

Présentation Travail de Master

05/02/24

Transcranial magnetic stimulation brain mapping of
the hand motor area:
comparison between healthy subjects and patients
with cervical myelopathy

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Supervisors: Prof. Philippe Bijlenga, PhD Giannina Rita Iannotti



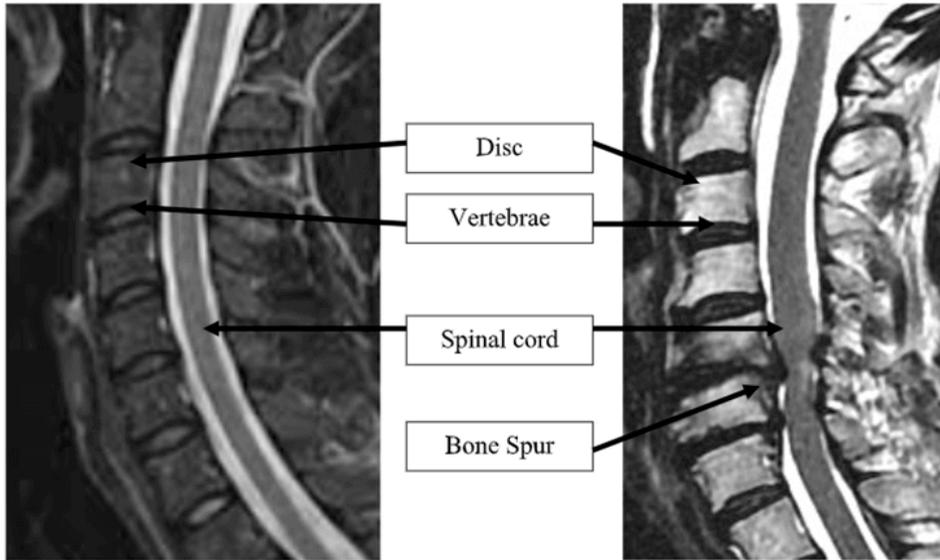
Cervical myelopathy

Cervical myelopathy results from **compression** on the spinal cord → **spondylotic myelopathy** (degenerative) is the most common cause

- It is the most common disorder of the spinal cord in persons older than 55 years of age
- Incidence of 4.04/100 persons-years

TTT:

- Conservative
- Surgical
 - anterior discectomy and fusion
 - posterior laminectomy and fusion



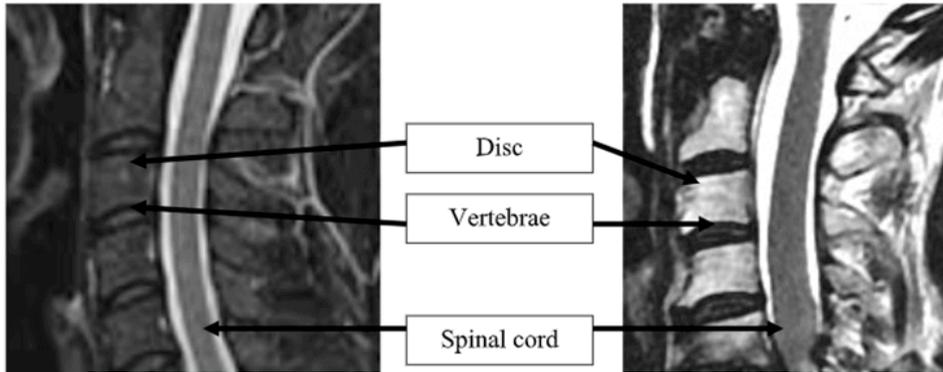
MRI Scan – Normal Cervical Spine

MRI Scan – Pressure on the spinal cord

	Number of patients (%)
Symptoms	
Neck pain and stiffness	19 (39%)
Numbness of arms	41 (84%)
Numbness of legs	33 (67%)
Hand clumsiness	33 (67%)
Leg stiffness	23 (47%)
Gait disturbance	39 (80%)
Lhermitte phenomenon	3 (6%)
Sphincter disturbances	19 (39%)
Sudden quadriplegia	7 (14%)
Signs	
Hyperreflexia of arms	36 (73%)
Hyperreflexia of legs	47 (96%)
Spastic gait	29 (59%)
Impaired vibration sense at wrist	23 (47%)
Impaired vibration sense at ankle	32 (65%)
Reduced pinprick sense in arm	30 (61%)
Reduced pinprick sense in leg	32 (65%)
Weakness of arms	23 (47%)
Weakness of legs (spastic paraparesis)	11 (22%)
Reduced pinprick sense with a level at trunk	9 (18%)

