ADVANCED QUANTITATIVE BRAIN MR MEASURES

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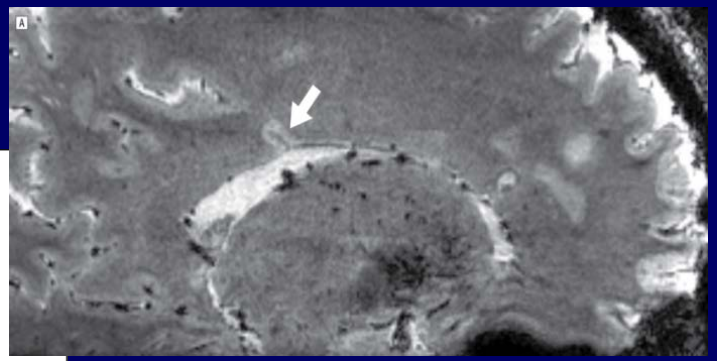
MRI IN MS

Outline of the presentation

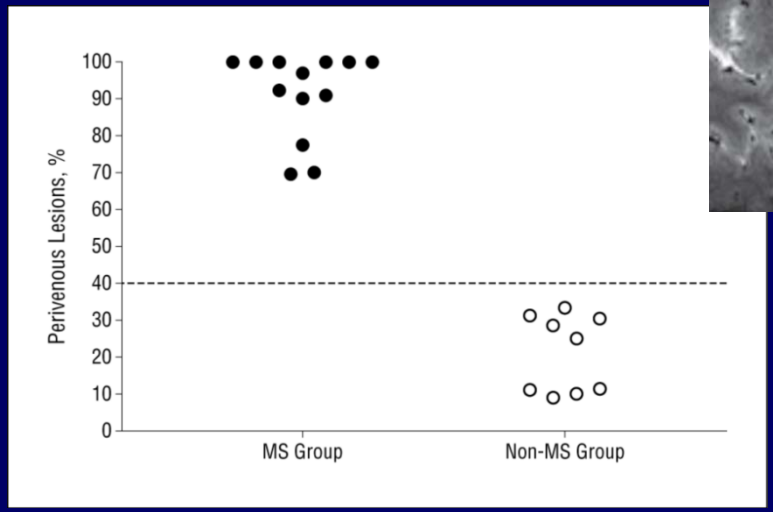
- **WM lesion nature**
- **Extent and topography of NAWM damage**
- **Cortical lesions**
- **Subpial demyelination**
- **“Diffuse” GM damage**
- **Regional damage**
- **CNS functional reorganization**
- **Conclusions**

MRI IN MS

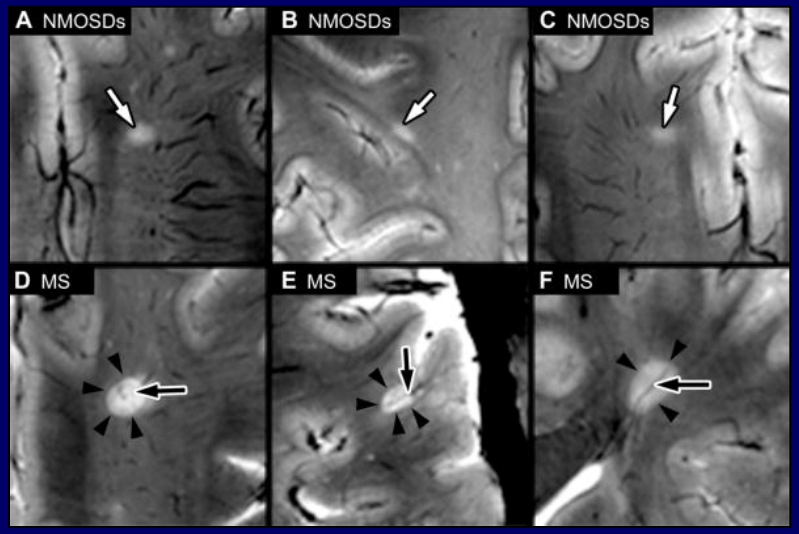
WM lesions



Mistry et al., JAMA Neurol 2013



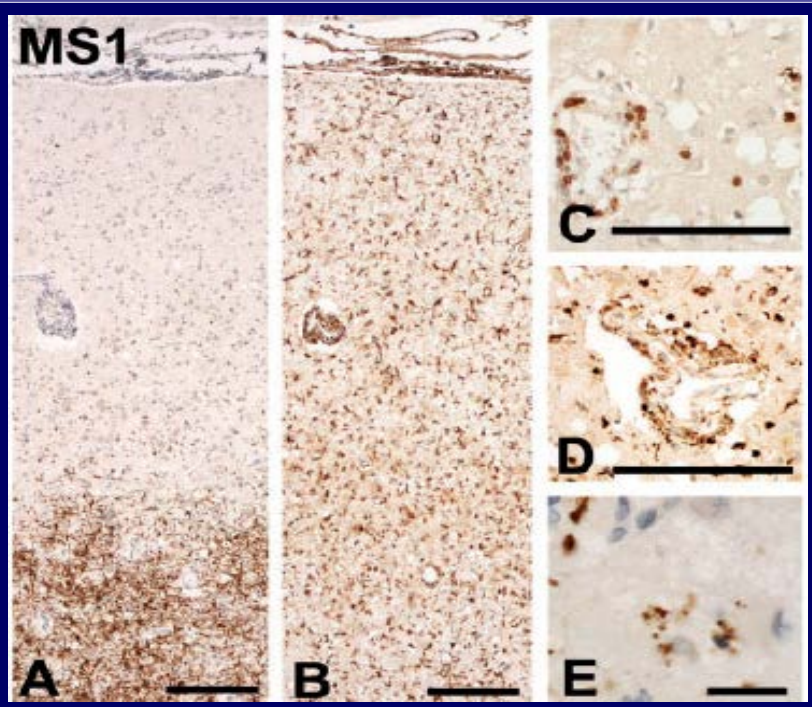
	Multiple sclerosis ($n = 3$)	Tuberculous meningitis ($n = 3$)	Alzheimer's disease ($n = 3$)	Controls ($n = 3$)
T cells	91 (55)	541 (860)	11 (9)	11 (24)
Microglia/macrophages	757 (596)	2301 (1449)	552 (218)	544 (252)
Extent of demyelination	41 (23)	1 (1)	0 (0)	0 (0)
Oligodendrocytes	23 (14)[+] / 105 (52)[#]	50 (32)	82 (23)	67 (107)
Neurons	154 (70)[+] / 221 (60)[#]	214 (24)	198 (43)	235 (15)
Axonal spheroids	8 (93)[+] / 6 (30)[#]	3 (7)	8 (26)	0 (2)



