National MS center Melsbroek

Nieuwe Inzichten in Beeldvorming bij MS

Spinaal Reserve als Nieuwe Prognostische Factor?

Prof. Dr. Miguel D'haeseleer, NMSC Melsbroek & UZ Brussel/VUB

Multiple Sclerose

- Belangrijke oorzaak van neurologische invaliditeit
- Ziekte verloopt **bij iedereen verschillend**
- Mechanismen?

National MS center Melsbroek

Multiple Sclerose

- Belangrijke oorzaak van neurologische invaliditeit
- Ziekte verloopt **bij iedereen verschillend**
- Mechanismen?
- **Concept van structurele en functionele “Reserve”**
- Intracranieel volume beschermt tegen cognitieve en fysieke achteruitgang

Multiple Sclerose

- Belangrijke oorzaak van neurologische invaliditeit
- Ziekte verloopt **bij iedereen verschillend**
- Mechanismen?
- **Concept van structurele en functionele “Reserve”**
- Intracranieel volume beschermt tegen cognitieve en fysieke achteruitgang
- **Klinische relevantie van pathologie in het ruggenmerg**
- Diameter van het spinal kanaal is weerspiegeling van de premorbide status

Spinal cord atrophy and disability in multiple sclerosis

A new reproducible and sensitive MRI method with potential to monitor disease progression

N. A. Losseff, S. L. Webb, J. I. O'Riordan, R. Page, L. Wang, G. J. Barker, P. S. Tofts, W. I. McDonald, D. H. Miller and A. J. Thompson

NMR Research Unit, Institute of Neurology, London, UK

Correspondence to Dr A. J. Thompson, NMR Research Unit, Institute of Neurology, Queen Square, London WC1N 3BG, UK

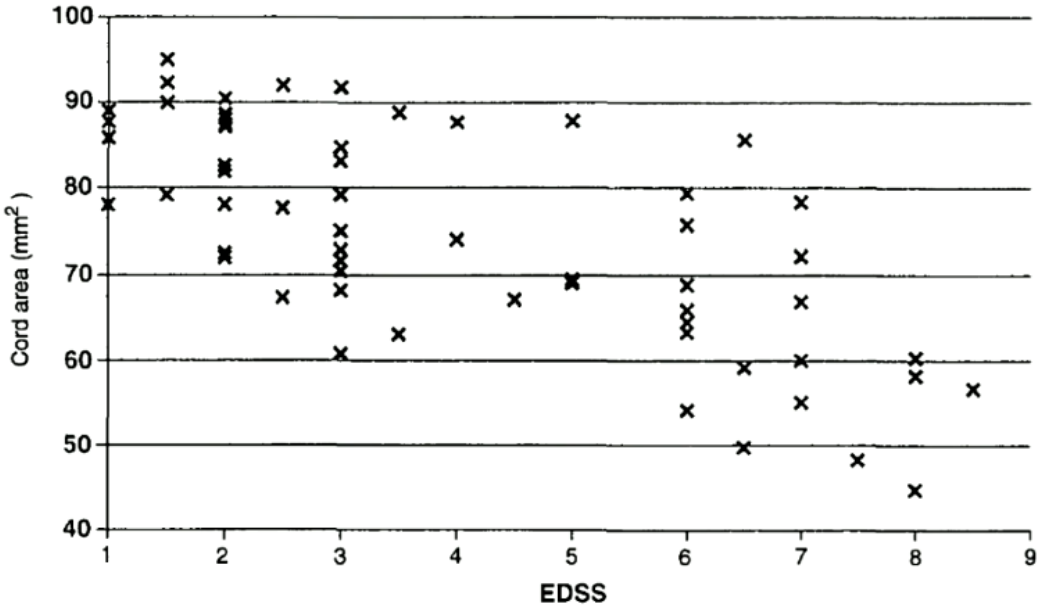


Fig. 3 Scatter chart of EDSS and C2 cord area in all patients ($r = -0.7$).

National MS center Melsbroek

Spinal cord atrophy and disability in multiple sclerosis

A new reproducible and sensitive MRI method with potential to monitor disease progression

N. A. Losseff, S. L. Webb, J. I. O'Riordan, R. Page, L. Wang, G. J. Barker, P. S. Tofts, W. I. McDonald, D. H. Miller and A. J. Thompson

NMR Research Unit, Institute of Neurology, London, UK

Correspondence to: Dr A. J. Thompson, NMR Research Unit, Institute of Neurology, Queen Square, London WC1N 3BG, UK

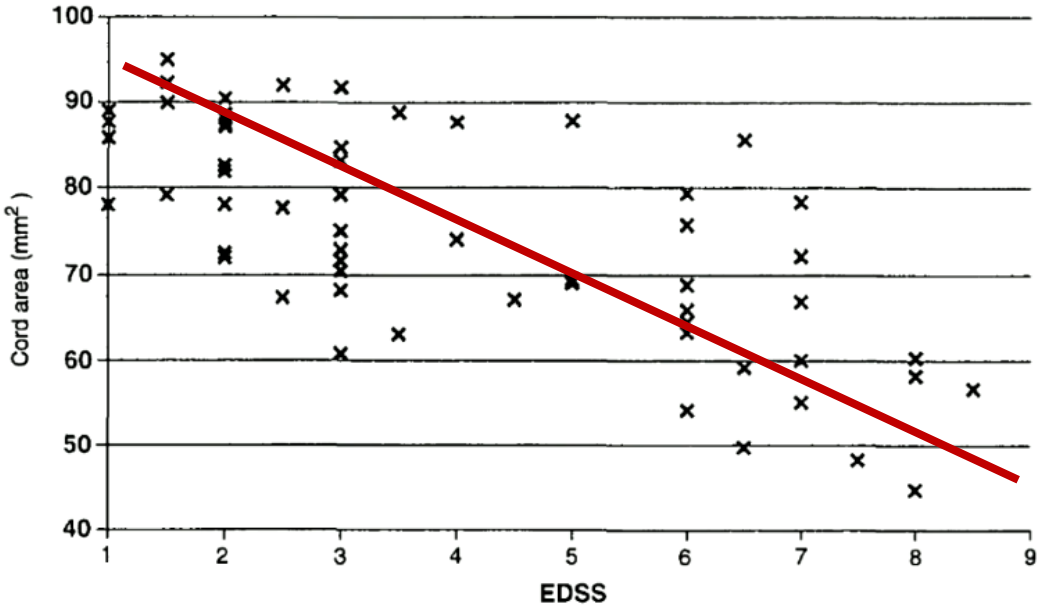


Fig. 3 Scatter chart of EDSS and C2 cord area in all patients ($r = -0.7$).

