[3] Peter van Gelderen,[3] Hellmut Merkle,[3] Fredric K. Cantor,[4] Hans Lassmann[2] and Jeff H. Duyn[3]

Exemple de 3 lésions chroniques actives



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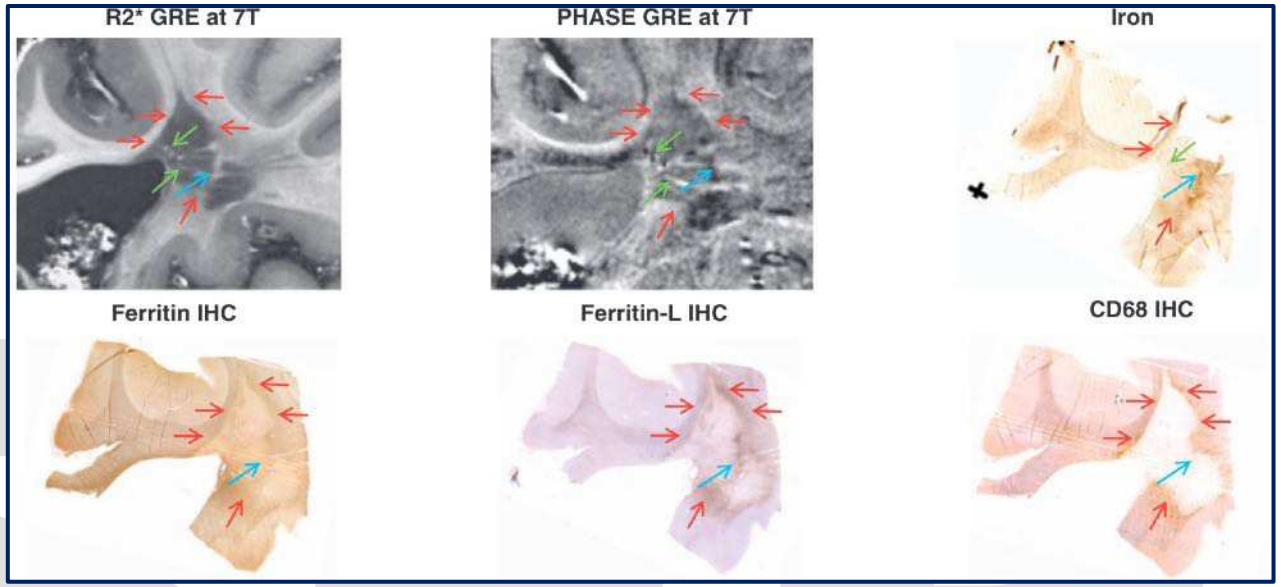

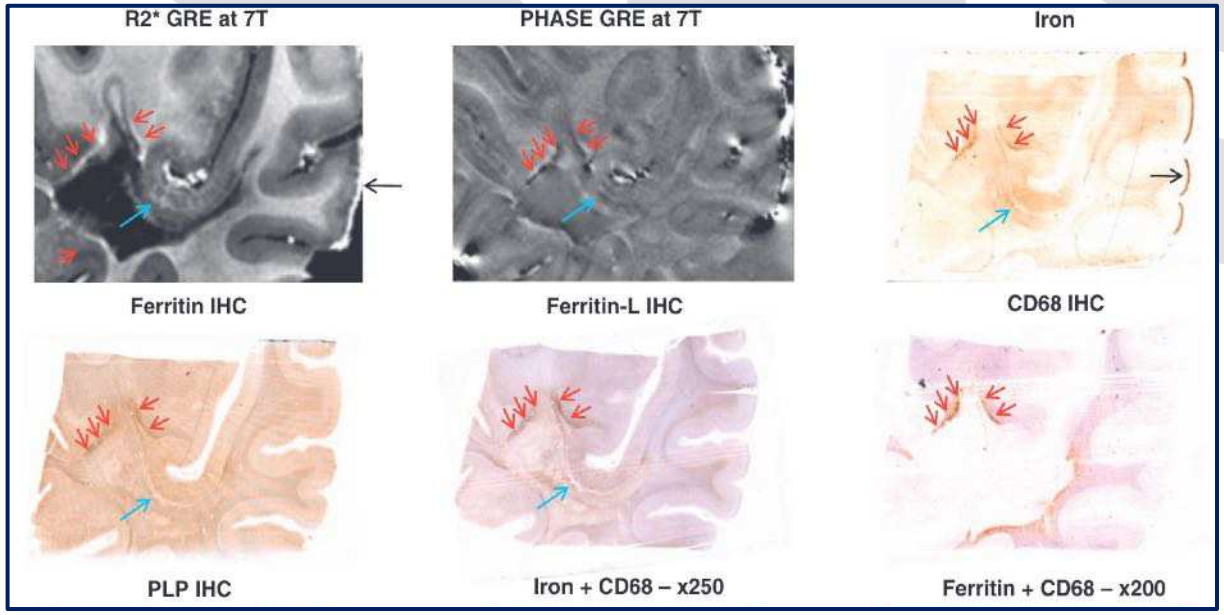

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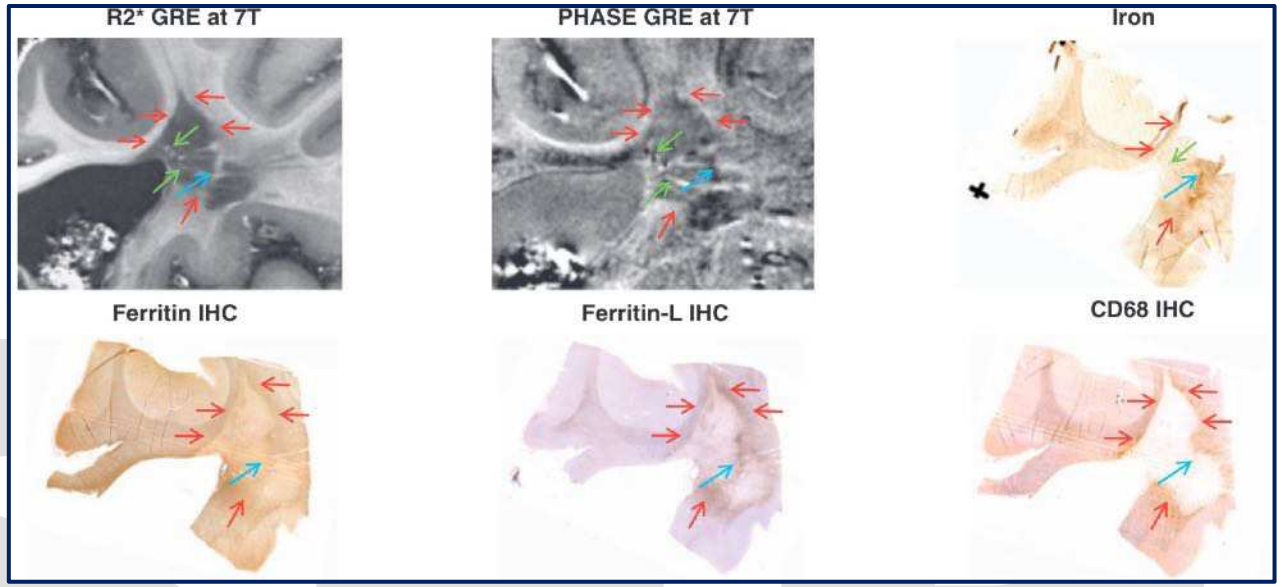
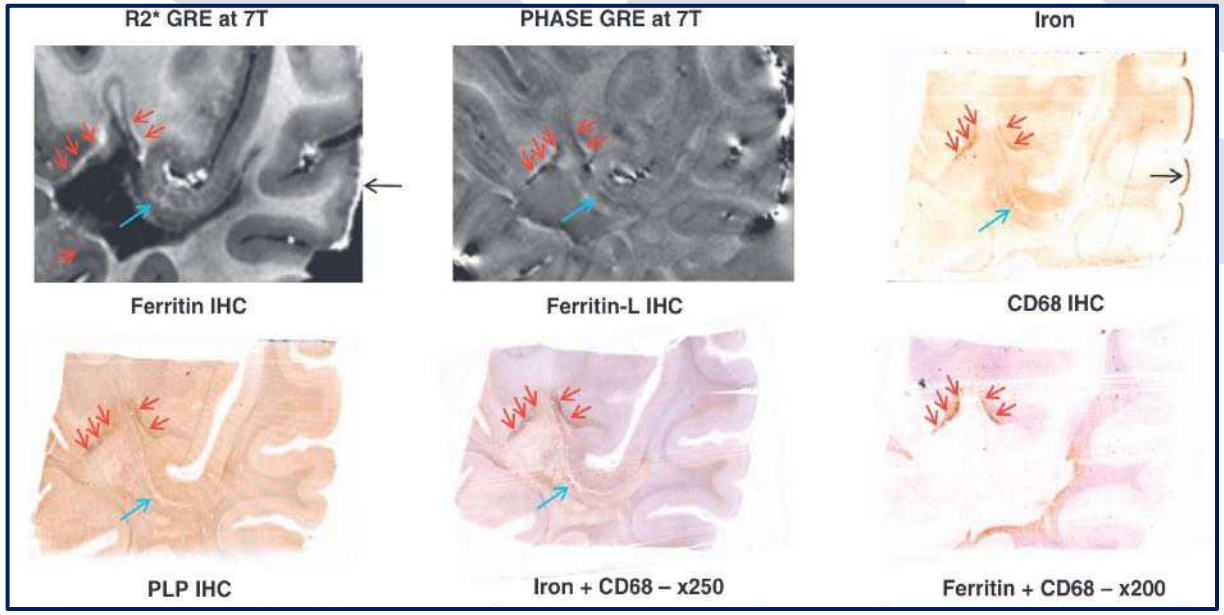
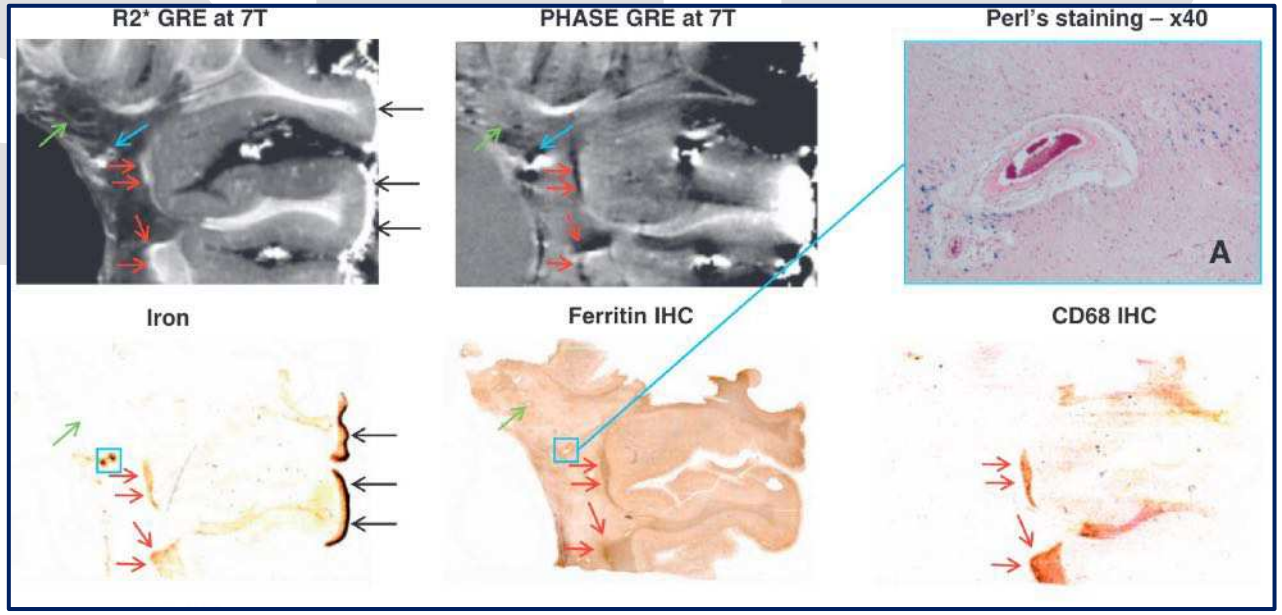






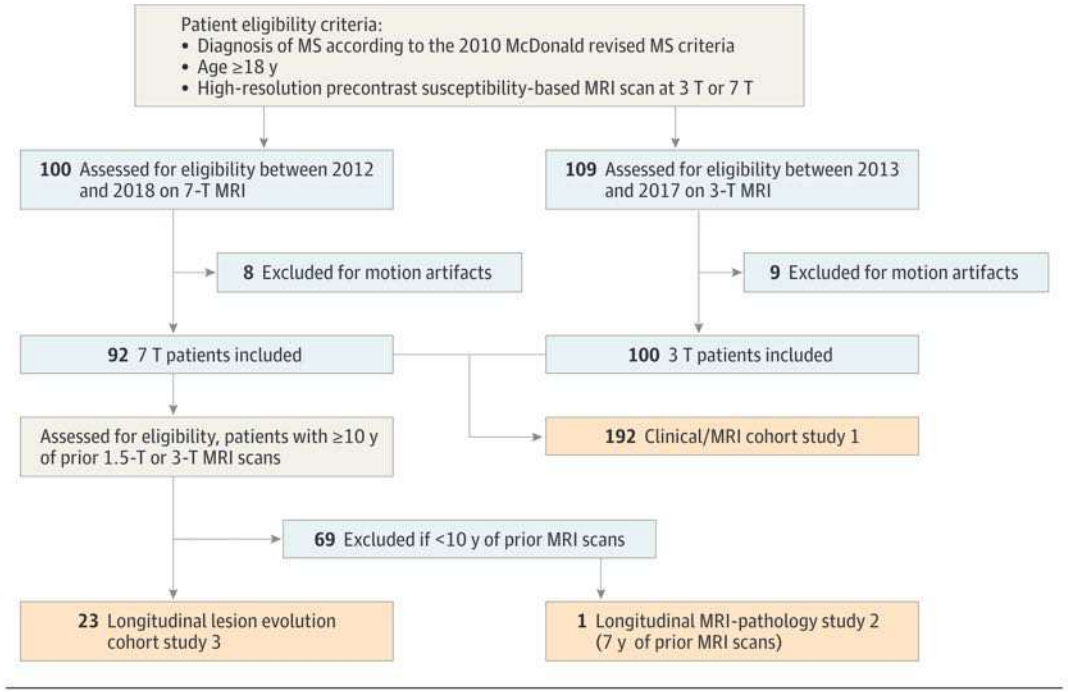
JAMA Neurology | Original Investigation

Association of Chronic Active Multiple Sclerosis Lesions With Disability In Vivo

Martina Absinta, MD, PhD; Pascal Sati, PhD; Federica Masuzzo, MD; Govind Nair, PhD; Varun Sethi, MD, PhD; Hadar Kolb, MD; Joan Ohayon, CRNP; Tianxia Wu, PhD; Irene C. M. Cortese, MD; Daniel S. Reich, MD, PhD

2019

Figure 1. Consolidated Standards of Reporting Trials Chart



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2019

56% des patients ont au moins une lésion PRL

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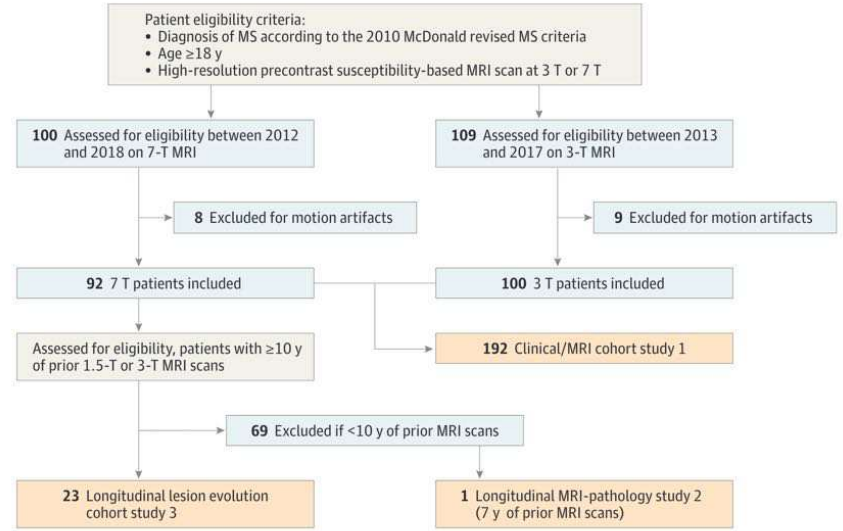

Table. Cohort Characteristics of 192 Patients With Multiple Sclerosis in the Cross-Sectional Cohort

Rim Category	No Detected Rims	1-3 Rims	≥4 Rims	Statistical Analysis[a]
Demographic and Clinical Data				
No. (%)	84 (44)	66 (34)	42 (22)	NA
Clinical phenotype, No. (%)				
CIS/RR	61 (73)	46 (70)	24 (57)	Fisher 2 × 3 P = .20, NS
SP	16 (19)	14 (21)	10 (24)	
PP	7 (8)	6 (9)	8 (19)	
Sex, Female, No. (%)	59 (70)	45 (68)		Fisher 2 × 3 P = .90, NS
Age, mean (SD), y	47.3 (14.5)	47.2 (11.4)	44.3 (11.1)	ANOVA P = .40, NS
Disease duration, mean (SD), y	13.4 (12.5)	12.9 (9.9)	12.2 (8.3)	ANOVA P = .80, NS
Patients never treated, No. (%)	27/84 (32)	11/66 (17)	5/42 (12)	Fisher 2 × 3 P = .01
African American, No. (%)	10 (12)	12 (18)	10 (24)	Fisher 2 × 3 P = .20, NS
*HLA-DRB1*15:01*, No. (%)	29/64 (45)	15/54 (28)	13/33 (41)	Fisher 2 × 3 P = .10, NS
EDSS score, median (range)	1.5 (0-7.5)*	2 (0-8)[&]	3 (1-7.5)*[&]	ANOVA P = .002
MSSS score, mean (SD)	3.0 (2.5)*	3.4 (2.5)[&]	4.9 (2.5)*[&]	ANOVA P < .001
PASAT score, mean (SD)	49.9 (8.6)*	48.4 (9.9)	44.6 (11.9)*	ANOVA P = .03
SDMT score, mean (SD)	53.4 (12.3)*	48.3 (13.4)	43.7 (17.8)*	ANOVA P = .001

Research

JAMA Neurology | Original Investigation

Association of Chronic Active Multiple Sclerosis Lesions With Disability In Vivo

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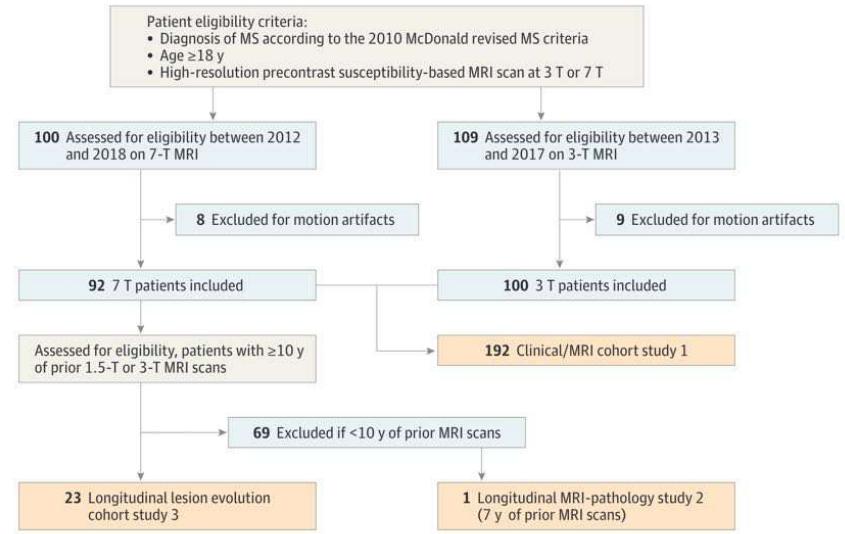

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*HLA-DRB1*15:01*, No. (%)	29/64 (45)	15/54 (28)	13/33 (41)	Fisher 2 × 3 P = .10, NS
EDSS score, median (range)	1.5 (0-7.5)*	2 (0-8)[&]	3 (1-7.5)*[&]	ANOVA P = .002
MSSS score, mean (SD)	3.0 (2.5)*	3.4 (2.5)[&]	4.9 (2.5)*[&]	ANOVA P < .001
PASAT score, mean (SD)	49.9 (8.6)*	48.4 (9.9)	44.6 (11.9)*	ANOVA P = .03
SDMT score, mean (SD)	53.4 (12.3)*	48.3 (13.4)	43.7 (17.8)*	ANOVA P = .001

Research

JAMA Neurology | Original Investigation

Association of Chronic Active Multiple Sclerosis Lesions With Disability In Vivo

Martina Absinta, MD, PhD; Pascal Sati, PhD; Federica Masuzzo, MD; Govind Nair, PhD; Varun Sethi, MD, PhD; Hadar Kolb, MD; Joan Ohayon, CRNP; Tianxia Wu, PhD; Irene C. M. Cortese, MD; Daniel S. Reich, MD, PhD

2019

Figure 1. Consolidated Standards of Reporting Trials Chart

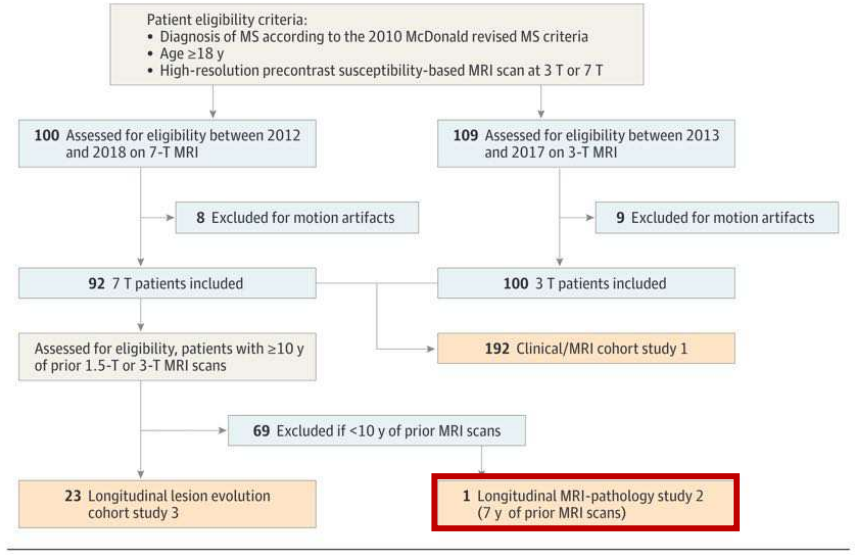
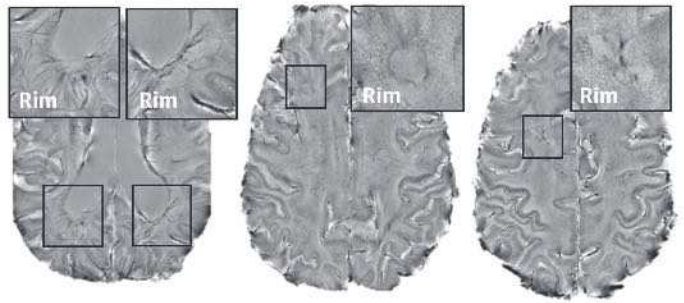


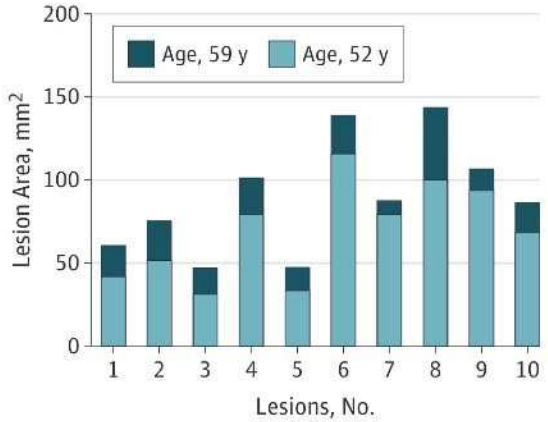
Figure 3. Man in His Late 50s With Progressive Multiple Sclerosis and Expanding Rim Lesions

A 7-T axial phase MRI

MRI acquired at age 59 years



B Histogram



All 10-rim lesions expanded over 7 years

Research

JAMA Neurology | Original Investigation

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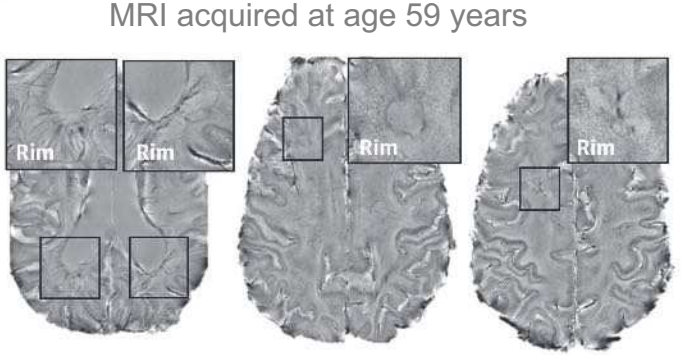

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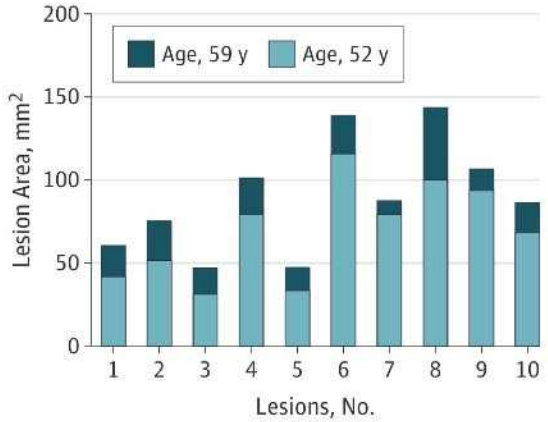
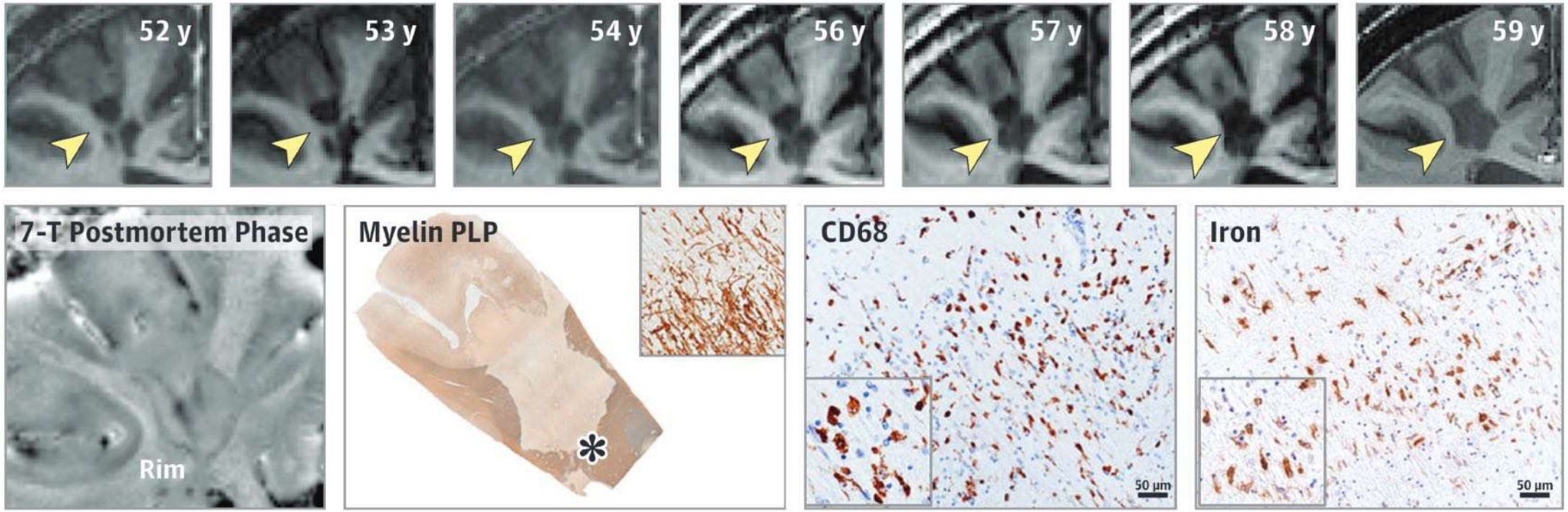


All 10-rim lesions expanded over 7 years

C MRI pathology of a frontal lesion that slowly expanded in vivo (lesion 4)



2020

MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

Occurrence and microstructural features of slowly expanding lesions on fingolimod or natalizumab treatment in multiple sclerosis

Paolo Preziosa, Elisabetta Pagani, Lucia Moiola, Mariaemma Rodegher, Massimo Filippi and Maria A Rocca

Table 1. Main demographic, clinical and conventional MRI findings at baseline in RRMS patients starting FTY or NAT.