Cervical myelopathy

Cervical myelopathy results from **compression** on the spinal cord → **spondylotic myelopathy** (degenerative) is the most common cause



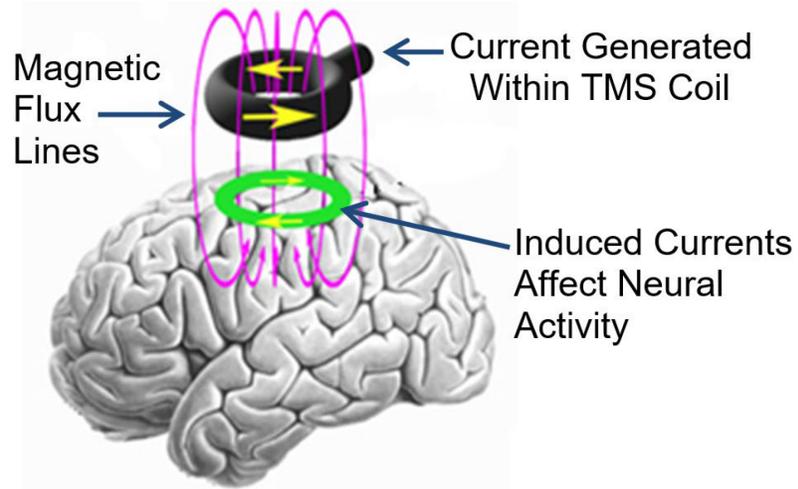
Question:

How spinal lesions can affect the cortical reorganization (of the hand)?

Gait disturbance	57 (60%)
Lhermitte phenomenon	3 (6%)
Sphincter disturbances	19 (39%)
Sudden quadriplegia	7 (14%)
Signs	
Hyperreflexia of arms	36 (73%)
Hyperreflexia of legs	47 (96%)
Spastic gait	29 (59%)
Impaired vibration sense at wrist	23 (47%)
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Weakness of legs (spastic paraparesis)	11 (22%)
Reduced pinprick sense with a level at trunk	9 (18%)

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- Surgical
 - anterior discectomy and fusion
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TMS