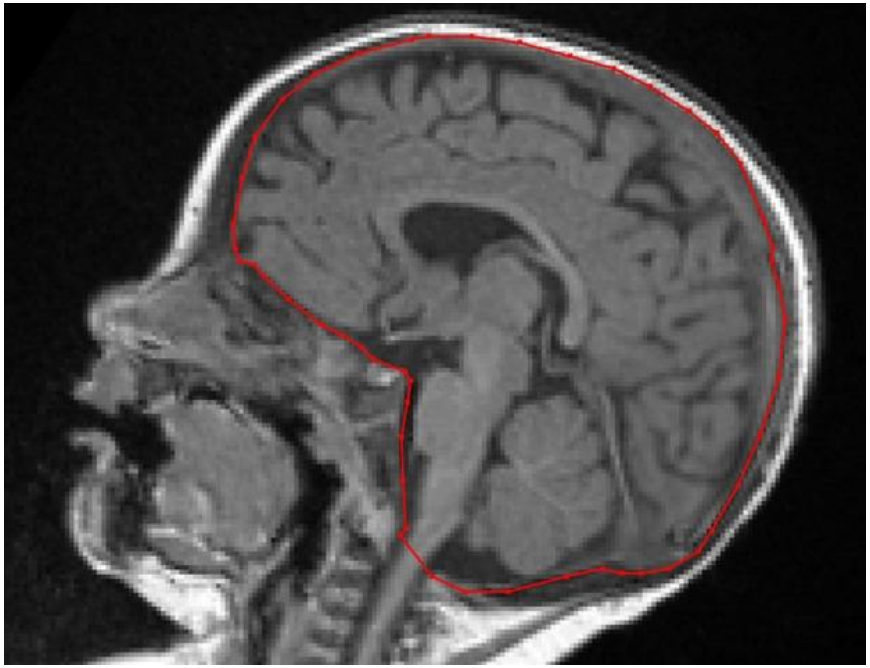
National MS center Melsbroek

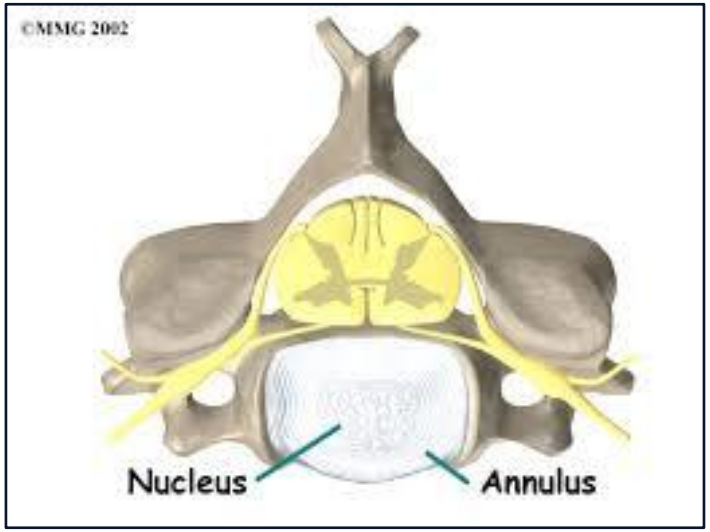
Multiple Sclerose

- Belangrijke oorzaak van neurologische invaliditeit
- Ziekte verloopt **bij iedereen verschillend**
- Mechanismen?
- **Concept van structurele en functionele “Reserve”**
- Intracranieel volume beschermt tegen cognitieve en fysieke achteruitgang
- **Klinische relevantie van pathologie in het ruggenmerg**
- Diameter van het spinal kanaal is weerspiegeling van de premorbide status

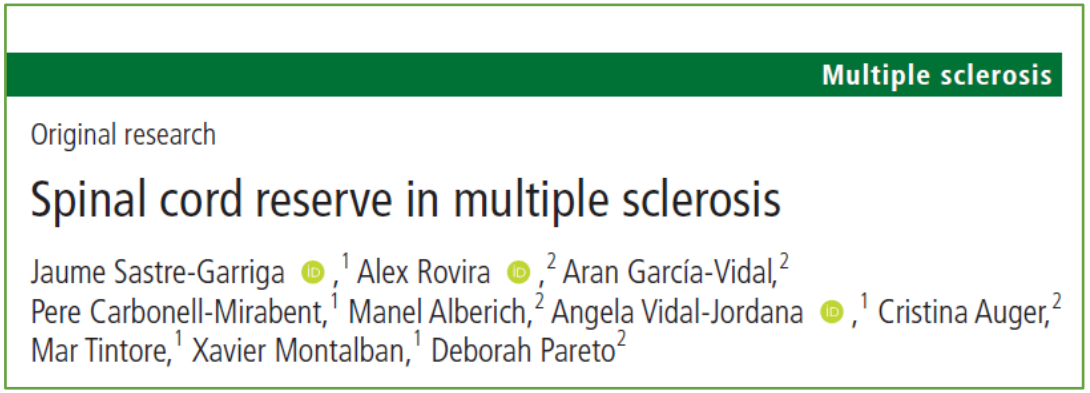
Multiple Sclerose

- Belangrijke oorzaak van neurologische invaliditeit
- Ziekte verloopt **bij iedereen verschillend**
- Mechanismen?
- **Concept van structurele en functionele “Reserve”**
- Intracranieel volume beschermt tegen cognitieve en fysieke achteruitgang
- **Klinische relevantie van pathologie in het ruggenmerg**
- Diameter van het spinal kanaal is weerspiegeling van de premorbide status
- **Spinaal reserve?**





National MS center Melsbroek



Multiple sclerosis

Original research

Spinal cord reserve in multiple sclerosis

Jaume Sastre-Garriga ,[1] Alex Rovira ,[2] Aran García-Vidal,[2]
Pere Carbonell-Mirabent,[1] Manel Alberich,[2] Angela Vidal-Jordana ,[1] Cristina Auger,[2]
Mar Tintore,[1] Xavier Montalban,[1] Deborah Pareto[2]

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ When applied to people with multiple sclerosis (MS), the brain reserve concept implies that the larger the brain at a premorbid stage, the lower is the risk of disability.

WHAT THIS STUDY ADDS

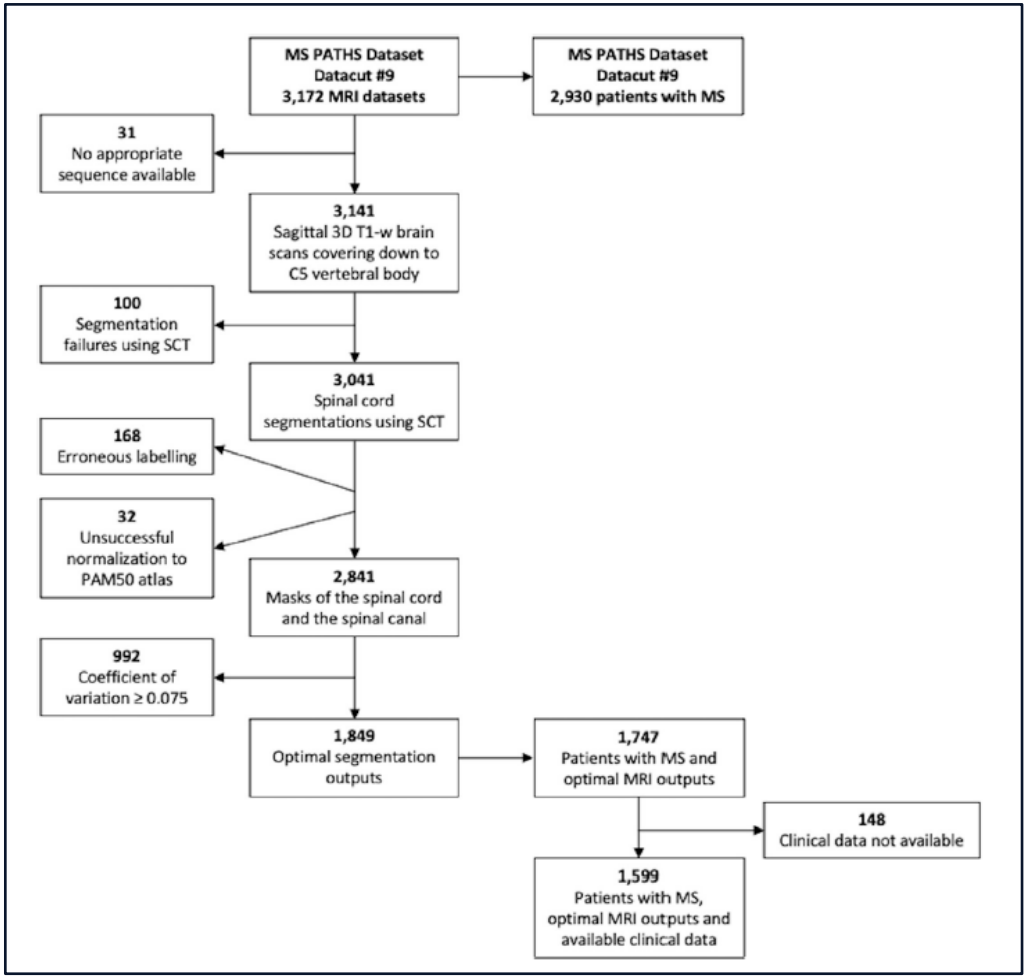
⇒ A larger area of the spinal canal, as a proxy of spinal cord (SC) maximal lifetime growth, is protective against disability in people with MS.