Variable	FTY (n=24)	NAT (n=28)	FTY versus NAT	
			Uncorrected p	Adjusted p
Women/men (%)	14 (58)/10 (42)	16 (57)/12 (43)	0.93[a]	
Mean age, years (SD)	37.4 (8.9)	36.3 (10.4)	0.68[b]	
Mean disease duration median, years (SD)	10.8 (6.5)	8.9 (6.5)	0.30[b]	
Median ARR (IQR)	1.0 (0.0; 1.0)	1.0 (1.0; 2.0)	0.67[c]	
Median ARR (IQR)	0.00 (0.00; 0.38)[a]	0.00 (0.00; 0.00)[a]	**0.02**[b]	**0.03**[b]
Number (%) of patients with relapse(s)	6 (25%)	1 (4%)	**0.03**[c]	0.05[c]
Median EDSS change (IQR)	0.0 (−0.5; 0.0)	0.0 (−0.5; 0.0)	0.99[d]	0.76[d]
Number (%) of patients with 3-month CDP	0 (0%)	2 (7%)	0.31[c]	0.37[c]
Median number of new T_2-hyperintense lesions (IQR)	1 (0; 2)	0 (0; 1)	**0.04**[b]	**0.01**[b,e]
Number (%) of patients with new T_2-hyperintense lesions	15 (63%)	10 (36%)	0.05[c]	**0.02**[c,e]
Number (%) of patients with ⩾1 Gd-enhancing lesions during the follow-up	2 (8%)	0 (0%)	0.21[c]	0.66[c]
Median T_2-hyperintense LV change, mL (IQR)	1.24 (0.33; 2.64)*	−0.21 (−1.00; 0.01)*	**<0.001**[d,e]	**<0.001**[d,e]
Mean percentage brain volume change (SD) (%)	−0.60 (0.59)	−0.80 (0.96)	0.40[d]	0.93[d]

2020

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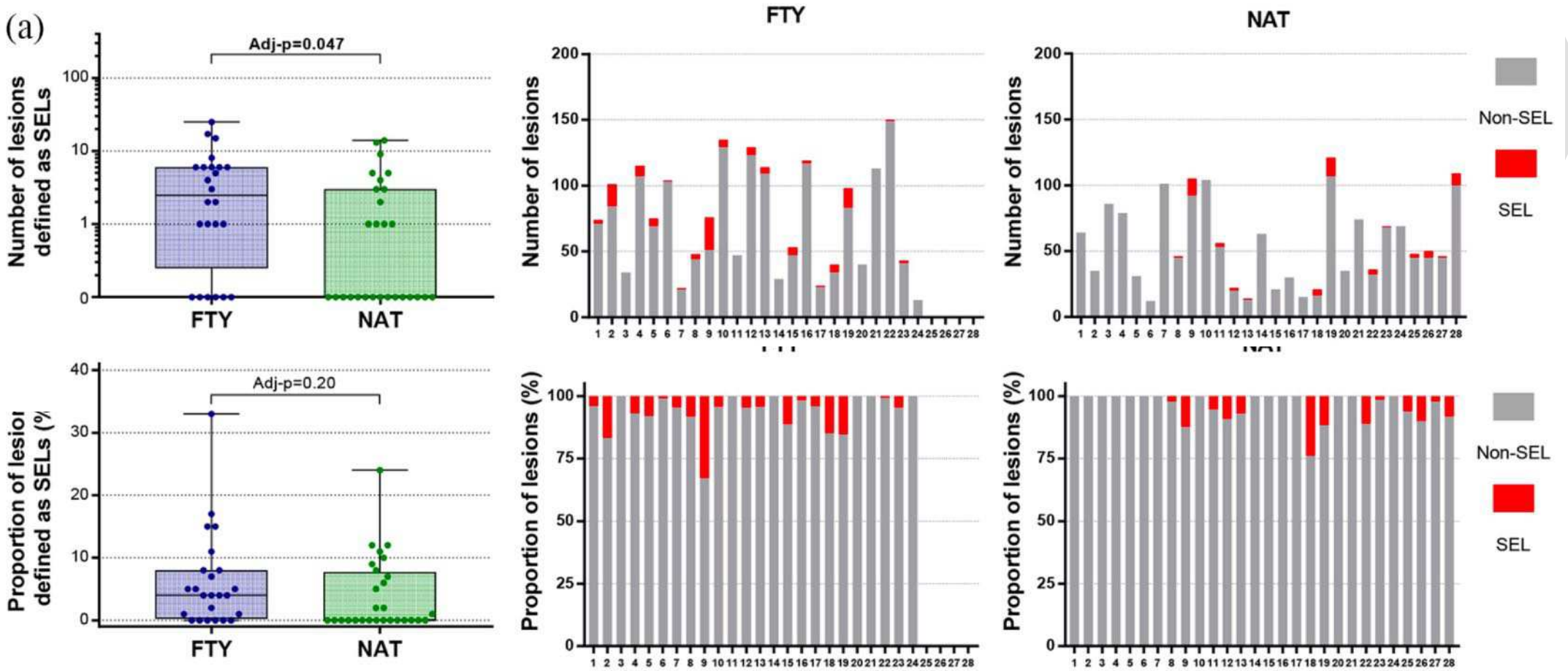
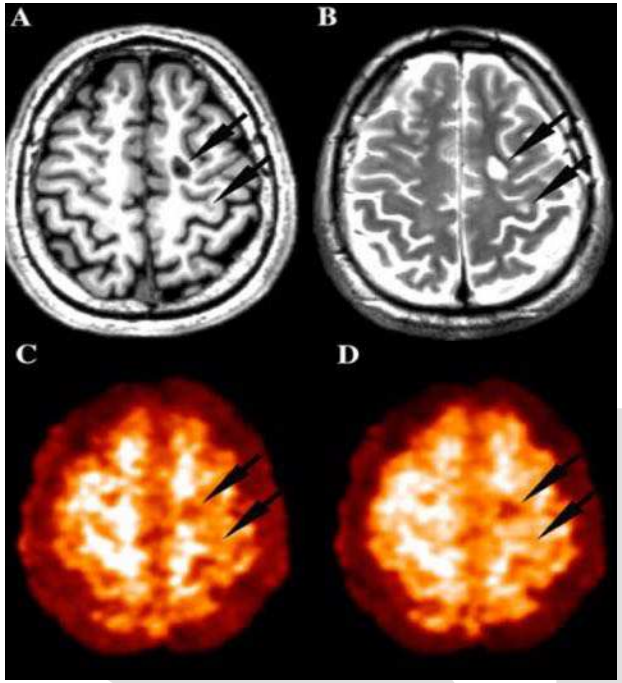


3. Cicatrisation ?

RESEARCH ARTICLE

Dynamic Imaging of Individual Remyelination Profiles in Multiple Sclerosis

Benedetta Bodini, MD, PhD,[1,2,3] Mattia Veronese, PhD,[2] Daniel García-Lorenzo, PhD,[1] Marco Battaglini, PhD,[4] Emilie Poirion,[1] Audrey Chardain, MD,[3,5] Léorah Freeman, MD, PhD,[1,3,6] Céline Louapre, MD, PhD,[1] Maya Tchikviladze, MD,[6] Caroline Papeix, MD,[6] Frédéric Dollé, PhD,[3] Bernard Zalc, MD, PhD,[1] Catherine Lubetzki, MD, PhD,[1,6] Michel Bottlaender, MD, PhD,[3] Federico Turkheimer, PhD,[2] and Bruno Stankoff, MD, PhD[1,3,5]



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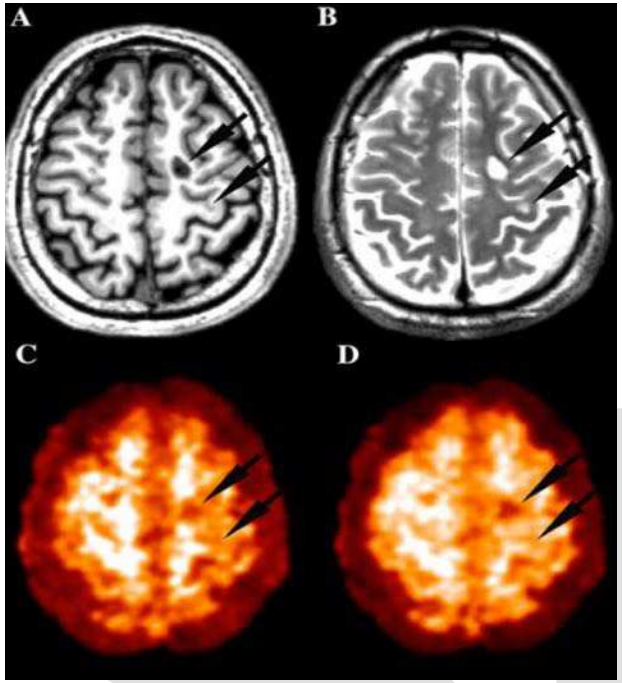

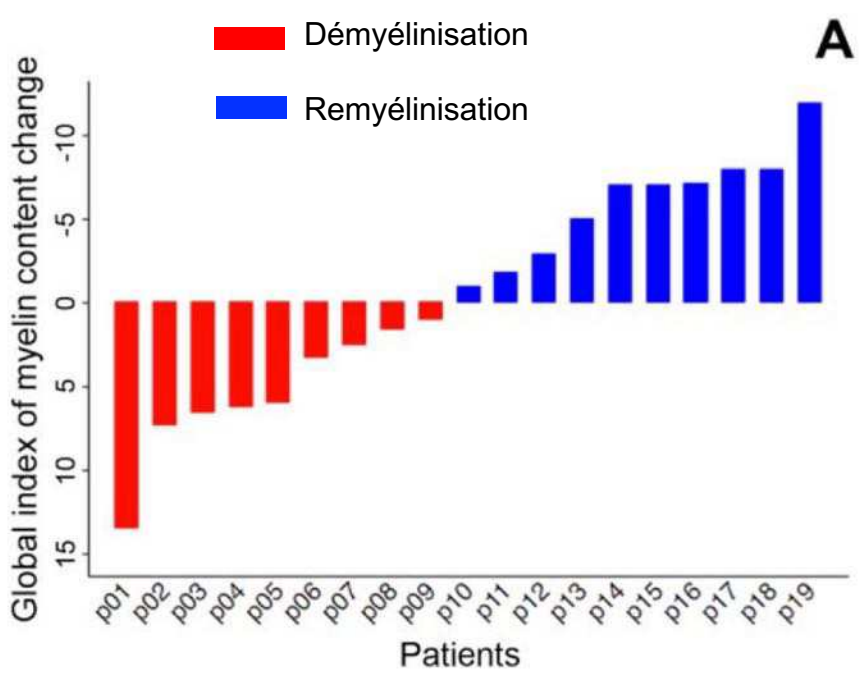

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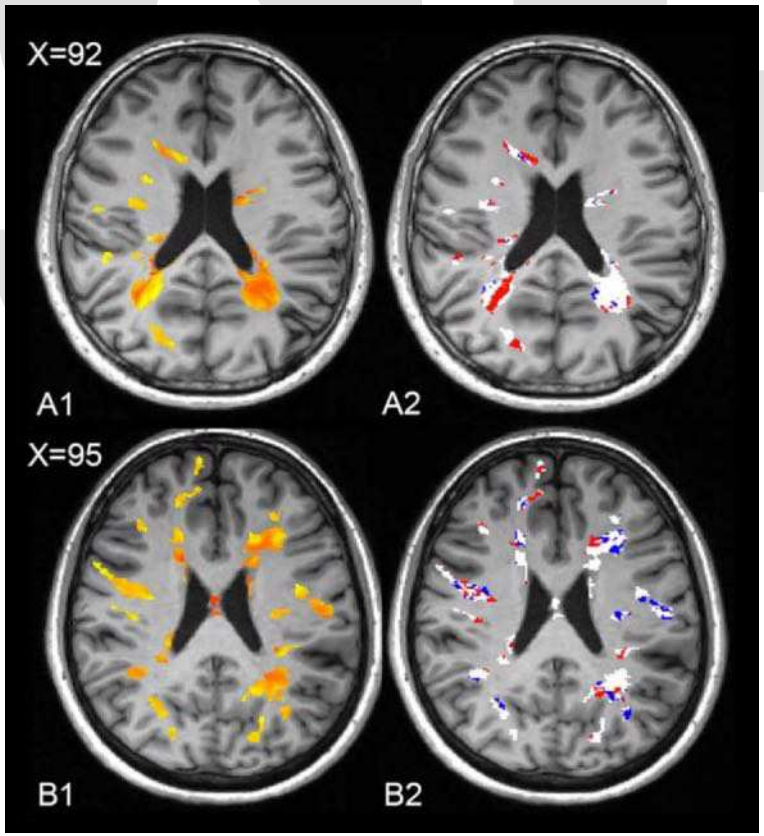

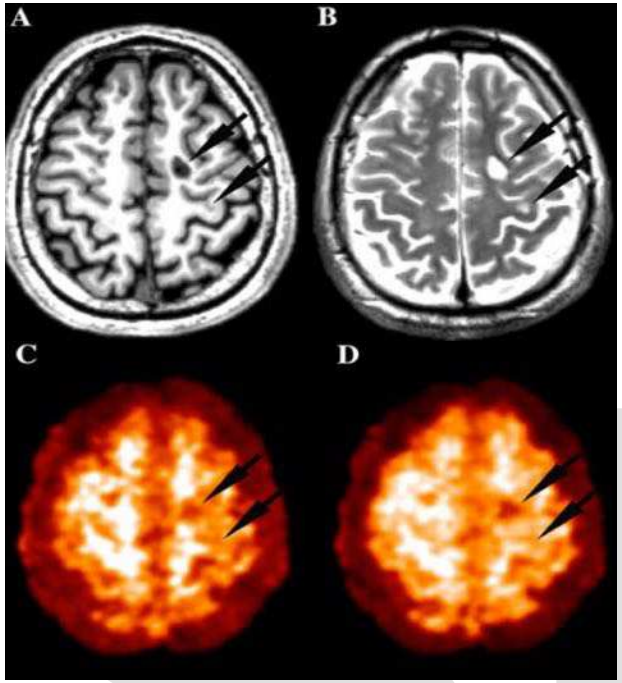

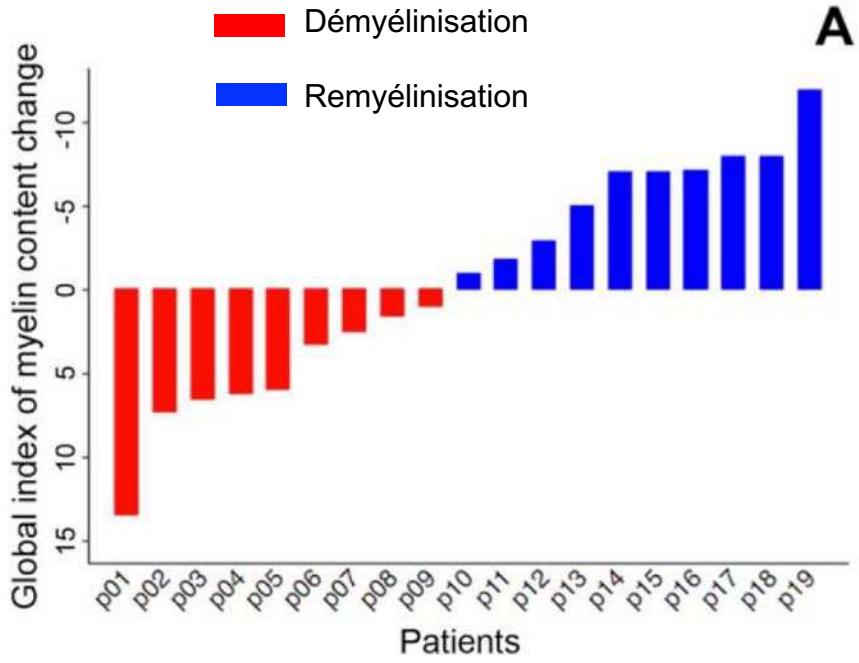

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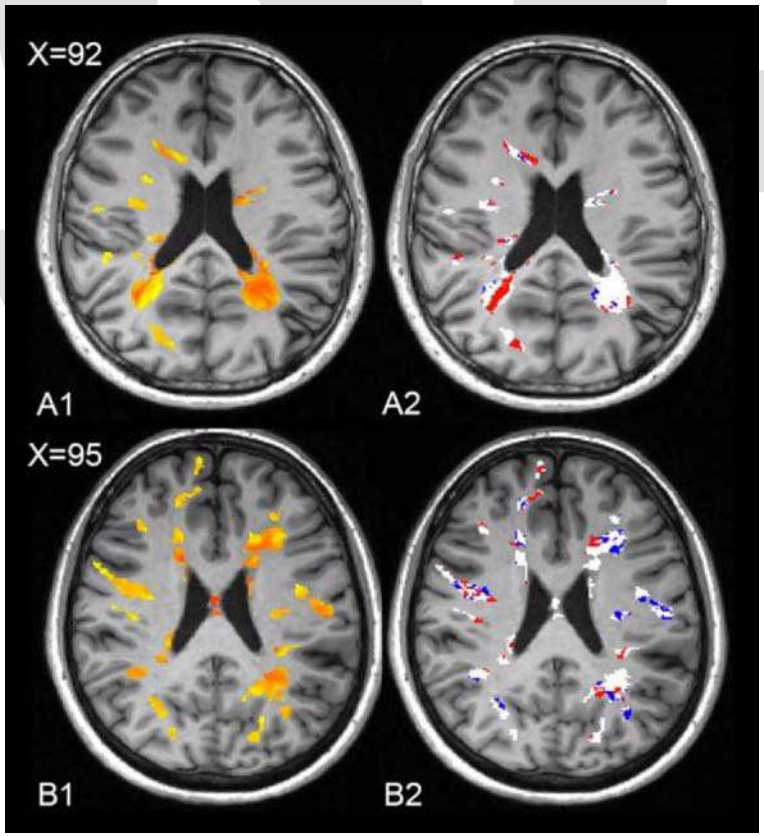

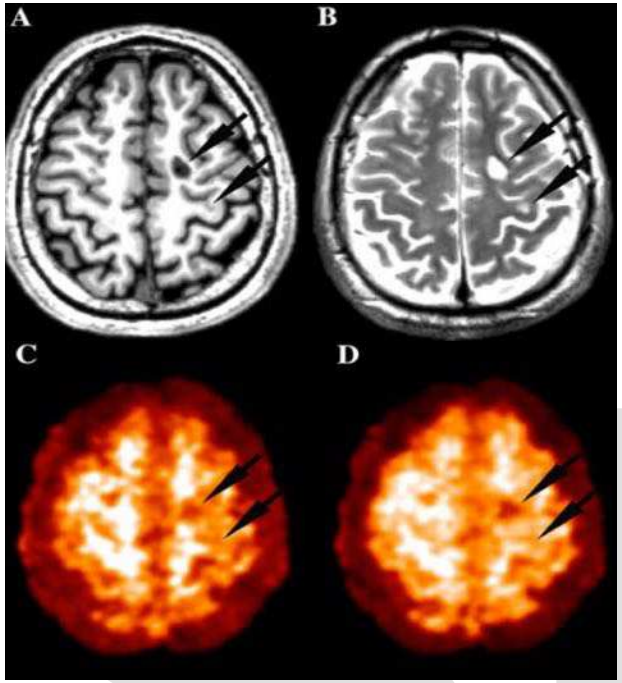

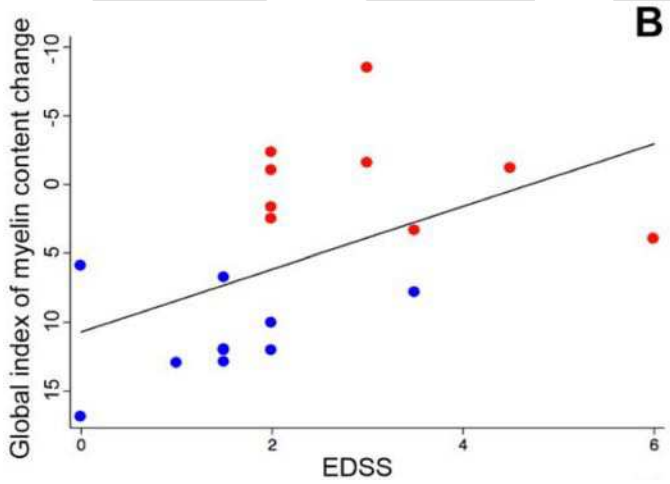

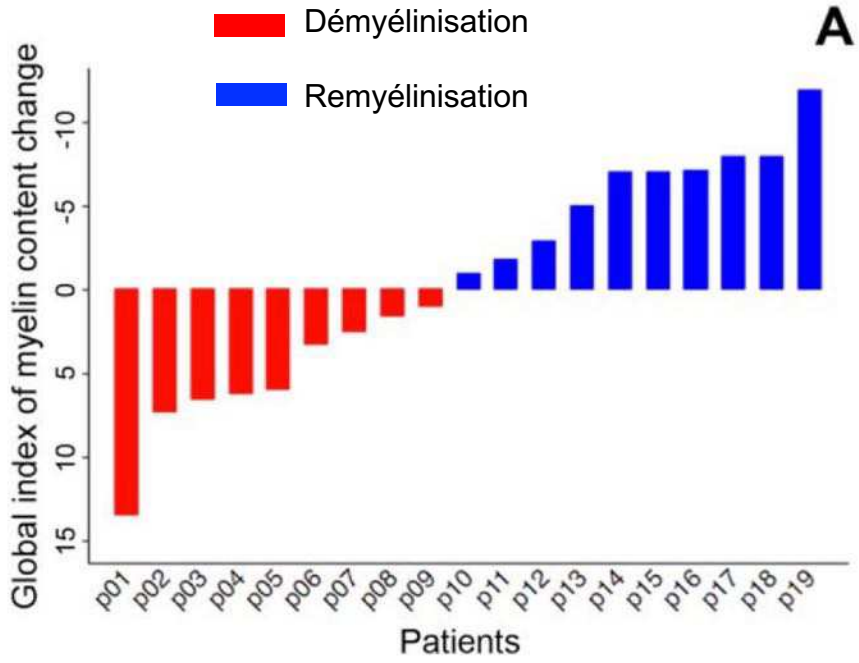

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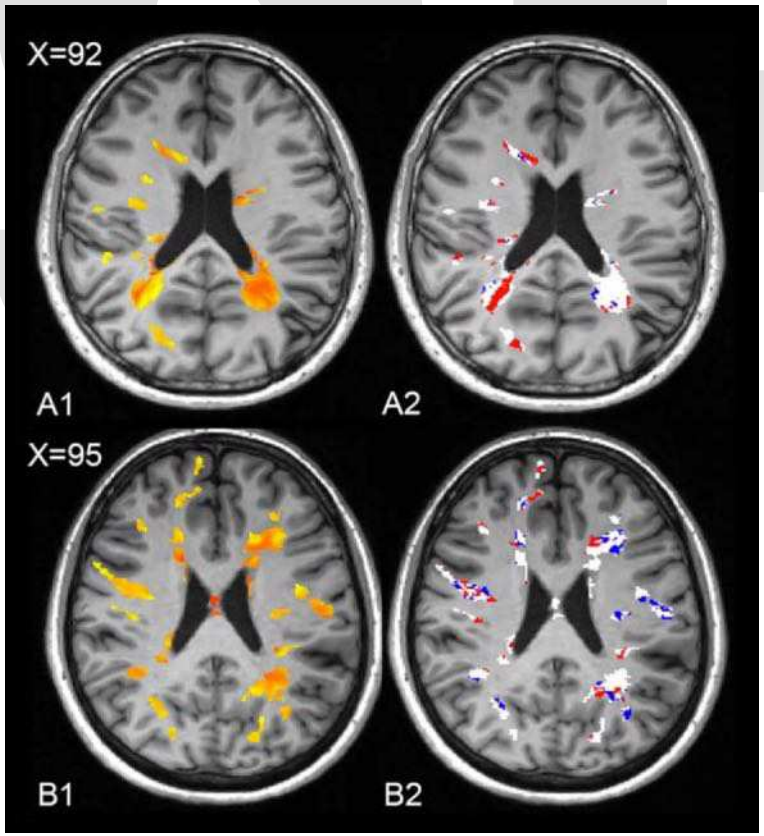

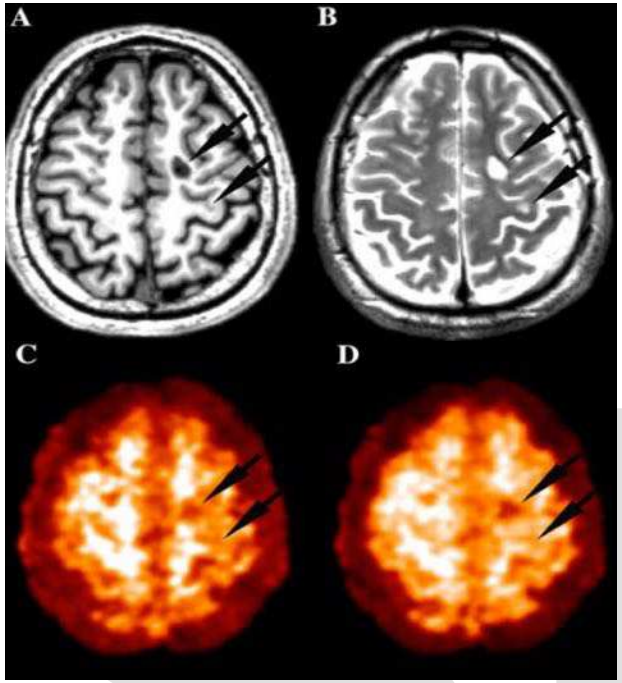

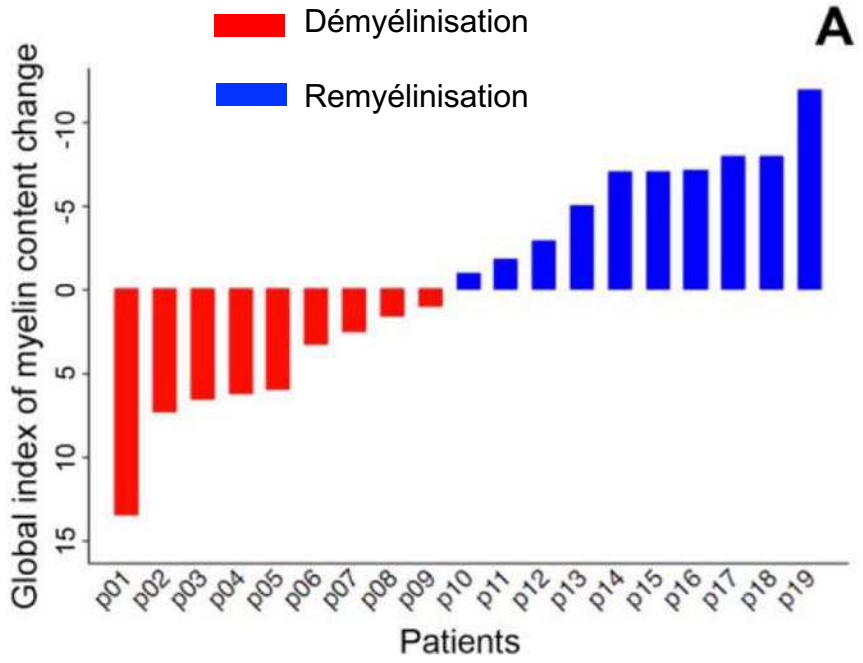

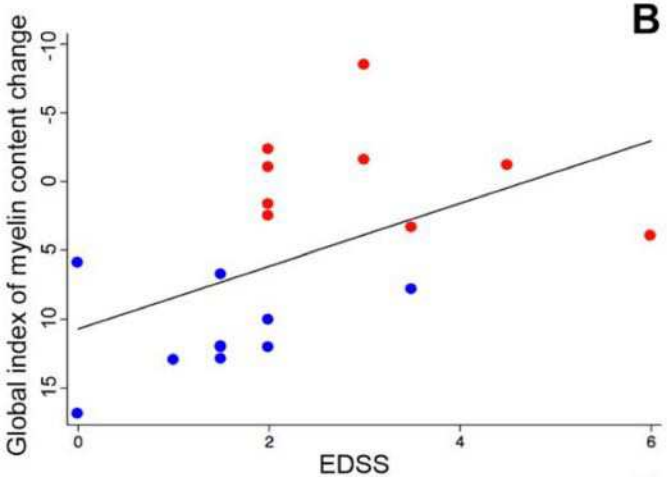

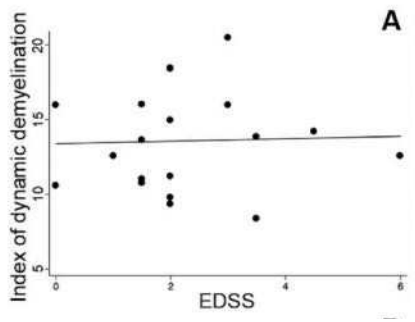

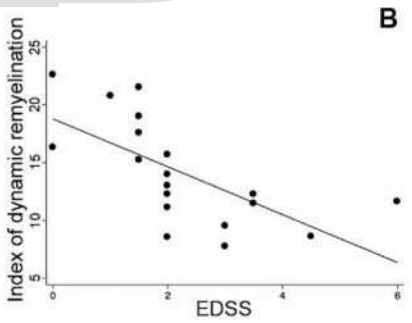

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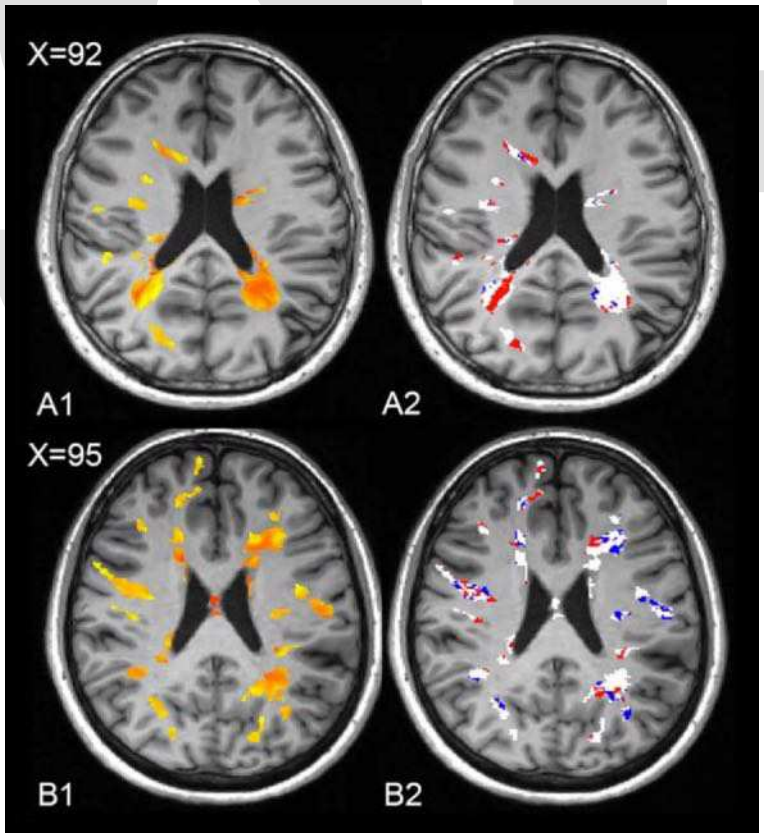
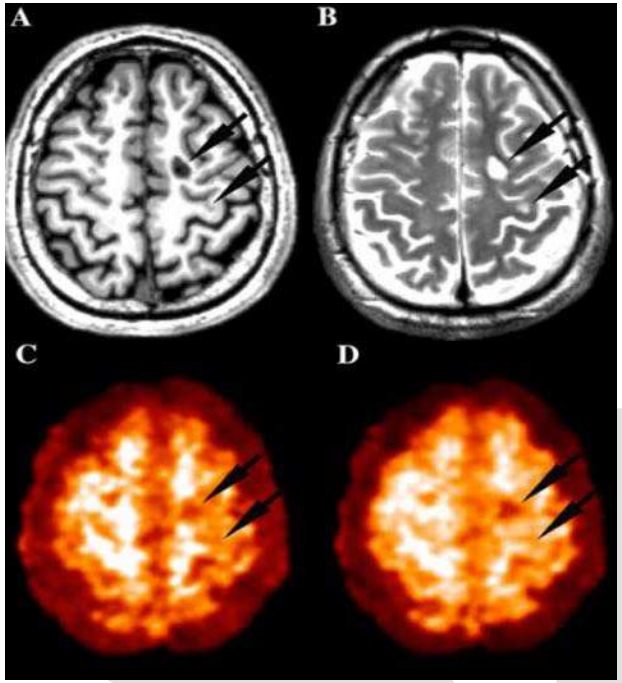
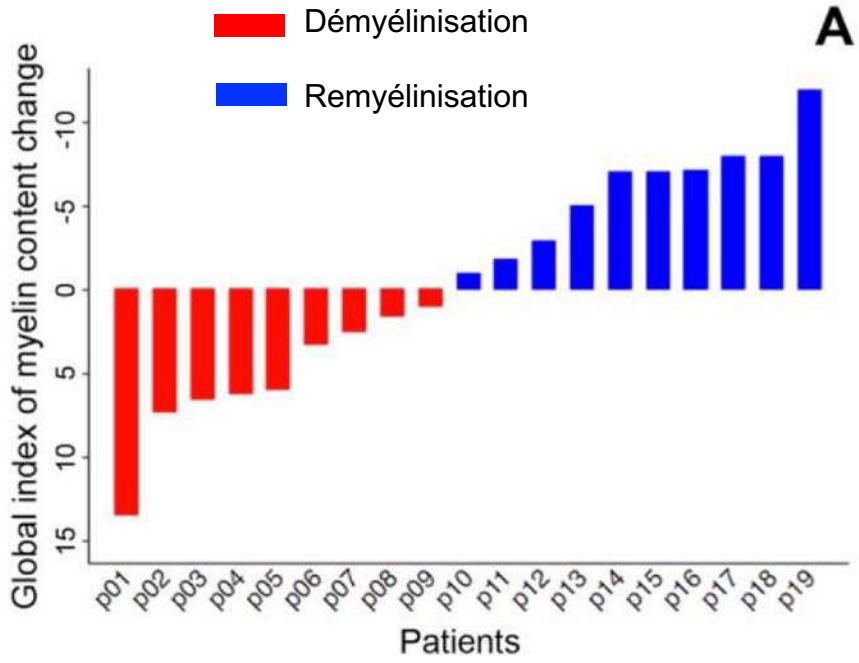
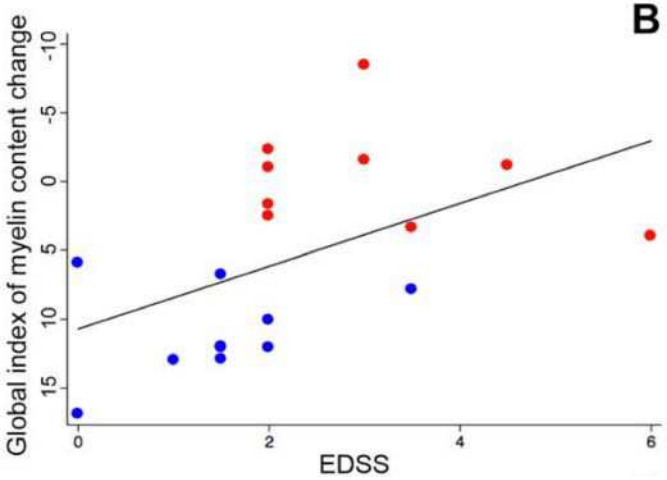
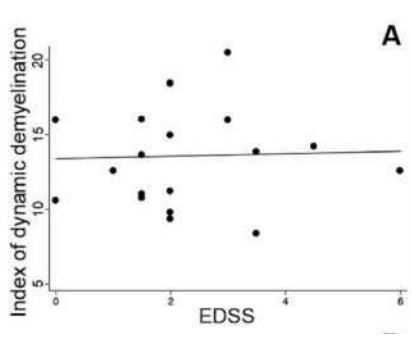
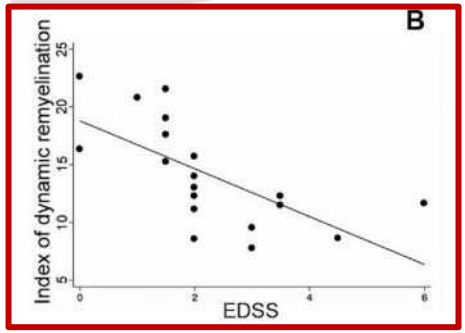