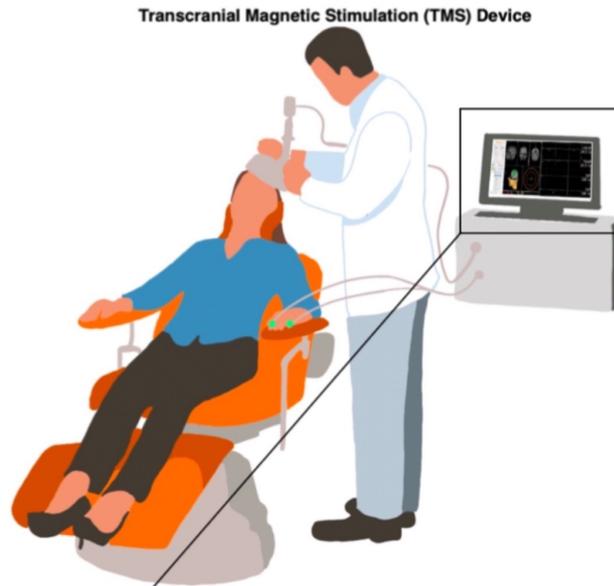
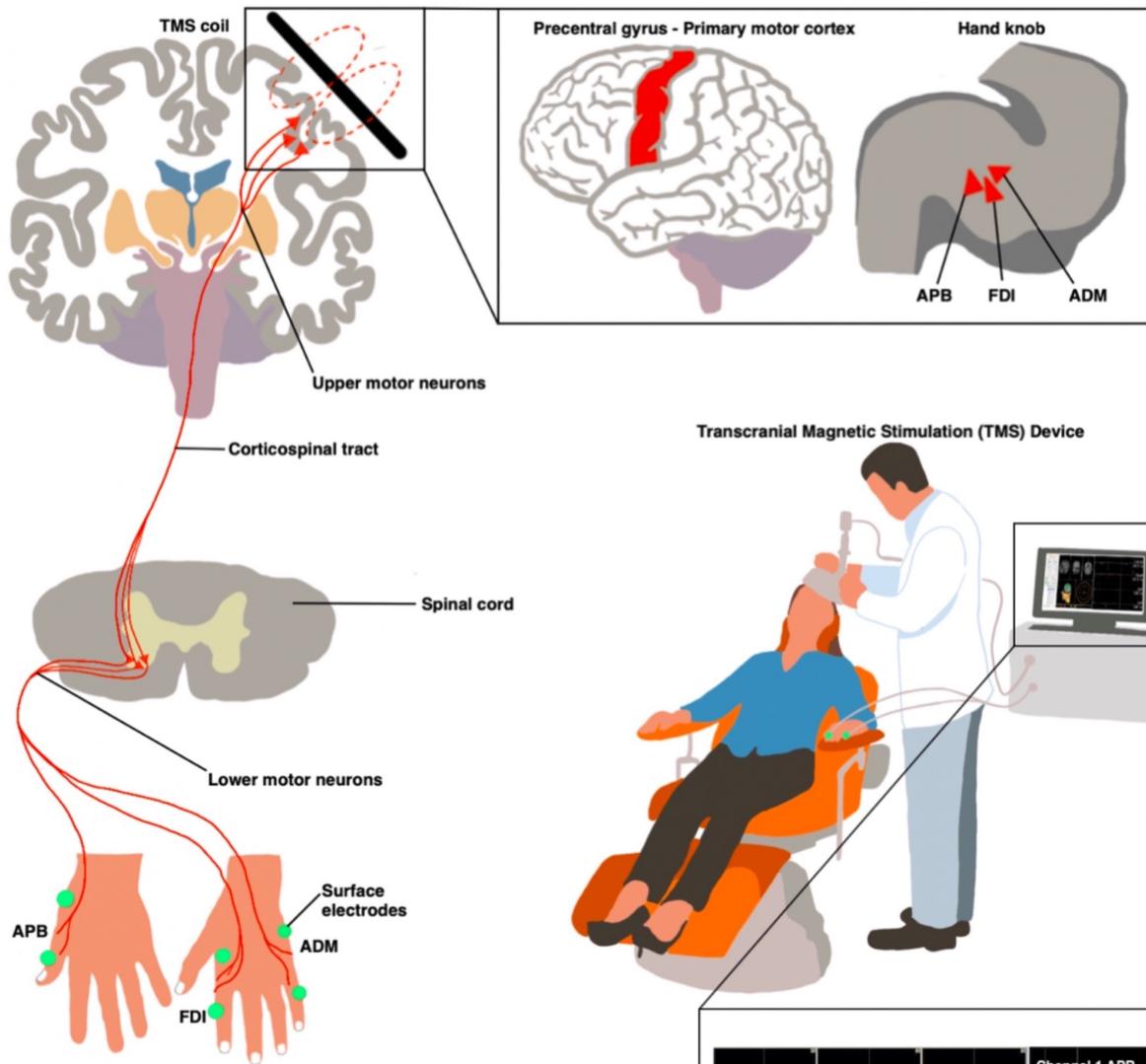


Nexstim® NBS System combining MRI-based stereotactic navigation and simultaneous electromyography (EMG)