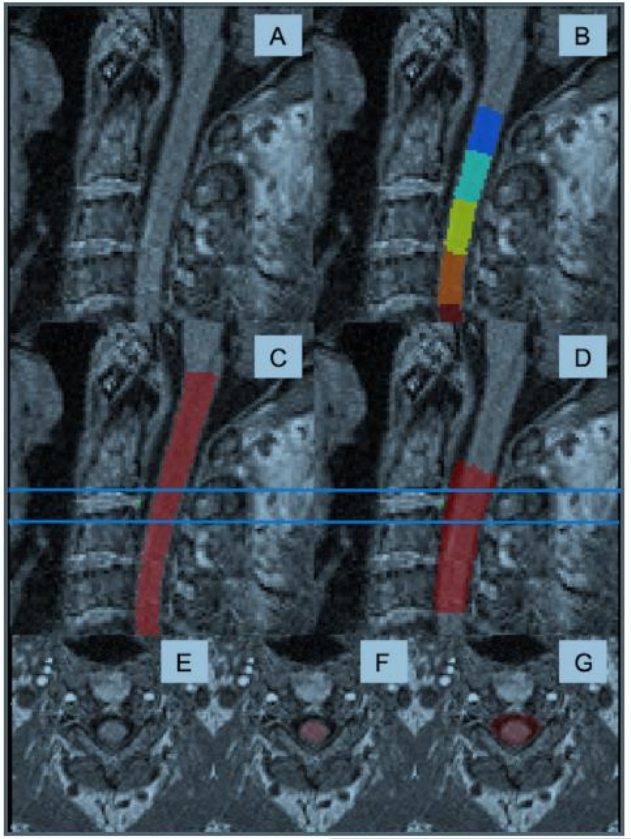
HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study extends the concept of brain reserve to an overarching concept of central nervous system reserve, supporting the need of brain and SC prehabilitation through cognitive and physical enrichment in MS.

J Neurol Neurosurg Psychiatry, Jan 2023

National MS center Melsbroek





National MS center Melsbroek

Multiple sclerosis

Table 1 Demographical, clinical and radiological features of patients with MS and healthy controls

	Healthy controls n=42	MS n=1747	P value*	SMD
Sex (female), n (%)†	33 (78.6%)	1171 (73.2%)	0.5513	0.125
Age, mean (SD)†	45.56 (9.64)	46.35 (12.17)	0.6041	0.072
Spinal cord canal area, median (IQR)	212.6 (210.1–216.0)	213.2 (208.2–220.2)	0.5503	0.286
Spinal cord area, median (IQR)	65.02 (61.79–68.87)	60.41 (54.86–65.94)	<0.001	0.709
Spinal cord parenchymal fraction, median (IQR)	0.31 (0.29–0.32)	0.28 (0.26–0.30)	<0.001	0.895
PDDS‡, median (IQR)	–	1 (0–3)	–	–
Brain T2 lesion volume§, median (IQR)	–	6.68 (3.17–14.55)	–	–

*P values correspond to univariate comparisons using parametric and non-parametric tests, as convenience. Age is expressed in years; spinal cord parenchymal fraction is expressed as percentage; spinal cord canal area and spinal cord area are expressed in mm^2; brain T2 lesion volume is expressed in mm^3.
†n=1599 for patients with MS (8.4% of missing data on the 1747 main dataset).
‡n=1554 (2.8% of missing data on the 1599 dataset for clinical associations).
§n=1453 for patients with MS (corresponding to 9.1% of missing data on the 1599 dataset for clinical associations).
MS, multiple sclerosis; PDDS, Patient Determined Disease Steps; SMD, standard mean differences/Cohen's d.

Multiple sclerosis

Table 1 Demographical, clinical and radiological features of patients with MS and healthy controls

	Healthy controls n=42	MS n=1747	P value*	SMD
Sex (female), n (%)†	33 (78.6%)	1171 (73.2%)	0.5513	0.125
Age, mean (SD)†	45.56 (9.64)	46.35 (12.17)	0.6041	0.072
Spinal cord canal area, median (IQR)	212.6 (210.1–216.0)	213.2 (208.2–220.2)	0.5503	0.286
Spinal cord area, median (IQR)	65.02 (61.79–68.87)	60.41 (54.86–65.94)	<0.001	0.709
Spinal cord parenchymal fraction, median (IQR)	0.31 (0.29–0.32)	0.28 (0.26–0.30)	<0.001	0.895
PDDS‡, median (IQR)	–	1 (0–3)	–	–
Brain T2 lesion volume§, median (IQR)	–	6.68 (3.17–14.55)	–	–

*P values correspond to univariate comparisons using parametric and non-parametric tests, as convenience. Age is expressed in years; spinal cord parenchymal fraction is expressed as percentage; spinal cord canal area and spinal cord area are expressed in mm^2; brain T2 lesion volume is expressed in mm^3.
†n=1599 for patients with MS (8.4% of missing data on the 1747 main dataset).
‡n=1554 (2.8% of missing data on the 1599 dataset for clinical associations).
§n=1453 for patients with MS (corresponding to 9.1% of missing data on the 1599 dataset for clinical associations).
MS, multiple sclerosis; PDDS, Patient Determined Disease Steps; SMD, standard mean differences/Cohen's d.

Relatie met Invaliditeit?

Multivariabele Lineaire Regressie

Leeftijd, Geslacht, SCPF, Brain T2 LV

National MS center Melsbroek

Relatie met Invaliditeit?

Multivariabele Lineaire Regressie

Leeftijd, Geslacht, SCPF, Brain T2 LV

Associatie van Spinaal Kanaal Diameter with PDDS (EDSS), PST (SDMT), LE-QoL

Relatie met Invaliditeit?

Multivariabele Lineaire Regressie

Leeftijd, Geslacht, SCPF, Brain T2 LV

Associatie van Spinaal Kanaal Diameter with PDDS (EDSS), PST (SDMT), LE-QoL

Niet met WST (T25FWT), MDT (9HPT), CST (visus), UE-QoL

Relatie met Invaliditeit?

Multivariabele Lineaire Regressie

Leeftijd, Geslacht, SCPF, Brain T2 LV

Associatie van Spinaal Kanaal Diameter with PDDS (EDSS), PST (SDMT), LE-QoL

Niet met WST (T25FWT), MDT (9HPT), CST (visus), UE-QoL

Algemene invaliditeit, cognitie, stapfunctie

Geen standaard, objectieve uitkomstmaten

Volgende Publicatie

Neurology®

MAGNIMS netwerk: Mongay-Ochoa, Neurology 2025 Jan 14;104(1):e210136.

MRI cervikale wervelzuil – C2/C3 and C3/C4 – EDSS – Longitudinaal opzet

National MS center Melsbroek

Volgende Publicatie

Neurology®

MAGNIMS netwerk: Mongay-Ochoa, Neurology 2025 Jan 14;104(1):e210136.

MRI cervikale wervelzuil – C2/C3 and C3/C4 – EDSS – Longitudinaal opzet

- Kleiner spinaal kanaal op C2/C3 bij progressieve MS
- Associatie met EDSS op C2/C3 and C3/C4
- Geen associatie met EDSS verslechtering na 5 jaar op C2/C3
- Kleiner kanaal op C3/C4 bij personen with EDSS verslechtering, significantie verdwijnt na correctie voor confounders