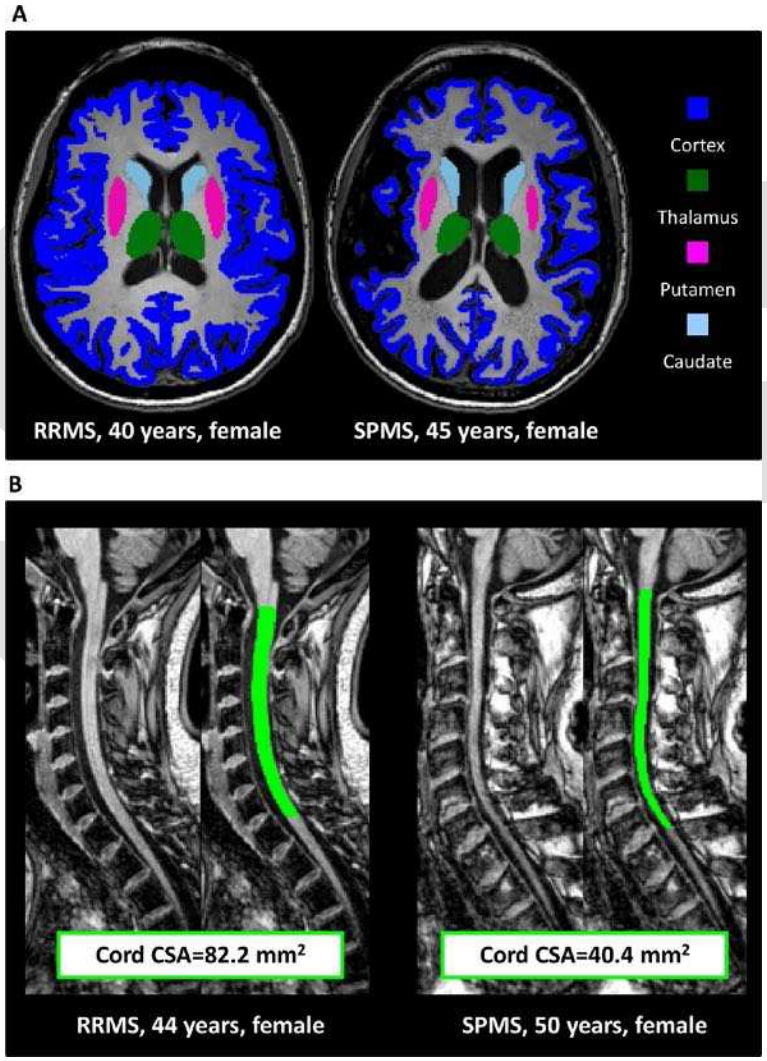






La corrélation est surtout liée aux lésions qui remyélinisent

Volumétrie



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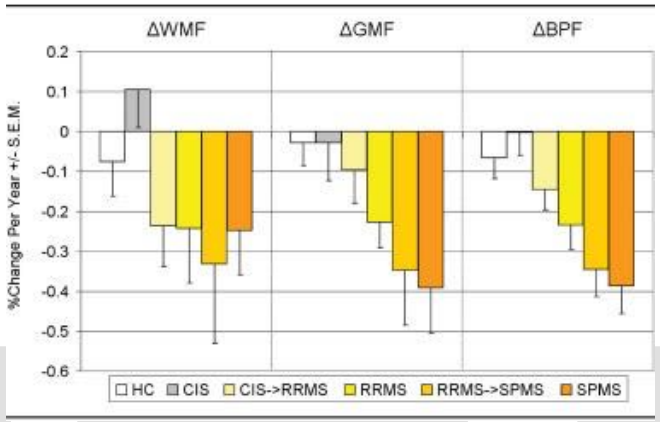

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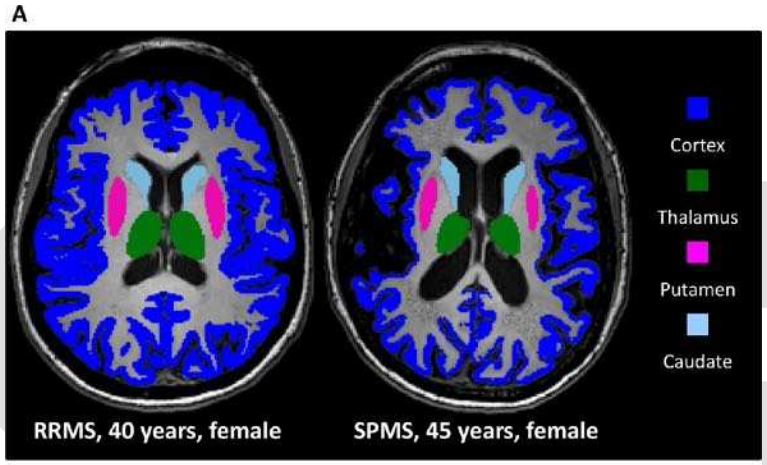

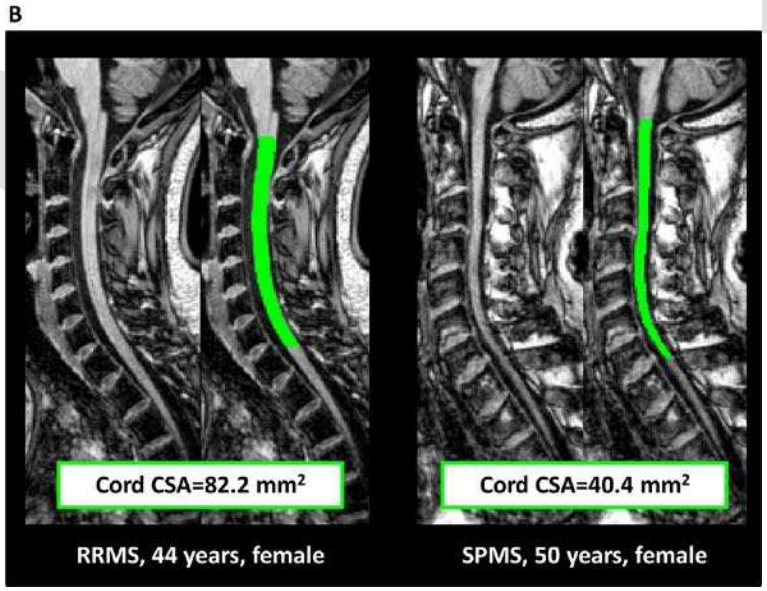

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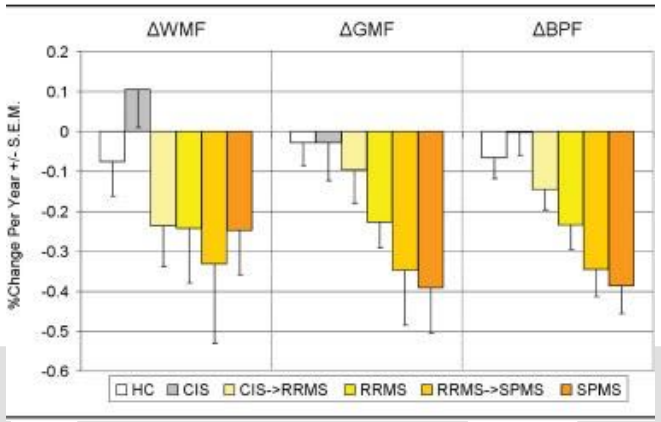

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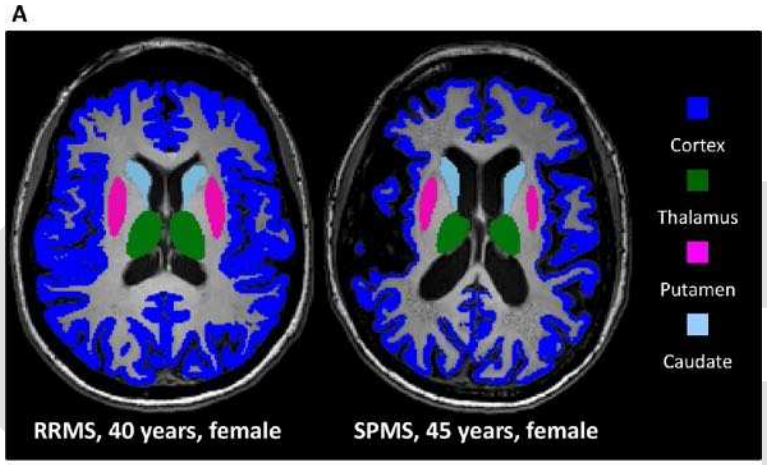

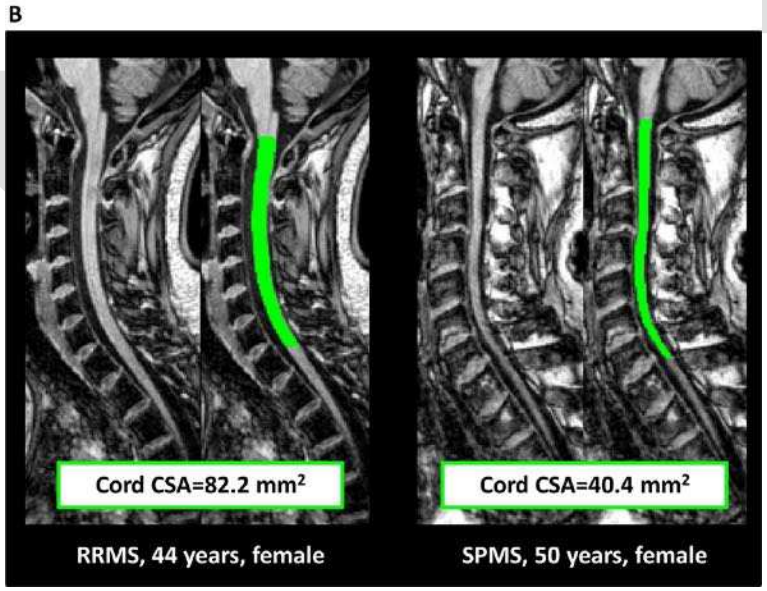

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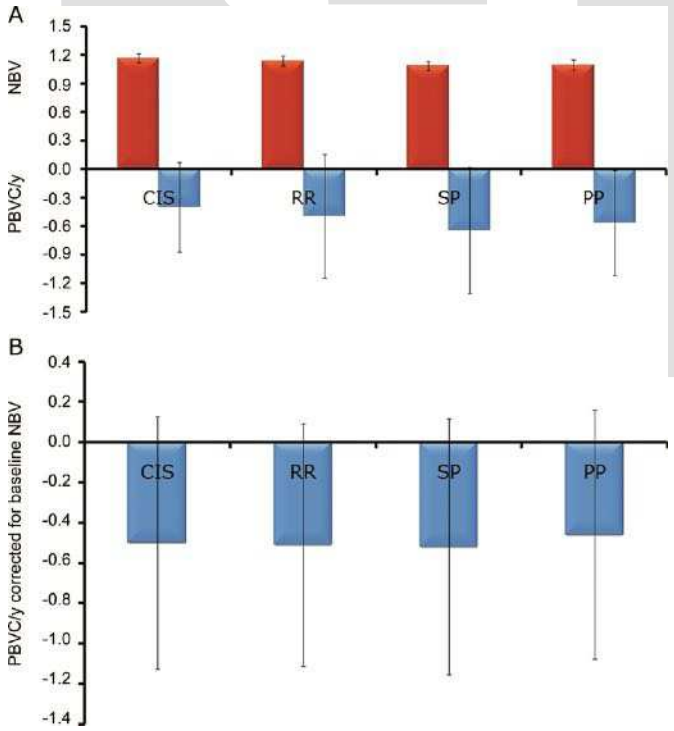
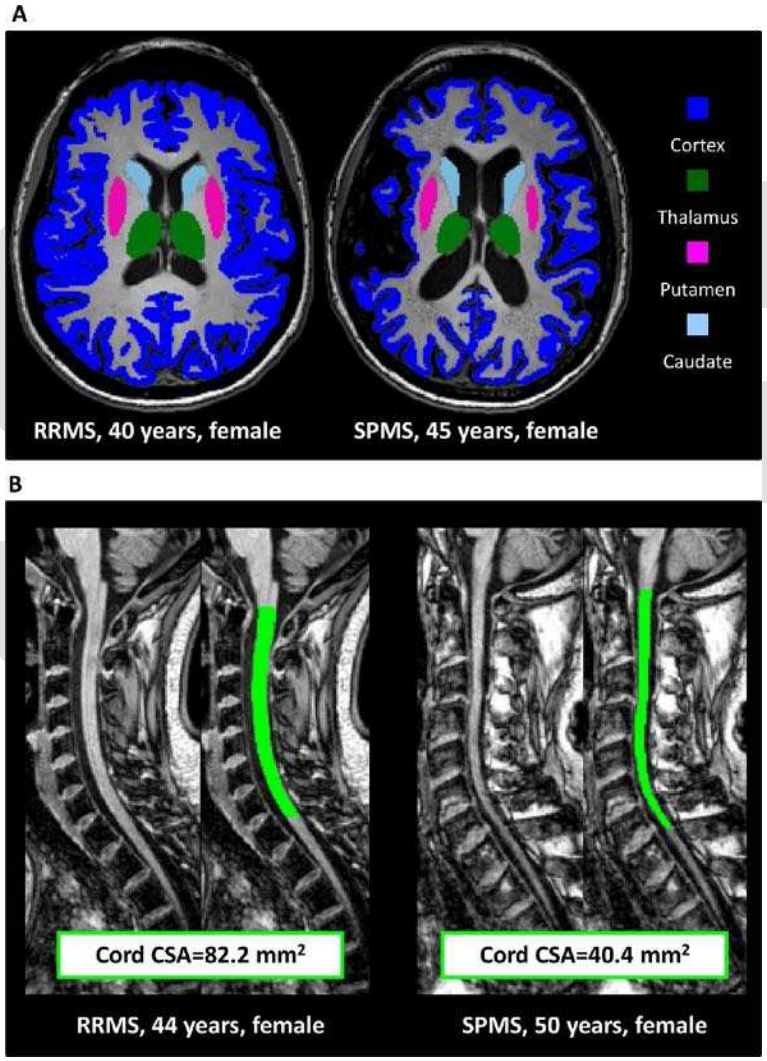


De Stefano et al. – Neurology 2010

Volumétrie



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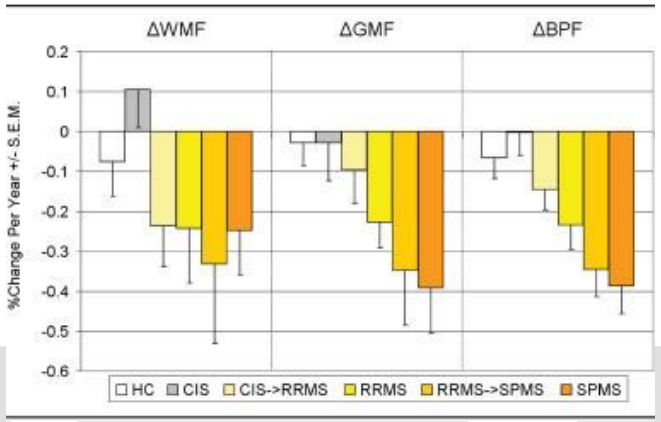

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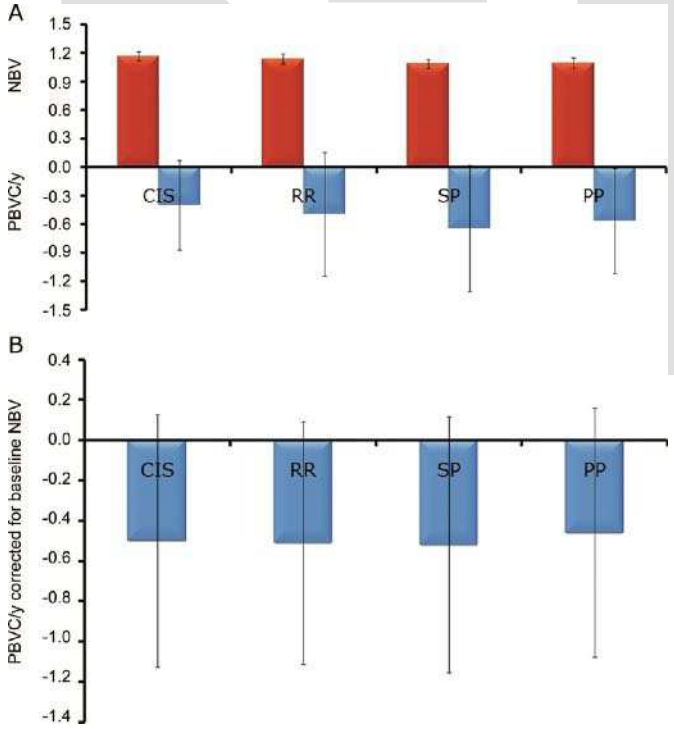

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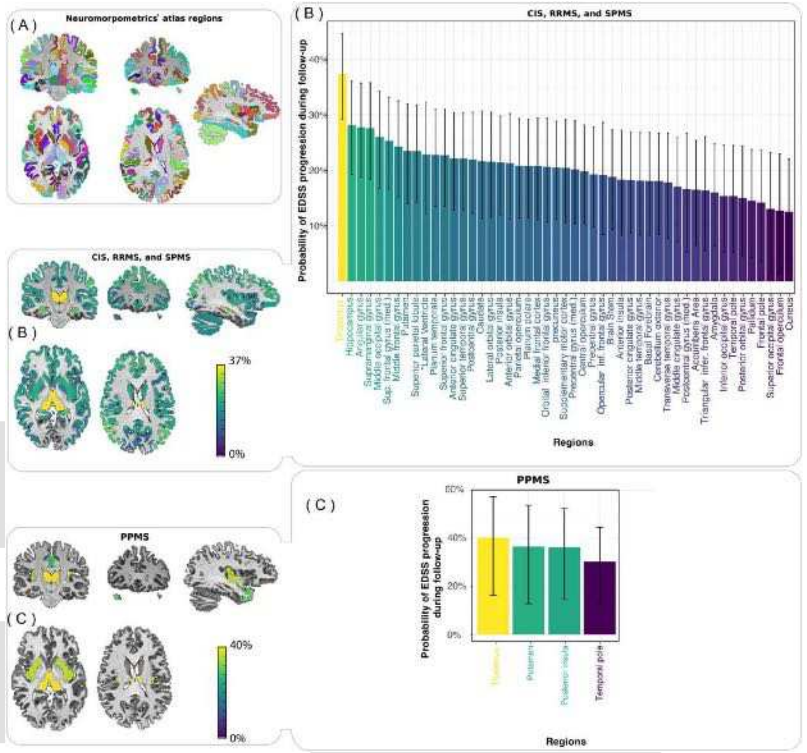
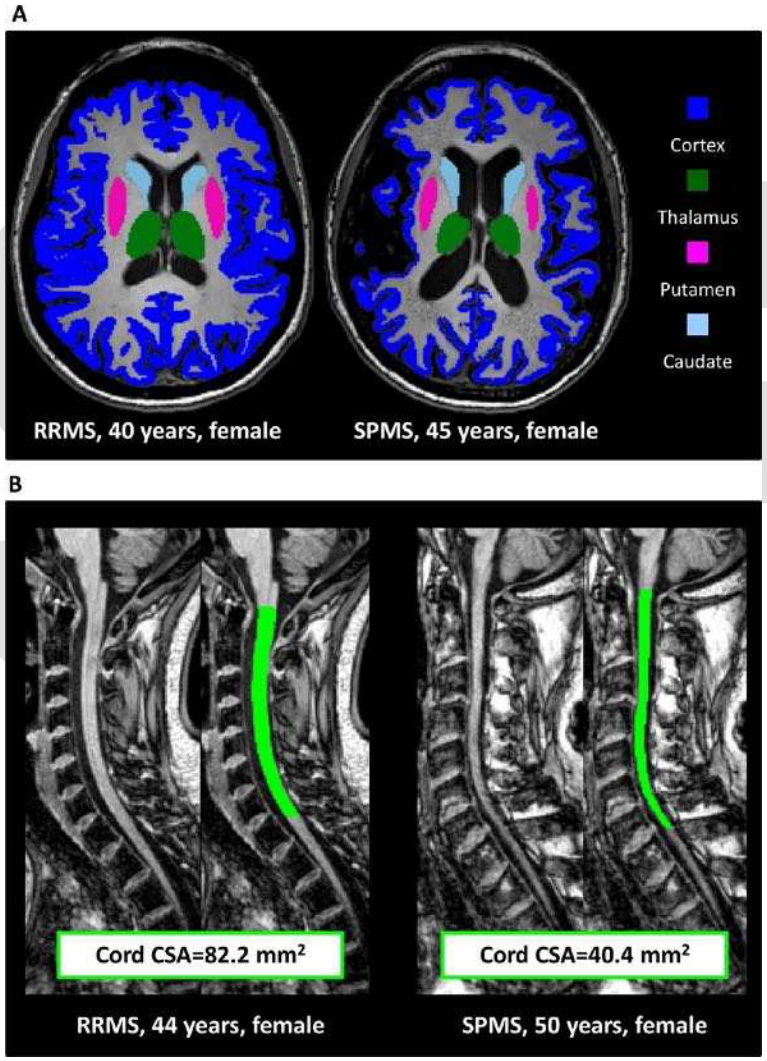
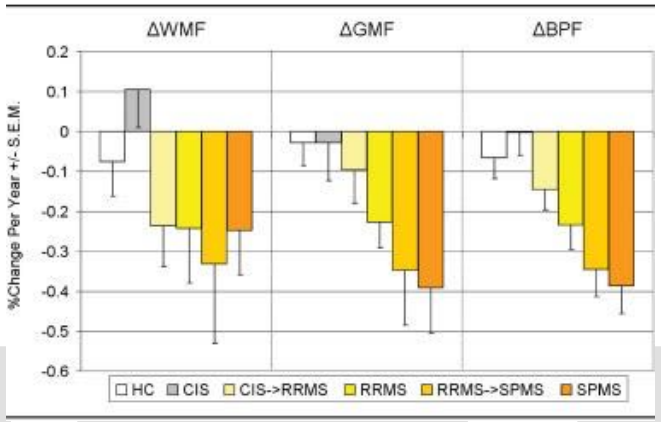


Eshaghi et al - Annals of Neurology 2018

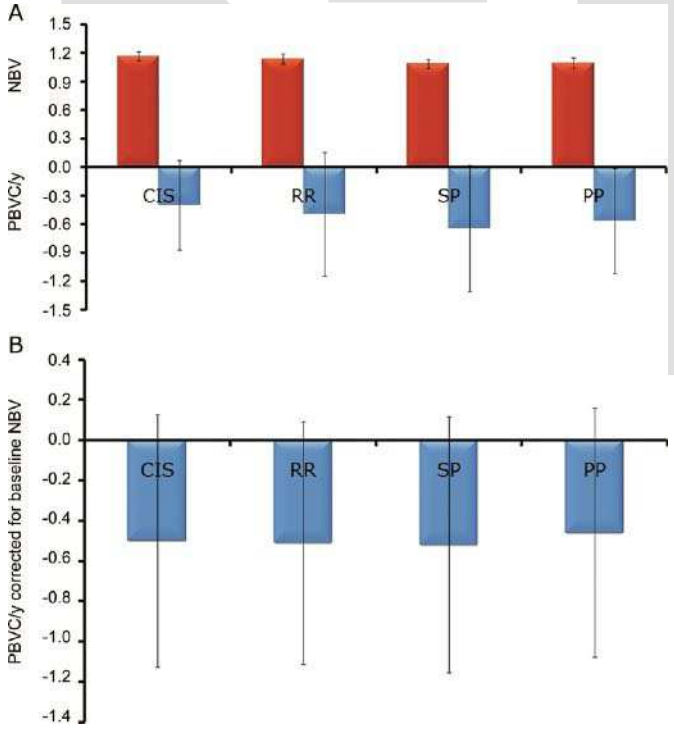
Volumétrie



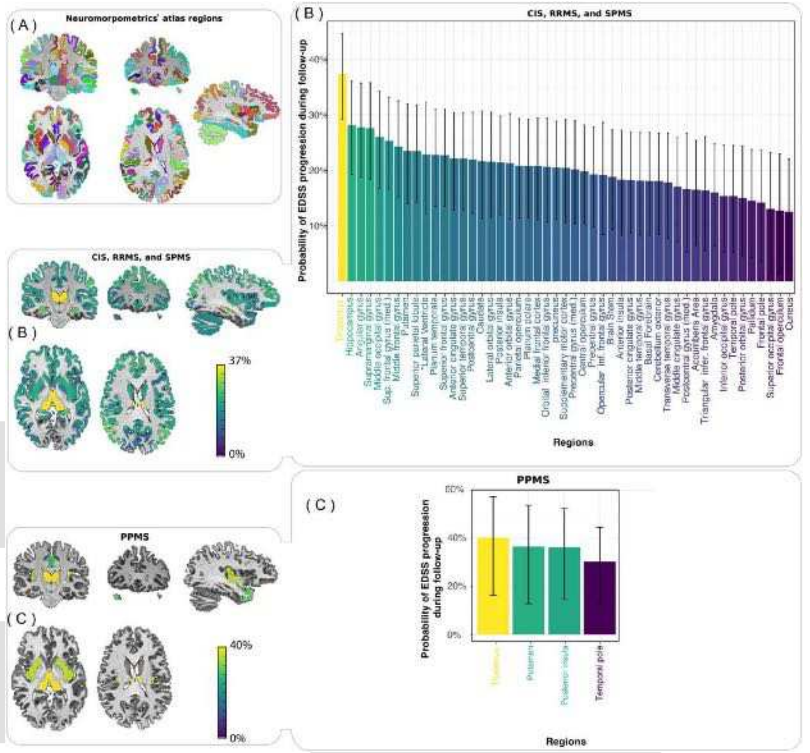
Filippi et al - Annals of Neurology 2020



Fisher et al - Annals of Neurology 2008



De Stefano et al. – Neurology 2010



Eshaghi et al - Annals of Neurology 2018

Atrophy of the thalami is correlated with the T2LL:

- right thalamus: ρ=0.57 p=0.001;
- left thalamus: ρ= 0.48 p=0.001

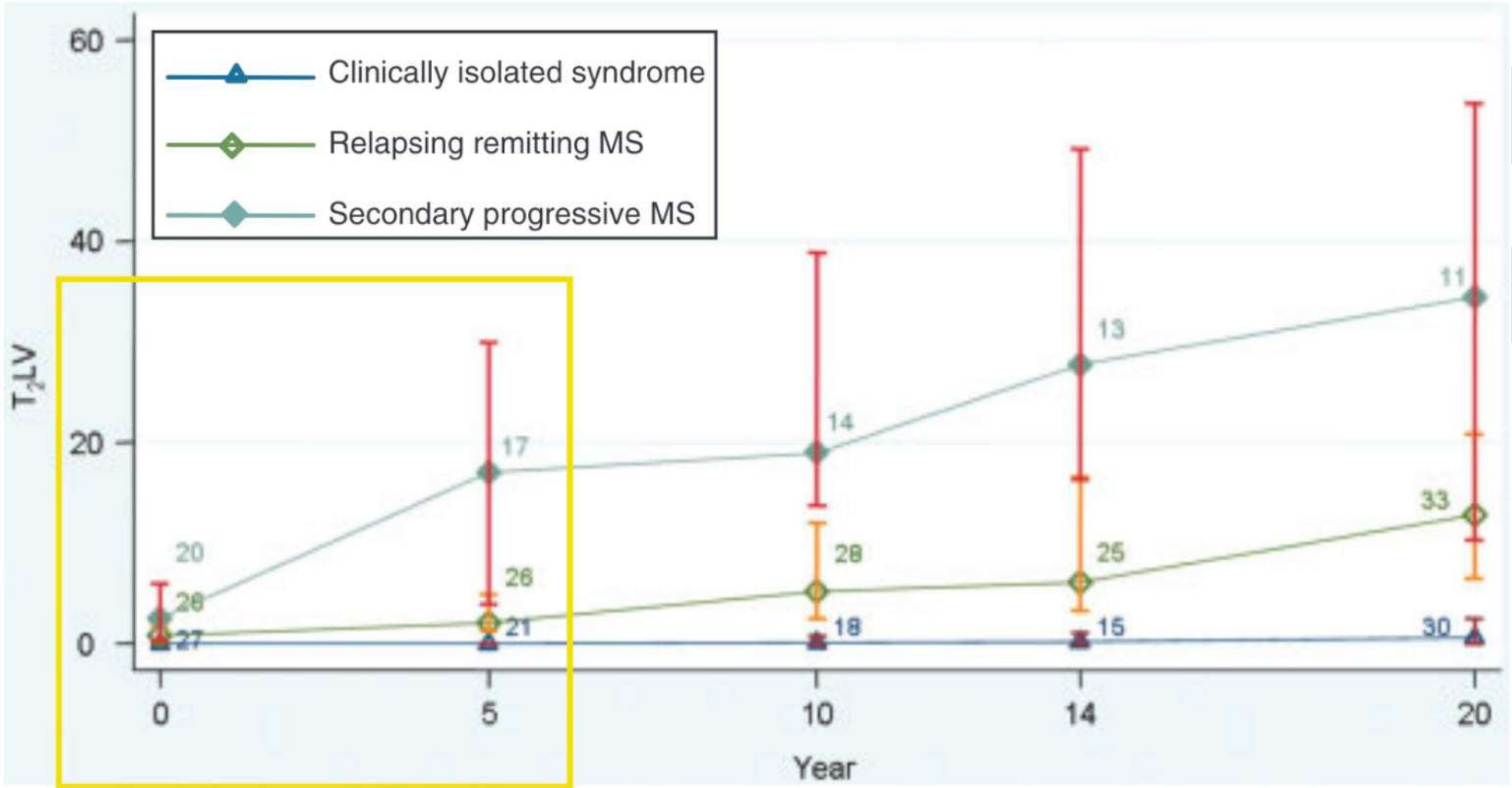
Audoin et al – JNNP 2010

4. Temporalité ?

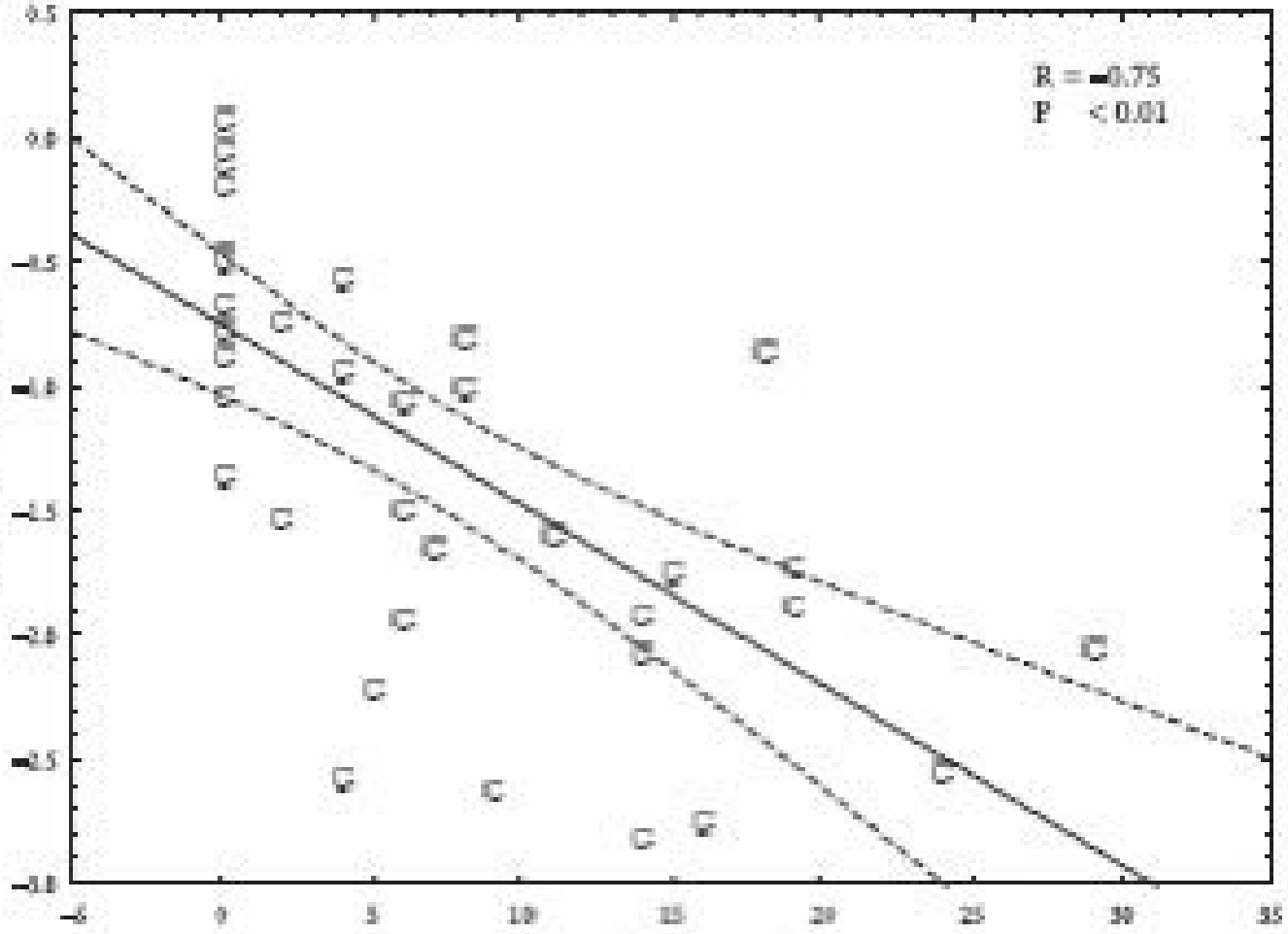
doi:10.1093/brain/awm329 *Brain* (2008), **131**, 808–817

Disability and T_2 MRI lesions: a 20-year follow-up of patients with relapse onset of multiple sclerosis

L. K. Fisniku,[1,2] P. A. Brex,[4] D. R. Altmann,[1,5] K. A. Miszkiel,[6] C. E. Benton,[6] R. Lanyon,[1,2] A. J. Thompson[1,3] and D. H. Miller[1,2]



Delayed effects of lesions on brain atrophy



The **number of new lesions in the first 6 months** does not correlate with brain volume at 6 months, well with brain volume at 12 months and very **well with brain volume at 18 months**

Paolillo et al,J Neurol, 2004

Qu'a-t-on appris de l'imagerie dans la sclérose en plaques ?