Sinneker et al., Neurology 2012

Perivascular: 92% MS *vs* 35% NMO lesions

Hypointense rim: 23% MS *vs* 2% NMO lesions

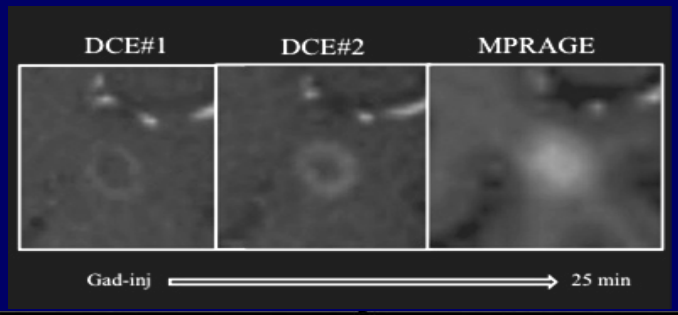


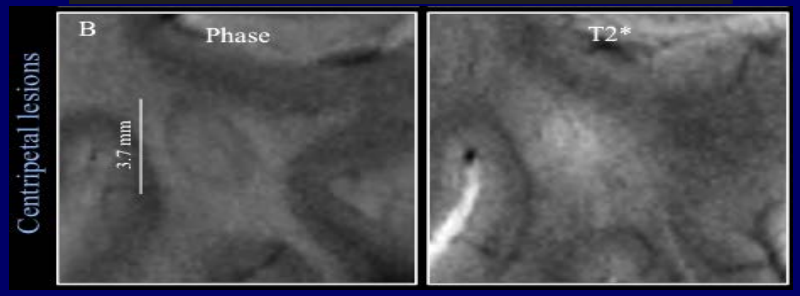
Fischer et al, Brain 2013

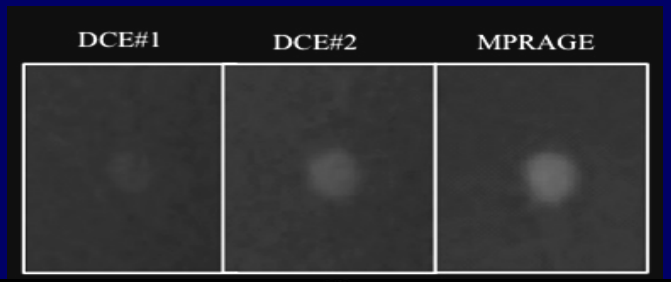
MRI IN MS

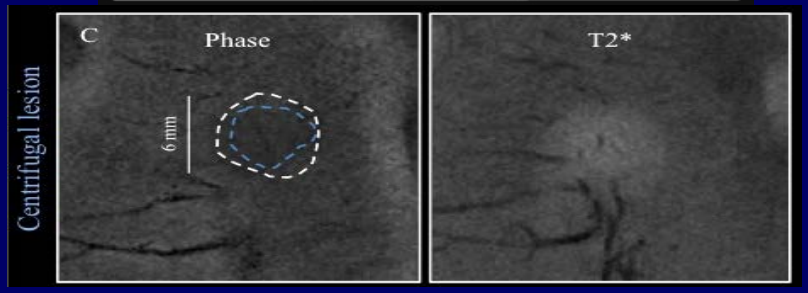
WM lesions

7 T



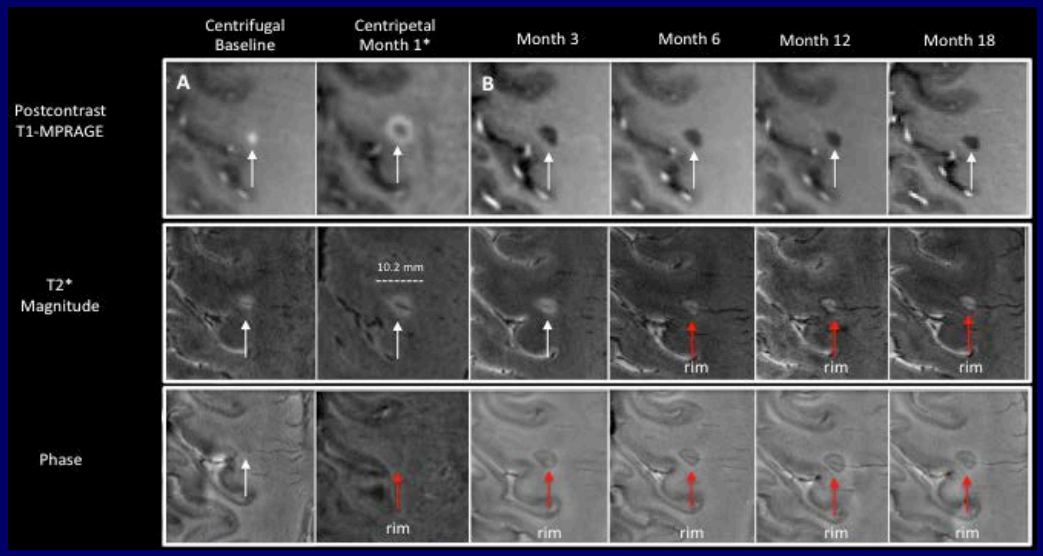




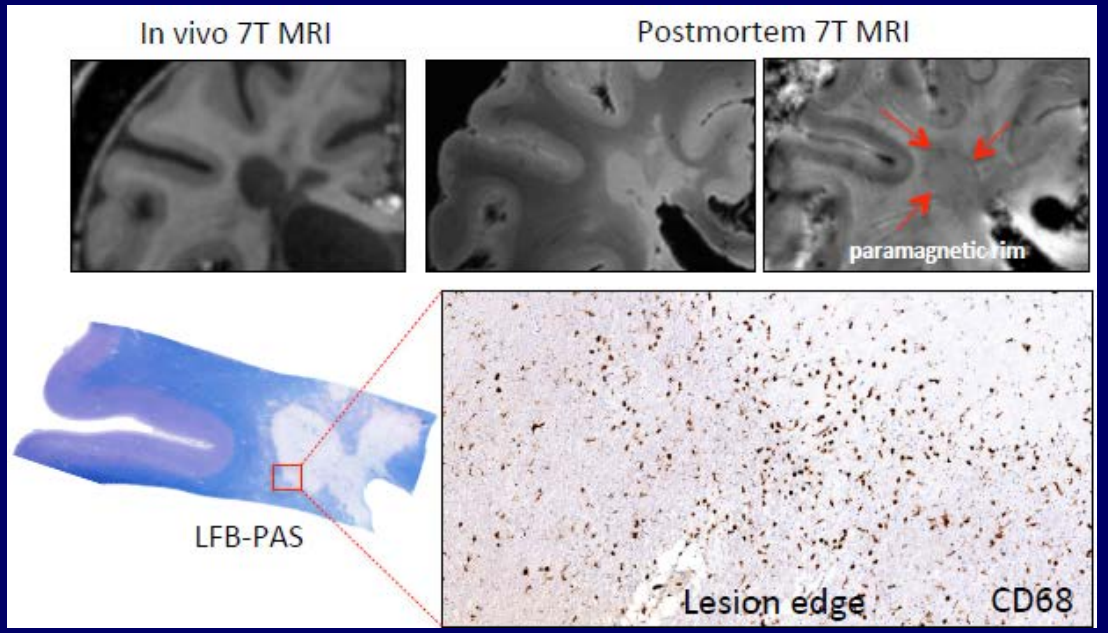


Absinta et al., Ann Neurol 2013

Persistent phase rim



Absinta et al., AAN 2014



MRI IN MS

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- WM lesion nature
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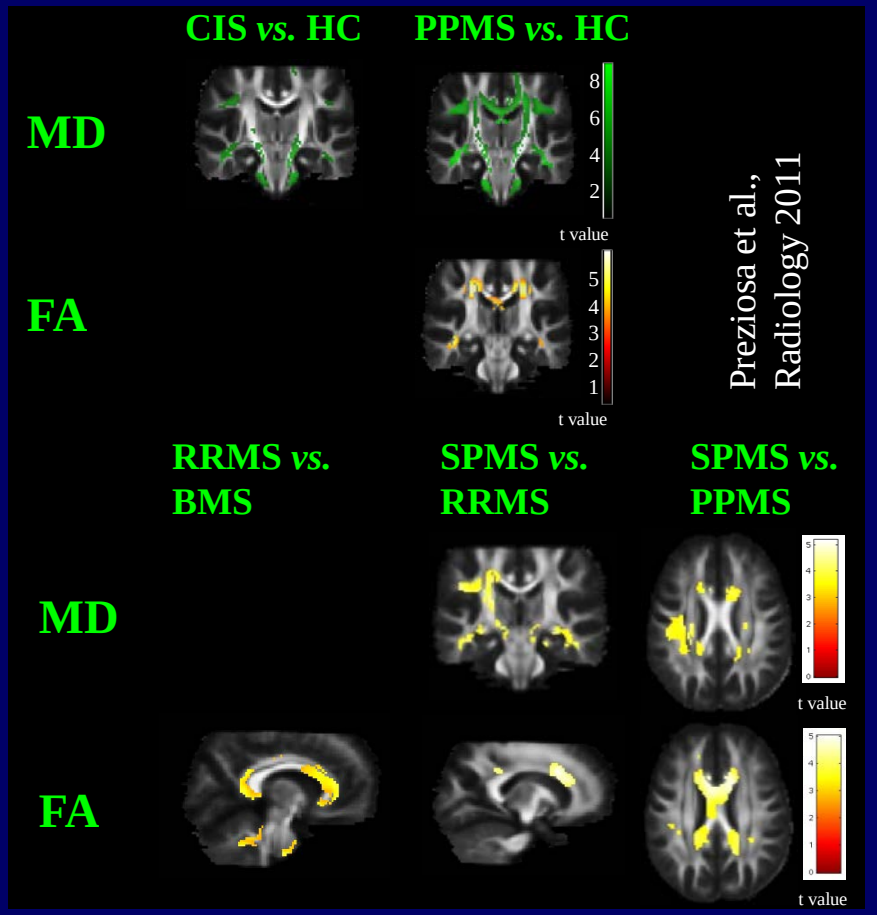
MRI IN MS

NAWM damage

	EDSS Score	
Independent Variable	*r* Value	*P* Value
T2 LV	0.55	<.001
WBNAA	−0.49	<.001
Mean lesion MD	0.50	<.001
Mean lesion FA	−0.36	.005
Mean NAWM FA	−0.52	.001
NAWM FA peak height	0.42	.001
Mean NAWM MD	0.26	.02
NAWM MD peak height	−0.31	.007

Pulizzi et al., Arch Neurol 2007



Relative contributions to cognitive impairment

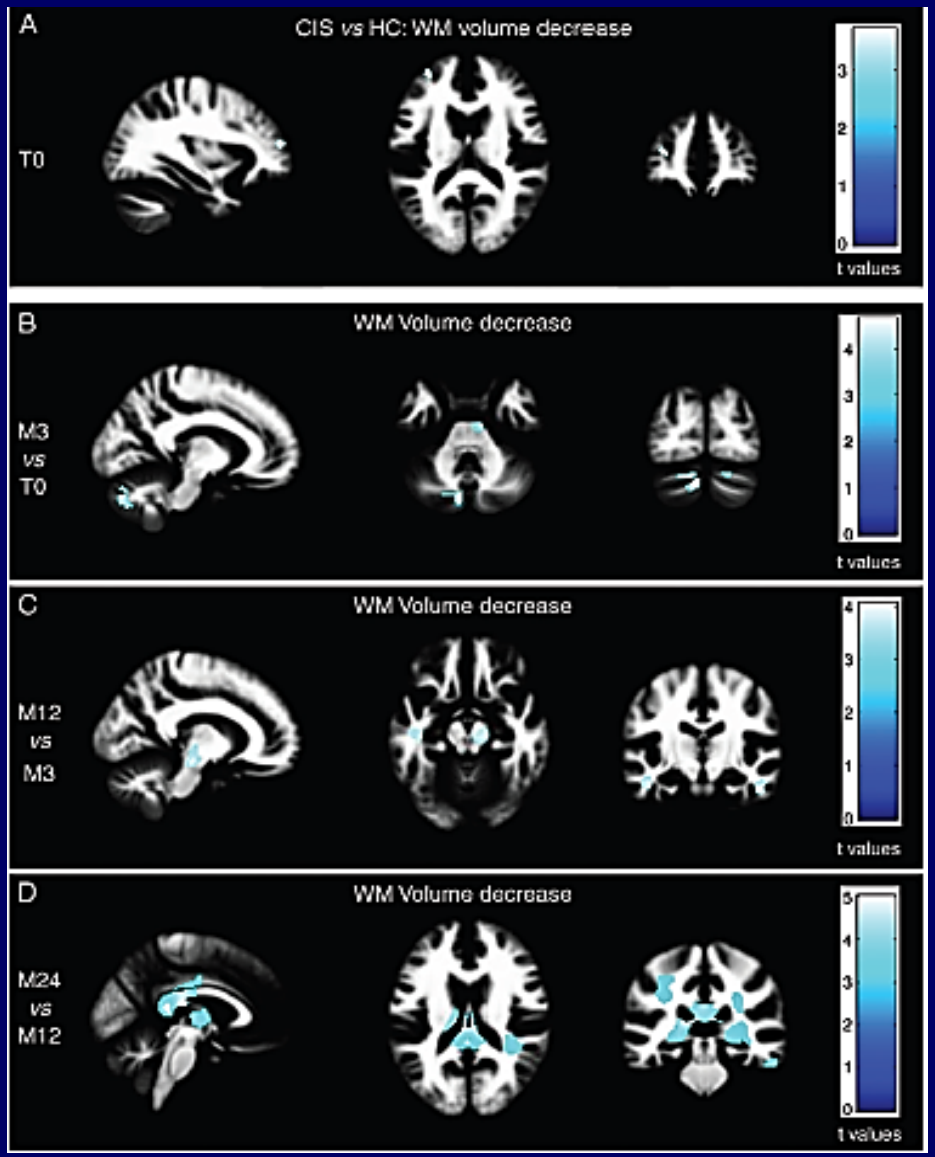
NAWM-MTR	68%
T1-LL	38%
T2-LL	37%
Lesion MTR	35%
Brain volume	21%