Nieuwe Validatie Studie

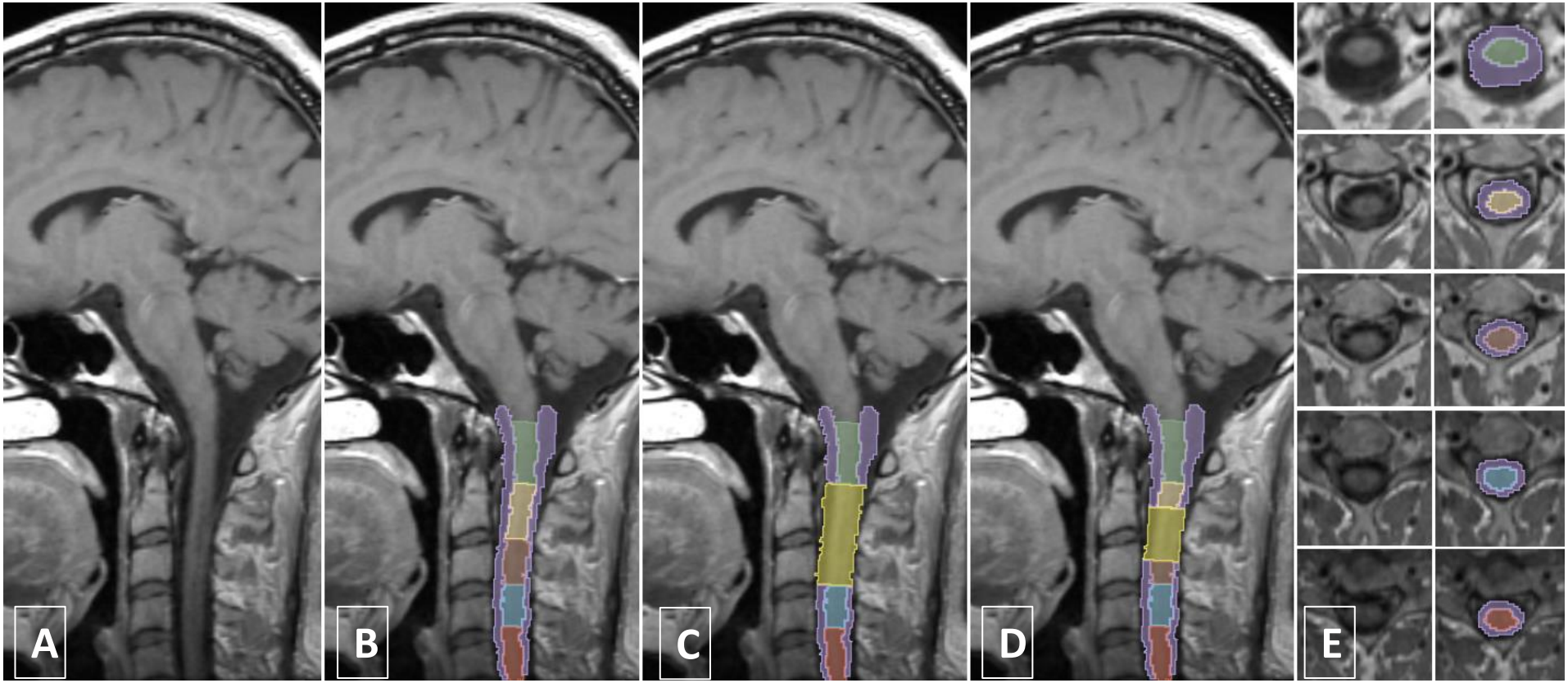
- Miguel D'Haeseleer, Marie D'hooghe, Stien Willems, Laetitia Della Faille, Ann Van Remoortel – **NMSC Melsbroek**
- Jaume Sastre-Garriga, Deborah Pareto, Neus Mongay-Ochoa – **CEMCAT and Vall d'Hebron Universiteit Barcelona**
- Guy Nagels, Jeroen Van Schependom – **Vrije Universiteit Brussel**
- Diana Sima, Arno Liseune – **Icometrix**

National MS center Melsbroek

New Validatie Studie

- Klinische en radiologische data bij > 2500 individuele patiënten @ **NMSC Melsbroek**
- MRI scans van de hersenen (2106 bij 873 personen)
- EDSS, T25FWT, 9HPT, SDMT
- EQ-5D VAS, MSSS, ARMSS, etc.
- Cross-sectionele and longitudinale evaluatie
- Twee verschillende meetmethodes

National MS center Melsbroek


A
B
C
D
E

New Validatie Studie

- Klinische en radiologische data bij > 2500 individuele patiënten @ **NMSC Melsbroek**
- MRI scans van de hersenen (2106 bij 873 personen)
- EDSS, T25FWT, 9HPT, SDMT
- EQ-5D VAS, MSSS, ARMSS, etc.
- Cross-sectionele and longitudinale evaluatie
- Twee verschillende meetmethodes
  - ➢ **“Icometrix” en “Barcelona” techniek**

National MS center Melsbroek

COMPLETE DATASET

10 slices model

	# scans	Mean SCaA	Std, Deviation SCaA	Mean CoV (SCaA)	Mean SCoA	Std, Deviation SCoA
Acrim Saint Pierre France	1	157,70		0,1267	43,00	
ASZ Aalst	17	205,21	23,94	0,0478	66,38	7,66
AZ Damiaan Oostende	1	247,00		0,0813	58,50	
AZ Delta	1	179,80		0,0842	59,80	
AZ Glorieux	2	199,45	28,78	0,0915	59,45	5,30
AZ Groeninge Kortrijk	1	267,60		0,0742	71,90	
AZ Herentals	1	215,50		0,0528	62,40	
AZ Jan Portaels Vilvoorde	4	163,50	14,55	0,0451	56,77	4,05
AZ Monica Deurne	4	160,75	36,34	0,0334	57,50	13,88
AZ Sint Jan Brugge	10	162,83	18,80	0,0816	55,09	7,34
AZ Sint Jozef Malle	2	138,90	1,27	0,0386	52,55	2,33
AZ West	1	167,80		0,0232	57,20	
AZ West Veurne	3	251,13	13,44	0,0769	70,77	10,65
CHU Brugmann	14	151,77	42,07	0,0693	48,65	14,92
CHWAPI Doornik	6	132,05	18,54	0,0686	50,92	5,46
Europa ziekenhuizen Ukkel	1	186,70		0,0181	64,40	
Europaziekenhuizen Sint Genesius Rode	2	199,20	12,16	0,034	65,85	8,98
GHDC Charleroi	1	207,90		0,0591	51,40	
HIS site Elsene	1	249,40		0,0334	59,10	
Instituut J. Bordet Brussel	1	182,00		0,0421	63,40	
Iris ziekenhuizen	5	233,12	34,40	0,063	69,04	7,88
Jan Yperman Veurne	2	234,30	28,85	0,0688	56,15	5,44
Jessa ziekenhuis	1	201,00		0,0376	70,70	
Koningin Fabiola ziekenhuis	2	233,50	2,40	0,0558	70,85	4,60
OLV zh Aalst	74	210,75	27,29	0,0596	61,18	9,16
Sint Elisabeth Ukkel	3	260,53	2,14	0,0406	75,73	1,43
Tivoli La Louvière	2	194,00	13,72	0,0258	54,05	2,47
ULB Erasme	24	187,85	25,33	0,0804	52,40	10,66
UZ Antwerpen	68	162,10	32,35	0,0494	52,27	8,56
UZ Brussel	304	200,88	30,84	0,0525	60,45	9,36
UZ Gent	19	197,28	18,25	0,0585	64,59	6,34
UZ Leuven	280	214,80	33,72	0,0567	64,93	8,91
Total	858	201,38	35,91	0,0558	61,08	10,05

DATASET ANALYSIS

Number of patients
- Total = 472
- With 1 scan = 254
- With > scan = 218 (of whom 120 with 2 scans)
- With > centers = 42

Number of centers = 32
Overlap: 42 patients with scans in > 1 center

National MS center Melsbroek

area model				
	Mean SCaA	Std, Deviation SCaA	Mean SCoA	Std, Deviation SCoA
Acrim Saint Pierre France	175,44		46,19	
ASZ Aalst	201,89	23,83	65,13	6,64
AZ Damiaan Oostende	247,86		58,18	
AZ Delta	189,17		61,46	
AZ Glorieux	204,66	41,00	62,49	5,88
AZ Groeninge Kortrijk	242,40		71,16	
AZ Herentals	224,54		65,26	
AZ Jan Portaels Vilvoorde	171,66	14,76	57,53	5,96
AZ Monica Deurne	169,65	26,68	59,70	11,18
AZ Sint Jan Brugge	168,66	22,02	55,15	6,00
AZ Sint Jozef Malle	144,10	0,47	53,88	3,10
AZ West	189,32		64,00	
AZ West Veurne	250,55	6,32	71,10	9,87
CHU Brugmann	163,91	33,79	53,39	11,18
CHWAPI Doornik	136,64	25,99	51,40	6,25
Europa ziekenhuizen Ukkel	199,97		63,58	
Europaziekenhuizen Sint Genesius Rode	203,39	6,31	67,61	8,81
GHDC Charleroi	228,60		54,54	
HIS site Elsene	252,23		59,90	
Instituut J. Bordet Brussel	179,93		63,49	
Iris ziekenhuizen	231,19	28,46	67,92	7,51
Jan Yperman Veurne	237,86	27,49	56,82	8,97
Jessa ziekenhuis	217,63		71,38	
Koningin Fabiola ziekenhuis	245,78	6,19	69,41	4,43
OLV zh Aalst	213,35	24,12	61,54	8,57
Sint Elisabeth Ukkel	268,16	2,59	77,72	0,54
Tivoli La Louvière	205,98	18,86	56,49	4,65
ULB Erasme	195,54	21,04	53,93	10,07
UZ Antwerpen	170,60	31,64	54,05	8,14
UZ Brussel	208,77	29,57	62,18	8,72
UZ Gent	205,41	19,37	65,92	6,25
UZ Leuven	220,20	31,43	65,82	7,94
Total	207,75	33,74	62,34	9,18