Partie II – Modifications fonctionnelles

Dr Adil MAAROUF

Neurologue

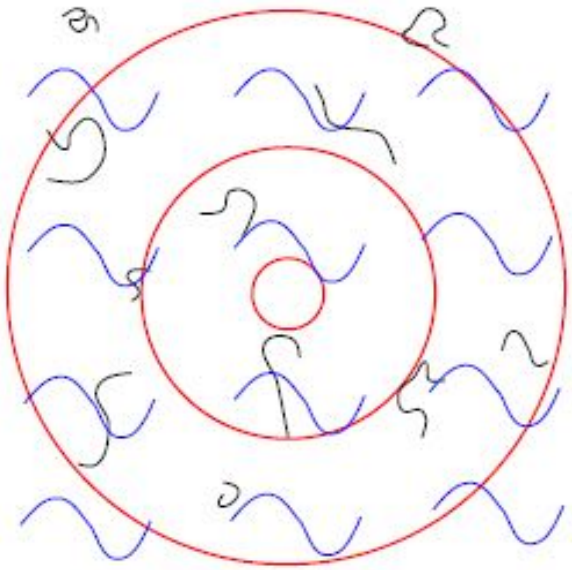
Maladie Inflammatoire du Cerveau et de la Moelle Epinière (MICeME)

Assistance Publique – Hôpitaux de Marseille

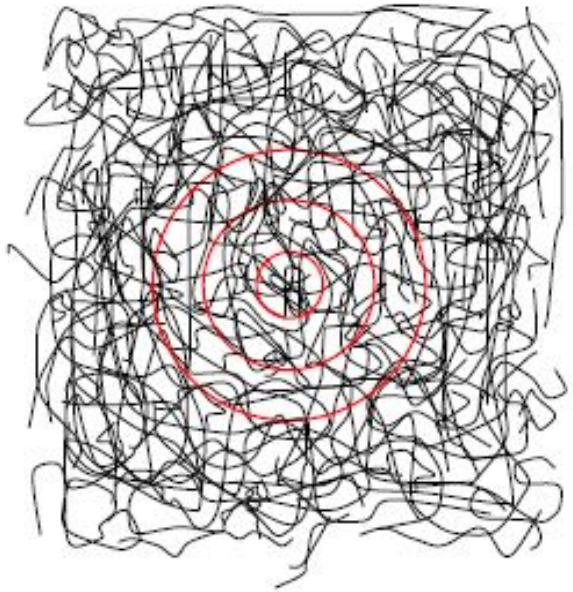
5. Comportement du système ?

Imagerie de diffusion

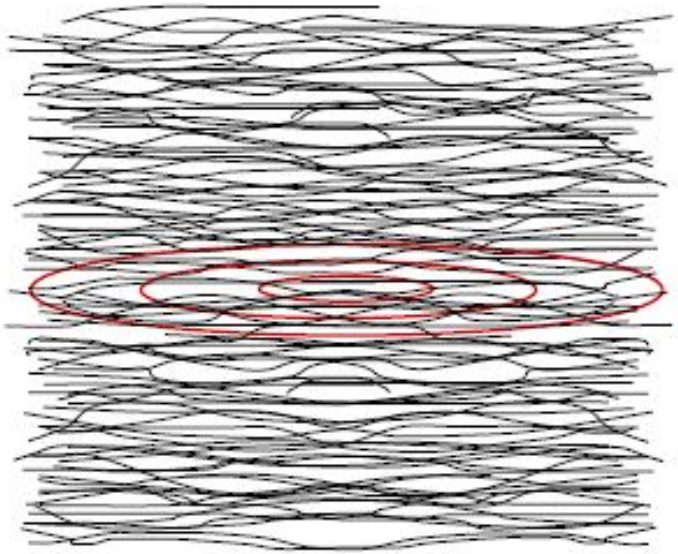
Mouvements brownien des molécules d'eau :



Diffusion libre

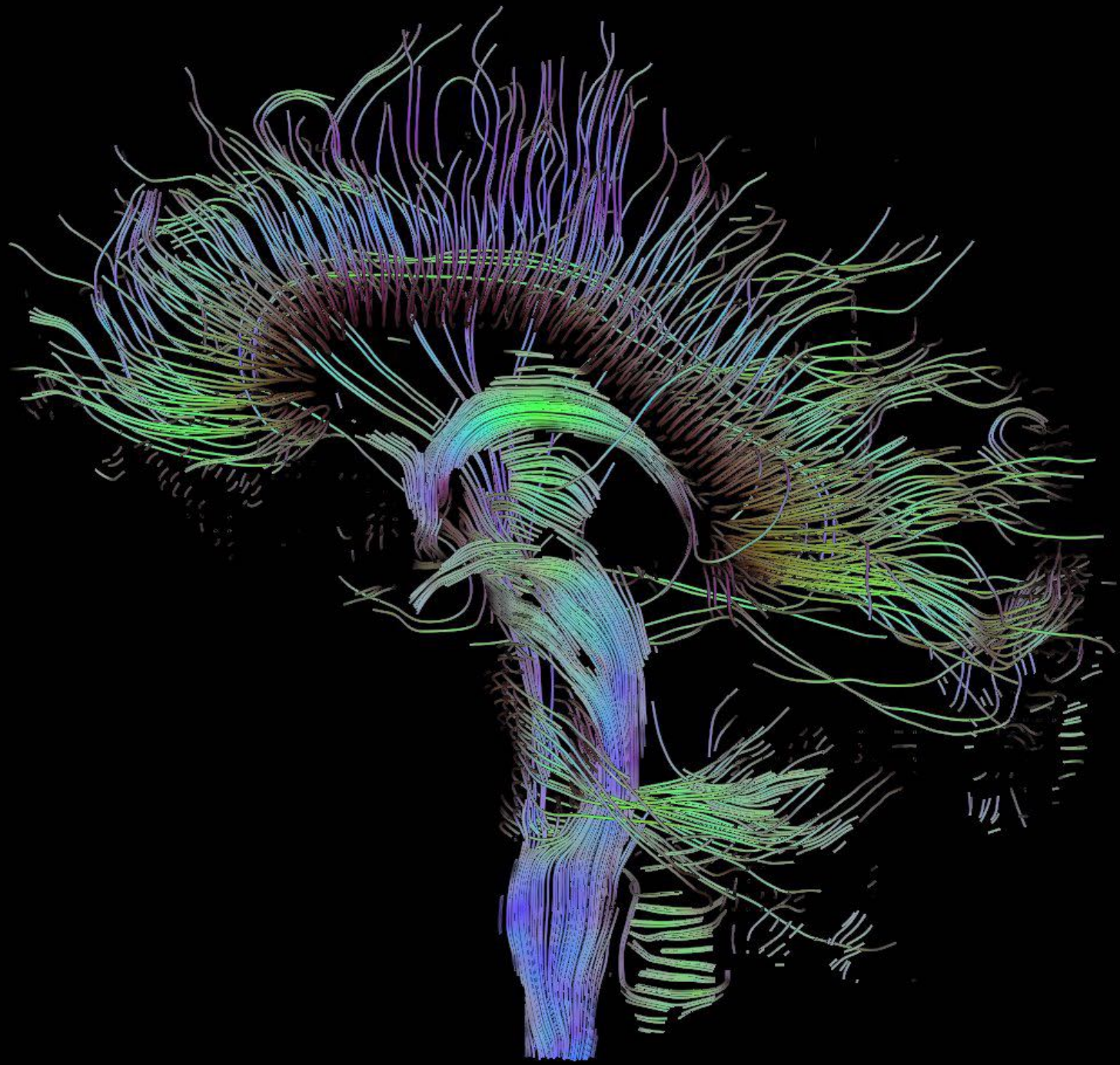


Diffusion restreinte isotrope



Diffusion restreinte anisotrope

S



P

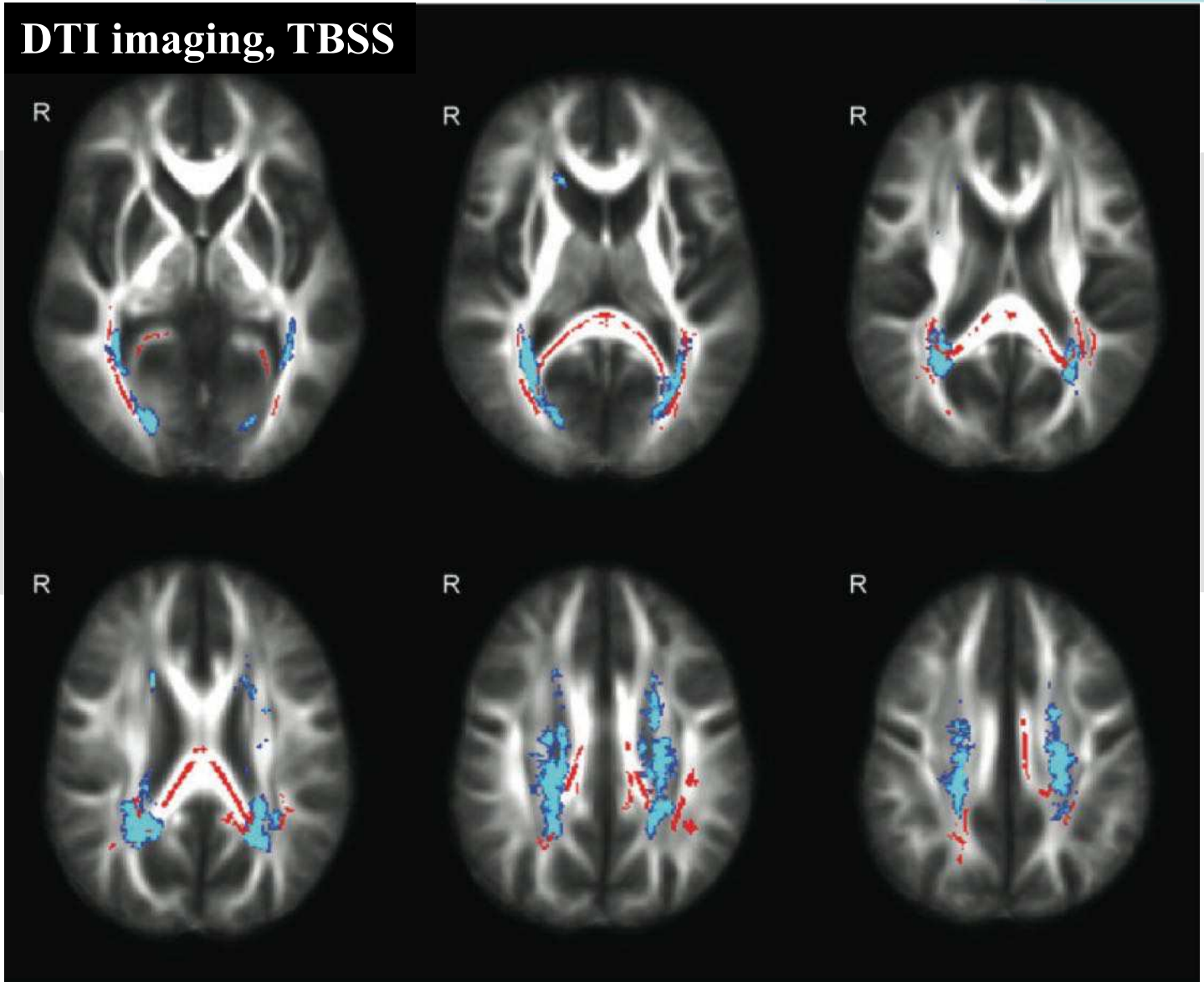
Disconnection as a mechanism for cognitive dysfunction in multiple sclerosis

R. A. Dineen,[1] J. Vilisaar,[2] J. Hlinka,[1] C. M. Bradshaw,[3] P. S. Morgan,[1] C. S. Constantinescu[2] and D. P. Auer[1]

Brain 2009: 132; 239–249 | 239

BRAIN
A JOURNAL OF NEUROLOGY

DTI imaging, TBSS



Regional correlation between **PASAT (composite)**, BVRT, CVLT II and Fractionnal Anisotropie

(37 patients, RRMS + SPMS, 10 years of disease duration)

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A JOURNAL OF NEUROLOGY

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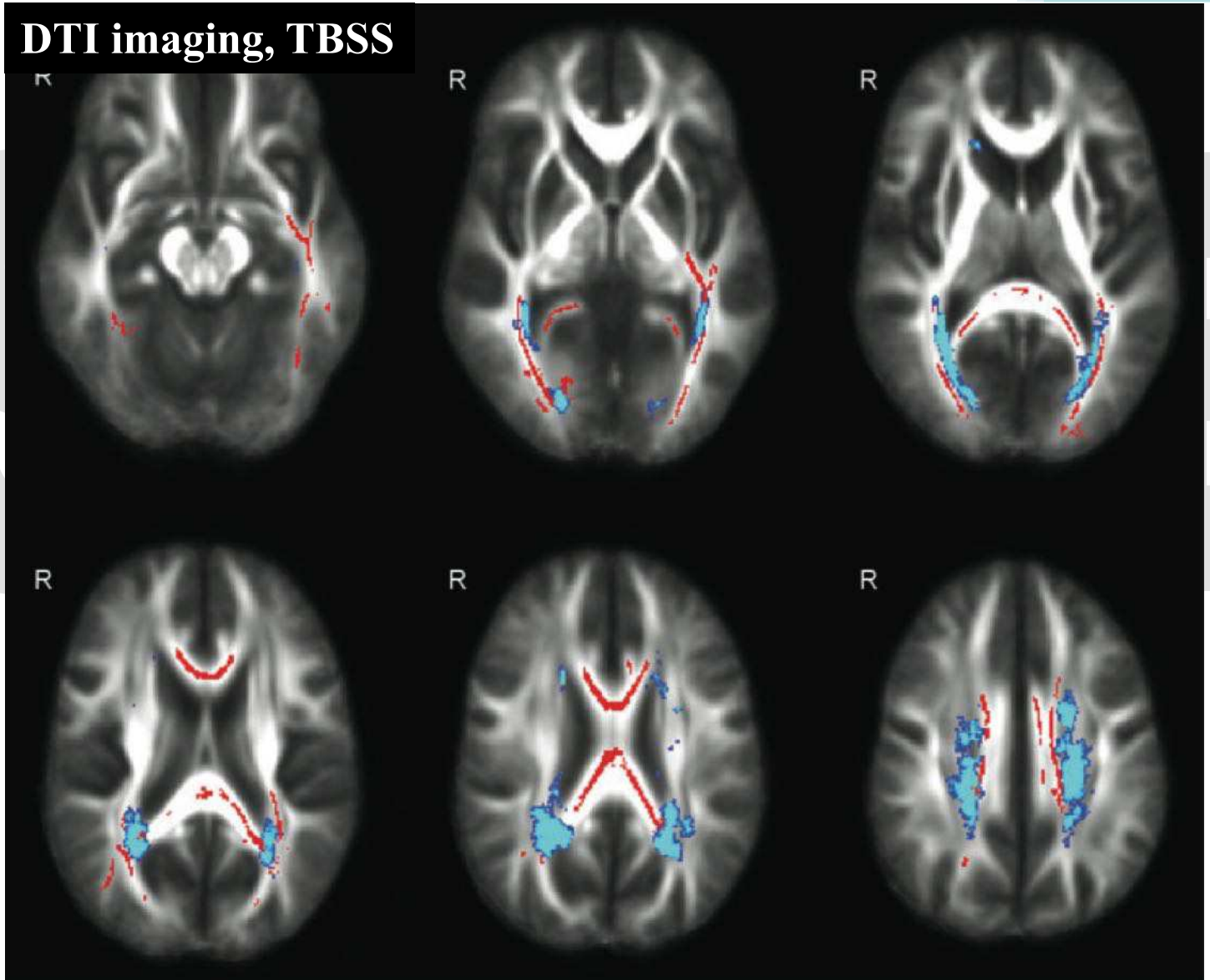

Regional correlation between PASAT, **BVRT (visual)**, CVLT II and Fractionnal Anisotropie

(37 patients, RRMS + SPMS, 10 years of disease duration)

Disconnection as a mechanism for cognitive dysfunction in multiple sclerosis

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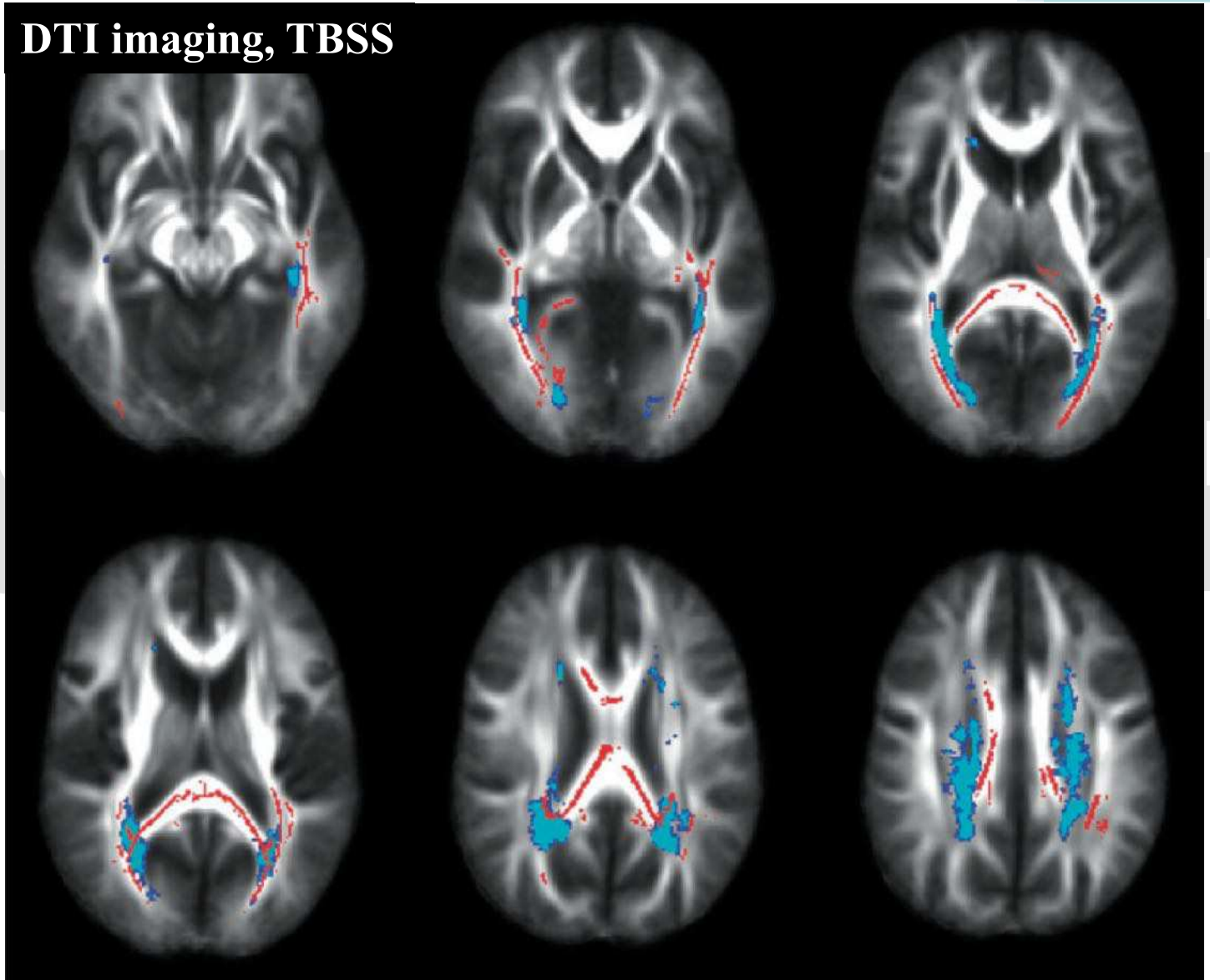
A JOURNAL OF NEUROLOGY



Regional correlation between PASAT, BVRT, **CVLT II (verbal)** and Fractionnal Anisotropie

(37 patients, RRMS + SPMS, 10 years of disease duration)

NAWM and cognitive impairment

- Thalamic radiations [1,2]
- Superior and inferior longitudinal fasciculus [3,4]
- Corpus callosum [1–6]
- Major forceps [3,4]
- Cingulate [3,4]

1 Schoonheim MM, Hum Brain Mapp. 2014

2 Yu HJ NeuroImage. 2012

3 Hecke WV J Magn Reson Imaging. 2010

4 Hulst HE Neurology. 2013

5 Llufriu S PLoS ONE. 2012

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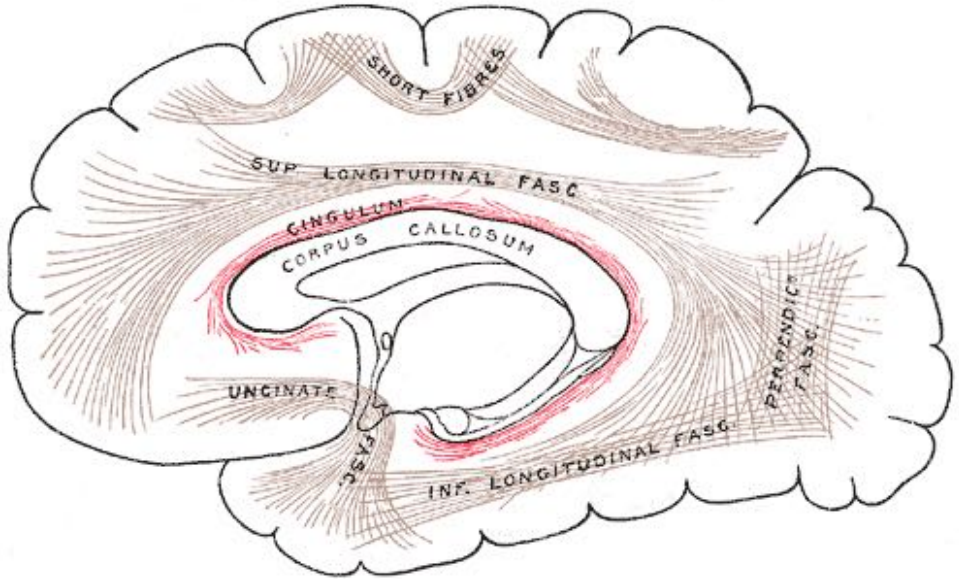
Disconnection hypothesis



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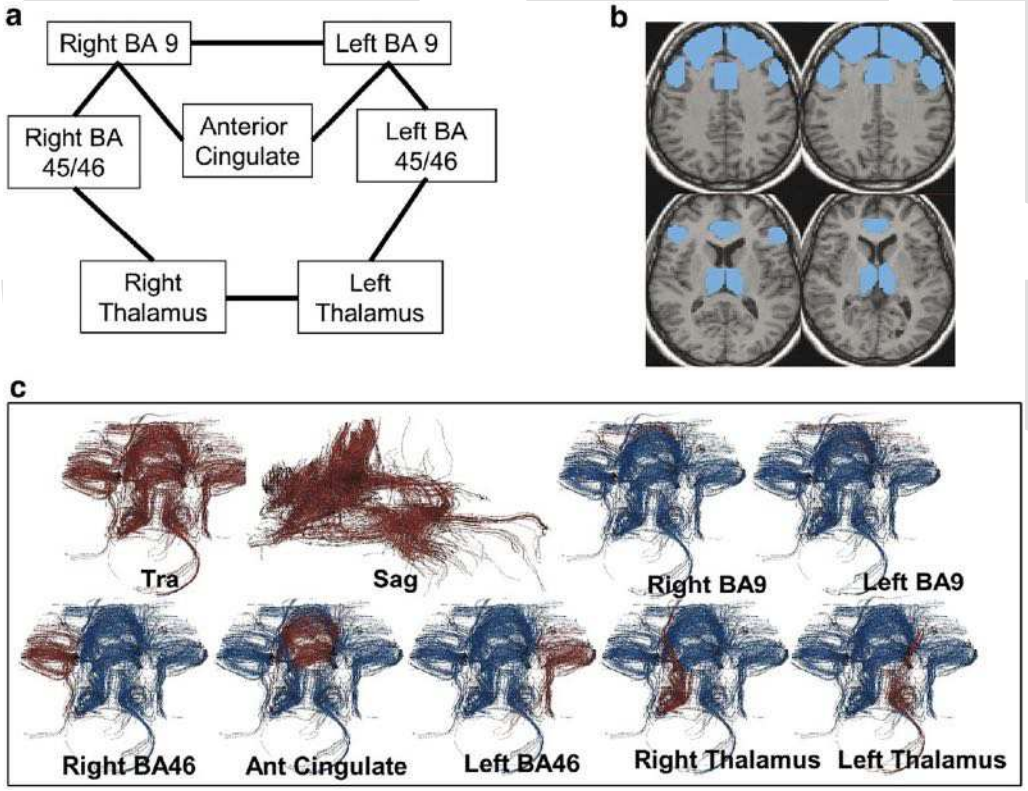
Structure of WM bundles constituting the working memory system in early multiple sclerosis: A quantitative DTI tractography study

Bertrand Audoin,[a,b] Maxime Guye,[a] Françoise Reuter,[a,b] My-Van Au Duong,[a] Sylviane Confort-Gouny,[a] Irina Malikova,[a,b] Elisabeth Soulier,[a] Patrick Viout,[a] André Ali Chérif,[b] Patrick J. Cozzone,[a] Jean Pelletier,[a,b] and Jean-Philippe Ranjeva[a,*]

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 36 (2007) 1324–1330

Role of reactive structural WM plasticity in compensation



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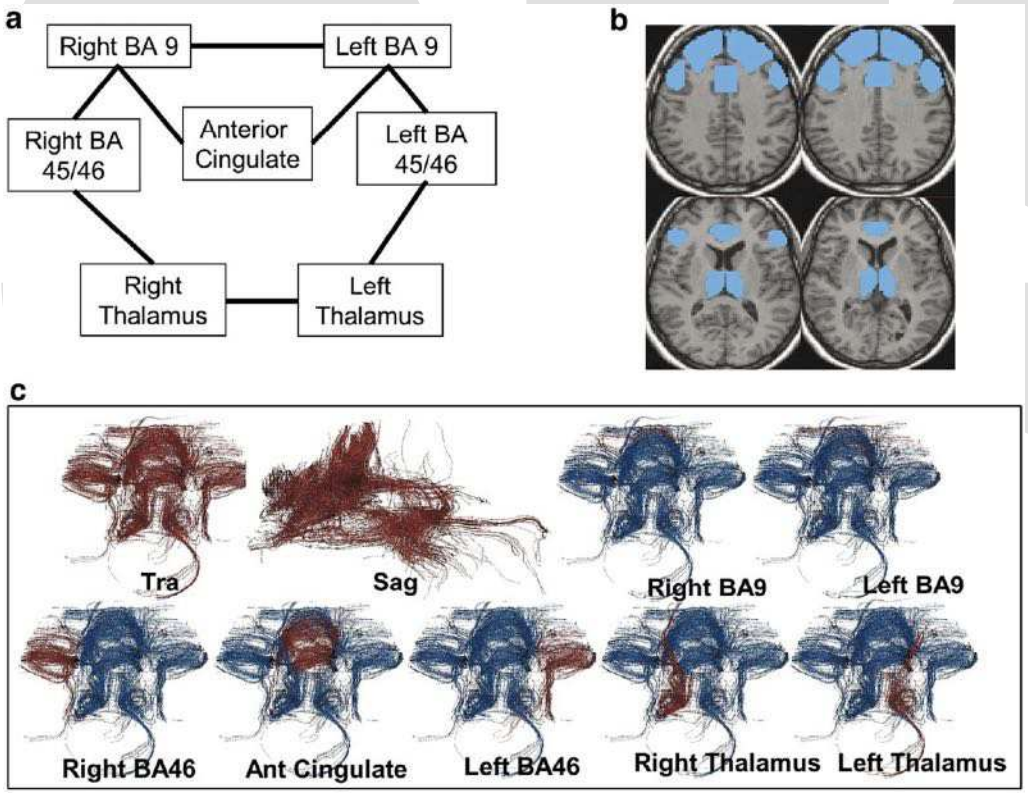

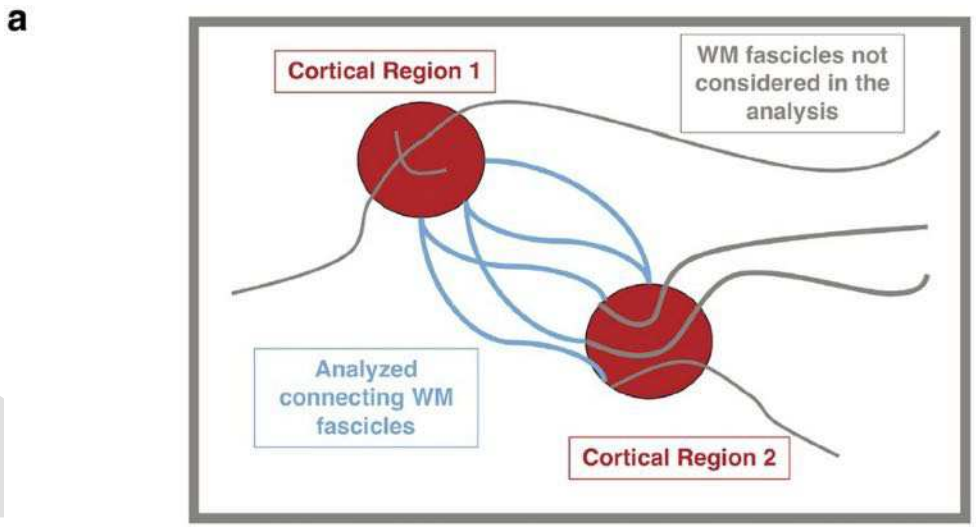

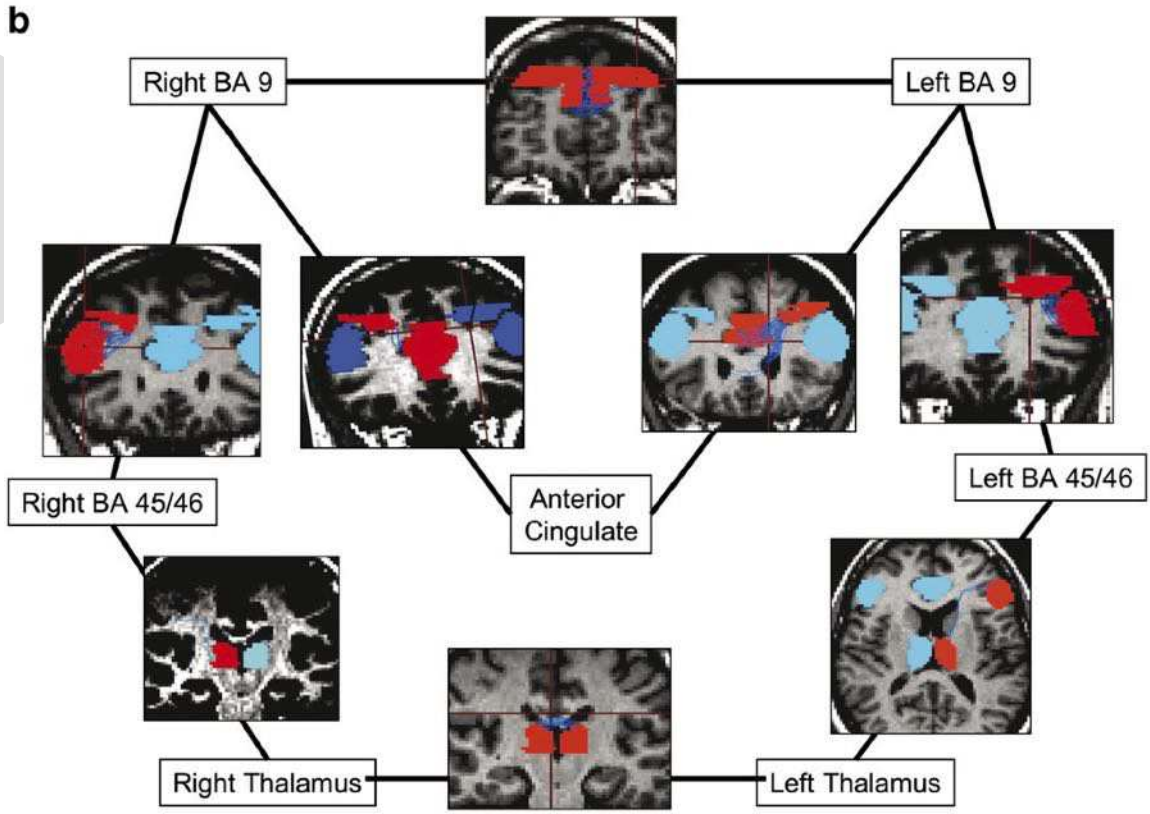

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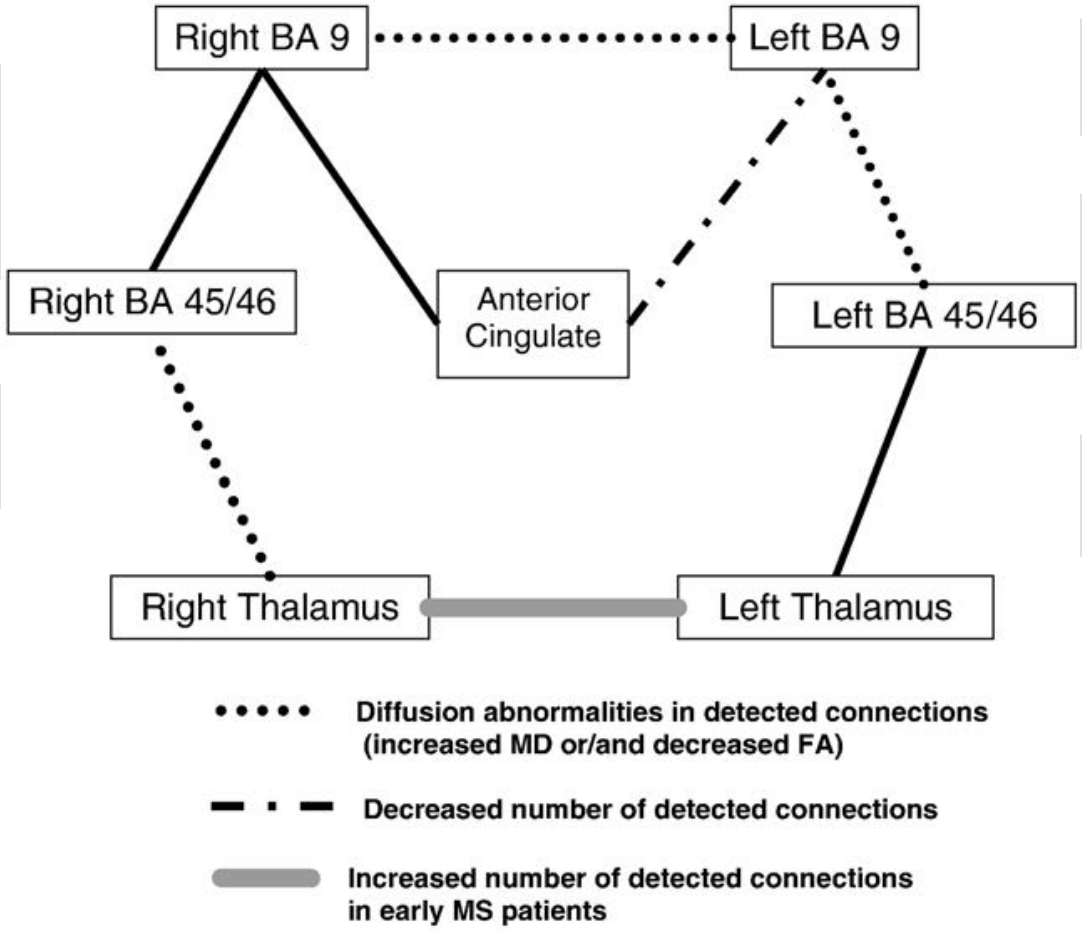