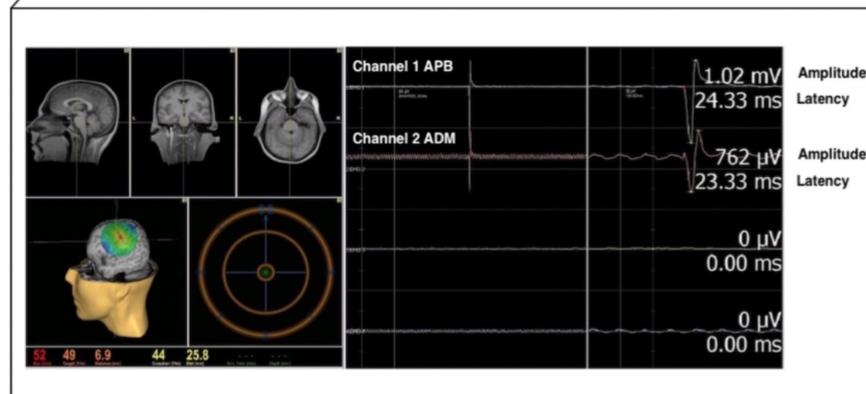


- Non-invasive and painless
- Frontal camera: neuro-navigation
- Coil
 - 2 Tesla
 - 2.54 cm deep stimulation
- EMG electrodes
- Mapping of the 2 hands: 2h
- Prior IRM needed

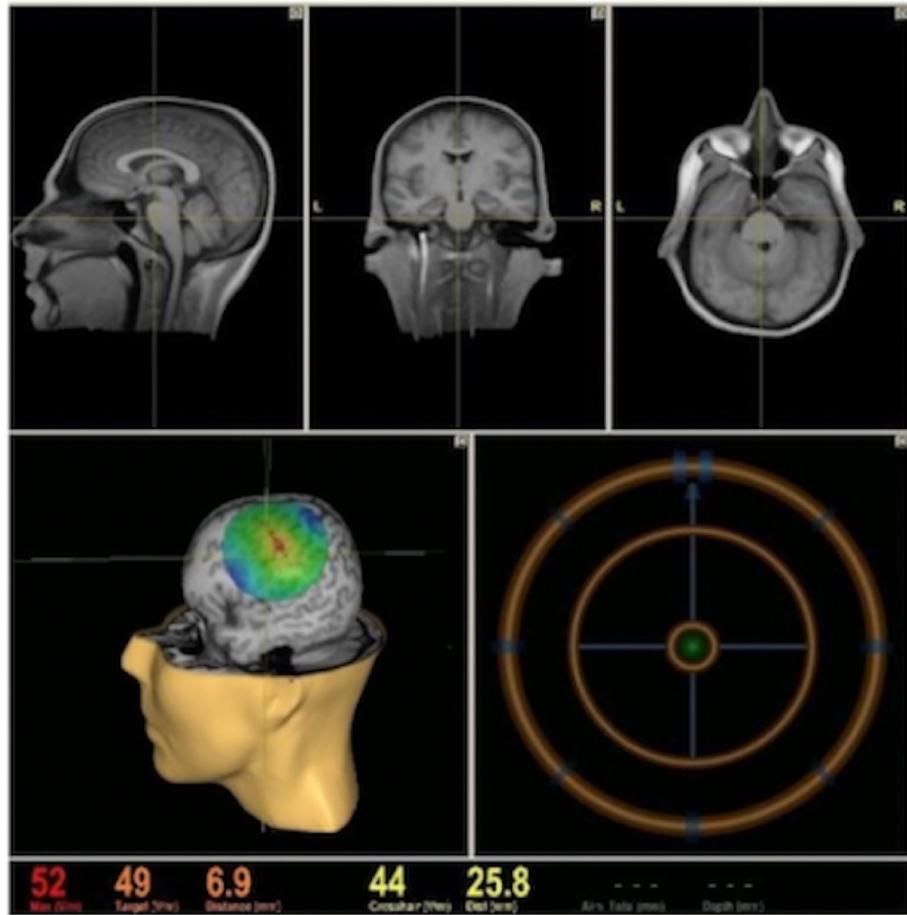
TMS



Magnetic field \rightarrow electric field
 \rightarrow stimulation of the corticospinal tractus \rightarrow detection of the motor evoked potential by transcutaneous electrodes