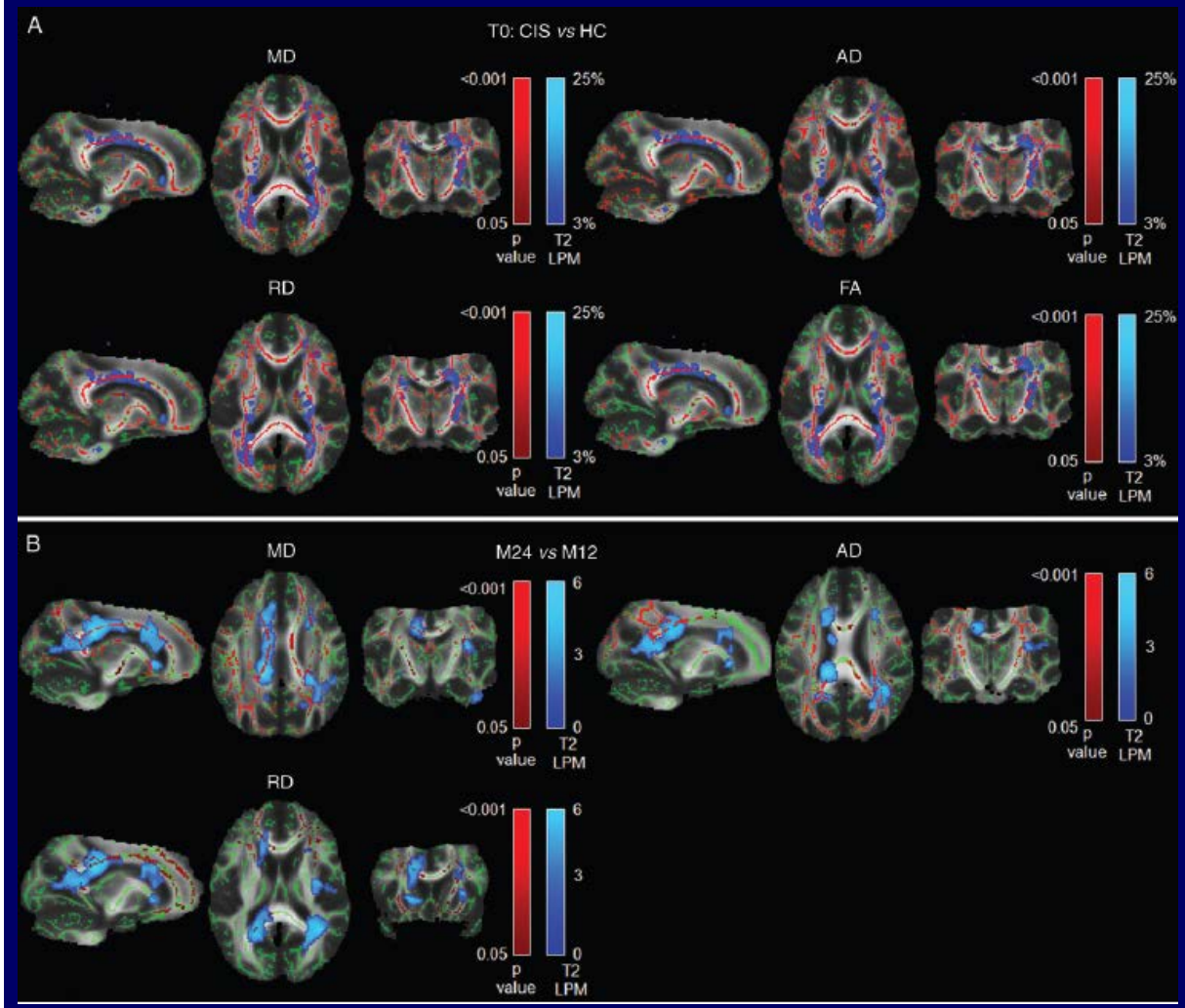
Filippi et al., JNNP 2000

MRI IN MS

NAWM damage

37 CIS patients, 2 years FU





Rocca et al., Radiology 2015

MRI IN MS

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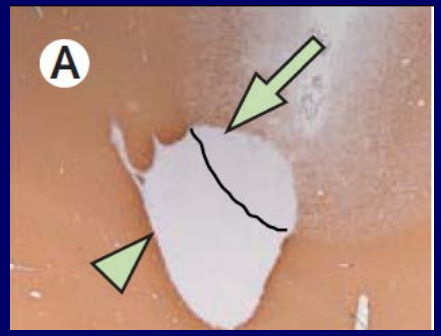
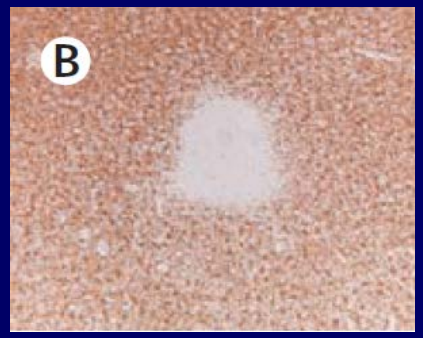
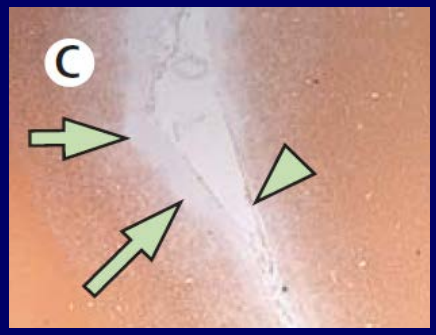
MRI IN MS
Cortical lesions