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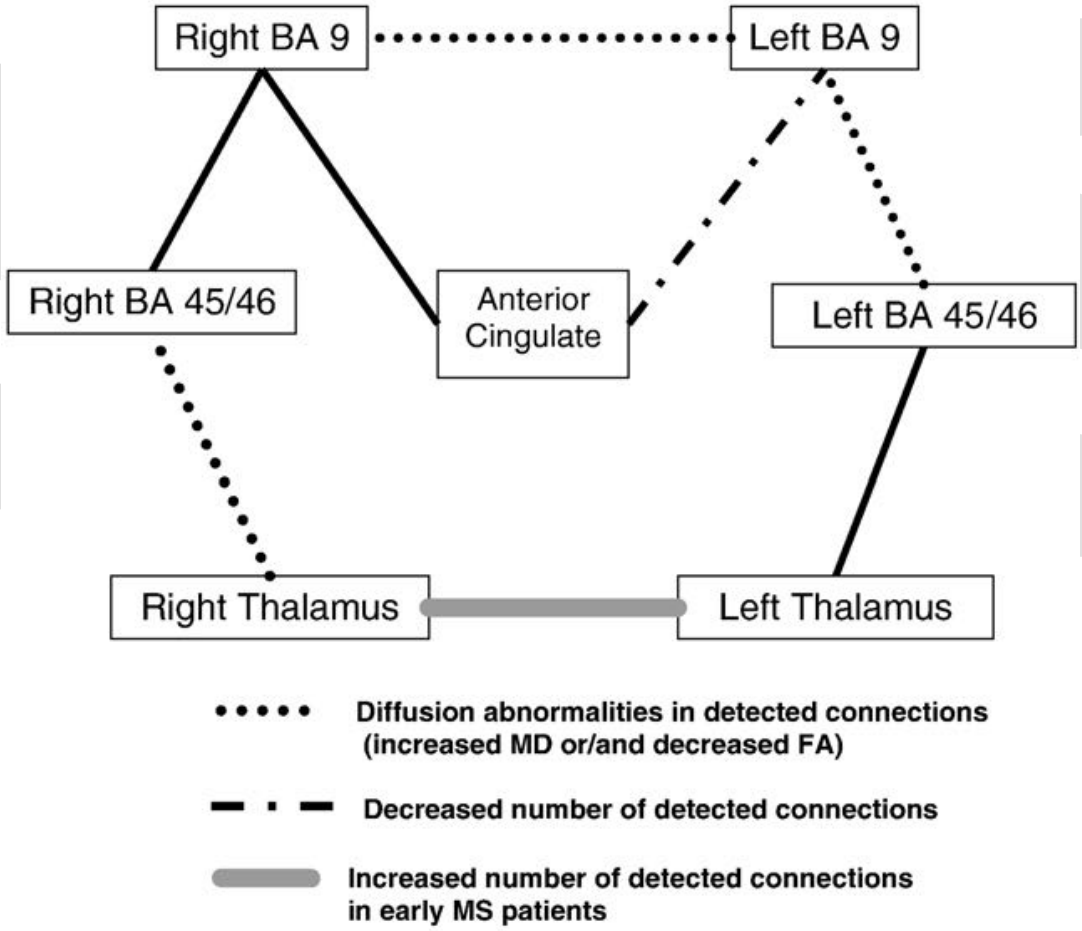

- ↑ number of connections between the 2 thalami was inversely correlated with the activation of the left BA 45/46 (Rho=−0.582, p=0.023)
- Number of connections between the **left** BA45/46 ⇔ BA9 was inversely correlated with the hyperactivation in the **right** BA 45/46 (Rho=−0.536, p=0.032)
- FA bundles **right** thalamus ⇔ BA 45/46 was correlated with the hyperactivation in the **right** BA 45/46 (Rho = 0.596, p = 0.032)
- FA bundles right thalamus ⇔ BA 45/46 was inversely correlated with f. connectivity between left and right BA 45/46

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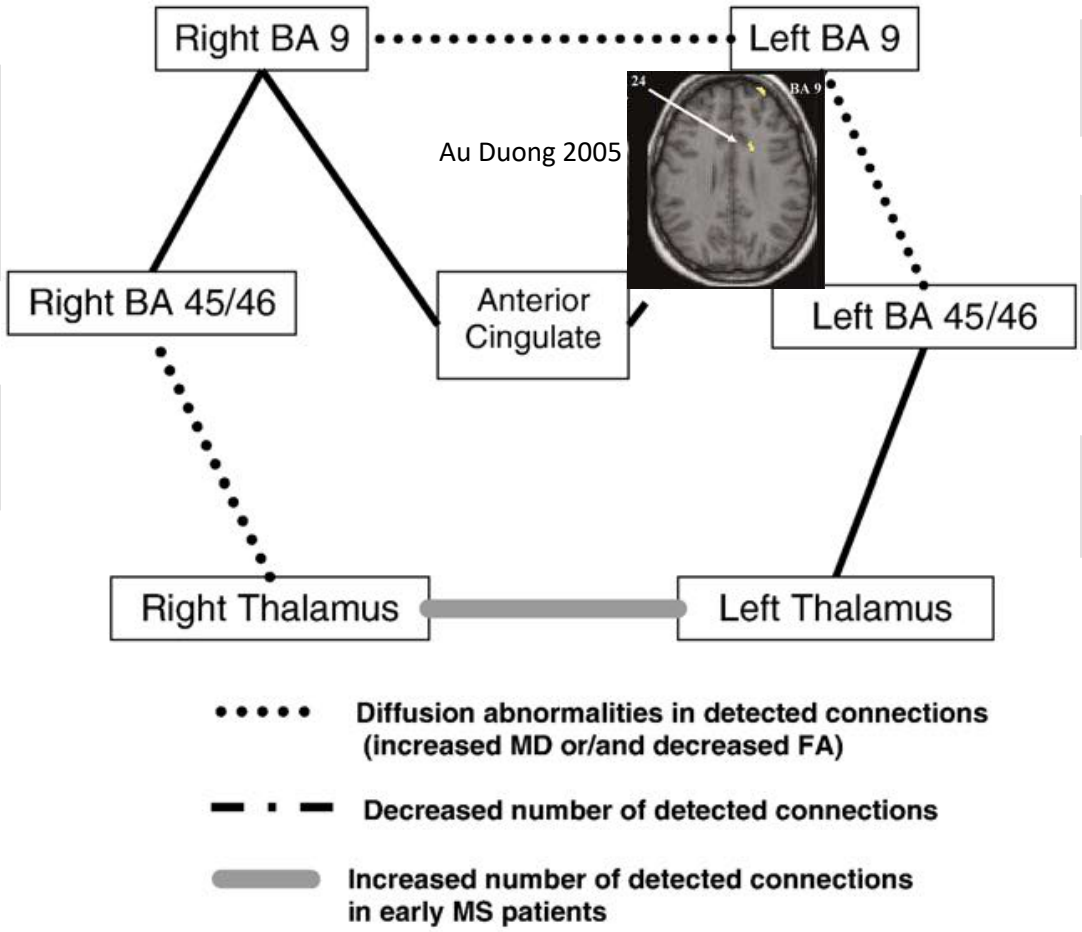

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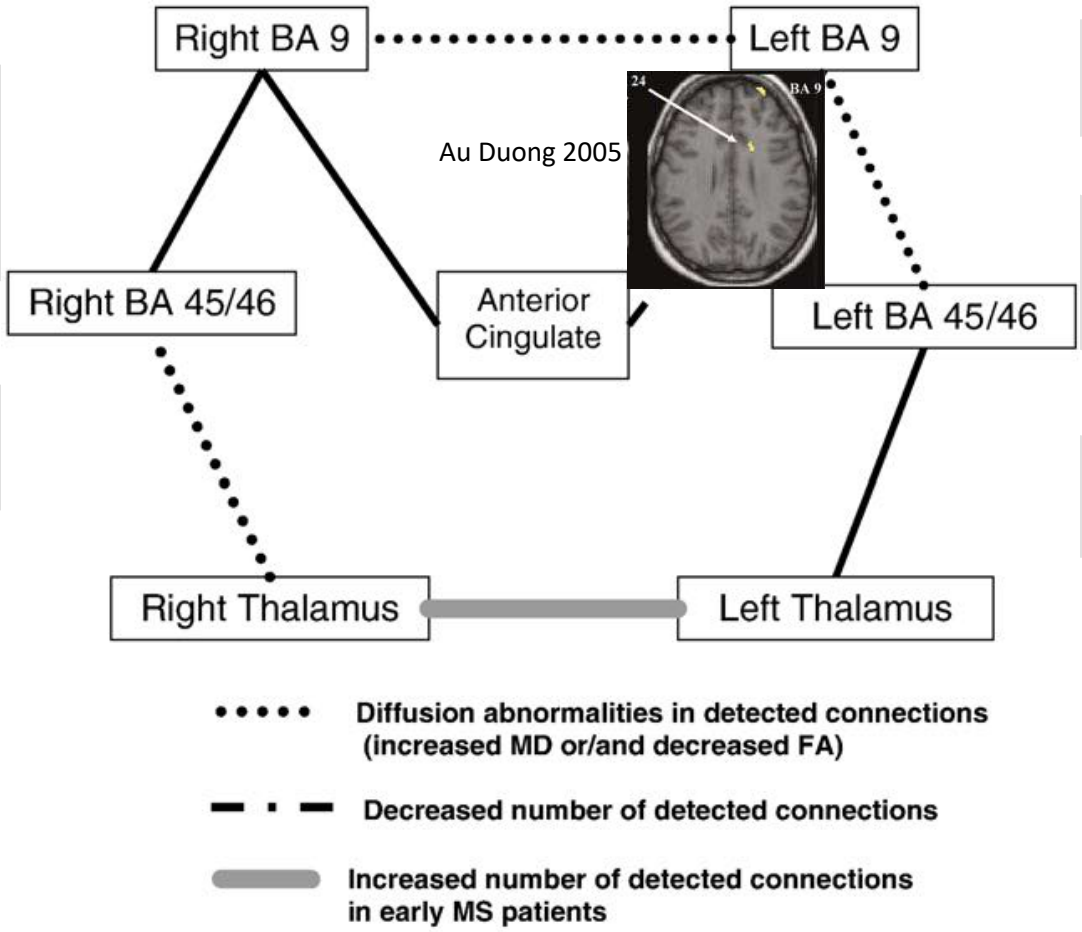

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These results suggest the occurrence of structural and functional brain reorganization processes shifting the left prefrontal activities involved in working memory towards alternative right hemispheric networks

Imagerie fonctionnelle

- Analyse du signal Blood Oxygen Level-Dependent
- Correspond à la réponse hémodynamique qui accompagne l'activité neuronale
- Détection des variations de signal IRM liées aux variations d'oxygénation du sang (désoxyhémoglobine) après la cascade hémodynamique consécutive à une activation neuronale (contraste BOLD)

Adaptive Functional Changes in the Cerebral Cortex of Patients with Nondisabling Multiple Sclerosis Correlate with the Extent of Brain Structural Damage

Maria A. Rocca, MD,[1] Andrea Falini, MD,[3] Bruno Colombo, MD,[2] Giuseppe Scotti, MD,[3] Giancarlo Comi, MD,[2] and Massimo Filippi, MD[1]

Ann Neurol . 2002

- contralateral (🔷) and ipsilateral (♣) primary somatomotor cortex,
- bilateral supplementary motor area (◗),
- contralateral (✔) and ipsilateral (●) SII,
- contralateral (⚡) and ipsilateral (▼) precentral gyrus,
- contralateral (†) and ipsilateral (*) inferior frontal gyrus,
- ipsilateral (✜) cerebellum

right-handed healthy volunteers	multiple sclerosis patients

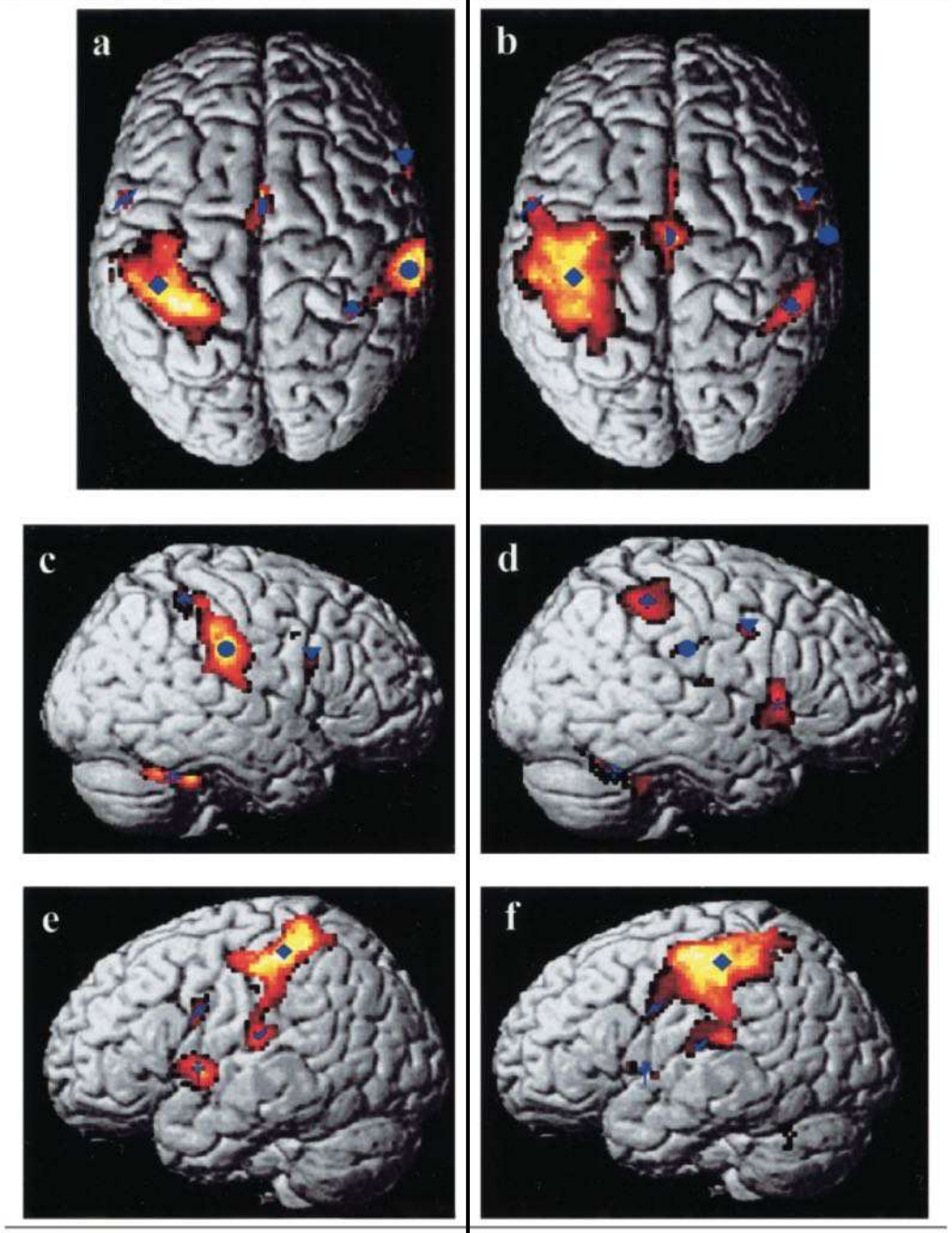

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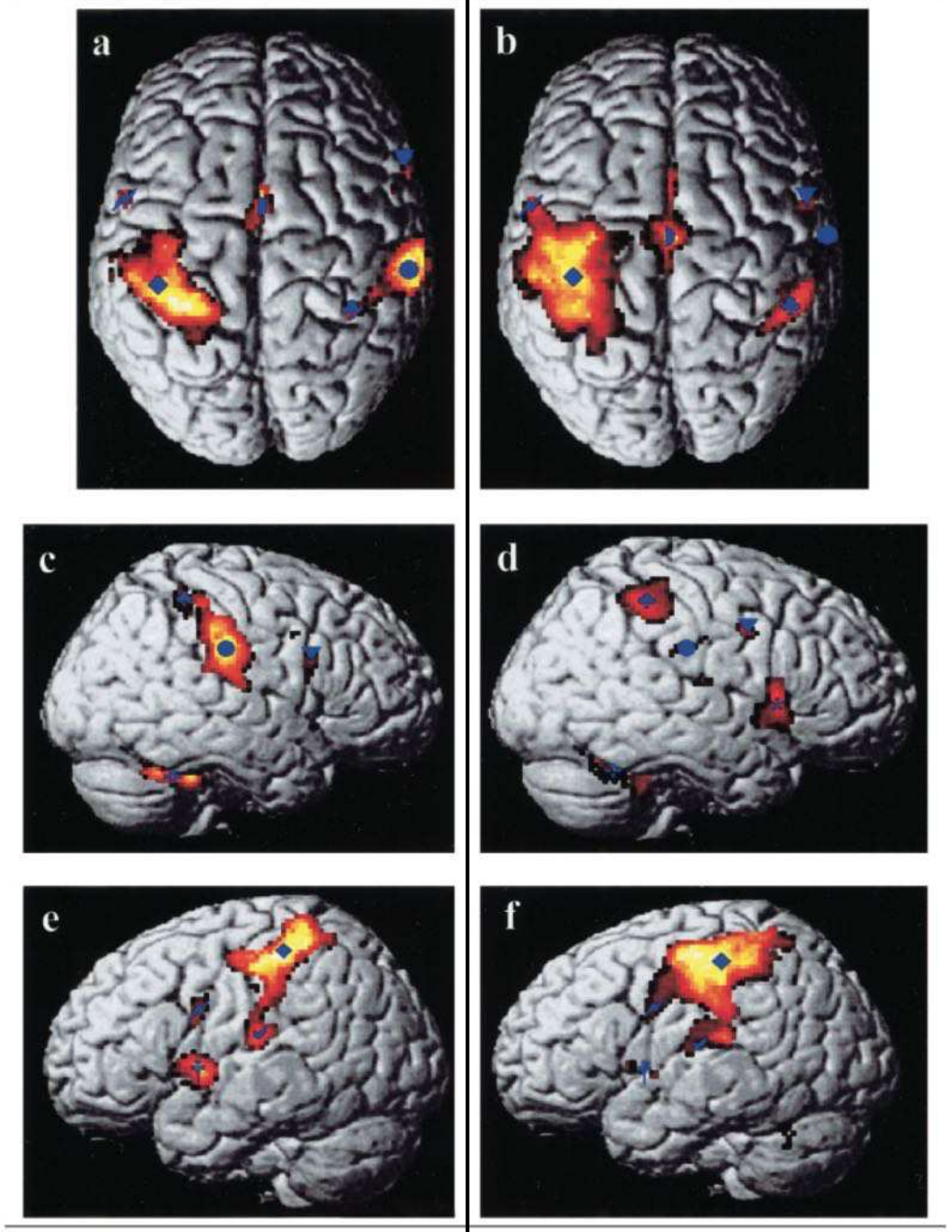
Table 2. Magnetization Transfer Ratio and $\bar{D}$ Histogram-Derived Metrics of the Normal-Appearing Brain Tissue from Healthy Volunteers and MS Patients

	Healthy Volunteers	MS Patients	*p*
Average MTR (SD, %)	40.4 (1.2)	39.5 (1.0)	n.s.
Mean MTR histogram peak height (SD)	115.1 (12.0)	107.5 (12.8)	0.05
Mean MTR histogram peak position (SD, %)	35.7 (1.6)	34.6 (1.5)	0.03
Average $\bar{D}$ (SD, $\times 10^{-3}$ mm^2 s^{-1})	0.91 (0.05)	0.96 (0.04)	0.006
Mean $\bar{D}$ histogram peak height (SD)	107.0 (13.6)	95.1 (16.2)	0.01
Mean $\bar{D}$ histogram peak position (SD, $\times 10^{-3}$ mm^2 s^{-1})	0.74 (0.03)	0.77 (0.04)	0.01

MTR = magnetization transfer ratio; $\bar{D}$ = mean diffusivity; SD = standard deviation; n.s. = not significant.

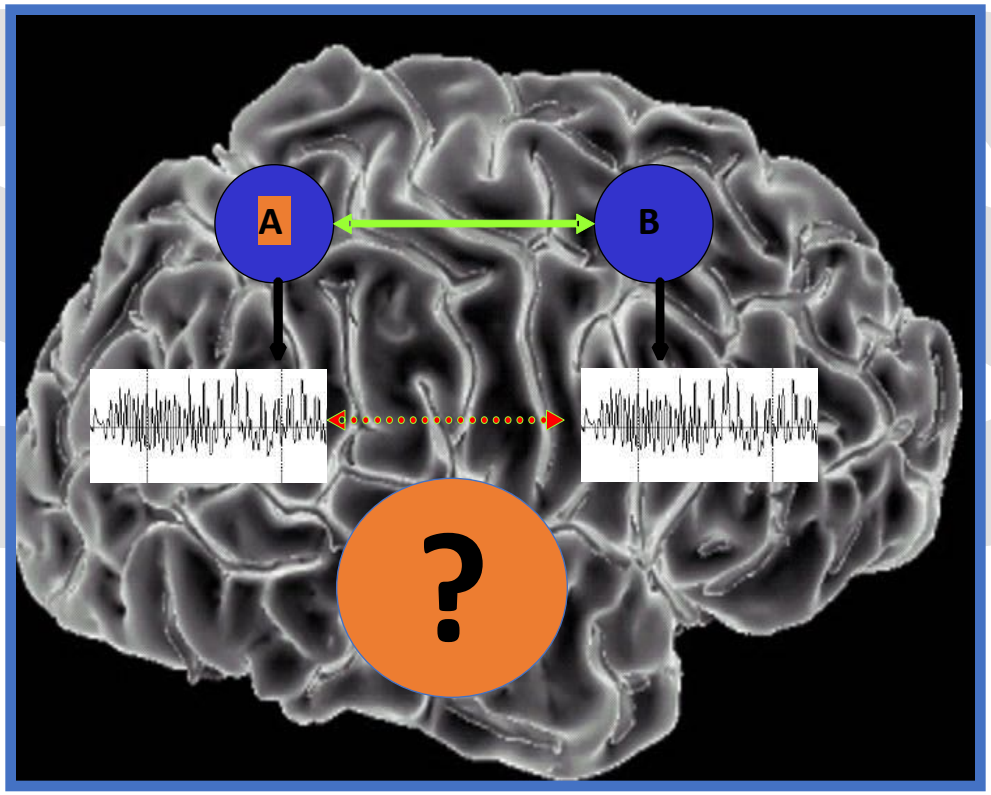
- T2 lesion volume was correlated with activations in the ipsilateral SMA (*r* = 0.80), and in the ipsilateral and contralateral Cingulate MA (*r* = 0.85)
- Average lesion MTR (*r* = -0.78) and average lesion MD (*r* = 0.88) were correlated with relative activation in the contralateral sensorimotor cortex

right-handed healthy volunteers | multiple sclerosis patients

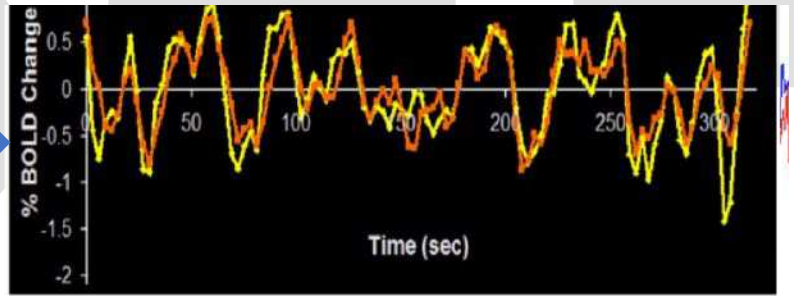


Connectivité cérébrale fonctionnelle et IRMf de repos

- **IRMf de repos**: fluctuations spontanées du signal BOLD à basse fréquence
  Biswald et al. 1995
- **Connectivité fonctionnelle cérébrale au repos**: recherche de corrélations entre les fluctuations au repos du signal BOLD dans différentes régions.



Raichle et Snyder, Neuroimage 2007



Interdépendance statistique entre séries temporelles de A & B
= Couplage fonctionnel entre A & B

MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

Depletion of brain functional connectivity enhancement leads to disability progression in multiple sclerosis: A longitudinal resting-state fMRI study

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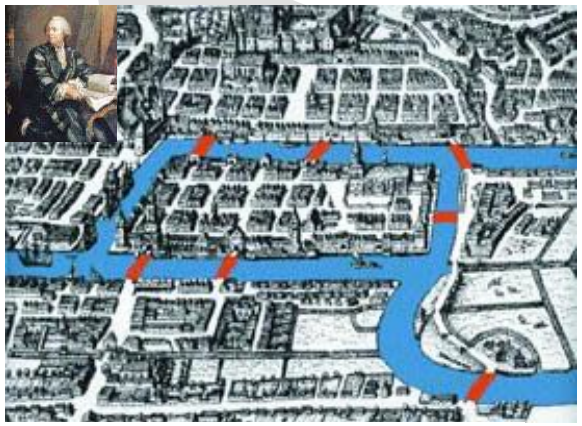
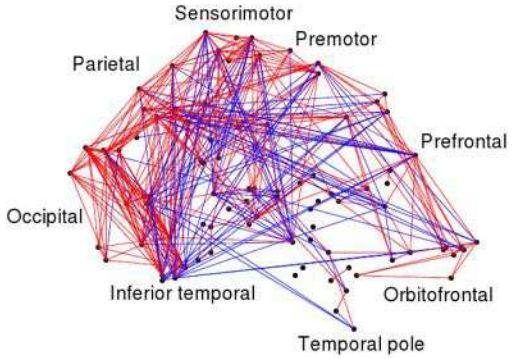
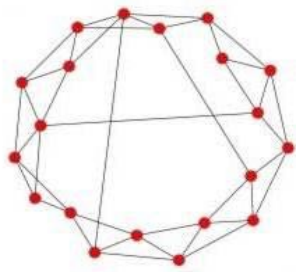
38 RRMS patients (DD= 120 ±32







Graph theory allows to quantify the global organization (not only the main network e.g., ICA)

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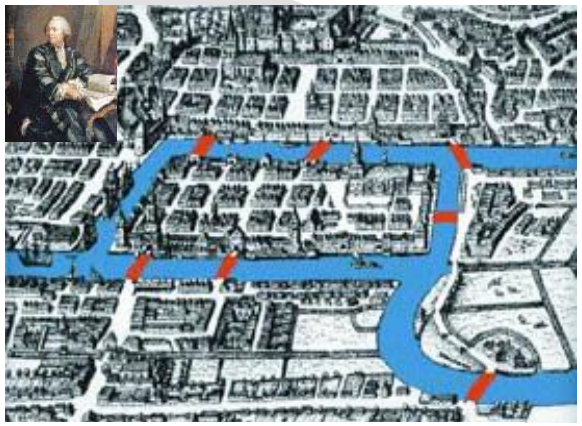

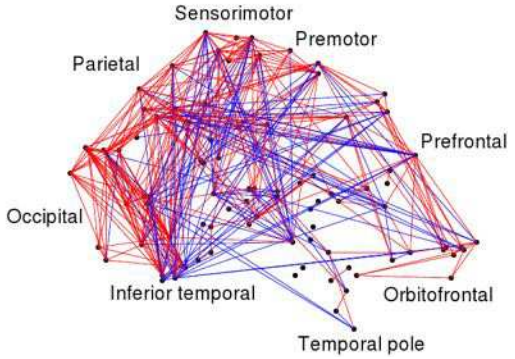

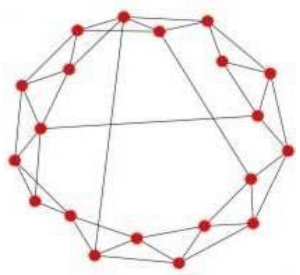

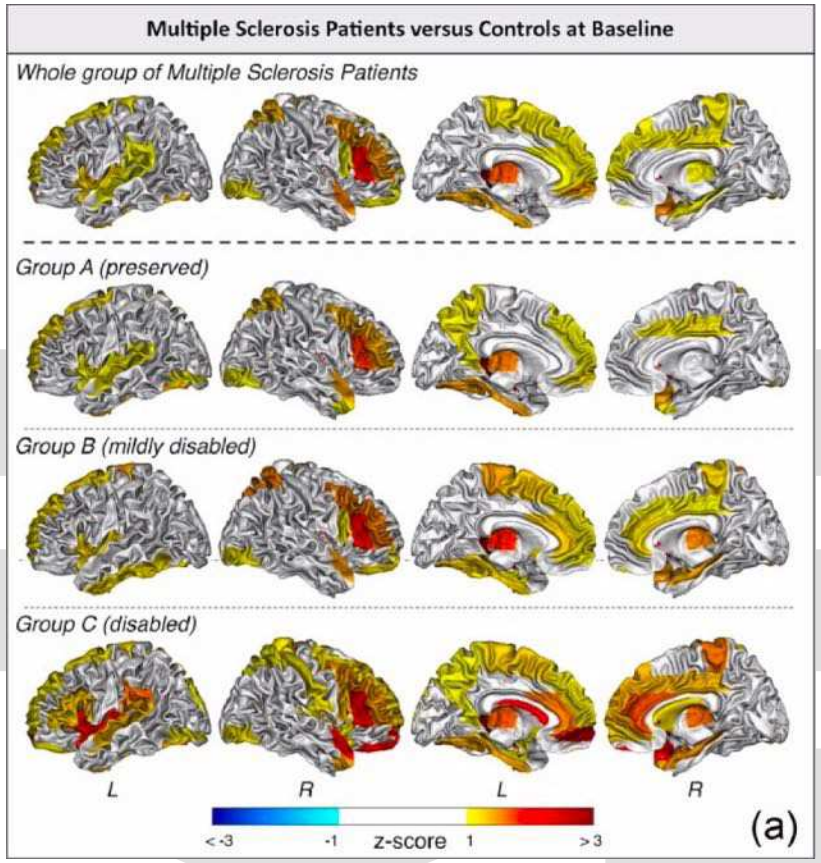

Higher global values of E_{nod} & E_{loc} in patients at baseline

Graph theory allows to quantify the global organization (not only the main network e.g., ICA)

MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

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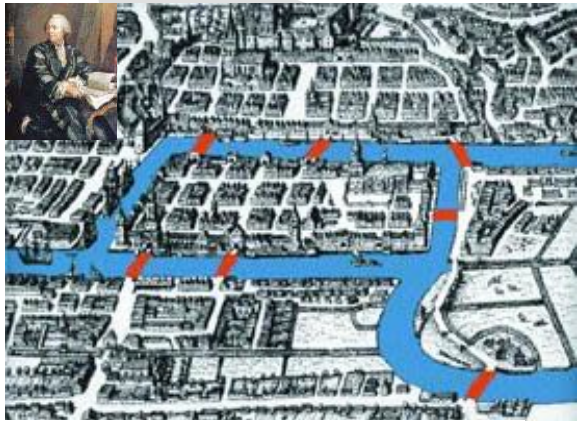
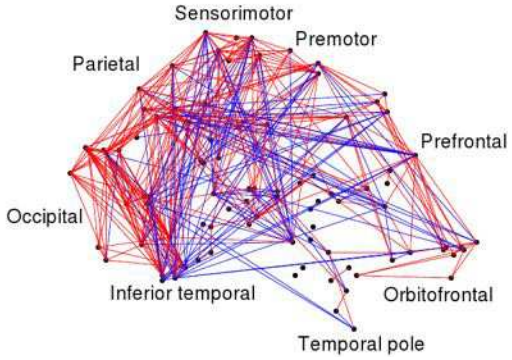
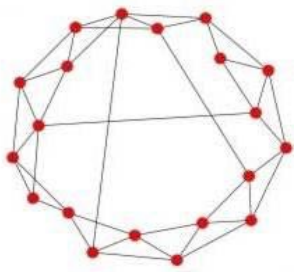
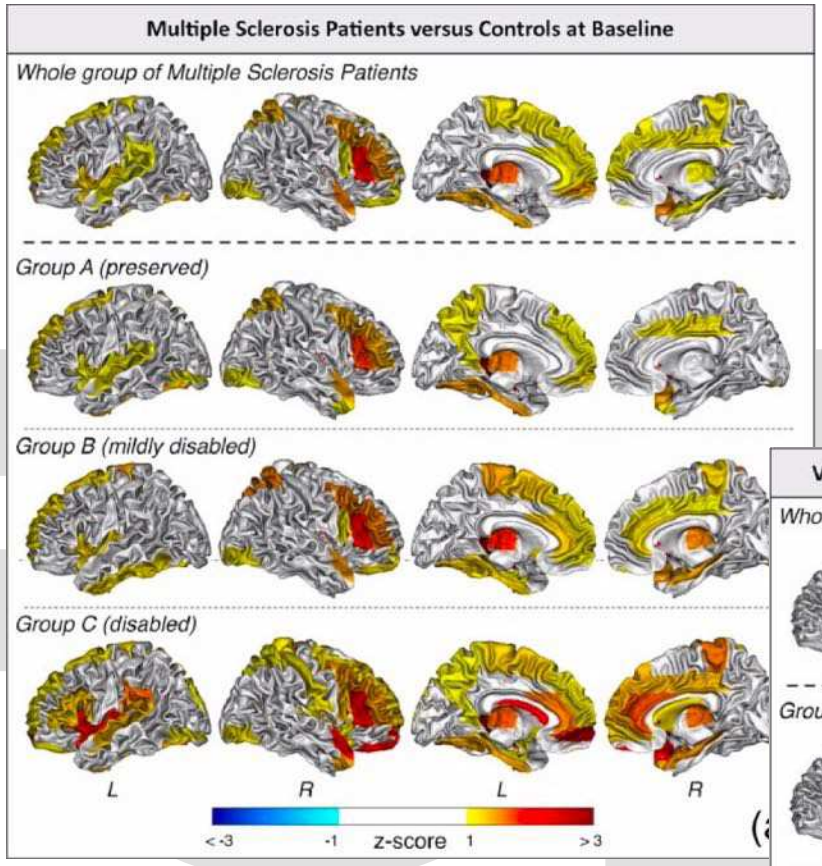




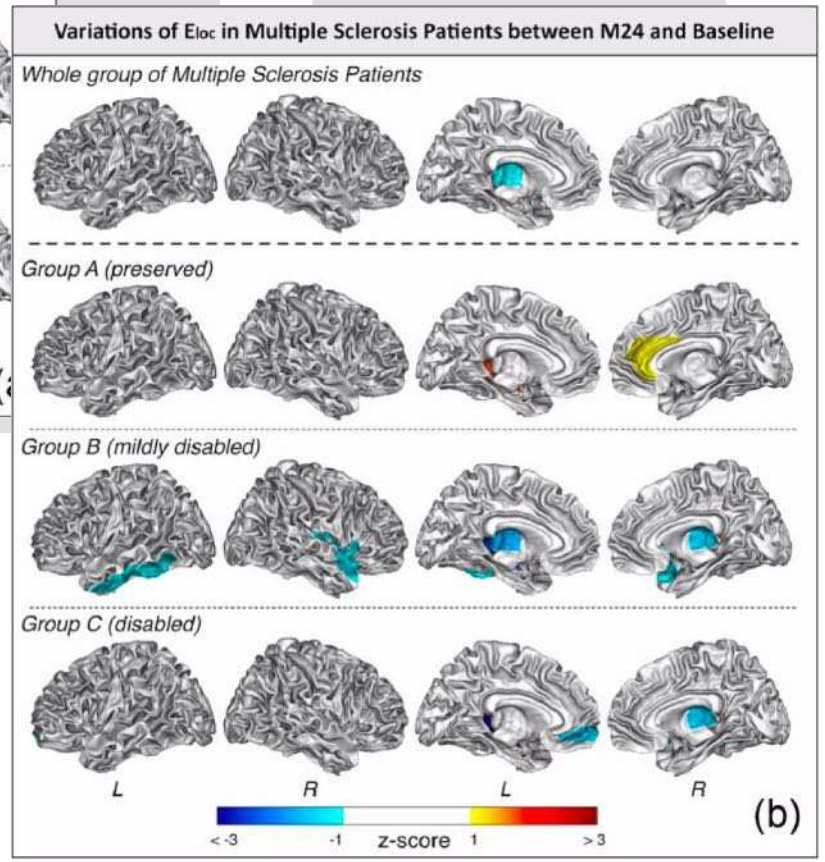




Higher global values of E_{nod} & E_{loc} in patients at baseline

Significant decrease in the whole group at year 2

- Increase in preserved patients
- Decrease in disabled patients



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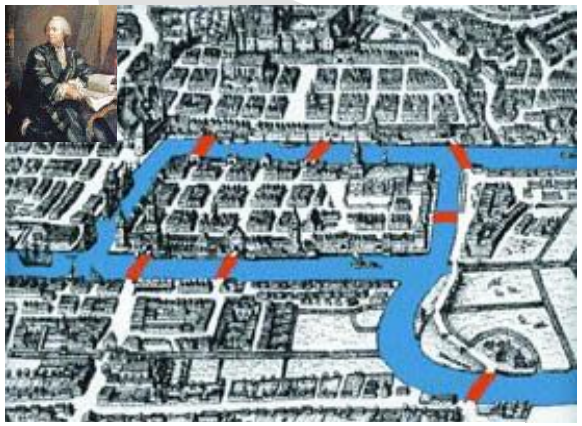
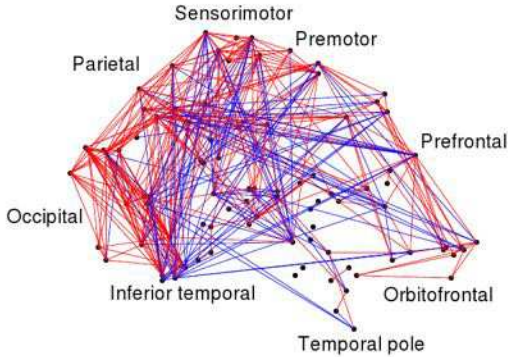
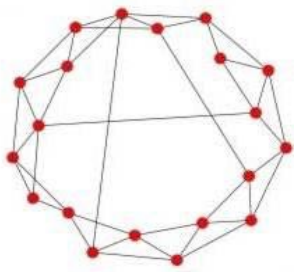
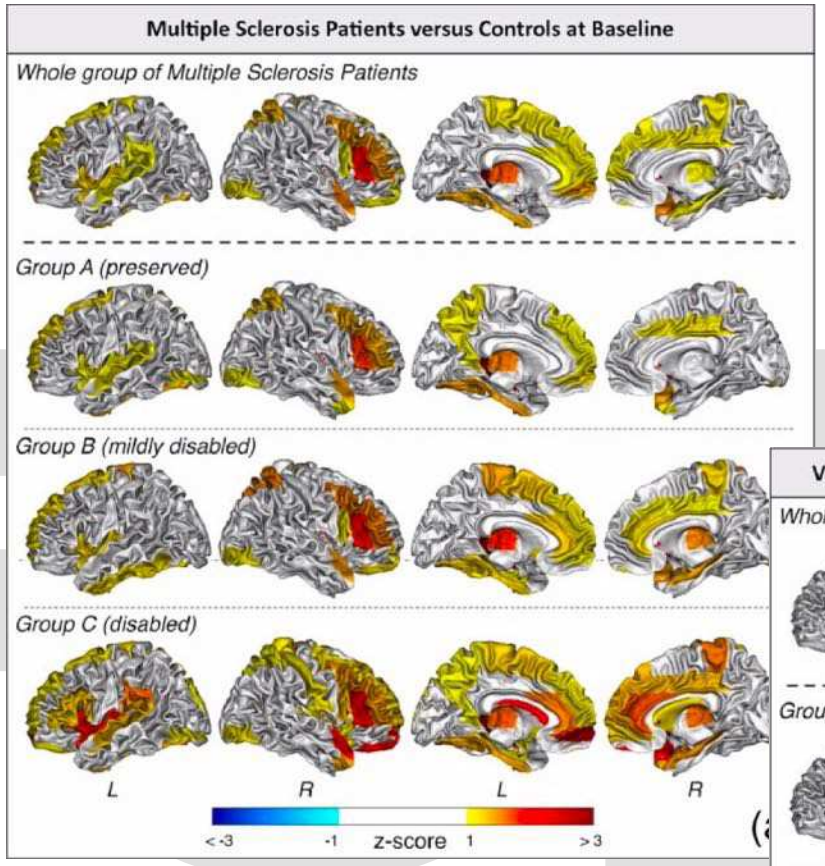
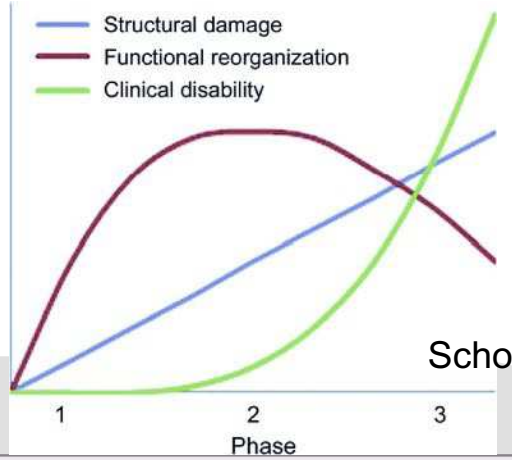


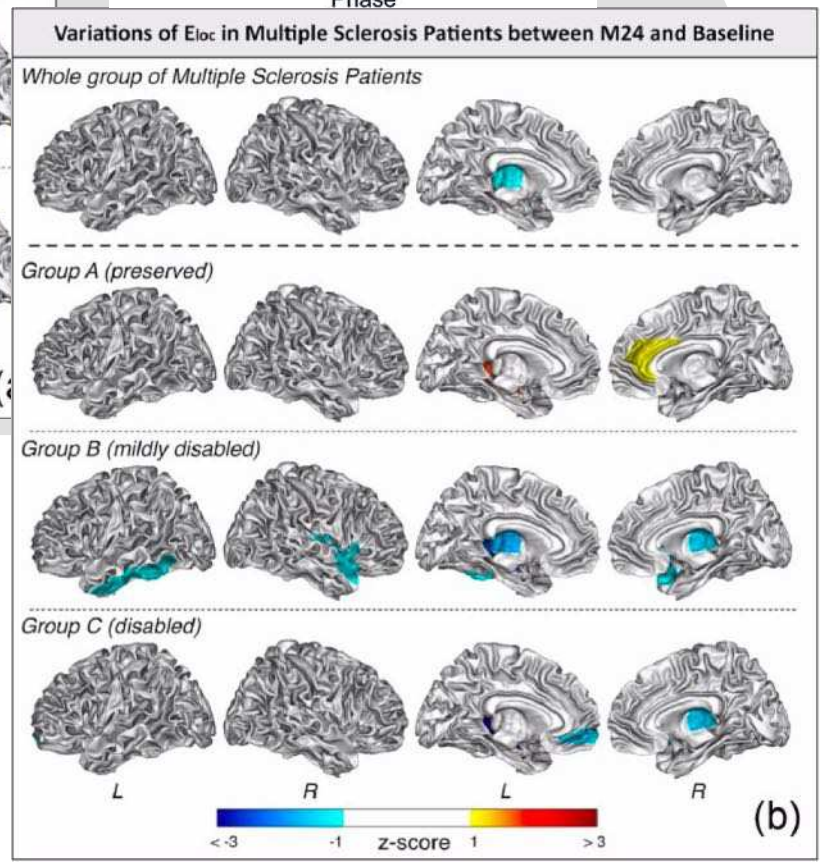








Schoonheim 2010



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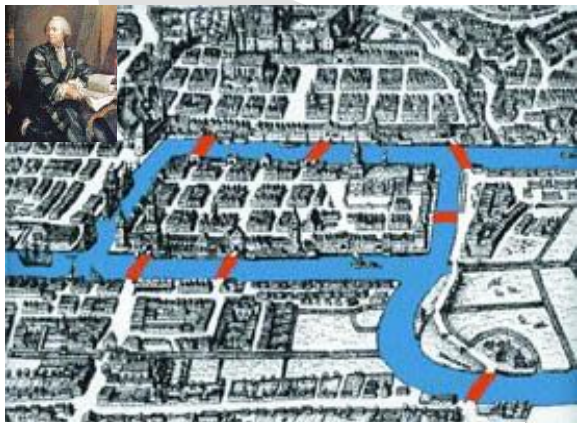
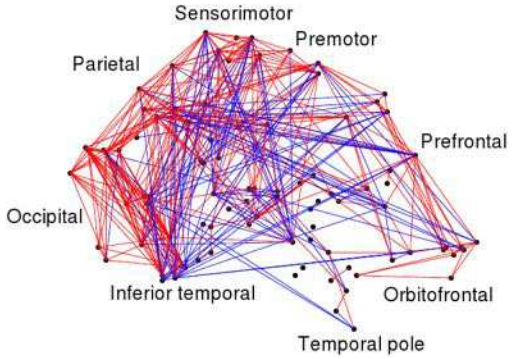
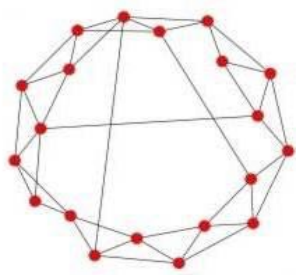
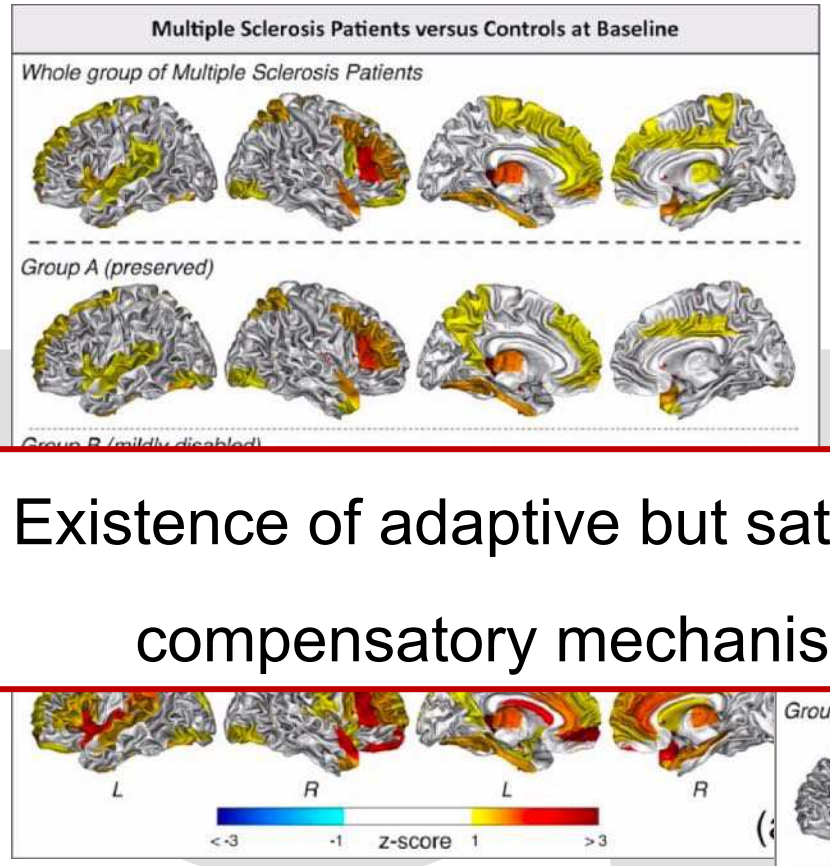
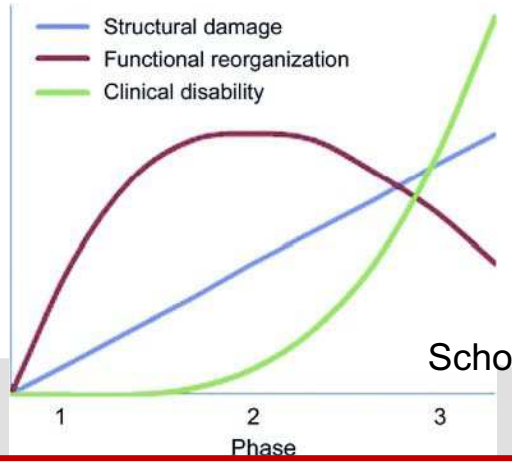






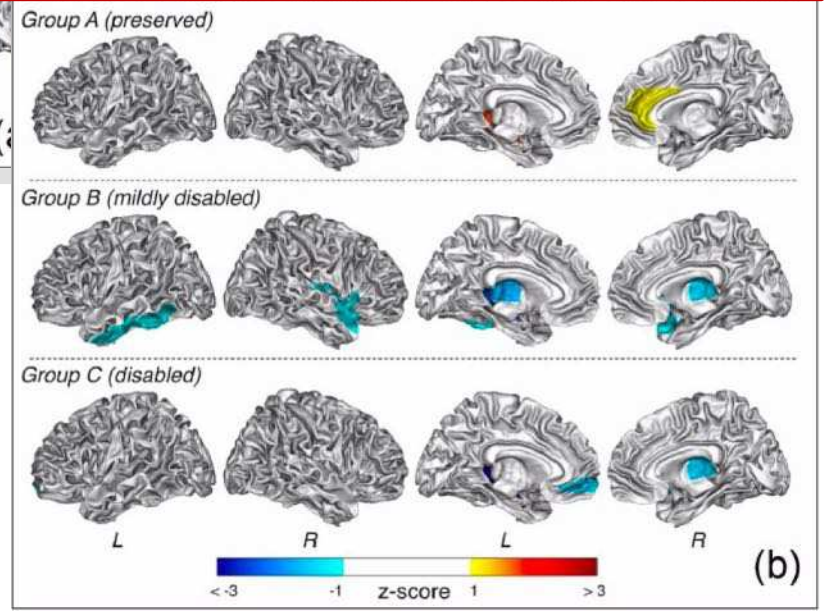




Schoonheim 2010

Existence of adaptive but saturable brain functional compensatory mechanisms in MS patients

Graph theory allows to quantify the global organization (not only the main network e.g., ICA)



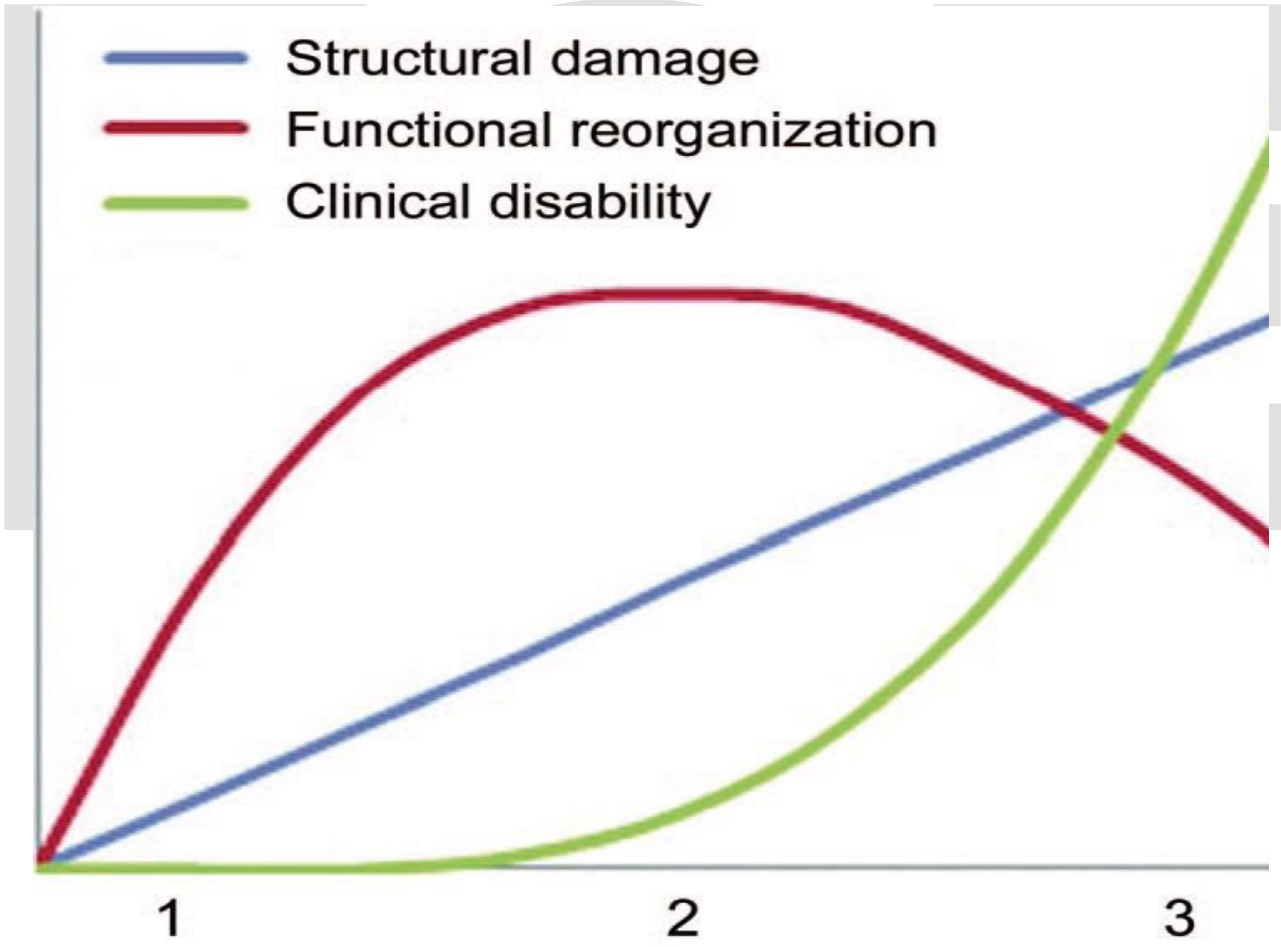
Comportement fonctionnel probable

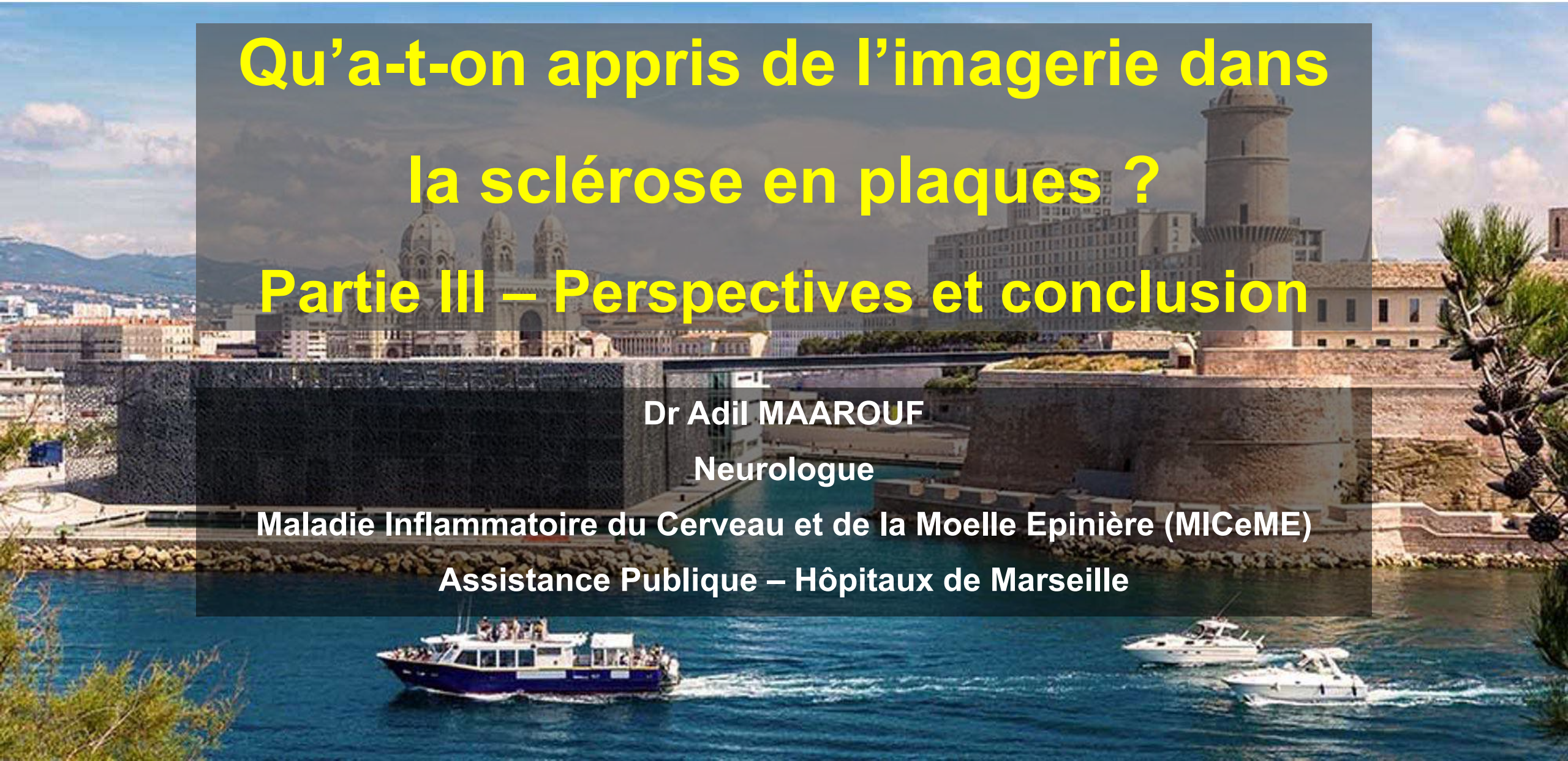
EDITORIAL

The limits of functional reorganization in multiple sclerosis

2010

Menno M. Schoonheim, MSc
Jeroen J.G. Geurts, PhD
Frederik Barkhof, MD





Qu'a-t-on appris de l'imagerie dans la sclérose en plaques ?

Partie III – Perspectives et conclusion

Dr Adil MAAROUF

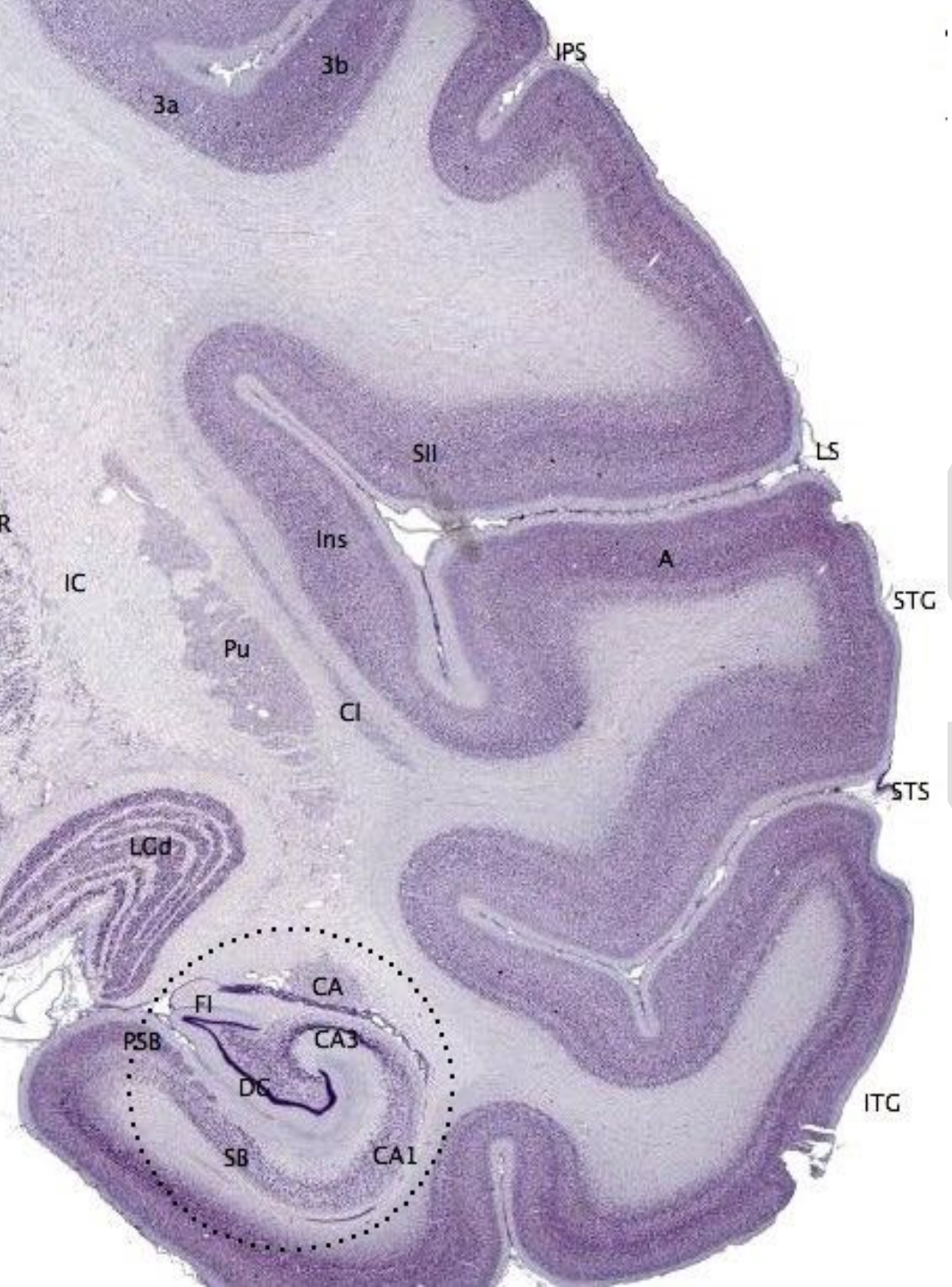
Neurologue

Maladie Inflammatoire du Cerveau et de la Moelle Epinière (MICeME)