DATASET ANALYSIS

Number of patients
- Total = 472
- With 1 scan = 254
- With > scan = 218 (of whom 120 with 2 scans)
- With > centers = 42

Number of centers = 32
Overlap: 42 patients with scans in > 1 center

National MS center Melsbroek

Uitzuiveren van onze Dataset

- CoV lager dan 0.075
- “Barcelona” methode
- 714 scans
- 426 unieke personen

	Cord Icometrix	Canal Icometrix	Cord Barcelona	Canal Barcelona
Number of values	714	714	714	714
Minimum	32,9	103,8	29,6	95,9
Maximum	85,7	304,5	86,6	304,6
Range	52,8	200,7	57,0	208,7
Mean	**62,7**	**209,6**	**61,5**	**203,5**
Std. Deviation	9,0	32,9	9,8	35,0
Std. Error of Mean	0,34	1,23	0,37	1,31

National MS center Melsbroek

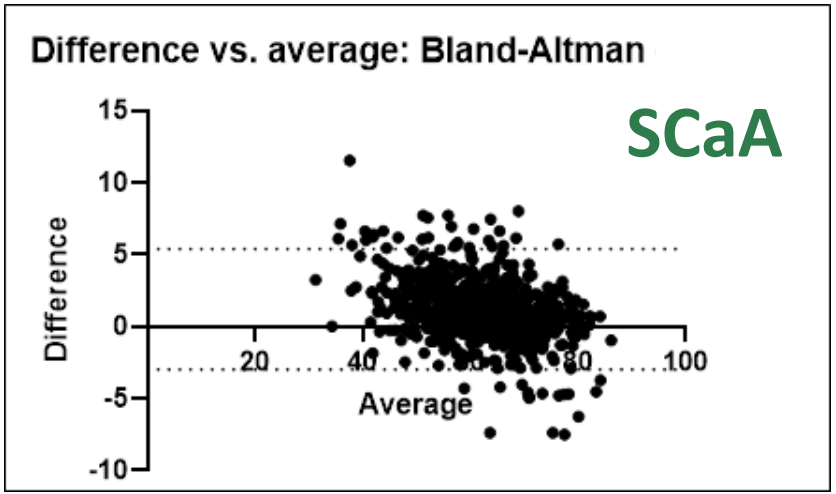
Uitzuiveren van onze Dataset

- CoV lager dan 0.075
- “Barcelona” methode
- 714 scans
- 426 unieke personen

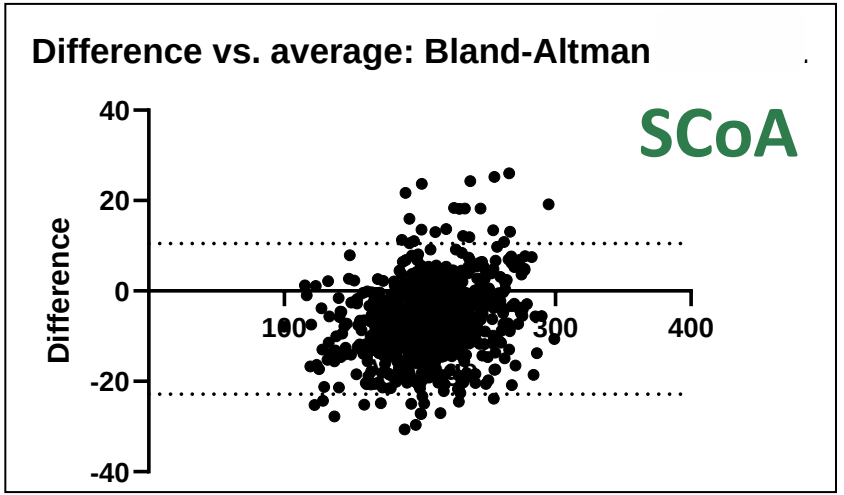
	Age vs. Cord Icometrix	Age vs. Canal Icometrix	Age vs. Cord Barcelona	Age vs. Canal Barcelona
Spearman r				
r	**-0,1707**	**-0,1085**	**-0,1471**	**-0,09157**
95% confidence interval	-0,2431 to -0,09640	-0,1825 to -0,03319	-0,2201 to -0,07233	-0,1660 to -0,01615
P (two-tailed)	**<0,0001**	**0,0037**	**<0,0001**	**0,0144**
Significant? (alpha = 0.05)	Yes	Yes	Yes	Yes
Number of XY Pairs	714	714	714	714

National MS center Melsbroek

Goede Overeenkomst tussen beide Technieken



ICC Cord = 0,96



ICC Canal = 0,95

National MS center Melsbroek

Cohorte voor Klinische Evaluaties

- Eén enkele MRI per individu
- Oudste scan weerhouden
- Demographics en klinische testen dichtste bij de MRI = T1, baseline
- Meest recente klinische testen = T2, follow-up
- EDSS, MSSS, ARMSS, T25FWT, NHPT, SDMT, 5Q-5D VAS
- N = 370, 34% met progressieve MS

	Total	RRMS	PMS	P
Number	370	244	126	-
Age; y	46 (16)	43 (15)	52 (16)	< 0.0001
Sex; % females	65.9	70.5	57.1	0.0102
Disease duration; y	13 (15)	11 (13)	19 (16)	< 0.0001
DMT; % treated	61.1	72.5	38.9	< 0.0001
Brain T2LV; mm^2	7.4 (12.2)	5.5 (10.0)	10.8 (15.8)	< 0.0001
SCaA, method 1; mm^2	206.0 ± 32.8	210.5 ± 33.4	197.2 ± 29.9	0.0002
SCoA, method 1; mm^2	61.7 ± 9.1	64.0 ± 8.5	57.4 ± 8.7	< 0.0001
SCPF, method 1	0.30 (0.05)	0.31 (0.05)	0.29 (0.05)	0.0005
SCaA, method 2; mm^2	199.7 ± 35.1	204.9 ± 35.8	189.7 ± 31.7	< 0.0001
SCoA, method 2; mm^2	60.6 ± 10.1	62.9 ± 9.5 $	56.1 ± 9.6	< 0.0001
SCPF, method 2	0.31 (0.05)	0.31 (0.05)	0.30 (0.05)	0.0041
EDSS score	4.0 (3.5)	3.0 (2.5)	6.5 (1.5)	< 0.0001
T25FWT score; s #	6.2 (7.2)[1]	5.3 (2.4)[2]	13.1 (30.4)[3]	< 0.0001
9HPT-dom score; s #	22.3 (11.9)[4]	20.8 (5.8)[5]	30.8 (20.8)[6]	< 0.0001
9HPT-ndom score; s #	23.4 (12.4)[4]	22.0 (7.4)[5]	32.4 (27.3)[6]	< 0.0001
SDMT score #	48.0 ± 14.8[7]	51.9 ± 13.6[8]	40.2 ± 14.2[9]	< 0.0001
EQ-5D VAS score #	70.0 (20.0)[10]	72.5 (19.2)[11]	67.0 (17.5)[12]	0.0056
MSSS	4.4 (4.9)	3.9 (4.2)	6.4 (3.3) £	< 0.0001
ARMSS score	6.2 (4.7)	5.3 (4.2)	7.8 (2.8)	< 0.0001