TMS



Channel 1 APB

10 μ V
20ms/100.2ms

Channel 2 ADM

10 μ V
20ms/100.2ms

10 μ V
20ms/100.2ms

10 μ V
20ms/100.2ms

1.02 mV
24.33 ms

762 μ V
23.33 ms

0 μ V
0.00 ms

0 μ V
0.00 ms

Amplitude
Latency

Amplitude
Latency

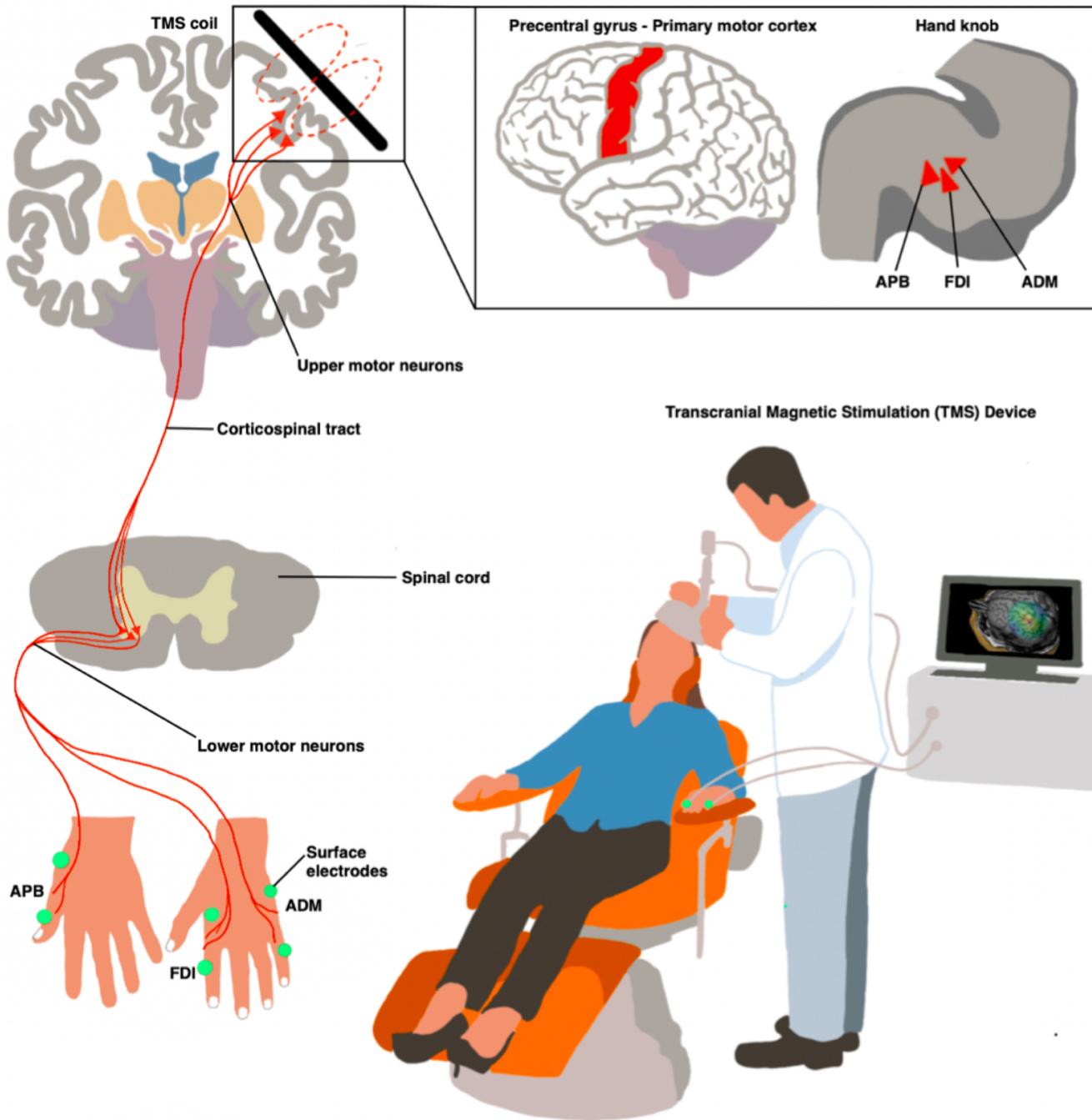
Amplitude
Latency

Amplitude
Latency

TMS

Sequence Description:																											
ID	Time (ms)	Stim. Type	Inter pulse Int. (ms)	First Intens. (%)	Second Intens. (%)	Target ID	Rep. Stim. ID	Peeling Depth (%)	User Resp.	Coil Loc. (mm)	Coil Normal			Coil Dir.			EF max. Loc. (mm)			EF max. Value (V/m)	EF at Target (V/m)	Ch1 Amp. (µV)	Ch1 Lat. (ms)	Ch2 Amp. (µV)	Ch2 Lat. (ms)	Ch3 Amp. (µV)	Ch3 Lat. (ms)
										x	y	z	x	y	z	x	y	z	x	y	z						
1.1.1.	69198	Single	-	30	-	-	-	30.2	-	132.7	223.1	106.4	0.5203	0.854	-0.0059	-0.203	0.1304	0.9705	115.3	193.8	95.6	30.6	-	-	-	-	-
1.1.2.	89485	Single	-	32	-	-	-	30.2	-	135.4	219.5	107.7	0.5603	0.8272	0.0412	0.4765	-0.3627	0.8009	114.2	194	98.8	33.6	-	-	-	-	-
1.1.3.	93123	Single	-	32	-	-	-	30.2	-	135.3	217	111.9	0.5741	0.8131	0.0962	-0.1323	-0.0238	0.9909	117.1	191.8	99.5	36.3	-	-	-	-	-
1.1.4.	100757	Single	-	32	-	-	-	30.2	-	130.6	220.6	114.9	0.5109	0.8525	0.111	-0.2678	0.0351	0.9628	113.9	193.2	103.2	35.3	-	73	24.3	-	-
1.1.5.	107559	Single	-	32	-	-	-	30.2	-	131.3	221.3	111.9	0.5069	0.8598	0.0624	-0.2671	0.0878	0.9596	114.7	193.5	99.7	35.1	-	-	-	-	-
1.1.6.	112654	Single	-	32	-	-	-	30.2	-	128.3	221.9	114.3	0.4691	0.8765	0.1081	-0.1108	-0.063	0.9918	112.1	194.6	102.6	36	-	-	-	-	-
1.1.7.	121390	Single	-	34	-	-	-	30.2	-	139.7	215.2	110.5	0.6866	0.7187	0.1103	-0.152	-0.0065	0.9884	119.7	190	98.5	37.3	-	-	-	-	-
1.1.8.	127230	Single	-	34	-	-	-	30.2	-	131.6	222.6	108.2	0.5115	0.8592	0.011	-0.6063	0.3518	0.7132	115.8	192.8	99.2	35.6	-	-	-	-	-
1.1.9.	131662	Single	-	34	-	-	-	30.2	-	129.5	223.1	107.6	0.4453	0.8931	0.0641	-0.5995	0.2442	0.7622	114.1	194	99.3	37.1	-	-	-	-	-