Type I: mixed WM/GM
34%



Type II: intracortical
16 %

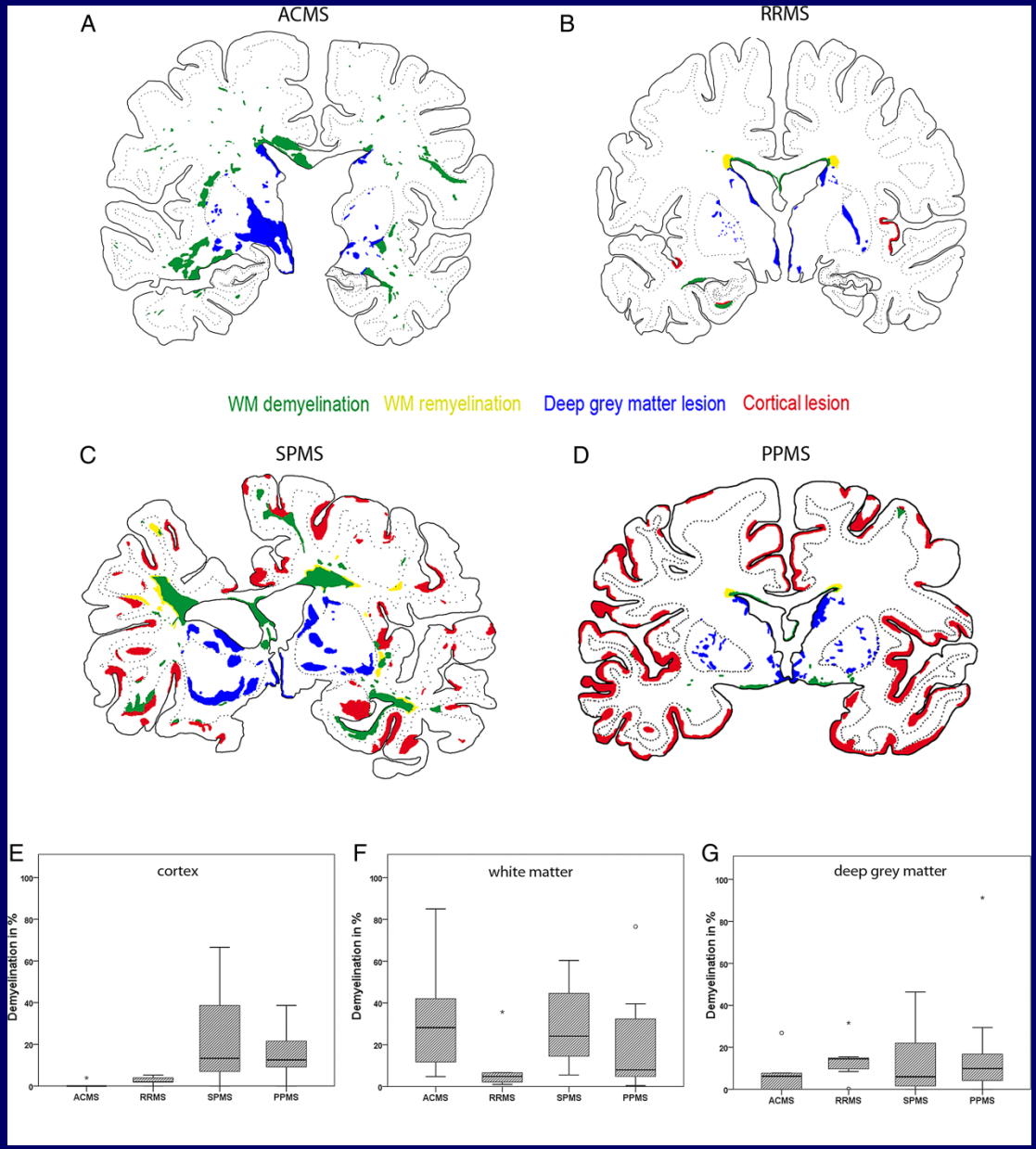


Type III: subpial cortical

Type IV: entire cortical ribbon

50%

Geurts and Barkhof, Lancet Neurol 2008

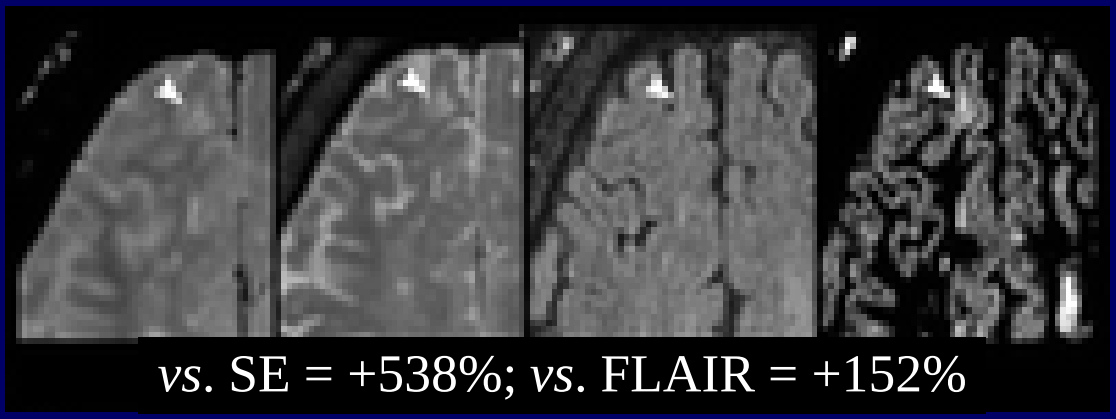


Haider et al., JNNP 2014

MRI IN MS

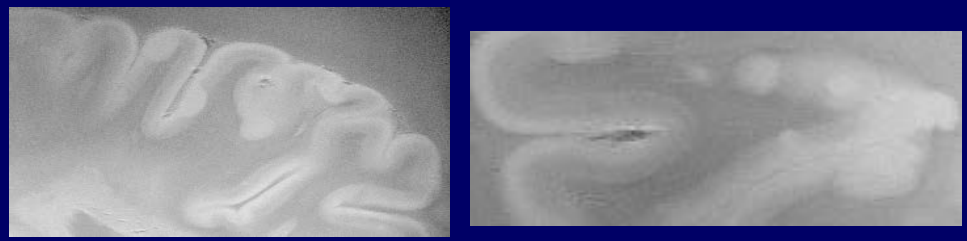
Cortical lesions

DIR



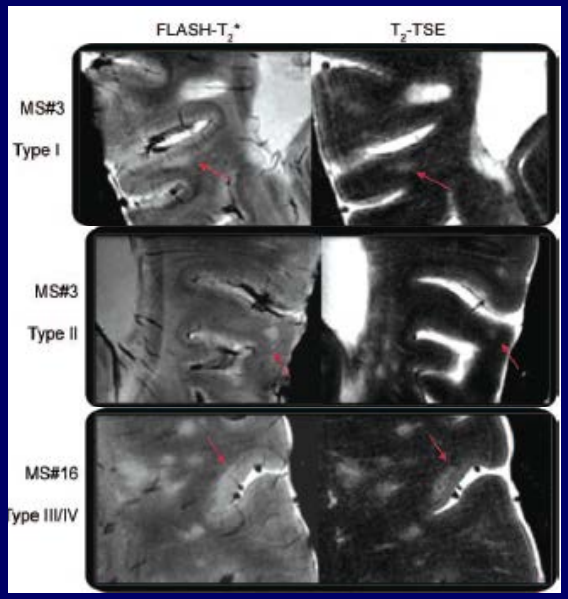
Geurts et al., Radiology 2005

8.0 T



Kangarlu et al., AJNR 2007

7.0 T



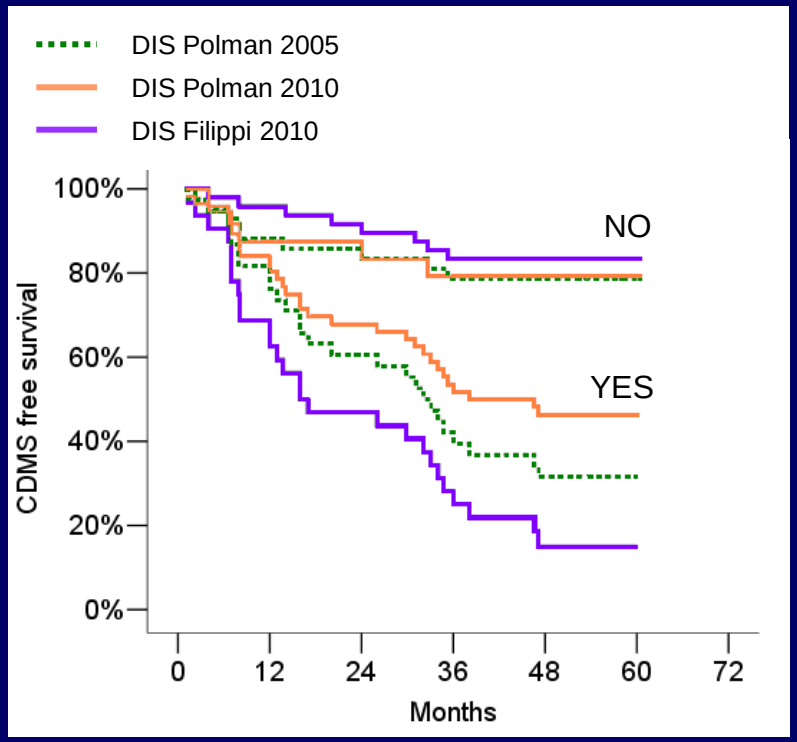
	7-T MRI		RRMS (n = 9)		SPMS (n = 7)		Pathology (study 1*), %	Pathology (study 2*), %
	%	(n)	Mean ± SE	Range	Mean ± SE	Range		
All types	100	(199)	9.4 ± 2.2	2-21	19 ± 6.9	8-53	100	100
Type I	36.2	(72)	3.9 ± 1.6	1-16	6.2 ± 4.0	0-26	34	38
Type II	13.6	(27)	1.1 ± 0.4	0-3	2.8 ± 1.5	0-10	16	18
Type III/IV	50.2	(100)	4.4 ± 1.3	0-11	10 ± 2.3	4-17†	50	44

Mainero et al., Neurology 2009

MRI IN MS

Cortical lesions

DIR in CIS (evolution to CDMS)



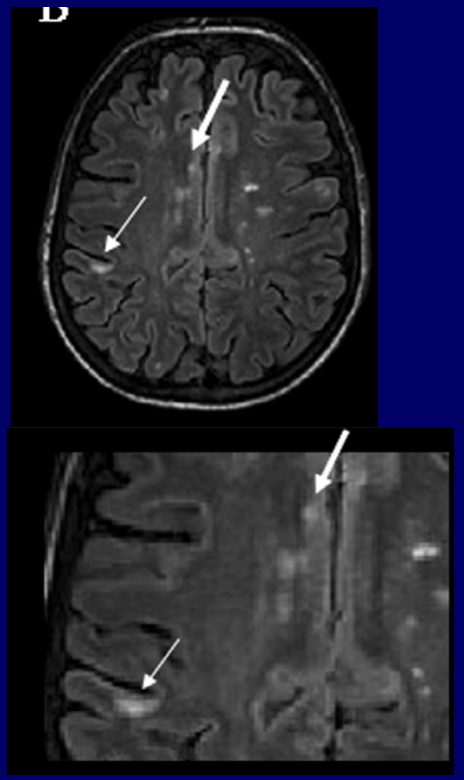
At least 2:

1 enhancing or 1 SC lesion
1 infratentorial lesion
1 cortical lesion

	Sensitivity	Specificity	Accuracy	OR
DIS Polman 2005	74 %	73%	74%	7.9
DIS Montalban 2010	86%	42%	61%	4.3
DIS Filippi 2010	**77%**	**93%**	**86%**	**47.3**

Filippi et al., Neurology 2010

DIR in pediatric MS



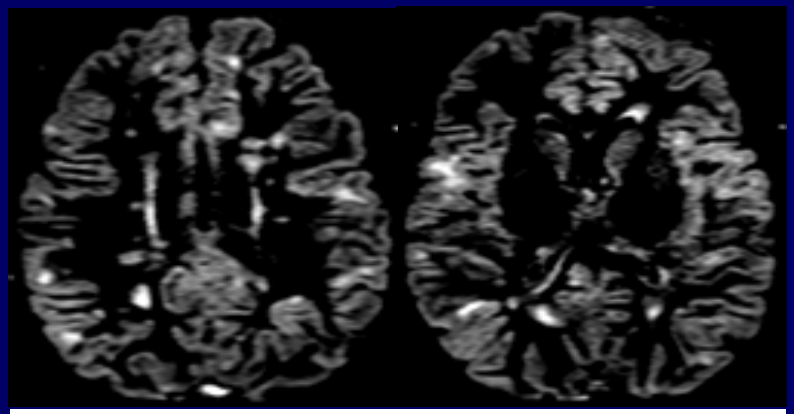
Absinta et al., Neurology 2011

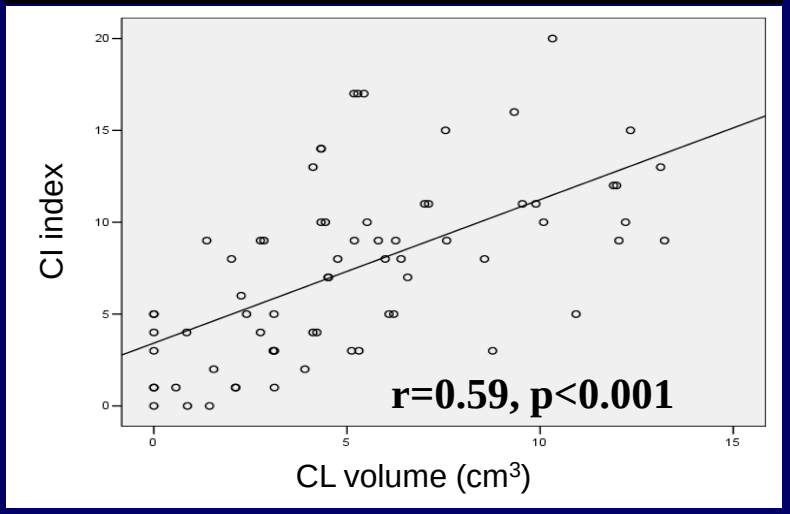
CLs: 8% pediatric MS, 66% adult MS.