National MS center Melsbroek

SCaA en Invaliditeit – Correlaties

- EDSS scores: -0,24; P < 0,0001
- ARMSS scores: -0,17 and -0,19; P = 0,0009 en 0,0003
- T25FWT: -0,19, P = 0,0004 en 0,0003
- NHPT scores dominante hand: -0,13 and -0,14; P = 0,0136 en 0,0073
- NHPT scores niet-dominante hand: -0,14 and -0,16; P = 0,0099 en 0,0037
- Trend voor MSSS en EQ-5D VAS scores

PS, alle klinische scores correleerden ook met SCoA and SCPF

SCaA en Invaliditeit – Multivariabele Regressie

- Lineaire regressie
- Modellen gecorrigeerd voor Leeftijd, Geslacht, SCPF, Brain T2LV
- SCaA op baseline voorspelt onafhankelijk de aanwezige klinische invaliditeit
    - EDSS, MSSS and ARMSS
    - T25FWT
    - NHPT dominante and niet-dominante hand

	SCaA $	
	Method 1	Method 2
EDSS	β -0.024, 95% CI -0.029 to -0.018, P < 0.0001*	β -0.020, 95% CI -0.026 to -0.015, P < 0.0001*
T25FWT	β -0.449, 95% CI -0.616 to -0.283, P < 0.0001*	β -0.392, 95% CI -0.545 to -0.240, P < 0.0001*
9HPT-d	β -0.282, 95% CI -0.451 to -0.113, P = 0.0011*	β -0.251, 95% CI -0.404 to -0.097, P = 0.0015*
9HPT-nd	β -0.318, 95% CI -0.466 to -0.171, P < 0.0001*	β -0.295, 95% CI -0.430 to -0.161, P < 0.0001*
SDMT	β 0.028, 95% CI -0.022 to 0.078, P = 0.2768	β 0.013, 95% CI -0.032 to 0.058, P = 0.5730
EQ-5D VAS	β 0.056, 95% CI -0.027 to 0.139, P = 0.1877	β 0.062, 95% CI -0.014 to 0.137, P = 0.1071
MSSS	β -0.020, 95% CI -0.030 to -0.011, P < 0.0001*	β -0.017, 95% CI -0.026 to -0.009, P < 0.0001*
ARMSS	β -0.029, 95% CI -0.036 to -0.021, P < 0.0001*	β -0.025, 95% CI -0.031 to -0.018, P < 0.0001*

SCaA en Invaliditeit – Multivariabele Regressie

- **EDSS score is geen continue variable!**

National MS center Melsbroek

SCaA en Invaliditeit – Multivariabele Regressie

- **EDSS score is geen continue variable!**
- Smaller kanaal geassocieerd met lager risico op EDSS score hoger dan 4,0
    - Gelijkaardige statistische aanpak, logistische regressie
    - OR 0,98; P < 0,0001

	Total	RRMS	PMS	P
Number	370	244	126	-
Age; y	46 (16)	43 (15)	52 (16)	< 0.0001
Sex; % females	65.9	70.5	57.1	0.0102
Disease duration; y	13 (15)	11 (13)	19 (16)	< 0.0001
DMT; % treated	61.1	72.5	38.9	< 0.0001
Brain T2LV; mm^2	7.4 (12.2)	5.5 (10.0)	10.8 (15.8)	< 0.0001
SCaA, method 1; mm^2	206.0 ± 32.8	210.5 ± 33.4	197.2 ± 29.9	0.0002
SCoA, method 1; mm^2	61.7 ± 9.1	64.0 ± 8.5	57.4 ± 8.7	< 0.0001
SCPF, method 1	0.30 (0.05)	0.31 (0.05)	0.29 (0.05)	0.0005
SCaA, method 2; mm^2	199.7 ± 35.1	204.9 ± 35.8	189.7 ± 31.7	< 0.0001
SCoA, method 2; mm^2	60.6 ± 10.1	62.9 ± 9.5 $	56.1 ± 9.6	< 0.0001
SCPF, method 2	0.31 (0.05)	0.31 (0.05)	0.30 (0.05)	0.0041
EDSS score	4.0 (3.5)	3.0 (2.5)	6.5 (1.5)	< 0.0001
T25FWT score; s #	6.2 (7.2)[1]	5.3 (2.4)[2]	13.1 (30.4)[3]	< 0.0001
9HPT-dom score; s #	22.3 (11.9)[4]	20.8 (5.8)[5]	30.8 (20.8)[6]	< 0.0001
9HPT-ndom score; s #	23.4 (12.4)[4]	22.0 (7.4)[5]	32.4 (27.3)[6]	< 0.0001
SDMT score #	48.0 ± 14.8[7]	51.9 ± 13.6[8]	40.2 ± 14.2[9]	< 0.0001
EQ-5D VAS score #	70.0 (20.0)[10]	72.5 (19.2)[11]	67.0 (17.5)[12]	0.0056
MSSS	4.4 (4.9)	3.9 (4.2)	6.4 (3.3) £	< 0.0001
ARMSS score	6.2 (4.7)	5.3 (4.2)	7.8 (2.8)	< 0.0001

National MS center Melsbroek

	Total	RRMS	PMS	P
Number	370	244	126	-
Age; y	46 (16)	43 (15)	52 (16)	< 0.0001
Sex; % females	65.9	70.5	57.1	0.0102
Disease duration; y	13 (15)	11 (13)	19 (16)	< 0.0001
DMT; % treated	61.1	72.5	38.9	< 0.0001
Brain T2LV; mm^2	7.4 (12.2)	5.5 (10.0)	10.8 (15.8)	< 0.0001
SCaA, method 1; mm^2	206.0 ± 32.8	210.5 ± 33.4	197.2 ± 29.9	0.0002
SCoA, method 1; mm^2	61.7 ± 9.1	64.0 ± 8.5	57.4 ± 8.7	< 0.0001
SCPF, method 1	0.30 (0.05)	0.31 (0.05)	0.29 (0.05)	0.0005
SCaA, method 2; mm^2	199.7 ± 35.1	204.9 ± 35.8	189.7 ± 31.7	< 0.0001
SCoA, method 2; mm^2	60.6 ± 10.1	62.9 ± 9.5 $	56.1 ± 9.6	< 0.0001
SCPF, method 2	0.31 (0.05)	0.31 (0.05)	0.30 (0.05)	0.0041
EDSS score	4.0 (3.5)	3.0 (2.5)	6.5 (1.5)	< 0.0001
T25FWT score; s #	6.2 (7.2)[1]	5.3 (2.4)[2]	13.1 (30.4)[3]	< 0.0001
9HPT-dom score; s #	22.3 (11.9)[4]	20.8 (5.8)[5]	30.8 (20.8)[6]	< 0.0001
9HPT-ndom score; s #	23.4 (12.4)[4]	22.0 (7.4)[5]	32.4 (27.3)[6]	< 0.0001
SDMT score #	48.0 ± 14.8[7]	51.9 ± 13.6[8]	40.2 ± 14.2[9]	< 0.0001
EQ-5D VAS score #	70.0 (20.0)[10]	72.5 (19.2)[11]	67.0 (17.5)[12]	0.0056
MSSS	4.4 (4.9)	3.9 (4.2)	6.4 (3.3) £	< 0.0001
ARMSS score	6.2 (4.7)	5.3 (4.2)	7.8 (2.8)	< 0.0001