1.1.10.	135925	Single	-	34	-	-	-	30.2	-	133.3	220.8	105.1	0.5151	0.8532	0.0822	0.3681	-0.3068	0.8777	113.3	194.9	96.6	36.7	-	-	-	-	-
1.1.11.	138477	Single	-	34	-	-	-	30.2	-	128.1	222.5	110.6	0.5084	0.855	0.1024	0.0706	-0.16	0.9846	111.5	195.5	100	38.7	-	-	-	-	-
1.1.12.	140698	Single	-	34	-	-	-	30.2	-	133.4	218.9	114.5	0.5296	0.8409	0.111	-0.2021	-0.002	0.9794	115.6	192.4	101.9	37.4	-	-	-	-	-
1.1.13.	142875	Single	-	34	-	-	-	30.2	-	131.7	221	111.3	0.4874	0.8705	0.0683	-0.2339	0.0548	0.9707	114.7	193.6	99.3	37.5	-	64	23	-	-
1.1.14.	155269	Single	-	37	-	-	-	30.2	-	130.1	223.4	109	0.5186	0.8543	0.0351	-0.3949	0.2029	0.896	114.3	193.9	98.7	39.1	-	-	-	-	-
1.1.15.	158753	Single	-	37	-	-	-	30.2	-	128.7	224.2	109.9	0.4966	0.8678	0.0182	-0.3111	0.1584	0.9371	113.2	194.6	98.8	39.4	-	-	-	-	-
1.1.16.	161138	Single	-	37	-	-	-	30.2	-	126.1	225.2	113.2	0.4208	0.9052	0.0602	-0.3164	0.0843	0.9449	111.3	195.3	101.4	39.1	-	-	-	-	-
1.1.17.	164856	Single	-	37	-	-	-	30.2	-	135.9	217.2	115	0.5704	0.8131	0.1163	-0.2401	0.0297	0.9703	117.3	191.1	102.1	40	-	-	-	97	19.7
1.1.18.	169080	Single	-	37	-	-	-	30.2	-	136.8	216.7	114.5	0.5763	0.811	0.1007	-0.2158	0.0321	0.9759	117.8	190.8	101.5	40.2	-	-	-	-	-
1.1.19.	172169	Single	-	37	-	-	-	30.2	-	133.2	220	112.3	0.5252	0.8482	0.068	-0.2387	0.0702	0.9685	115.8	192.7	99.7	40.1	-	-	-	-	-
1.1.20.	174963	Single	-	37	-	-	-	30.2	-	133.9	220.8	107.3	0.5169	0.8555	0.0311	-0.2259	0.1013	0.9689	116.2	193	96.4	39.6	-	-	-	89	15.3
1.1.21.	178441	Single	-	37	-	-	-	30.2	-	142.3	211.6	111.2	0.7132	0.6922	0.1104	-0.4091	0.2832	0.8674	123.1	186.5	99.7	42	-	-	-	-	-
1.1.22.	180795	Single	-	37	-	-	-	30.2	-	140.3	214.3	112.7	0.6986	0.7103	0.0863	-0.3995	0.2871	0.8706	121.4	187.9	100.8	40.5	-	-	-	76	20
1.1.23.	187198	Single	-	37	-	-	-	30.2	-	119.2	228.2	108.3	0.3636	0.926	0.1019	-0.5636	0.1316	0.8155	107.8	197.3	100.3	40.5	-	-	-	-	-