Mean CL volume:
0.002 ml (SD=0.009) pediatric MS
0.2 ml (SD=0.3) adult MS (p=0.0003)

MRI IN MS
Cortical lesions

CLs and cognitive impairment





Calabrese et al., Arch Neurol 2009

Age, CL volume, and NCV independent predictors of the cognitive impairment index: R^2=0.55, p<0.001

CLs and clinical disability accumulation

107 relapse-onset MS patients, 3 years FU

Baseline CL volume: entire group: B=0.511; p<0.001
RRMS: B=0.512; p<0.001
SPMS: B=0.495; p<0.001

Calabrese et al., Ann Neurol 2010

CLs and disease evolution

334 relapse-onset MS patients, 5 years FU

Age: OR 1.2, p =0.001
Baseline CL volume: OR 1.7, p <0.001
Baseline cerebellar cortical volume: OR 0.2, p <0.001

Calabrese et al., Ann Neurol 2013

48 PPMS patients, 2 years FU

Baseline CL volume: B: -0.525, p <0.001
Baseline T2-WM-LV: B: -0.448, p <0.001

Calabrese et al., Neurology 2009

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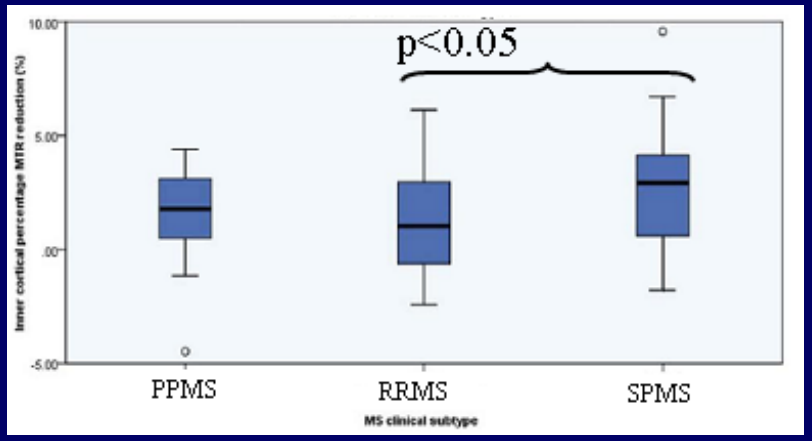
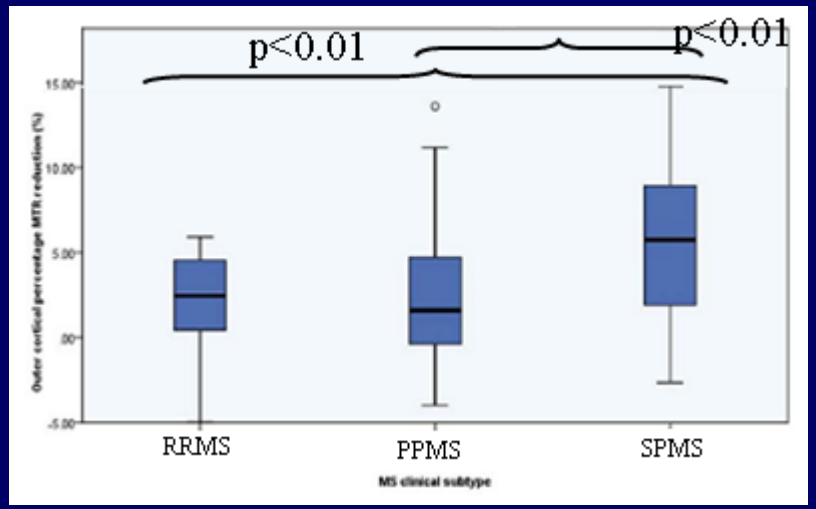
MRI IN MS

Subpial demyelination

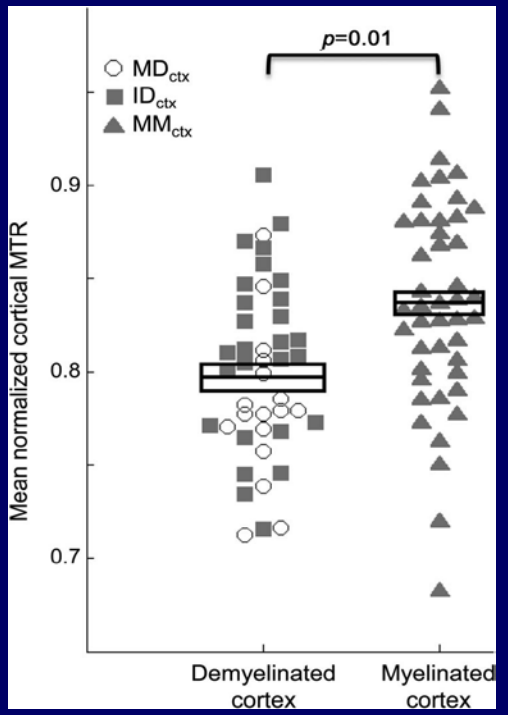
Inner cortical MTR



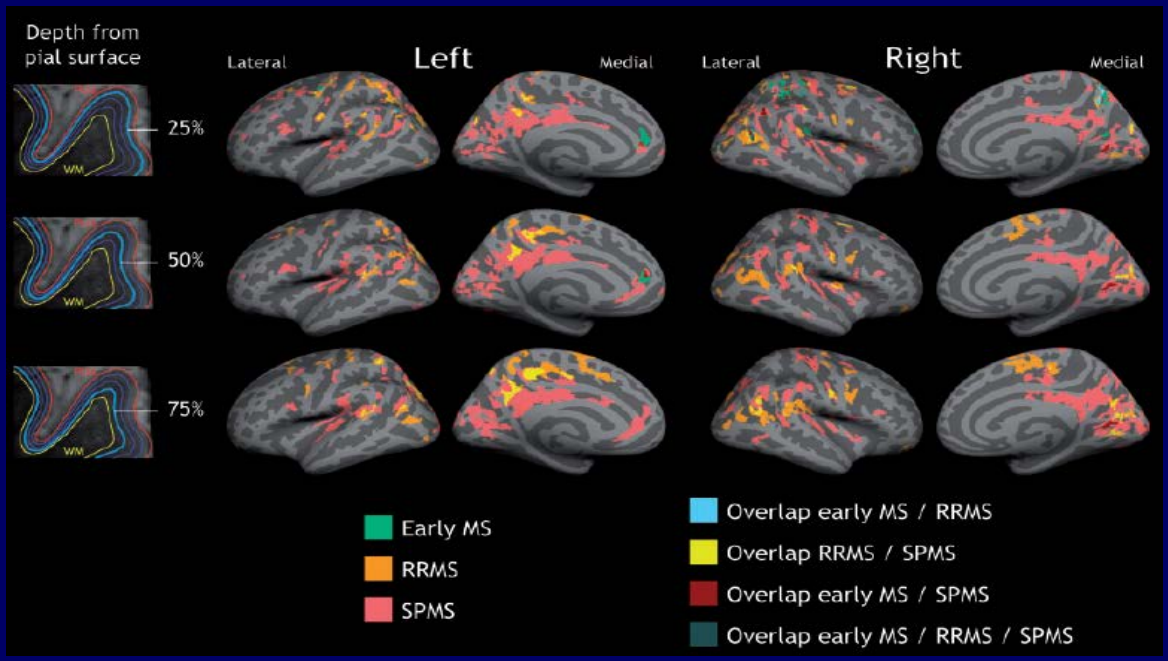
Outer cortical MTR



Samson et al., Mult Scler 2014



Chen et al., Neurology 2013



Mainero et al., Brain 2015

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MRI IN MS

"Diffuse" GM damage

54 PPMS, 5-year FW & EDSS

Baseline EDSS: OR: 0.48, p = 0.03

GM MD: OR: 1.21, p = 0.005

Nagelkerke R^2: 0.44

Rovaris et al., Brain 2006

73 relapse-onset MS, 8-year FW & EDSS

GM MTR: OR 0.97, p=0.03

Lesion MTR % change: OR 0.88, p=0.02

Nagelkerke R^2: 0.28

Agosta et al., Brain 2006

73 relapse-onset MS,13-year FW & EDSS

Baseline GMF: OR 0.79, p=0.01

C index: 69%

Evolution to SPMS:

Baseline T2 LV (OR=1.13, p=0.005)

Baseline GMF (OR=0.71, p=0.04)

C-index: 84%

Cognitive deterioration:

Baseline average GM MTR (OR=0.87, p=0.03)

Baseline disease duration (OR=1.50, p=0.08)

C-index: 97%

Filippi et al., Neurology 2013

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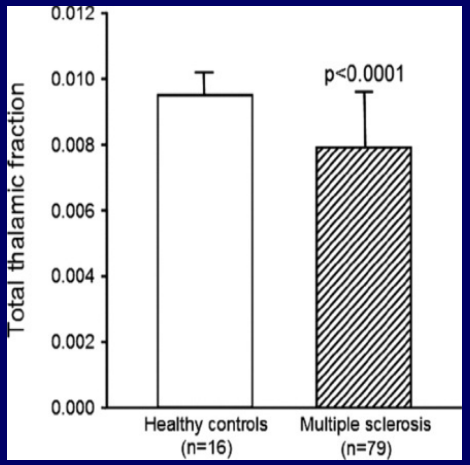
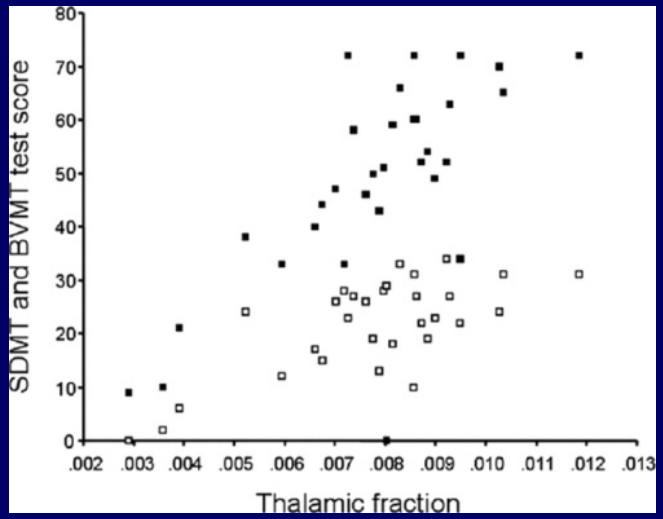
MRI IN MS
Regional damage / Thalamus