National MS center Melsbroek

	Total	RRMS	PMS	P
Number	370	244	126	-
Age; y	46 (16)	43 (15)	52 (16)	< 0.0001
Sex; % females	65.9	70.5	57.1	0.0102
Disease duration; y	13 (15)	11 (13)	19 (16)	< 0.0001
DMT; % treated	61.1	72.5	38.9	< 0.0001
Brain T2LV; mm^2	7.4 (12.2)	5.5 (10.0)	10.8 (15.8)	< 0.0001
SCaA, method 1; mm^2	206.0 ± 32.8	210.5 ± 33.4	197.2 ± 29.9	0.0002
SCoA, method 1; mm^2	61.7 ± 9.1	64.0 ± 8.5	57.4 ± 8.7	< 0.0001
SCPF, method 1	0.30 (0.05)	0.31 (0.05)	0.29 (0.05)	0.0005
SCaA, method 2; mm^2	199.7 ± 35.1	204.9 ± 35.8	189.7 ± 31.7	< 0.0001
SCoA, method 2; mm^2	60.6 ± 10.1	62.9 ± 9.5 $	56.1 ± 9.6	< 0.0001
SCPF, method 2	0.31 (0.05)	0.31 (0.05)	0.30 (0.05)	0.0041
EDSS score	4.0 (3.5)	3.0 (2.5)	6.5 (1.5)	< 0.0001
T25FWT score; s #	6.2 (7.2)[1]	5.3 (2.4)[2]	13.1 (30.4)[3]	< 0.0001
9HPT-dom score; s #	22.3 (11.9)[4]	20.8 (5.8)[5]	30.8 (20.8)[6]	< 0.0001
9HPT-ndom score; s #	23.4 (12.4)[4]	22.0 (7.4)[5]	32.4 (27.3)[6]	< 0.0001
SDMT score #	48.0 ± 14.8[7]	51.9 ± 13.6[8]	40.2 ± 14.2[9]	< 0.0001
EQ-5D VAS score #	70.0 (20.0)[10]	72.5 (19.2)[11]	67.0 (17.5)[12]	0.0056
MSSS	4.4 (4.9)	3.9 (4.2)	6.4 (3.3) £	< 0.0001
ARMSS score	6.2 (4.7)	5.3 (4.2)	7.8 (2.8)	< 0.0001

National MS center Melsbroek

	Total	RRMS	PMS	P
Number	370	244	126	-
Age; y	46 (16)	43 (15)	52 (16)	< 0.0001
Sex; % females	65.9	70.5	57.1	0.0102
Disease duration; y	13 (15)	11 (13)	19 (16)	< 0.0001
DMT; % treated	61.1	72.5	38.9	< 0.0001
Brain T2LV; mm^2	7.4 (12.2)	5.5 (10.0)	10.8 (15.8)	< 0.0001
SCaA, method 1; mm^2	206.0 ± 32.8	210.5 ± 33.4	197.2 ± 29.9	0.0002
SCoA, method 1; mm^2	61.7 ± 9.1	64.0 ± 8.5	57.4 ± 8.7	< 0.0001
SCPF, method 1	0.30 (0.05)	0.31 (0.05)	0.29 (0.05)	0.0005
SCaA, method 2; mm^2	199.7 ± 35.1	204.9 ± 35.8	189.7 ± 31.7	< 0.0001
SCoA, method 2; mm^2	60.6 ± 10.1	62.9 ± 9.5 $	56.1 ± 9.6	< 0.0001
SCPF, method 2	0.31 (0.05)	0.31 (0.05)	0.30 (0.05)	0.0041
EDSS score	4.0 (3.5)	3.0 (2.5)	6.5 (1.5)	< 0.0001
T25FWT score; s #	6.2 (7.2)[1]	5.3 (2.4)[2]	13.1 (30.4)[3]	< 0.0001
9HPT-dom score; s #	22.3 (11.9)[4]	20.8 (5.8)[5]	30.8 (20.8)[6]	< 0.0001
9HPT-ndom score; s #	23.4 (12.4)[4]	22.0 (7.4)[5]	32.4 (27.3)[6]	< 0.0001
SDMT score #	48.0 ± 14.8[7]	51.9 ± 13.6[8]	40.2 ± 14.2[9]	< 0.0001
EQ-5D VAS score #	70.0 (20.0)[10]	72.5 (19.2)[11]	67.0 (17.5)[12]	0.0056
MSSS	4.4 (4.9)	3.9 (4.2)	6.4 (3.3) £	< 0.0001
ARMSS score	6.2 (4.7)	5.3 (4.2)	7.8 (2.8)	< 0.0001

MV Linear Regression
Progressive Disease ~ SCaA
Corrected for age
Beta -0,10 and -0,13
P < 0,0050

National MS center Melsbroek

Toename Invaliditeit – Longitudinale Analyses

- EDSS, MSSS, ARMSS: 79 +/- 30 maanden
  - N = 370
- T25FWT, NHPT: 74 +/- 30 maanden
  - N = 333 and 332, respectievelijk
- SDMT: 72 +/- 29 maanden
  - N = 299
- EQ-5D VAS: 73 +/- 30 maanden
  - N = 204

Toename Invaliditeit – Correlaties

- Delta MSSS scores: -0,13 and -0,16; P = 0,0108 en 0,0023
- Delta NHPT scores dominant hand: -0,15 and -0,19; P = 0,0053 en 0,0007
- Delta NHPT scores non-dominant hand: -0,12 and -0,14; P = 0,0359 en 0,0002
- Delta SDMT scores: 0,12 and 0,13; P = 0,0441 en 0,0214

PS, SCoA bleek significant gecorreleerd met delta T25FWT, NHPT en MSSS scores, SCPF met delta T25FWT scores

Toename Invaliditeit – Multivariabele Regressie

- Lineare regressie
- Correctie voor Leeftijd, Geslacht, Brain T2LV, SCPF, T1 score, tijdsinterval
- SCaA op baseline voorspelt absolute verandering in invaliditeit
    - EDSS, MSSS and ARMSS
    - T25FWT
    - NHPT dominante and niet-dominante hand

National MS center Melsbroek

	SCaA $	
	Method 1	Method 2
Delta EDSS	β -0.004, 95% CI -0.009 to < -0.001, P = 0.0508	β -0.004, 95% CI -0.008 to < -0.001, P = 0.0269*
Delta T25FWT	β -0.271, 95% CI -0.464 to -0.078, P = 0.0061*	β -0.252, 95% CI -0.428 to -0.076, P = 0.0052*
Delta 9HPT-d	β -0.434, 95% CI -0.713 to -0.156, P = 0.0023*	β -0.441, 95% CI -0.695 to -0.187, P = 0.0007*
Delta 9HPT-nd	β -0.280, 95% CI -0.516 to -0.043, P = 0.0206*	β -0.302, 95% CI -0.518 to -0.085, P = 0.0065*
Delta SDMT	β 0.027, 95% CI -0.011 to -0.064, P = 0.1620	β 0.024, 95% CI -0.010 to -0.058, P = 0.1595
Delta EQ-5D VAS	B -0.016, 95% CI -0.087 to -0.056, P = 0.6628	β -0.012, 95% CI -0.077 to -0.053, P = 0.7221
Delta MSSS	β -0.010, 95% CI -0.016 to -0.005, P = 0.0003*	β -0.010, 95% CI -0.015 to -0.005, P = 0.0002*
Delta ARMSS	β -0.006, 95% CI -0.012 to -0.001, P = 0.0308*	β -0.006, 95% CI -0.011 to -0.001, P = 0.0175*

Toename Invaliditeit – Relevant in de Praktijk?

- Klinisch relevante verslechtering op EDSS wordt gedefinieerd als:
  - Toename van 1,5 of meer indien baseline score 0,0
  - Toename van 1,0 of meer indien baseline score 1,0-5,5 inclusief
  - Toename van 0,5 of meer indien baseline score 6,0 of meer
- T25FWT, NHPT: toename van minstens 20%
- SDMT: toename van minstens 10% en/of 4 punten

Toename Invaliditeit – Relevant in de Praktijk?

- EDSS: 40,8%
- T25FWT: 37,8%
- NHPT dominante and niet-dominante hand: 28,9% and 29,2%, respectievelijk
- SDMT: 35,8%

Ter herinnering, opvolging over 6 tot 6,5 jaar

Toename Invaliditeit – Relevant in de Praktijk?

- Multivariabele logistische regressie
- Gecorrigeerde modellen: Leeftijd, Geslacht, Brain T2LV, SCPF, T1 score, tijdsinterval
- SCaA op baseline voorspelt risico op klinisch relevante achteruitgang
    - EDSS: OR 0,99; P = 0,0005
    - T25FWT: OR 0,99; P < 0,0001 and P = 0,0507
    - NHPT dominant hand: OR 0,98; P = 0,0375 and 0,0001
    - NHPT non-dominant hand: OR 0,99; P = 0,0283 and 0,0285

Conclusies van ons Onderzoek

- Betrouwbare meting van diameter spinaal kanaal en ruggenmerg op MRI hersenen
- Bevestiging van het concept **SPINALE RESERVE**
    - Staat van het ruggenmerg voor de ziekte
    - Associatie met EDSS, T25FWT, en NHPT
    - Algemene invaliditeit, stapfunctie en handfunctie
    - Voorspellend voor verergering van invaliditeit over ongeveer 6 jaar
- Lager bij progressieve MS
    - Oorzaak, gevolg, of beiden?