1.1.24.	201712	Single	-	40	-	-	-	30.2	-	131.5	222.3	110.1	0.485	0.8727	0.0565	-0.2829	0.0954	0.9544	114.7	193.8	98.4	42.6	-	-	-	-	-
1.1.25.	205477	Single	-	40	-	-	-	30.2	-	128.5	224	112.4	0.4869	0.8722	0.0467	-0.2812	0.1059	0.9538	112.9	194.5	100.4	42.3	-	-	-	-	-
1.1.26.	208657	Single	-	40	-	-	-	30.2	-	136.9	216.4	114.1	0.6085	0.7805	0.1434	-0.2352	0.0048	0.9719	118	190.6	101.6	43.6	-	-	-	84	20.7
1.1.27.	211562	Single	-	40	-	-	-	30.2	-	142.8	211.8	110.2	0.655	0.7471	0.1127	-0.0757	-0.0834	0.9936	121.3	188.6	98.3	44.9	-	-	-	-	-
1.1.28.	218547	Single	-	40	-	-	-	30.2	-	133	221.8	102.2	0.5517	0.8252	0.1212	0.5606	-0.4745	0.6786	113.4	194.9	96.7	41.1	-	-	-	94	-
1.1.29.	220842	Single	-	40	-	-	-	30.2	-	131.7	222.3	103.3	0.5471	0.8303	0.1063	0.5767	-0.4659	0.6711	112.4	195.4	97.5	41.8	-	-	-	-	-
1.1.30.	223576	Single	-	40	-	-	-	30.2	-	136.4	218.4	107.9	0.5527	0.823	0.1314	0.6143	-0.5088	0.6031	115	193.1	100.7	42.2	-	-	-	-	-
1.1.31.	227049	Single	-	40	-	-	-	30.2	-	123	226	110.6	0.4396	0.8903	0.1188	-0.2264	-0.0182	0.9739	109.7	196.5	99.9	44.3	-	-	-	-	-
1.1.32.	251017	Single	-	42	-	-	-	30.2	-	132.1	222.2	105.6	0.5212	0.8521	0.0484	-0.366	0.1719	0.9146	115.7	193.5	96	44.7	-	-	-	274	21
1.1.33.	256272	Single	-	42	-	-	-	30.2	-	134.5	220.5	107	0.5311	0.8462	0.0438	-0.1457	-0.1422	0.9791	114.8	194	96.4	44.1	-	-	-	-	-
1.1.34.	259282	Single	-	42	-	-	-	30.2	-	133.6	219.2	113.1	0.6248	0.7751	0.0939	0.1452	-0.2335	0.9614	114.4	193.4	101.1	46	-	-	-	-	-
1.1.35.	262634	Single	-	42	-	-	-	30.2	-	127.9	223.1	110.2	0.5521	0.8209	0.1459	0.0459	-0.2047	0.9778	111.5	195.5	99.9	47.3	-	-	-	-	-
1.1.36.	272324	Single	-	42	-	-	-	30.2	-	132.4	221	102.3	0.5593	0.8246	0.0848	-0.7022	0.4169	0.5771	116.7	192.7	96.5	44.9	-	-	-	-	-
1.1.37.	280246	Single	-	42	-	-	-	30.2	-	129.4	224	104.3	0.4957	0.8677	0.038	-0.6326	0.3307	0.7003	114.4	194.1	97.7	44.3	-	-	-	-	-
1.1.38.	283213	Single	-	42	-	-	-	30.2	-	129.6	223.8	100.8	0.4781	0.8781	0.0173	-0.6393	0.3345	0.6924	114.5	194.4	95.2	44.2	-	63	21	-	-