Thalamic fraction *vs* cognitive test

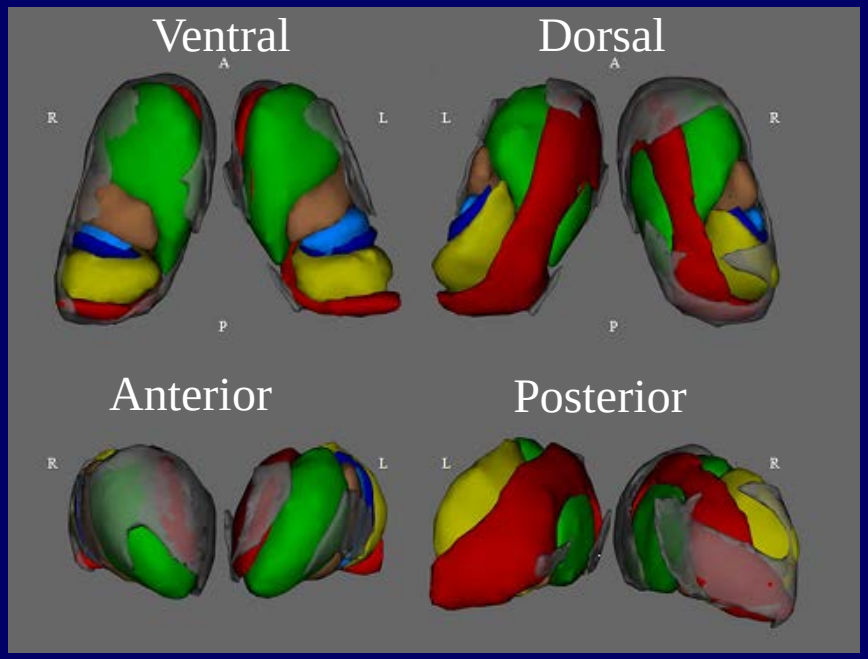




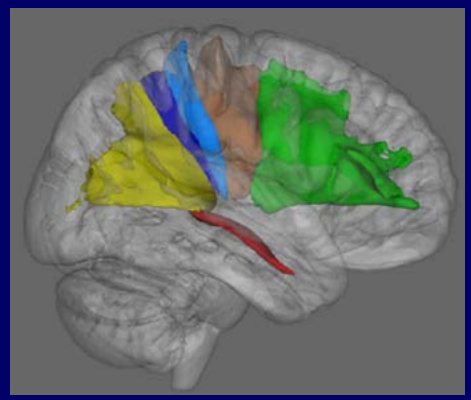
Houtchens et al., Neurology 2007

Thalamic connectivity defined regions (CDRs)

CI (22) *vs* CP (30) MS



Cortico-thalamic tracts



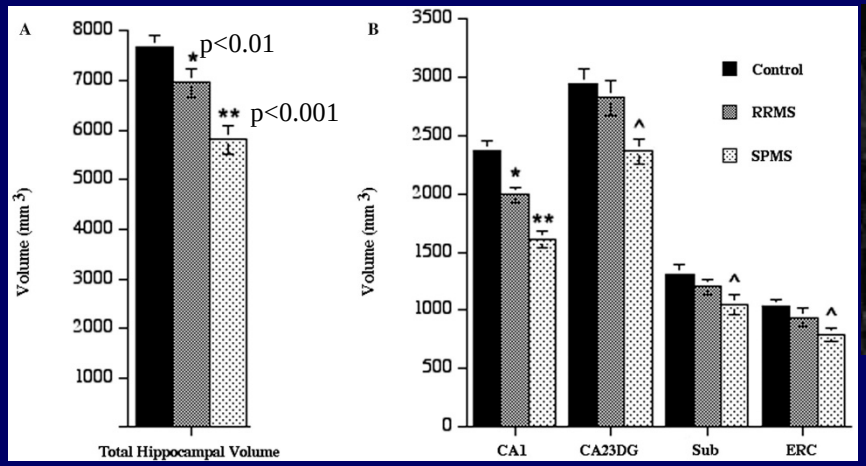
Frontal CDR
Motor CDR
Post-Central CDR
Posterior Parietal CDR
Temporal CDR
Occipital CDR

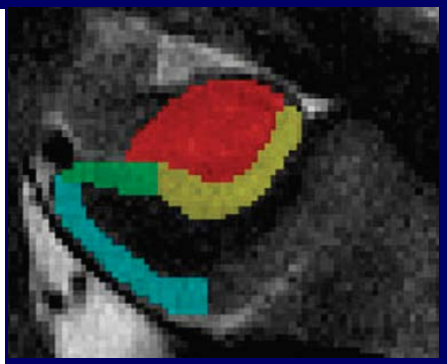
Damage of specific cortico-thalamic tracts explained global cognitive dysfunction and impairment of selected cognitive domains better than all other MRI variables