Wat betekent dit nu?

National MS center Melsbroek

Wat betekent dit nu?

Kunnen we onze spinale reserve moduleren?

Kunnen we dit gebruiken bij beslissingen over behandeling?

Brain Reserve: is it fixed?

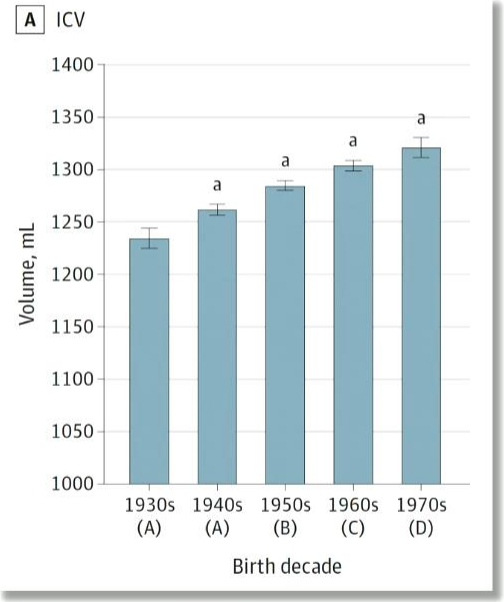
JAMA Neurology | Original Investigation

Trends in Intracranial and Cerebral Volumes of Framingham Heart Study Participants Born 1930 to 1970

Charles DeCarli, MD; Pauline Maillard, PhD; Matthew P. Pase, PhD; Alexa S. Beiser, PhD; Daniel Kojis, BA; Claudia L. Satizabal, PhD; Jayandra J. Himali, PhD; Hugo J. Aparicio, MD, MPH; Evan Fletcher, PhD; Sudha Seshadri, MD

Conclusions

This study extends current knowledge by showing that secular trends in brain structure are occurring. The larger brain structure, which may reflect improved brain development and brain health, is at least 1 manifestation of improved brain reserve that could buffer the effect of late-life diseases on incident dementia.



DeCarli et al, JAMA Neurol 2024

Jaume Sastre-Garriga

Cemcat

ECTRIMS 2025

Minder Gunstige Prognostische Factoren

- Meerdere opflakkeringen in het eerste jaar, slecht herstel
- Progressieve ziekte
- Veel MRI letsels, ruggenmergaantasting
- Etnische factoren
- Laag vitamine D, roken, co-morbiditeiten
- Socio-economische achtergrond

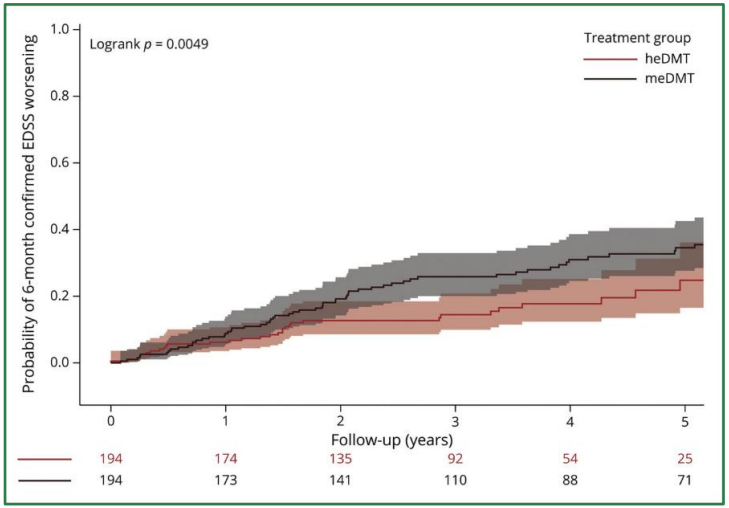
Open access | Review article | First published online October 16, 2024 | Request permissions

Beyond lines of treatment: embracing early high-efficacy disease-modifying treatments for multiple sclerosis management

Celia Oreja-Guevara, Sergio Martínez-Yélamos, [...], and José E. Meca-Lallana +24 View all authors and affiliations

All Articles | https://doi.org/10.1177/17562864241284372

profiles between early heDMTs and meDMTs, though long-term safety data are still lacking. The review also addresses the need for a personalized approach based on patient characteristics, prognostic factors, and preferences, explores the importance of therapeutic inertia, and highlights the evolving landscape of international and national guidelines that increasingly advocate for early intensive treatment approaches. The article also addresses the challenges of ensuring access to these therapies and the importance of further research to establish long-term safety and effectiveness of DMTs in MS.



ARTICLE | July 7, 2020 Check for updates

Initial high-efficacy disease-modifying therapy in multiple sclerosis

A nationwide cohort study

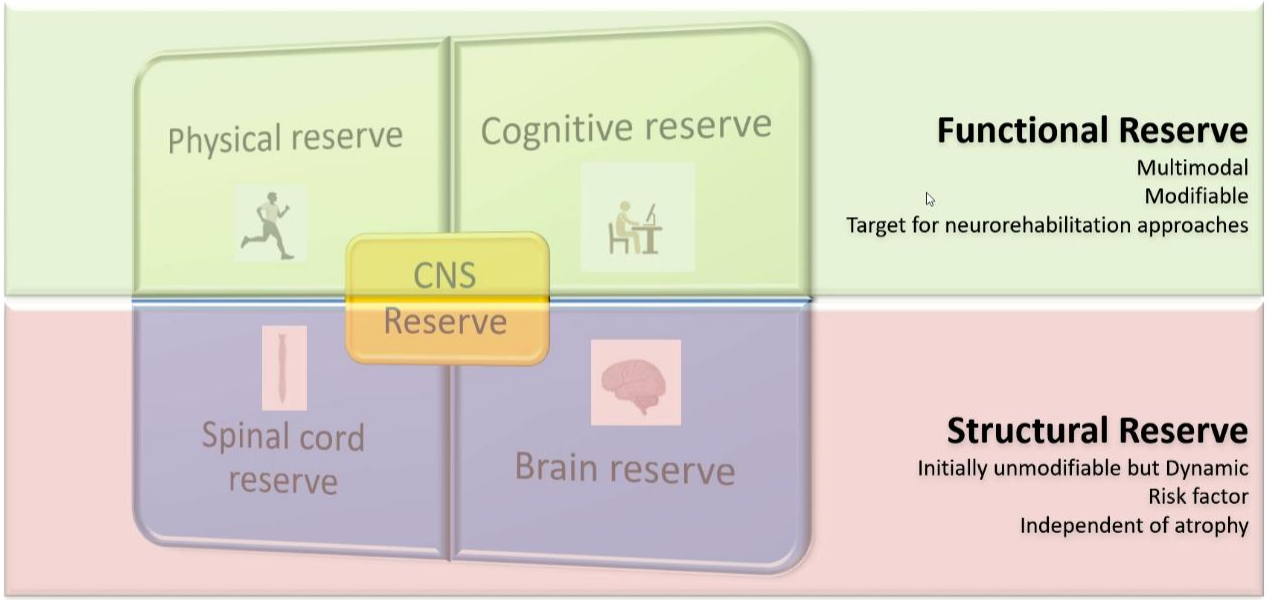
This article has been corrected. VIEW CORRECTION

Mathias Due Buron, MD, Thor Ameri Chalmer, MD, Finn Sellebjerg, MD, DMsc, Ismael Barzinji, MD, Danny Bech, MD, Jeppe Romme Christensen, MD, PhD, Mette Kirstine Christensen, MD, PhD, ... SHOW ALL ... , and Melinda Magyari, MD, PhD | AUTHORS INFO & AFFILIATIONS

August 25, 2020 issue • 95 (8) e1041-e1051 • https://doi.org/10.1212/WNL.0000000000010135

National MS center Melsbroek

CNS Reserve



Jaume Sastre-Garriga

Cemcat

ECTRIMS 2025

National
MS center
Melsbroek