Assistance Publique – Hôpitaux de Marseille

6. Exhaustivité ?

Cortex


3b
3a
IPS
SII
LS
Ins
A
IC
STG
Pu
Cl
STS
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CA
Fl
PSB
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CA1
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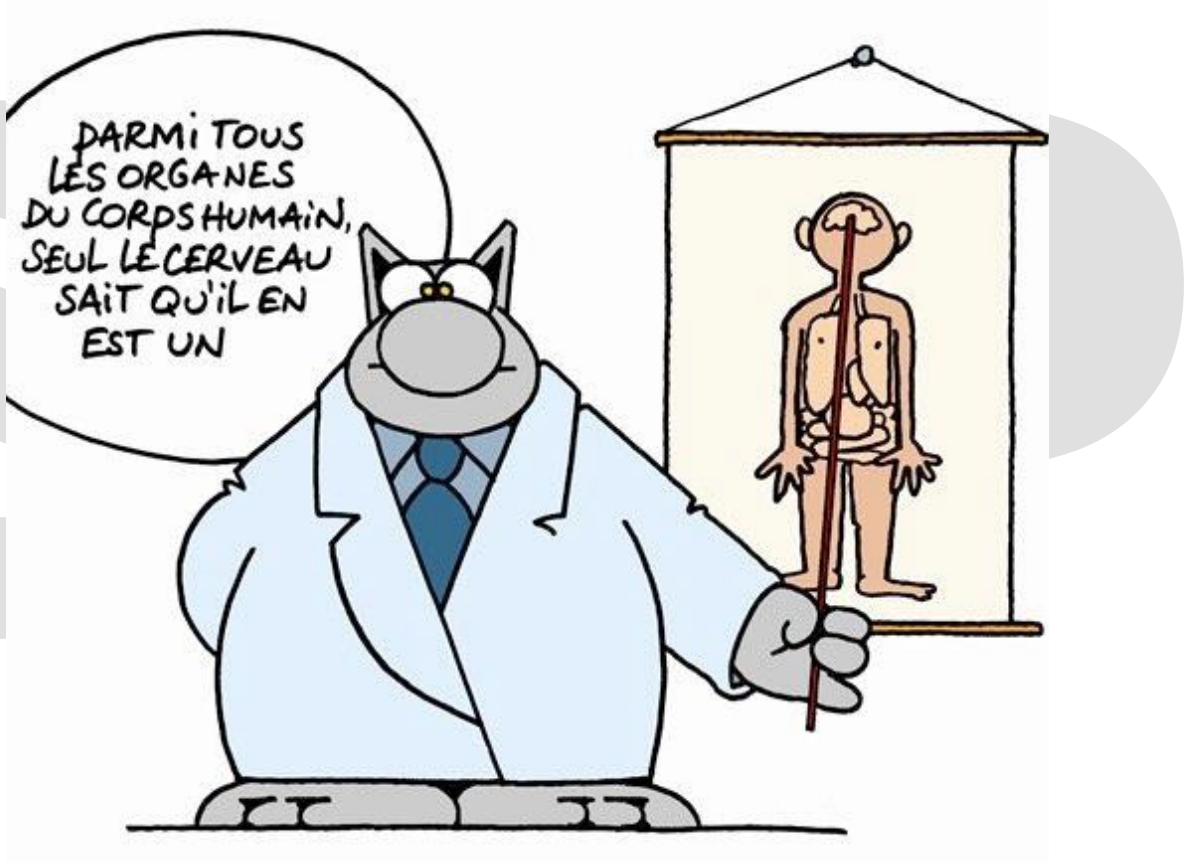
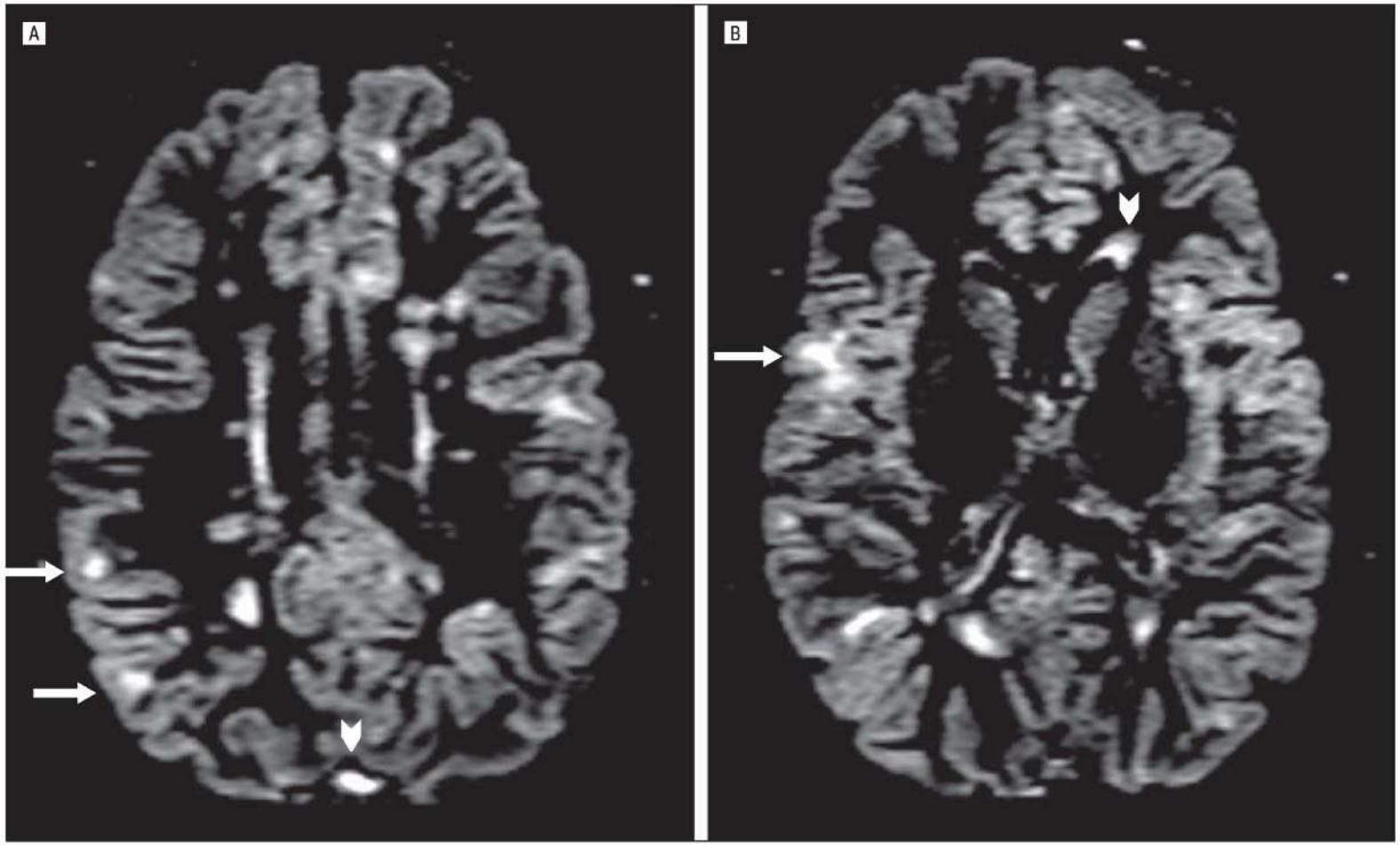
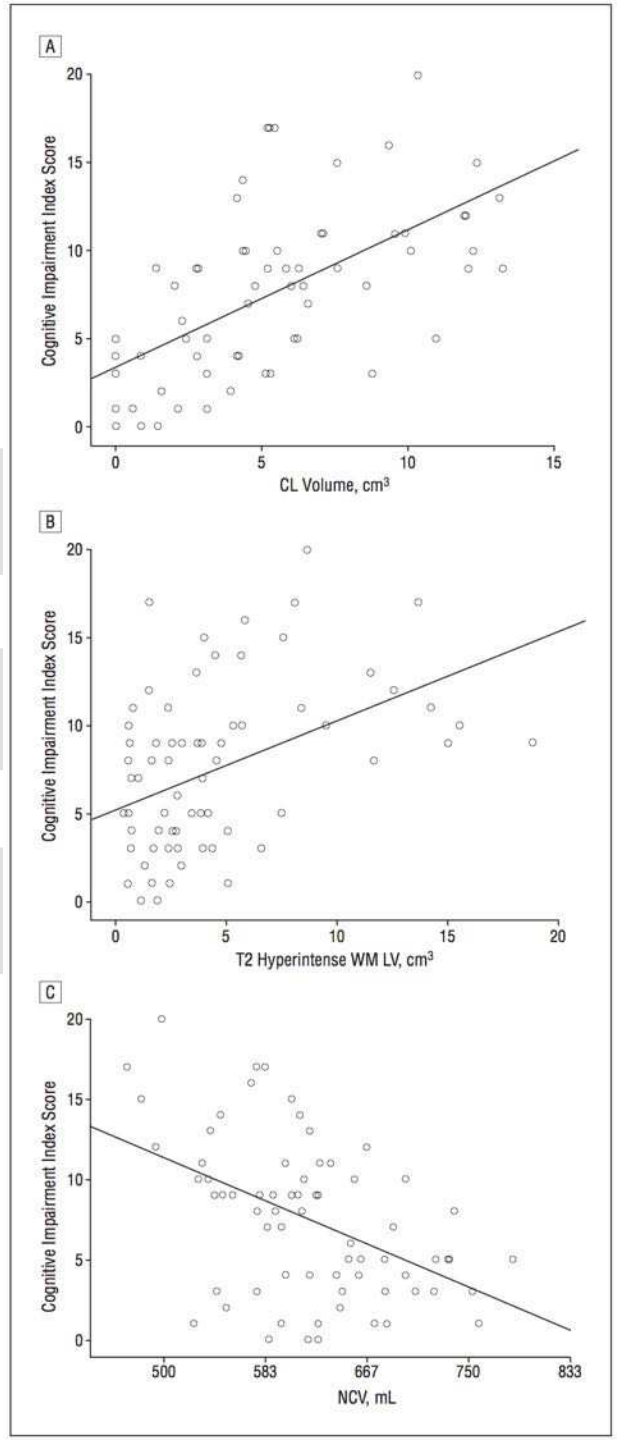

PARMI TOUS LES ORGANES DU CORPS HUMAIN, SEUL LE CERVEAU SAIT QU'IL EN EST UN

Cortical Lesions and Atrophy Associated With Cognitive Impairment in Relapsing-Remitting Multiple Sclerosis

Massimiliano Calabrese, MD; Federica Agosta, MD; Francesca Rinaldi, MD; Irene Mattisi, MD; Paola Grossi, PhD; Alice Favaretto, MD; Matteo Atzori, MD; Valentina Bernardi, MD; Luigi Barachino, RT; Luciano Rinaldi, MD, PhD; Paola Perini, MD; Paolo Gallo, MD, PhD; Massimo Filippi, MD

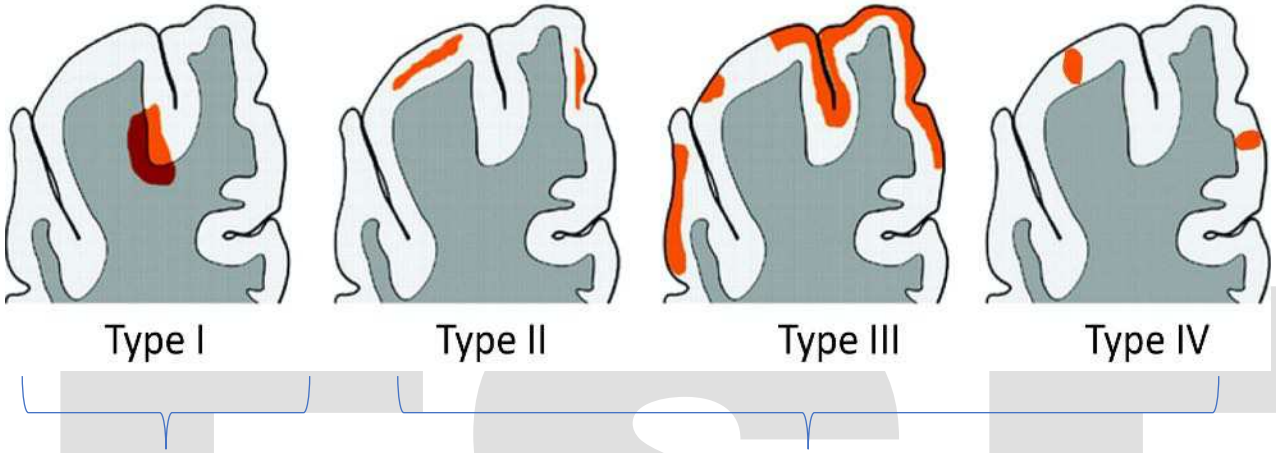




Mutivariate : age / **cortical lesions** / **neocortical** volume (r^2=0,55 p<0.001)

No difference T2LL CP vs CI

- Pathological hallmark of multiple sclerosis, highly specific



From Dutta et Trapp, Neurology 2007

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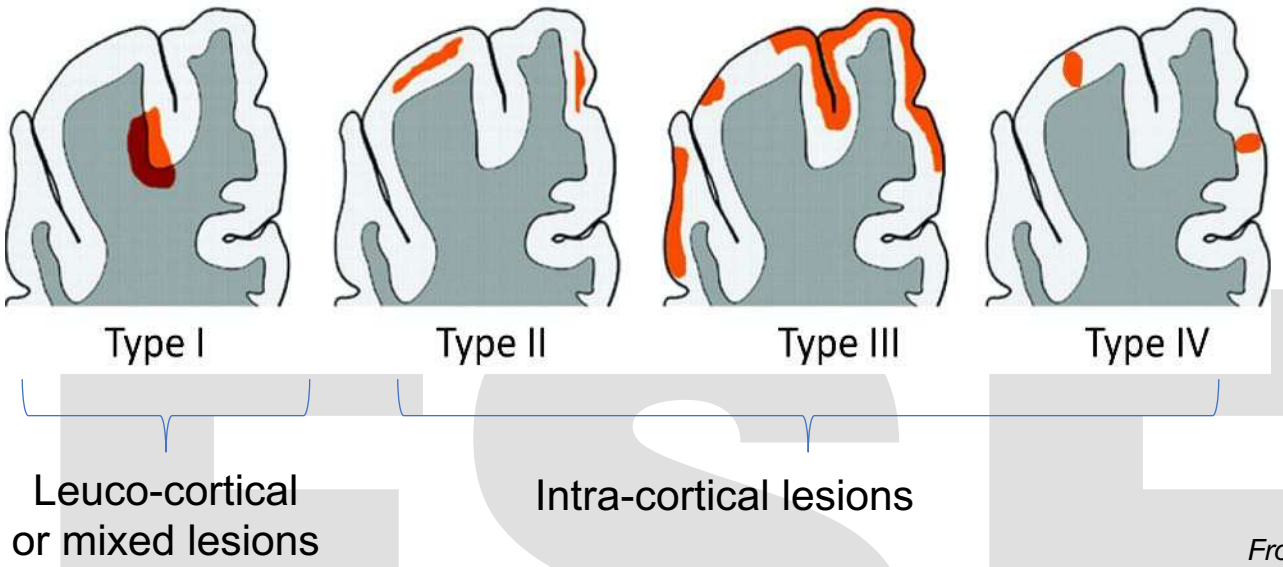
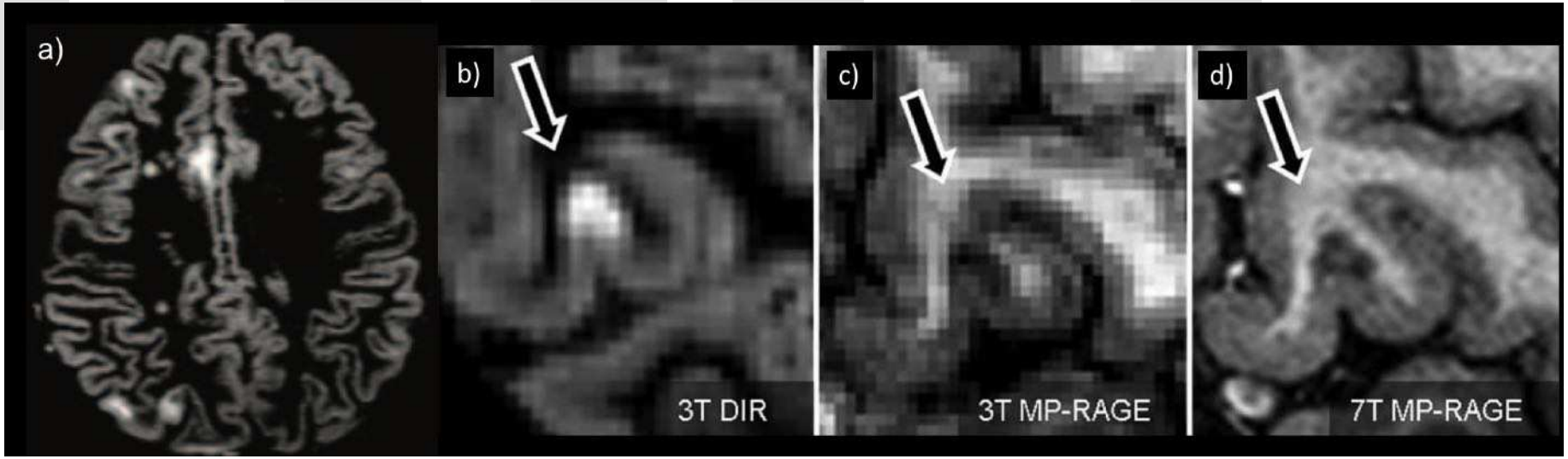
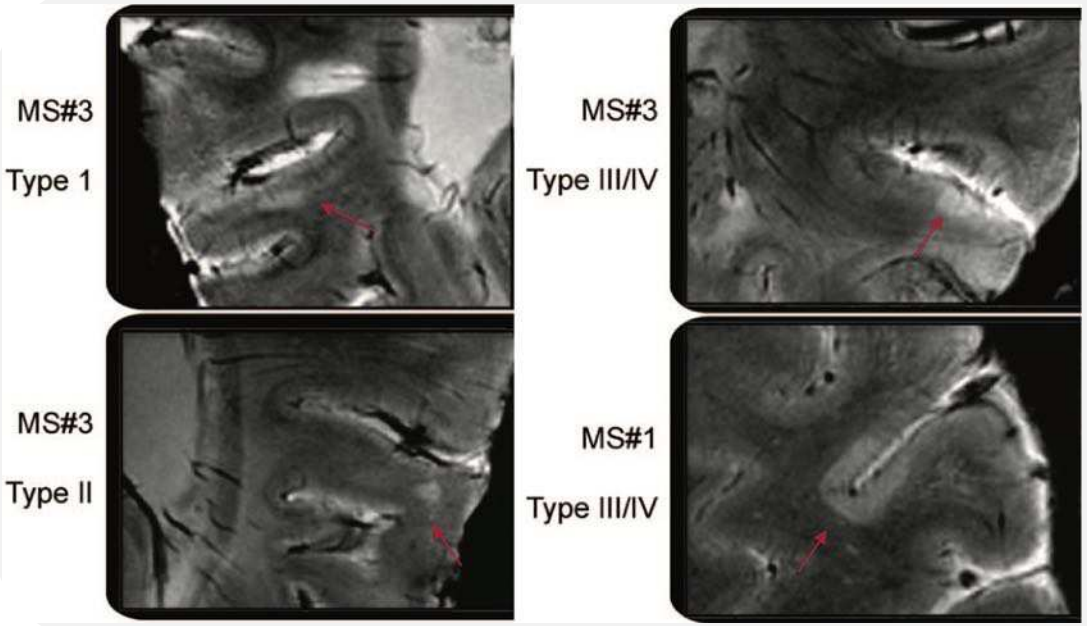


From Dutta et Trapp, Neurology 2007

- Multiple previous studies tried to depict them at 1.5 & 3T using MRI sequences like double inversion recovery (DIR)
- But strongly lack of specificity
- 7T brings a huge gap for *in vivo* visualisation of cortical lesions

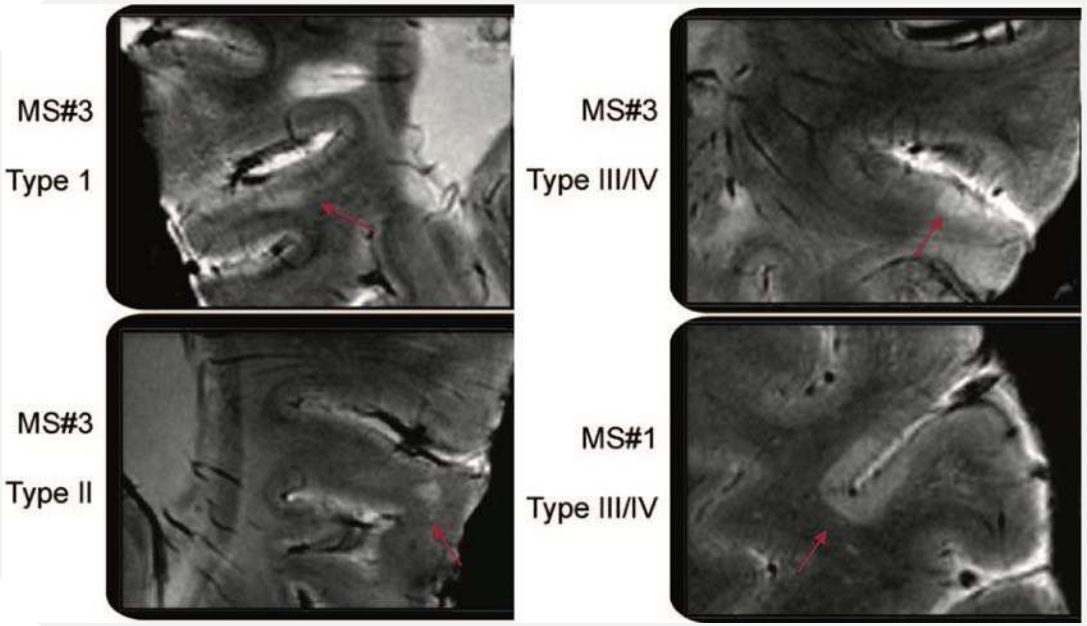


From Tallantyre et al, JMRI 2010



Maneiro el al, 2009 :

- First study performed *in vivo* at 7T in a group of MS patients
- 199 cortical lesions in 16 patients (9 RRMS and 7 SPMS):
  - Type I 36%
  - Type II 14%
  - Type III/IV 50%
- Independent from the number of white matter lesions
- Cortical lesions were more frequent in SPMS patients



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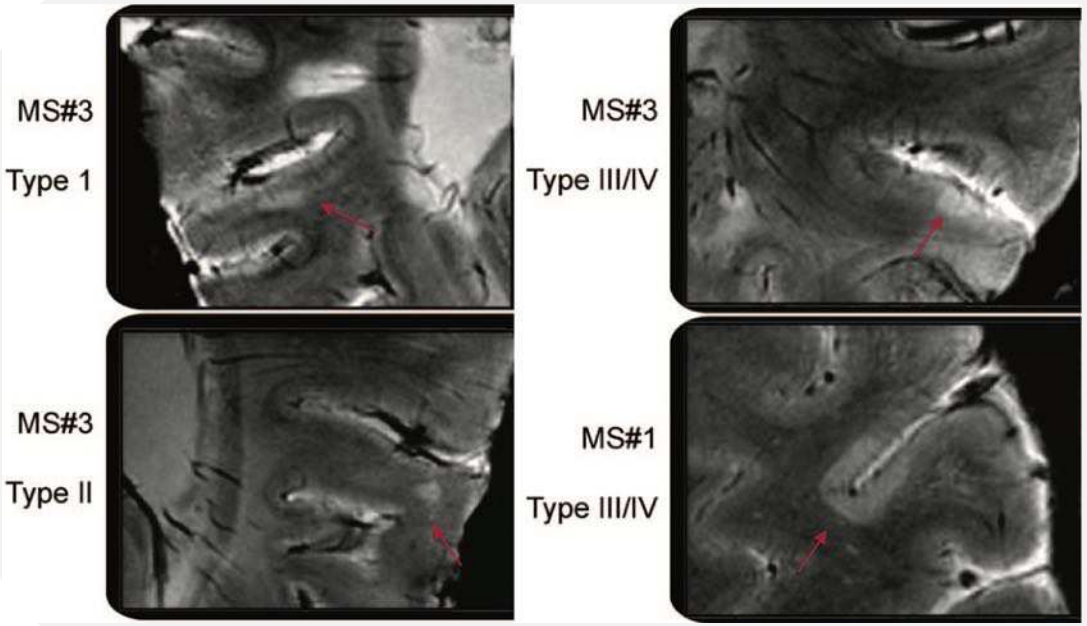
Harrison et al, 2015

- 36 individuals with MS (30 RRMS, 6 SPMS)
- Cognitive and physical deficits were significantly associated with cortical lesions
- But leukocortical lesions (type I) mainly drive the risk of cognitive deficits



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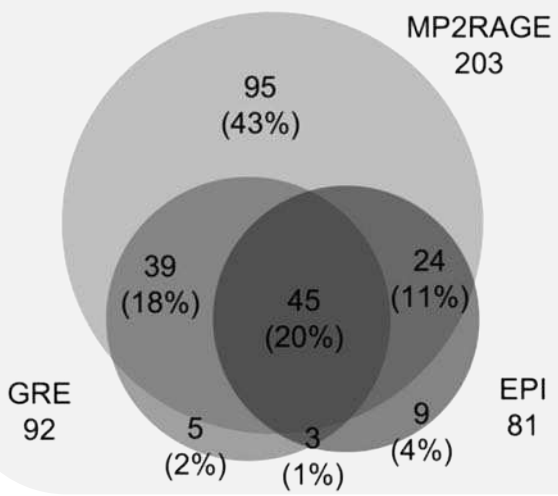
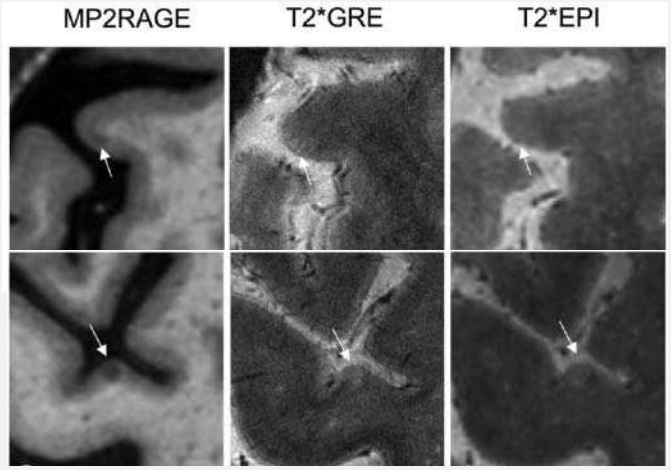
Beck et al, 2018

- Combined MP2RAGE and T2*-w at 7T improved detection

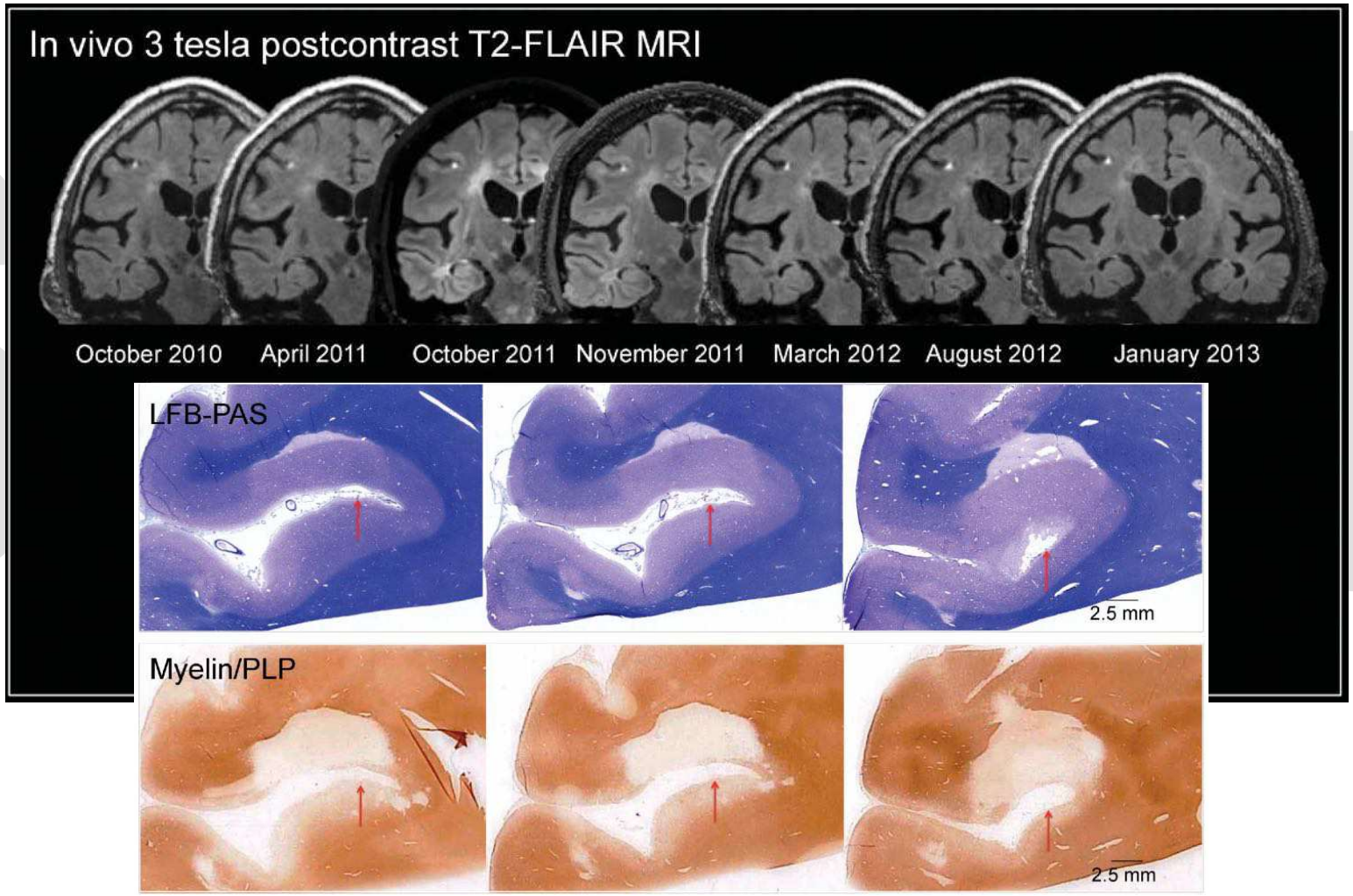




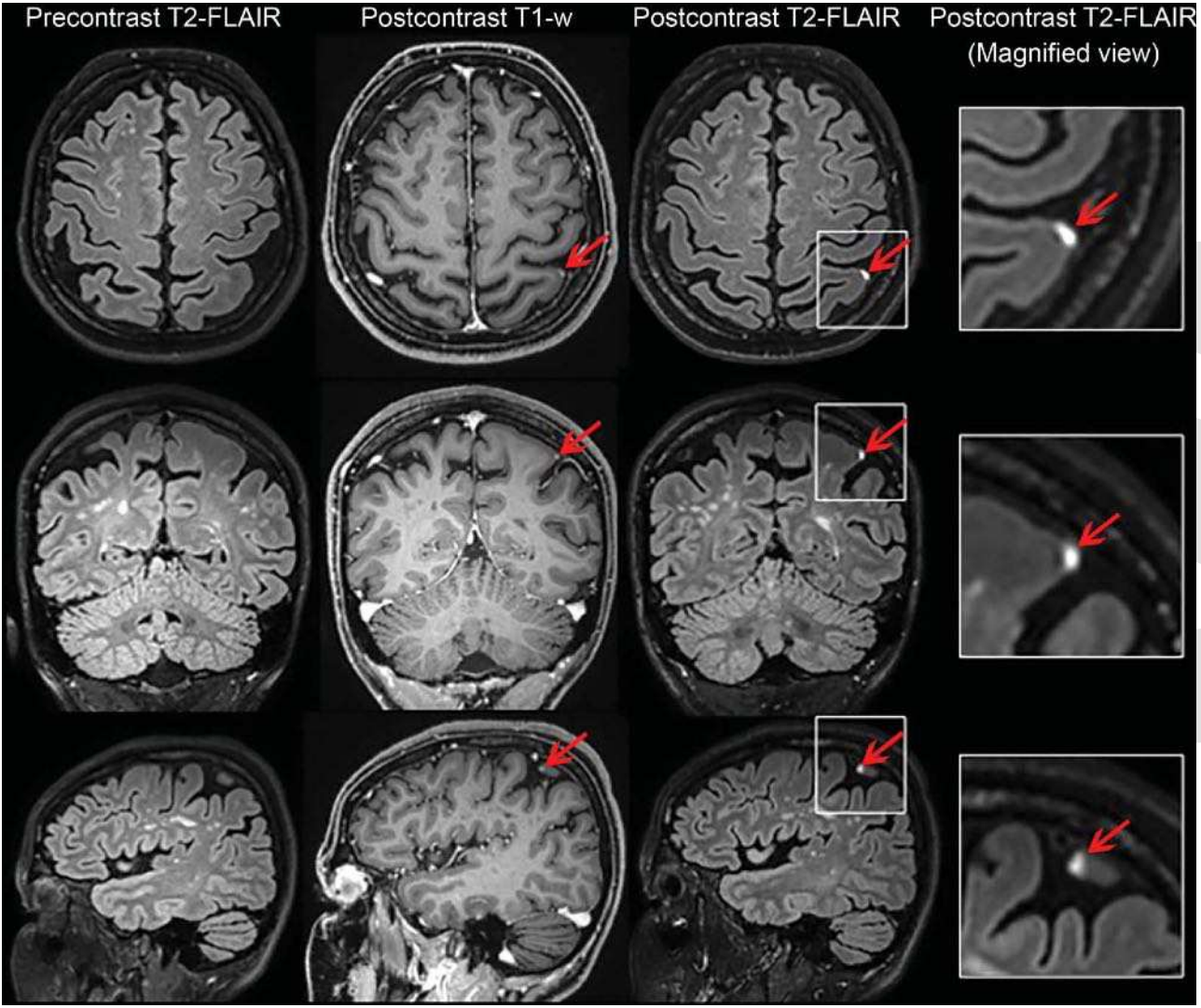
ARTICLES

Gadolinium-based MRI characterization of leptomeningeal inflammation in multiple sclerosis