Bisecco et al., Hum Brain Mapp 2015

MRI IN MS
Regional damage / Hippocampus

Hippocampal atrophy



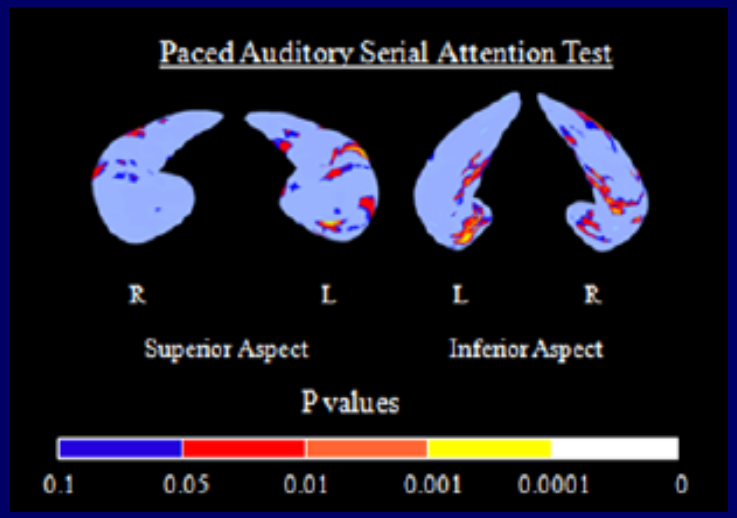


Dentate and CA2&3 CA1
Subiculum ERC

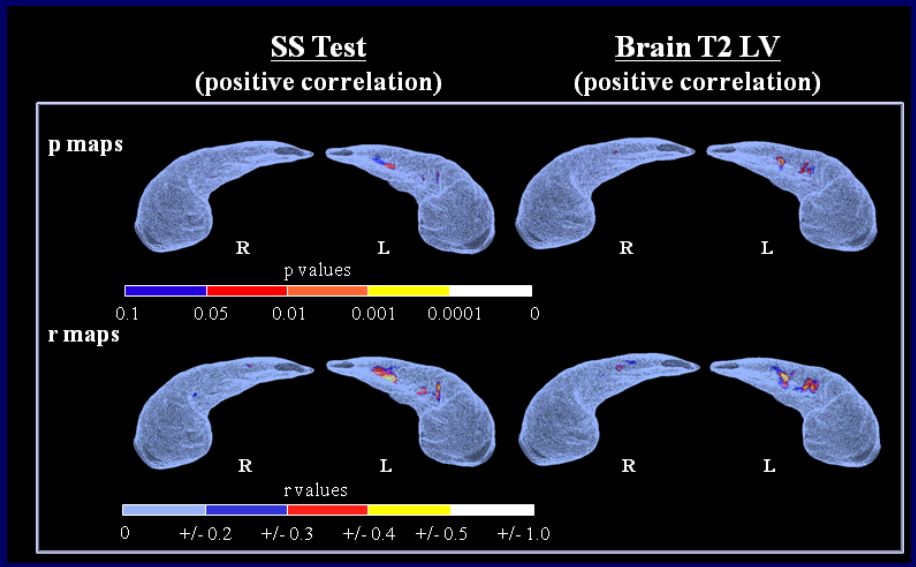
Sicotte et al., Brain 2008

Hippocampal DG hypertrophy

Hippocampal atrophy *vs* PASAT test

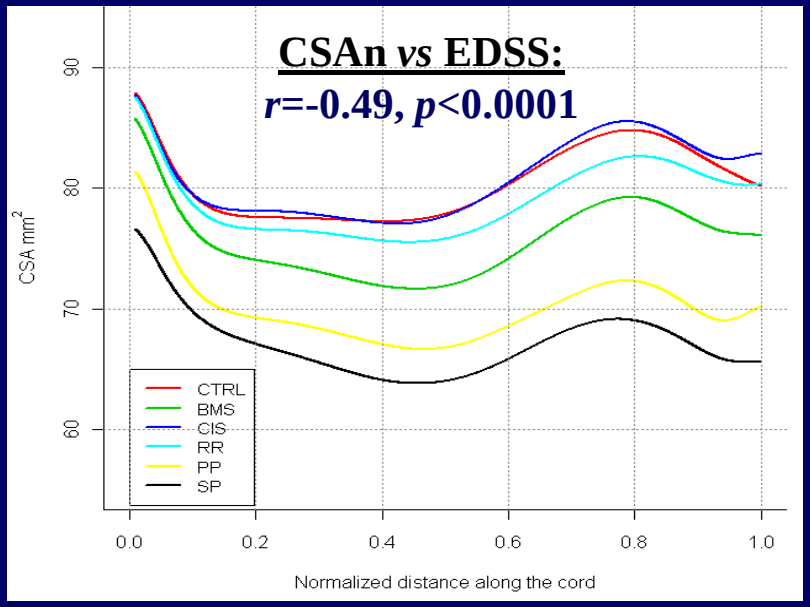


Longoni et al., Brain Struct Funct 2013



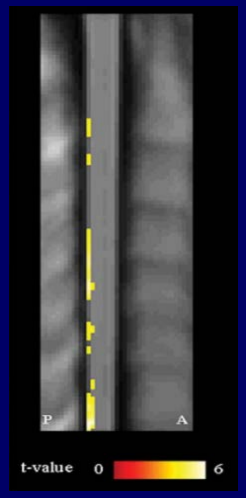
Rocca et al., Hum Brain Mapp 2015

MRI IN MS
Regional damage / Spinal cord

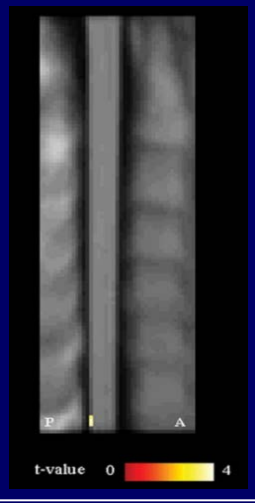


Rocca et al., Neurology 2011

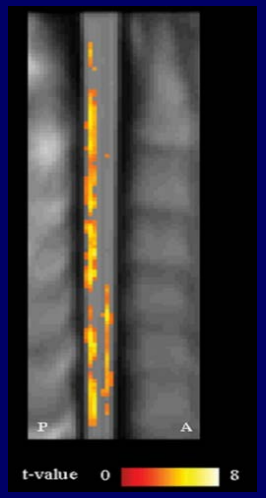
MS *vs* controls



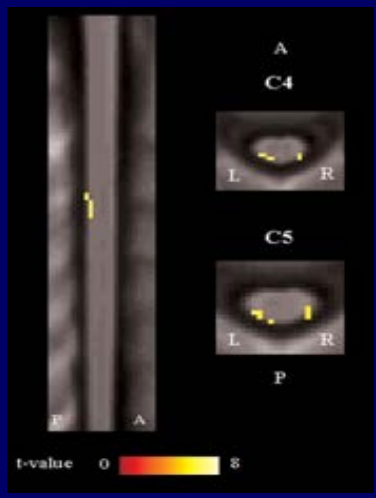
RRMS *vs* controls



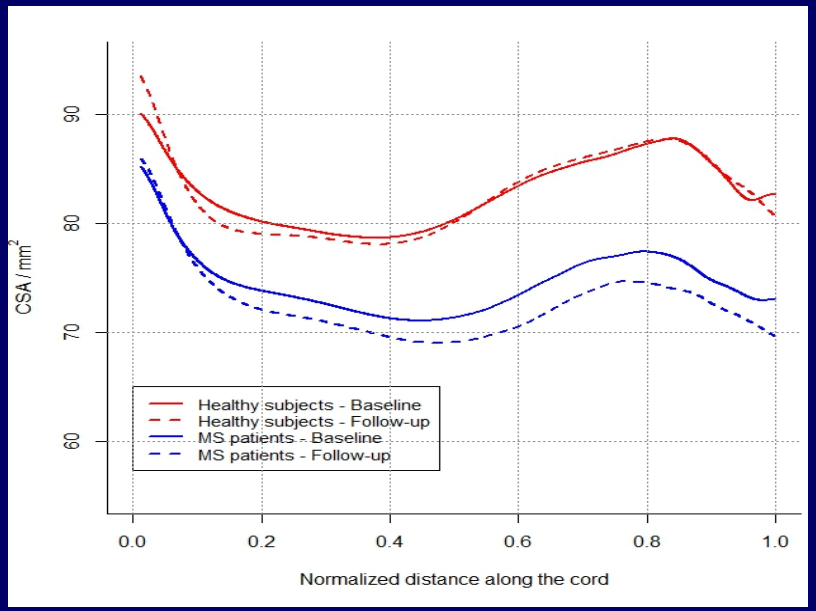
SPMS *vs* RRMS



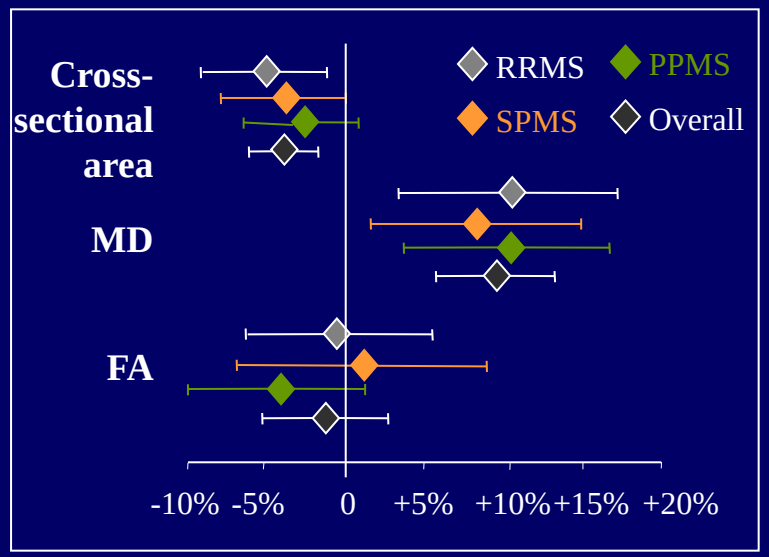
Atrophy *vs* EDSS



Valsasina et al., Radiology 2012



Valsasina et al., J Neurol 2015



42 MS patients
Baseline cross-sectional area and FA *vs*. EDSS at follow –up:
r = -0.40; p = 0.01

Agosta et al., Brain 2007

MRI IN MS

Outline of the presentation

- WM lesion nature
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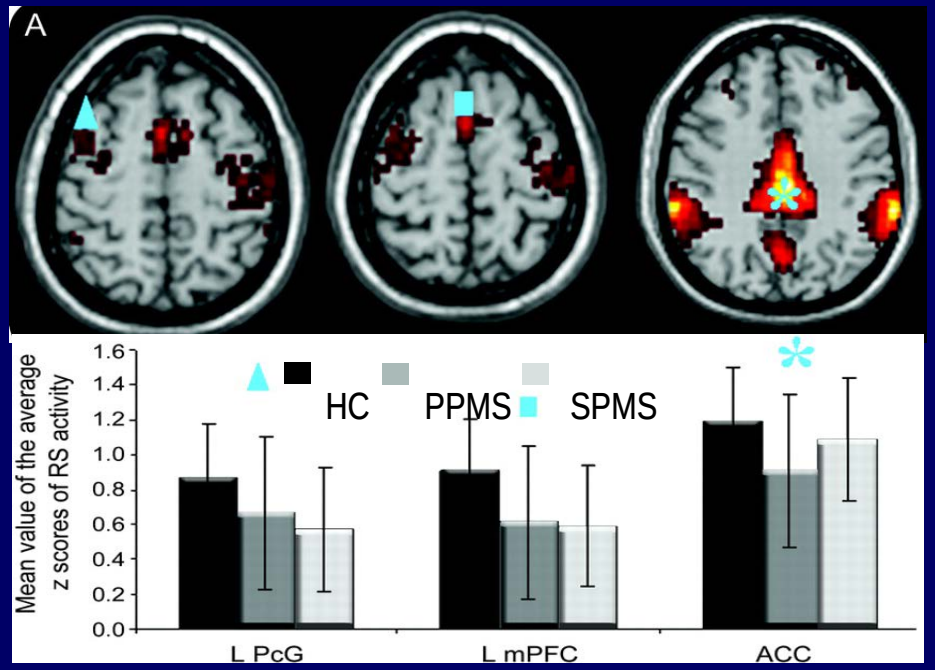
MRI IN MS

CNS functional reorganization

DMN in progressive MS patients

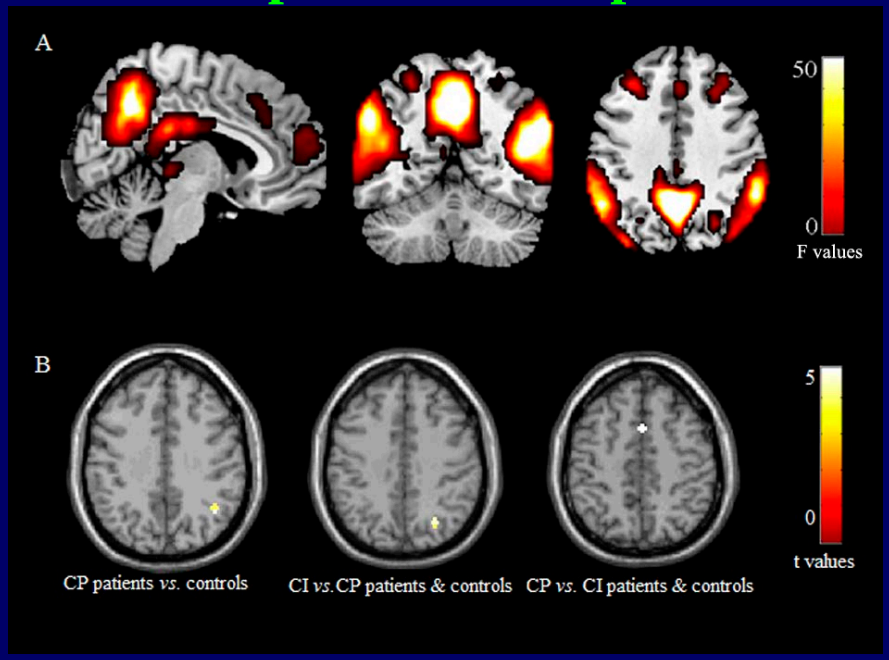


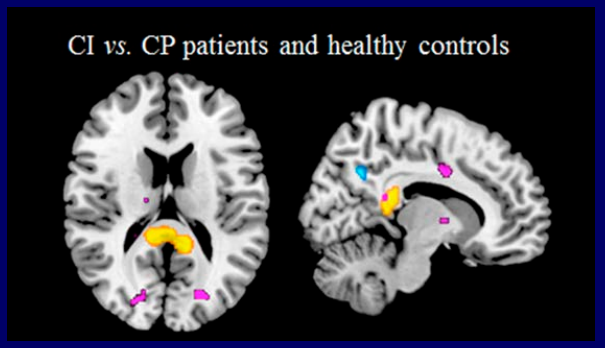
Correlations between ↓ DMN fluctuations and:

PASAT (r=0.42, p<0.001)
CC FA and JD (r from 0.54 to 0.87, p<0.001)
Cingulum FA (r=0.83, p<0.001)