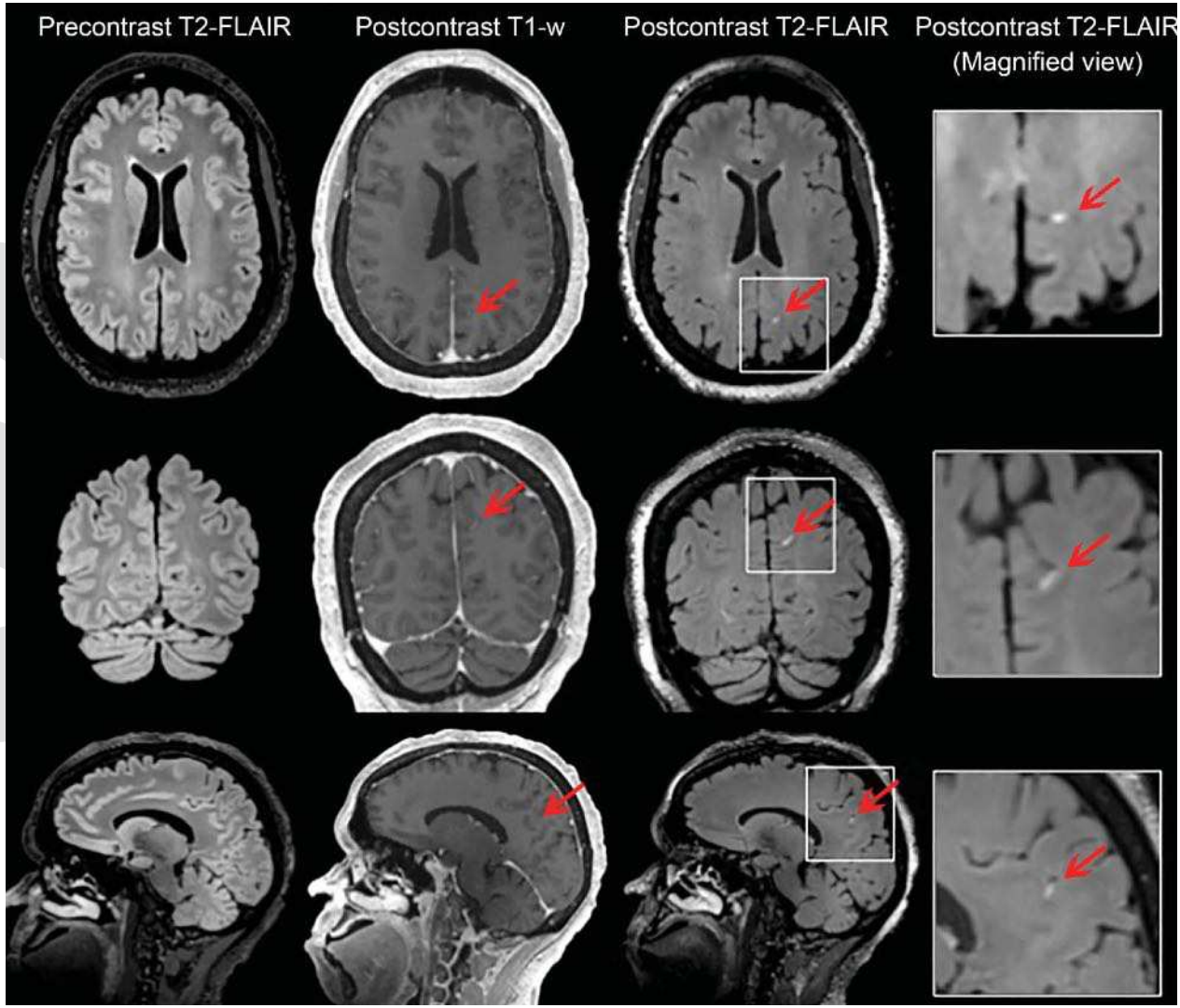
Absinta et al. – Neurology 2015



25 % des patients, plus fréquent dans les formes progressives



Maladie de Behçet



HTLV-1

Leptomeningeal gadolinium enhancement across the spectrum of chronic neuroinflammatory diseases

Absinta et al. – Neurology 2017

22% des patients non MS (56/254)
25% des patients MS (74/299)

Figure 3 Odds ratios of leptomeningeal enhancement in disease groups compared to healthy controls

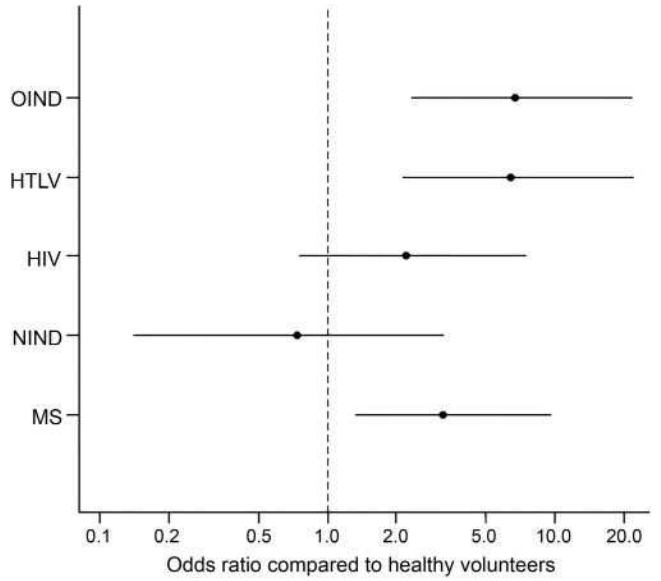


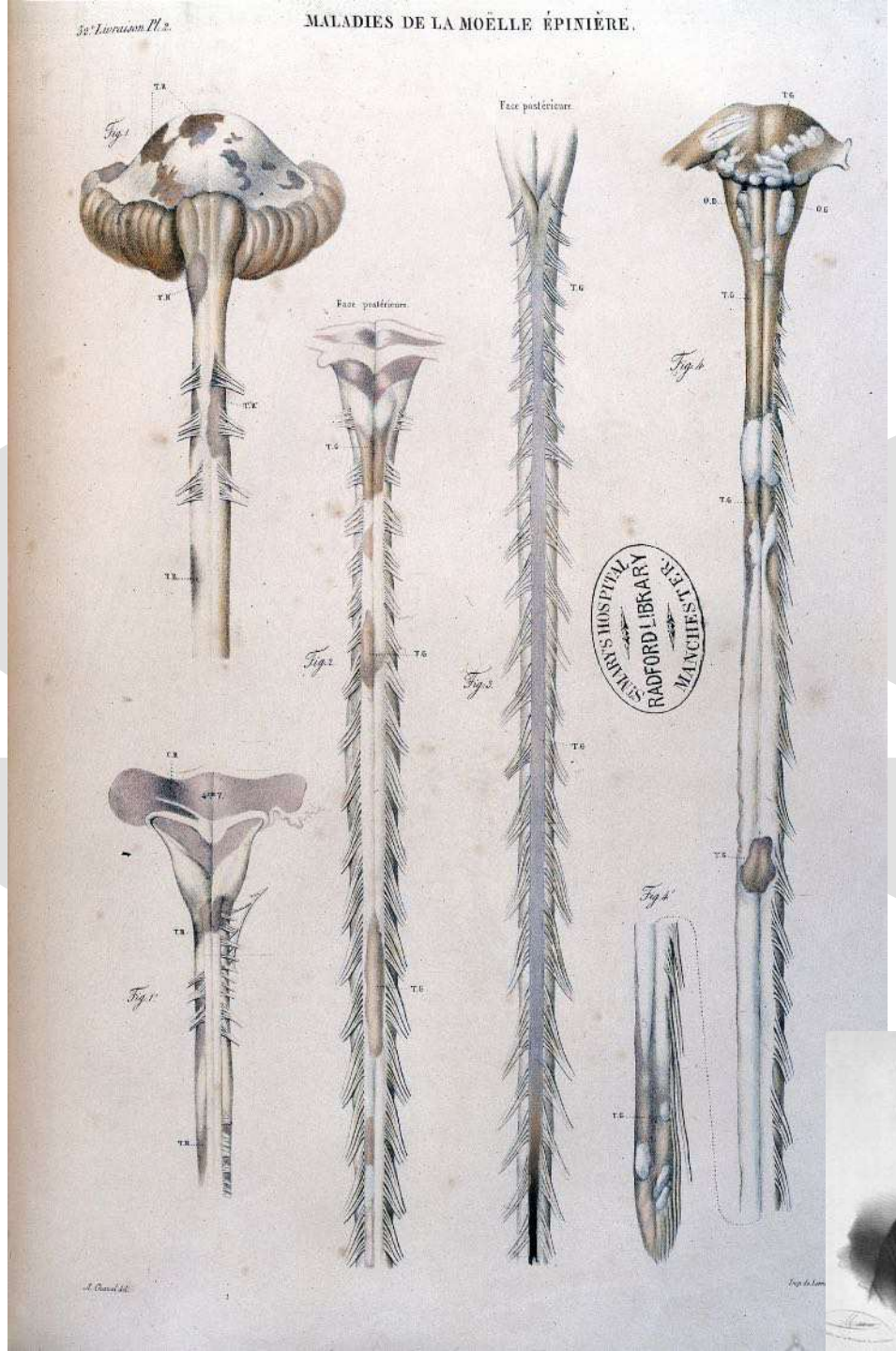
Table Cohort characteristics

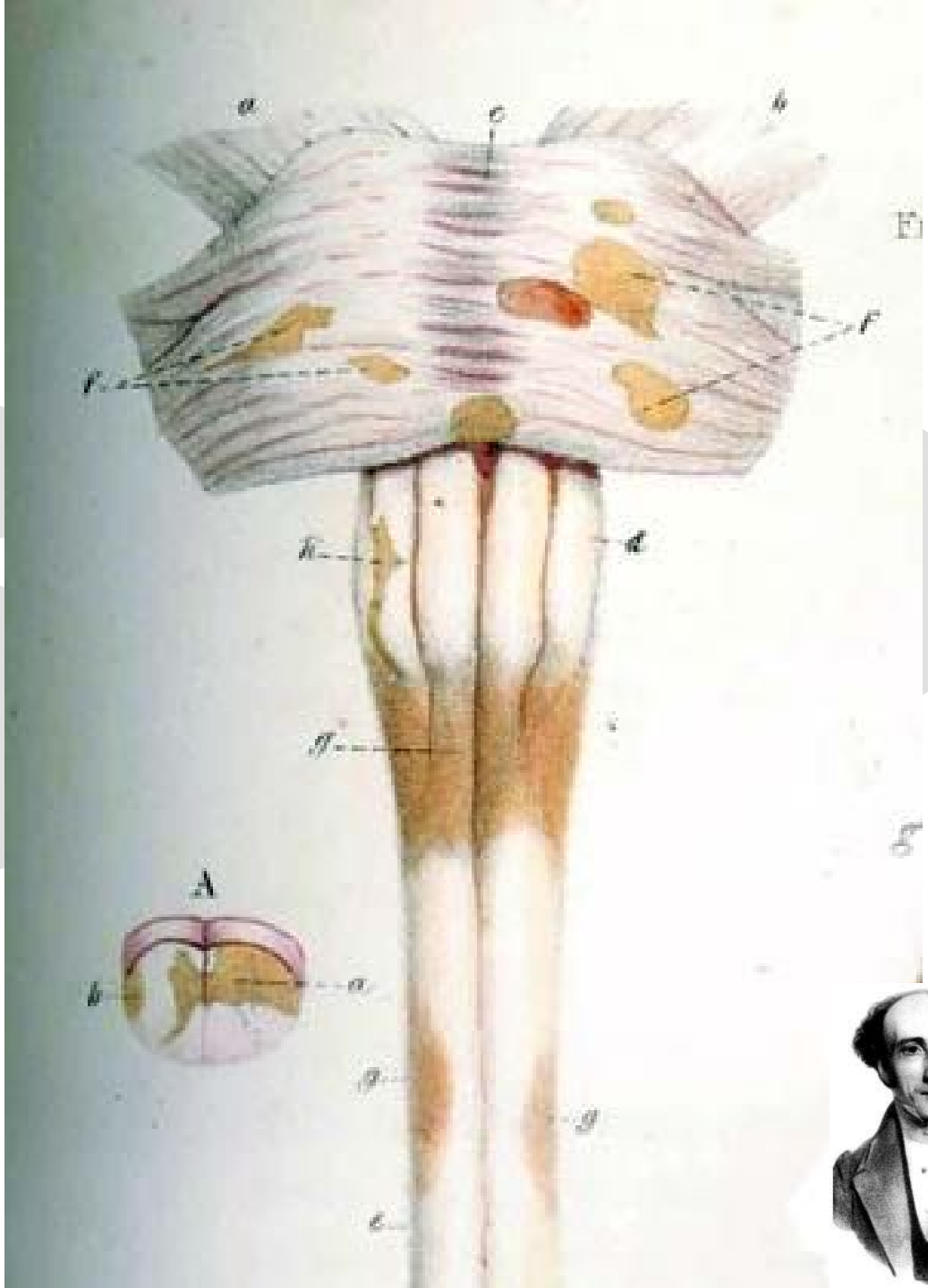
	OIND	NIND	HTLV-infected	HIV-infected	MS[a]	Healthy volunteers
No. of participants	52	38	38	61	299	66
No. of women, %	32 (61)	27 (71)	25 (66)	25 (41)	177 (59)	32 (48)
Mean age (range), y	43 (20-62)	50 (29-70)	53 (24-75)			
CSF data available, %	37 (71)	27 (71)	28 (74)	18 (49)	242 (81)	8 (12)
LME detection on postcontrast T2-FLAIR images						
No. of cases with LME, %	18 (35)	3 (8)	17 (45)	13 (21)	75 (25)	5 (8)
No. of cases with multiple foci of LME, %	7 (39)	0	5 (29)	2 (15)	26 (35)	0

56% HTLV-associated myelopathy (14/25)

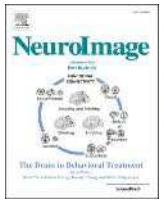
3e Livraison Pl. 2.

MALADIES DE LA MOELLE ÉPINIÈRE.





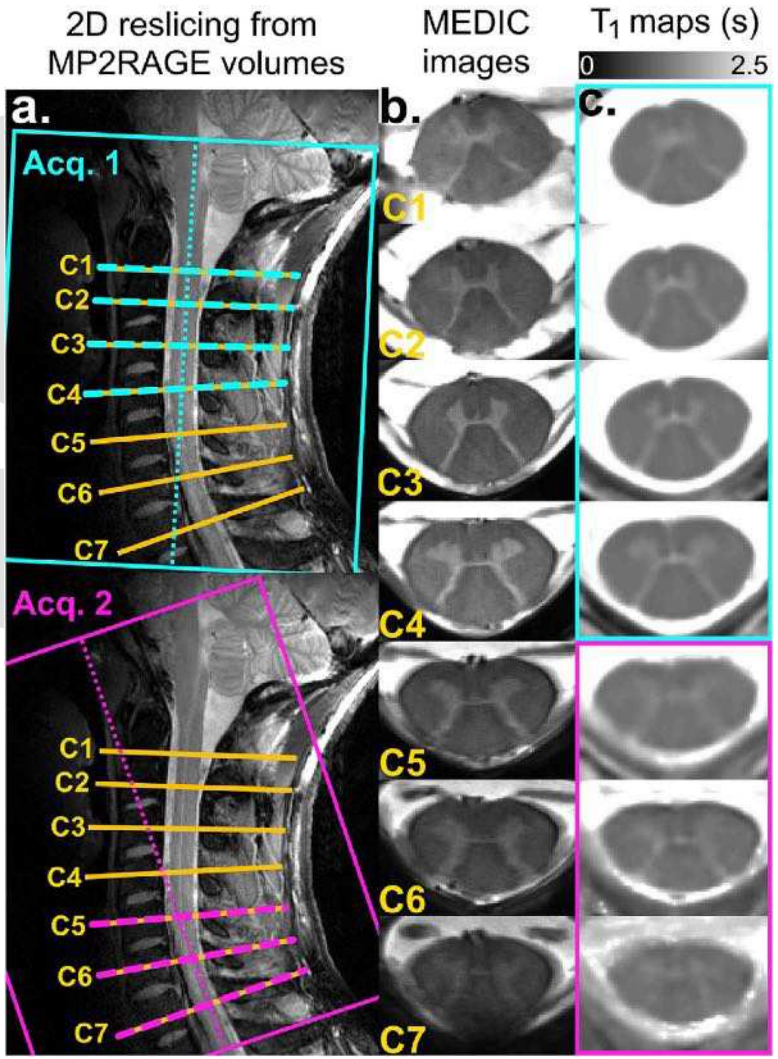
7T study



Anterior fissure, central canal, posterior septum and more: New insights into the cervical spinal cord gray and white matter regional organization using T_1 mapping at 7T

Aurélien Massire [a,b,c], Henitsoa Rasoanandrianina [a,b,c], Maxime Guye [a,b], Virginie Callot [a,b,c,*]

NeuroImage143(2016)58–69
NeuroImage 205 (2020) 116275



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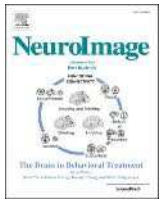

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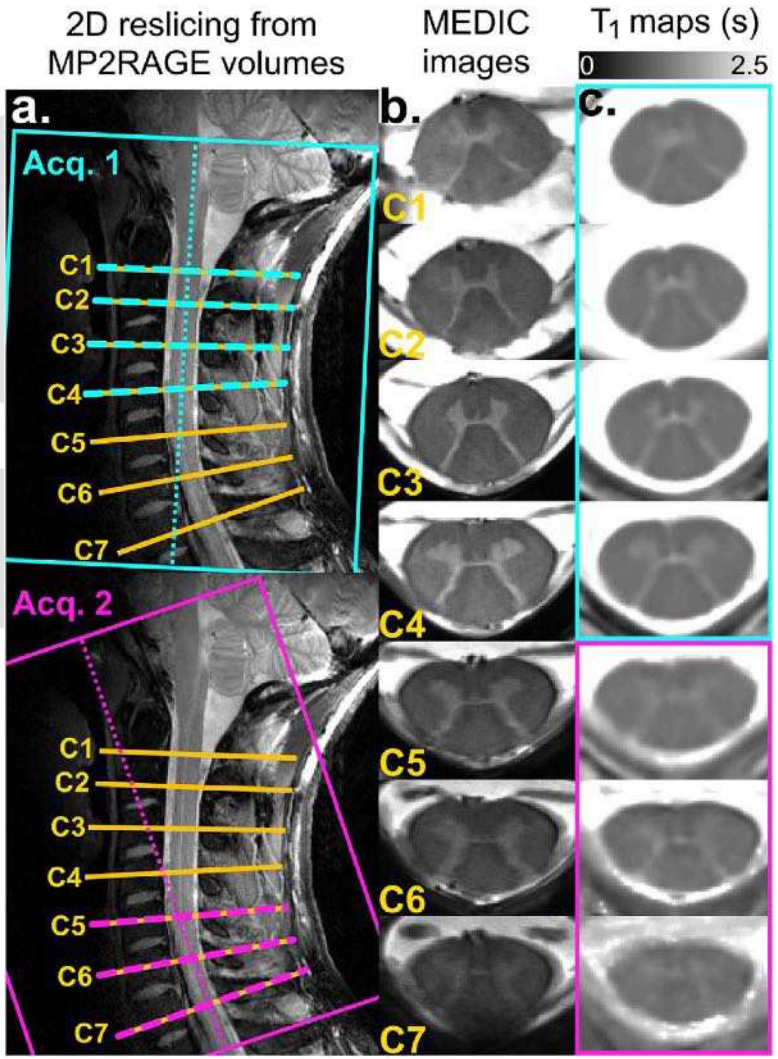
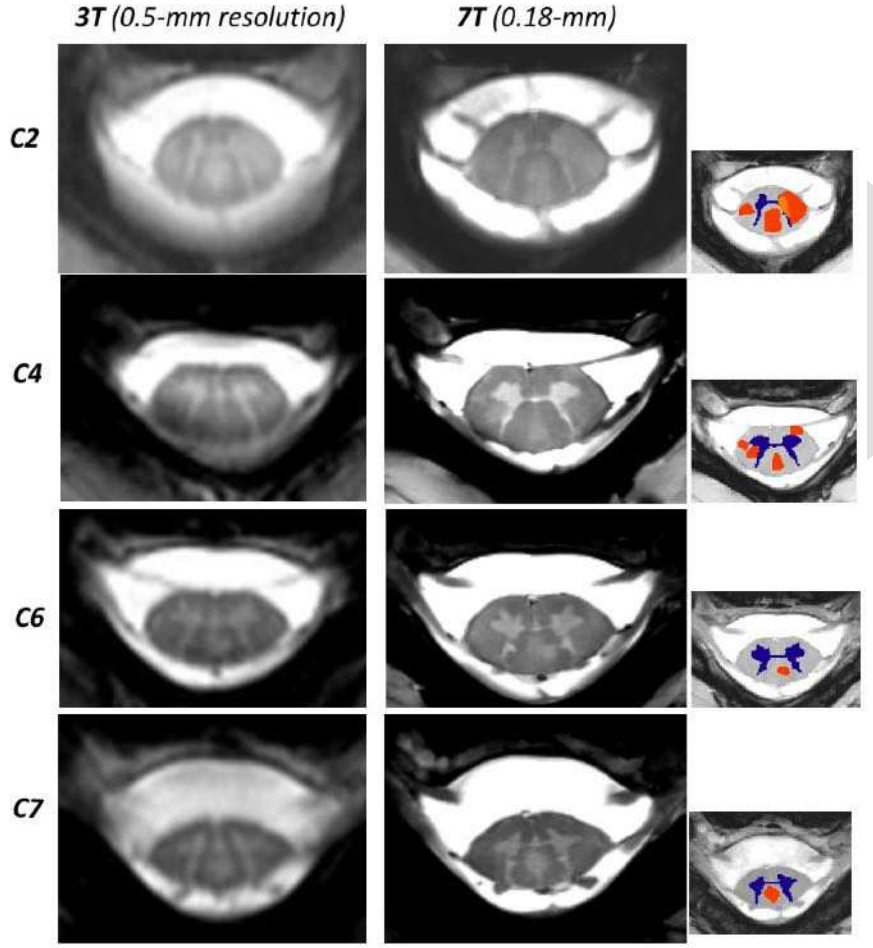
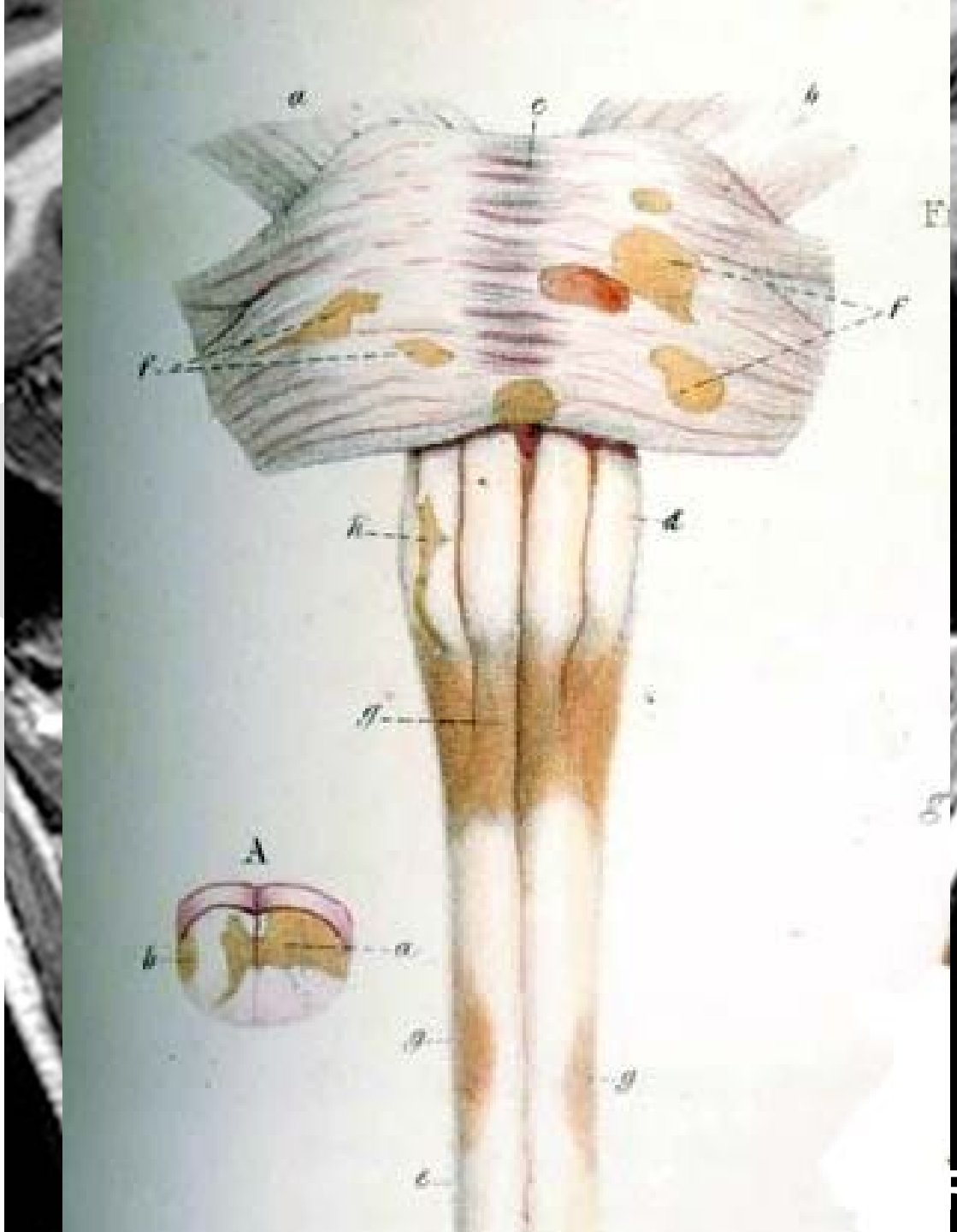
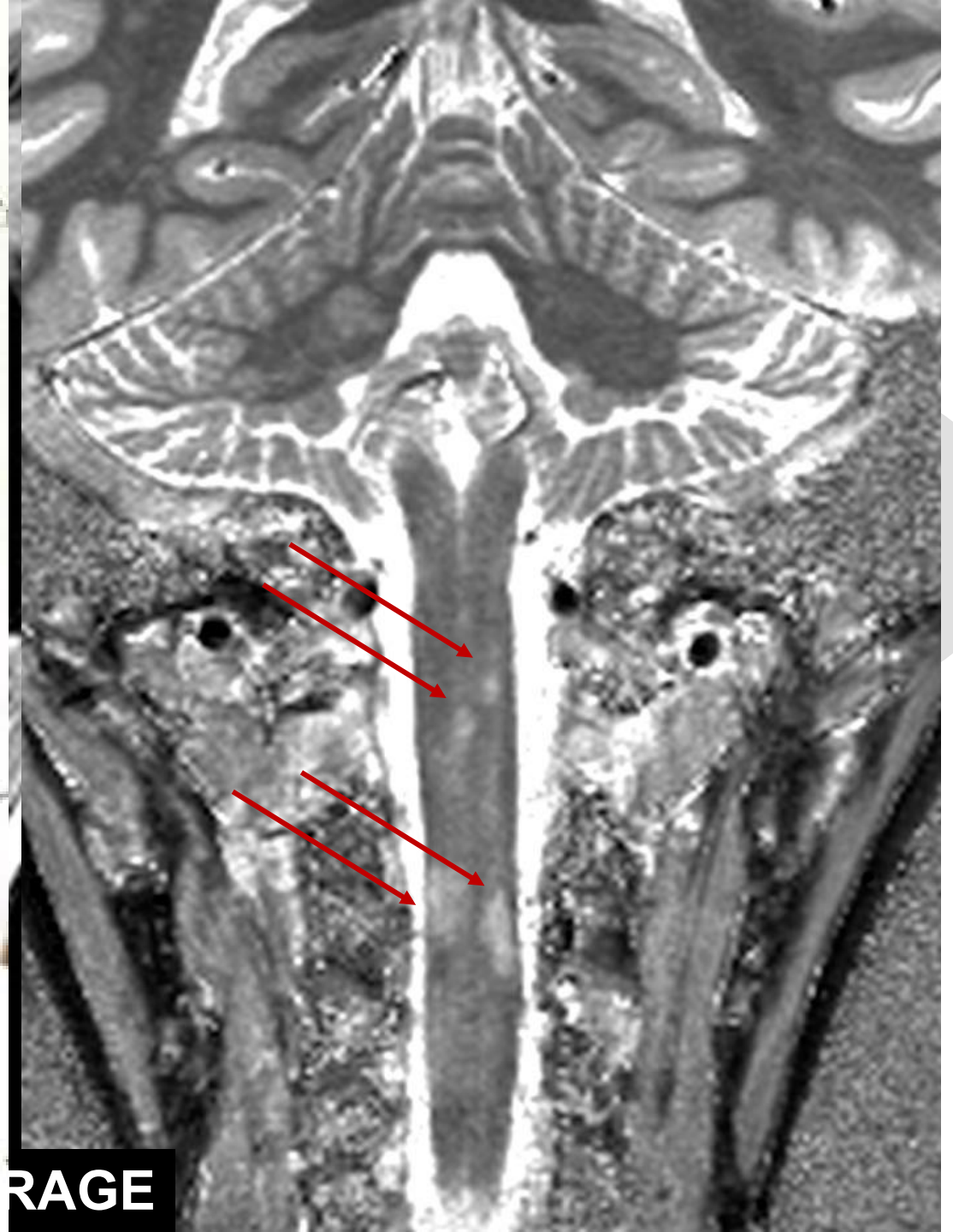
NeuroImage143(2016)58–69
NeuroImage 205 (2020) 116275





1st read : 17% of missed lesions at 3T vs. 7T evaluation - (4/23 lesions)
2nd read (after 7T) : only 9% remain unseen at 3T (2/23)





RAGE

In conclusion

1. Key role of lesions in MS pathology and disability – heterogenicity

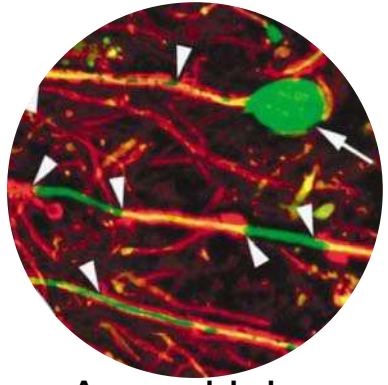
2. Compensatory mechanism in response to structural damage (WM bundles), by means of functional reorganization :
    i. increased activation
    ii. or synchronization of specific structures or networks

3. Adaptative but saturable brain functional compensatory mechanisms

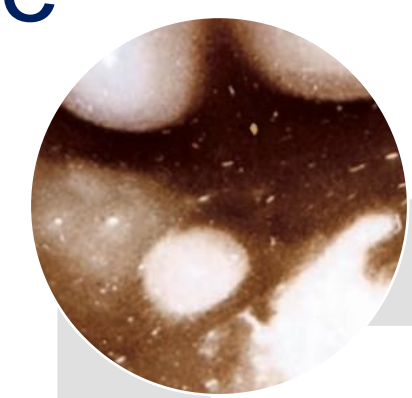
4. Emerging technique to assess lesions heterogenicity and their consequences

5. Unmet needs for progression, role of advanced MRI ?

Physio -pathologie



Axonal injury

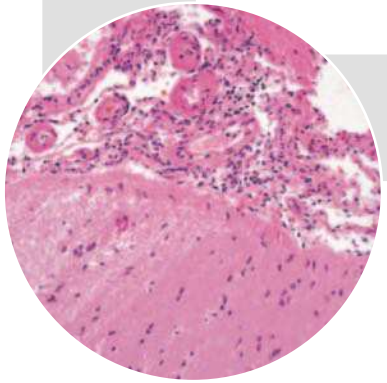


WM lesions

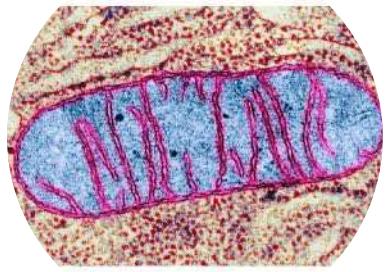
GM/subpial lesions

Pathological processes underlying progression in MS

Smoldering lesions



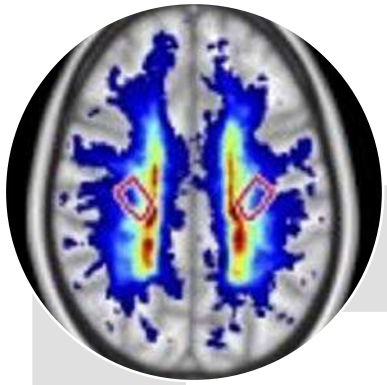
Meningeal follicles



Virtual hypoxia

Techniques avancées

Axonal injury



WM lesions

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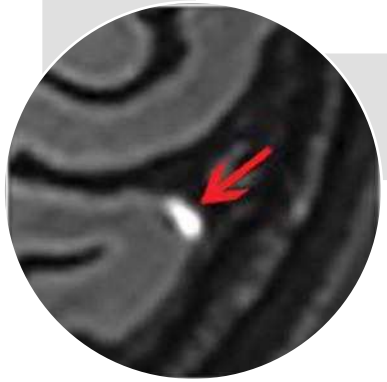
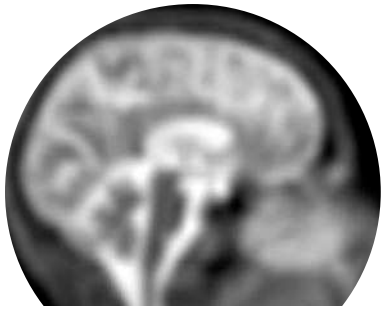
Pathological processes underlying progression in MS

Smoldering lesions



Meningeal follicles



Virtual hypoxia

Merci pour votre attention

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