Rocca et al., Neurology 2010

DMN in pediatric MS patients





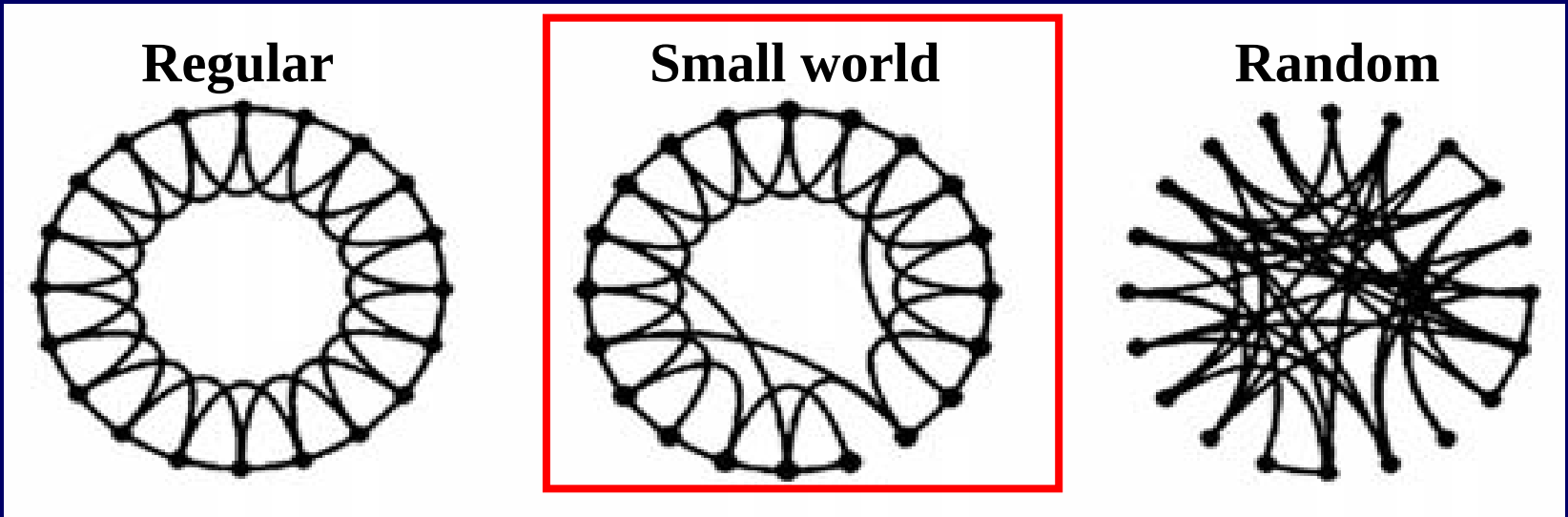
CI explained by:
- **cingulum FA**
- **CC MD**
- **R precuneus RS FC**

C-index=0.99

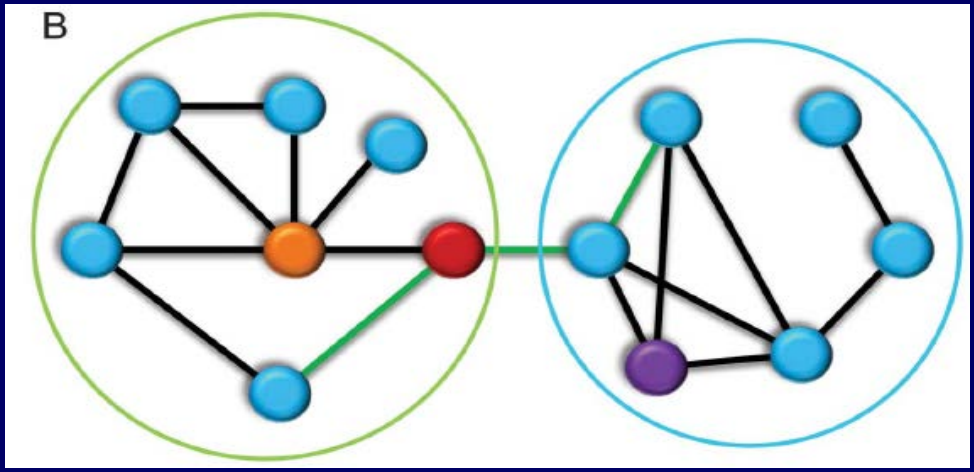
Rocca et al., Neurology 2014

MRI IN MS

CNS functional reorganization



Small world network: high clustering coefficient, short characteristic path length



Shortest path length

Highest degree

Connecter hub

Highest clustering coefficient (its neighbours are all neighbours of each other)

Global properties

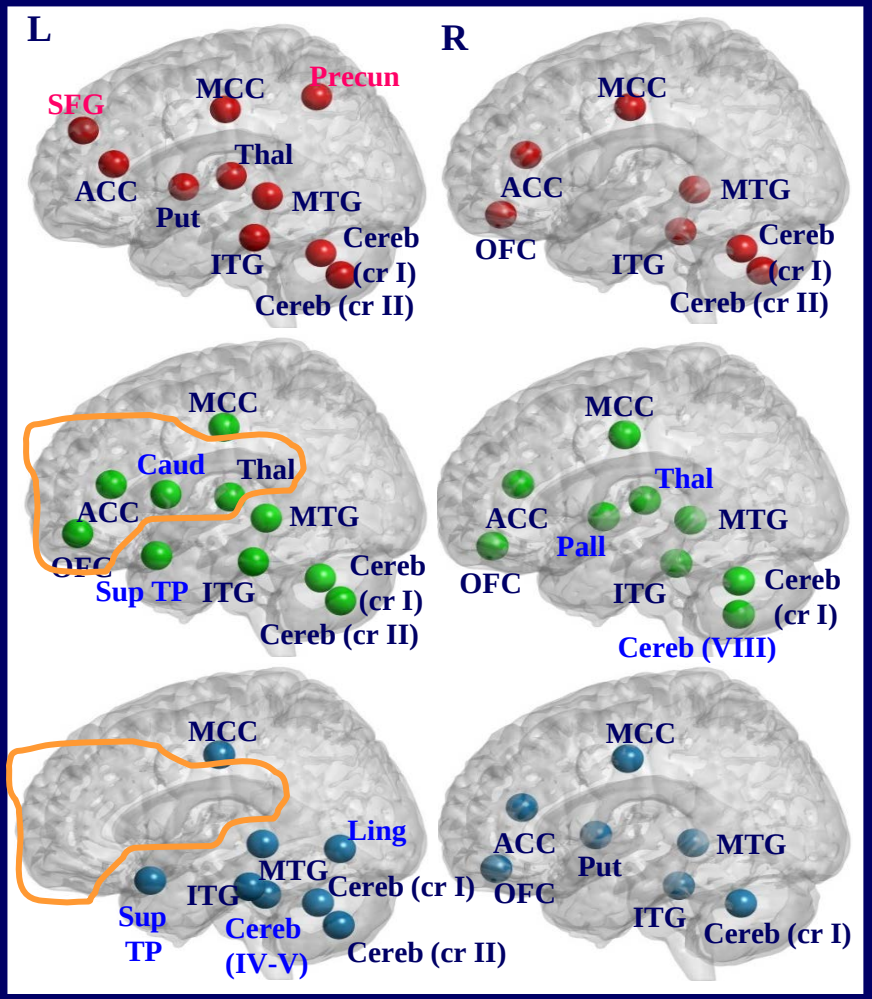
Regional properties

MRI IN MS

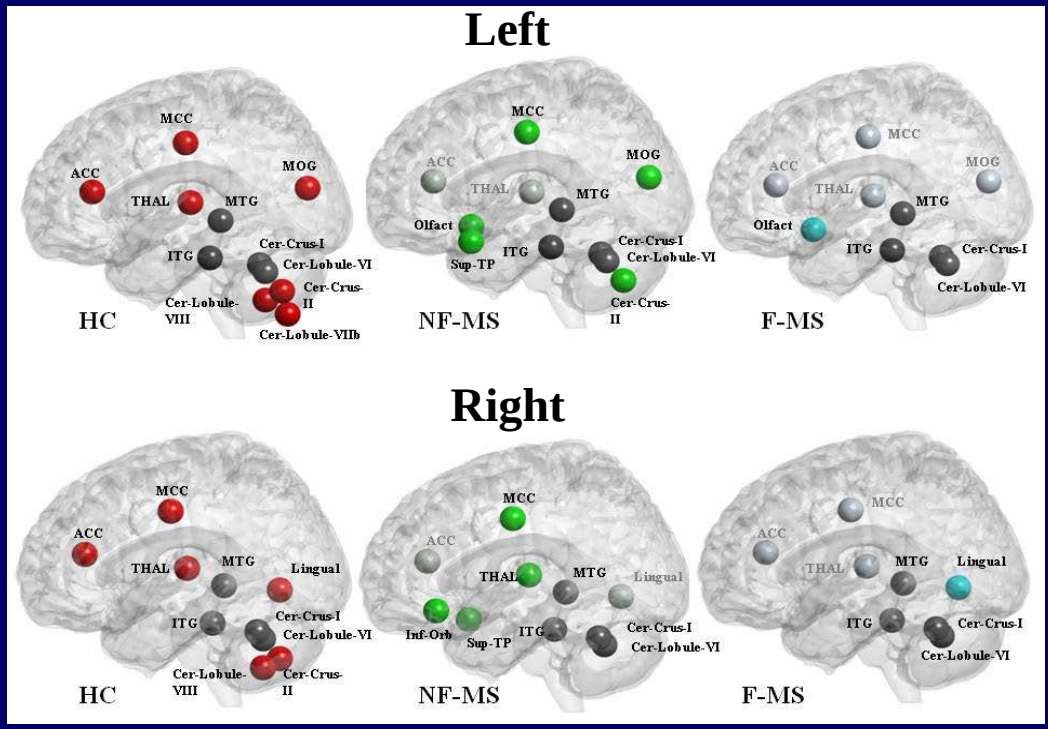
CNS functional reorganization

Functional hubs

246 MS (34 % CI) *vs* 55 controls



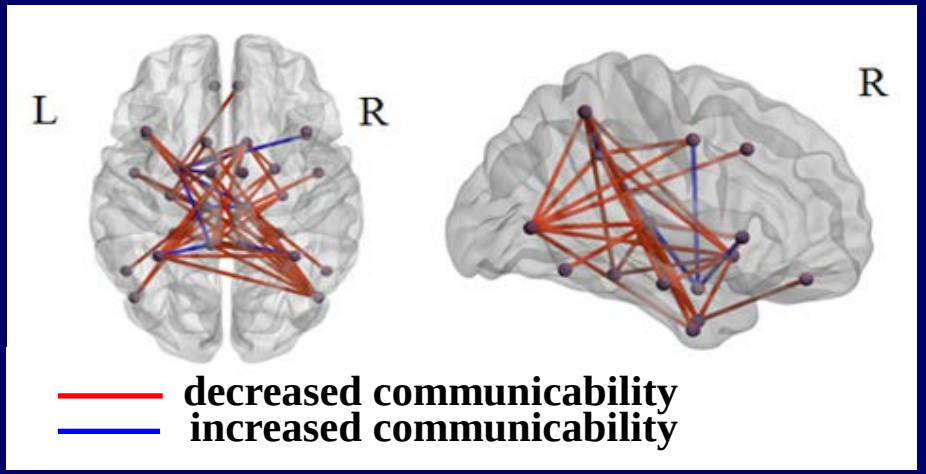
Rocca et al., Brain Struct Funct 2014



Filippi et al., AAN 2014

Hippocampal structural connectivity

Edge graphical properties



Llufriu et al., ECTRIMS 2015

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MRI IN MS

Conclusions