1.1.39.	293011	Single	-	42	-	-	-	30.2	-	130.2	222.3	111.6	0.5416	0.8371	0.0772	0.2351	-0.239	0.9421	111.7	195.3	100.1	45.5	-	-	-	-	-
1.1.40.	297015	Single	-	42	-	-	-	30.2	-	121.4	227.6	112.8	0.3775	0.9242	0.0574	-0.3537	0.0866	0.9313	108.9	196.6	101.4	44.6	-	-	-	-	-
1.1.41.	299949	Single	-	42	-	-	-	30.2	-	118.9	229.7	105.6	0.3772	0.9257	0.0298	-0.541	0.1941	0.8183	108	197.6	97.7	43.8	-	-	-	-	-
1.1.42.	303583	Single	-	42	-	-	-	30.2	-	137	217.3	109.8	0.578	0.8137	0.0619	-0.0989	-0.0054	0.9951	117.8	191.6	97.8	46.2	-	-	-	-	-
1.1.43.	308640	Single	-	42	-	-	-	30.2	-	133.2	220.6	110.9	0.528	0.8483	0.0392	-0.0906	0.0104	0.9958	115	193.5	98.6	45.2	-	-	-	323	21.7
1.1.44.	327170	Single	-	42	-	-	-	30.2	-	129.9	220.8	115.8	0.5762	0.7997	0.1687	0.0253	-0.2238	0.9743	112.3	194	104.4	46.6	-	-	-	-	-
1.1.45.	370339	Single	-	42	-	-	-	30.2	-	140.3	214.6	107	0.6868	0.7192	0.1048	-0.4041	0.2581	0.8775	121.7	188.6	96.2	46.7	-	-	-	174	19
1.1.46.	382259	Single	-	42	-	-	-	30.2	-	138.2	215.5	111.6	0.6097	0.7759	0.1624	-0.2667	0.0079	0.9637	118.9	190.2	100	47.1	-	-	-	-	-
1.1.47.	385266	Single	-	42	-	-	-	30.2	-	138.9	215.3	108	0.6368	0.755	0.1564	-0.2608	0.0201	0.9652	119.7	190.2	97.2	47.1	-	-	-	-	-
1.1.48.	388201	Single	-	42	-	-	-	30.2	-	142.3	212	107.2	0.7105	0.6918	0.1286	-0.3568	0.1968	0.9132	123.2	187.2	96.4	48.7	-	-	-	-	-

Background



- Inter-individual **heterogeneity** of the hand «hot spot» [1]
- There is a **somatotopic representation** of the hand muscles within the «hand knob» [2-6]
- Impact of laterality → **incongruent results** [7-15]
- Damage to the spinal → **posterior shift towards the somatosensory cortex** [16-18]

Our hypothesis:

1. The dominant hand:

- smaller area
- lower intensities of stimulation
- lower latencies

2. Patients with cervical myelopathy:

- posterior extension reorganization – with bigger area
- bigger intensities of stimulation
- bigger latencies

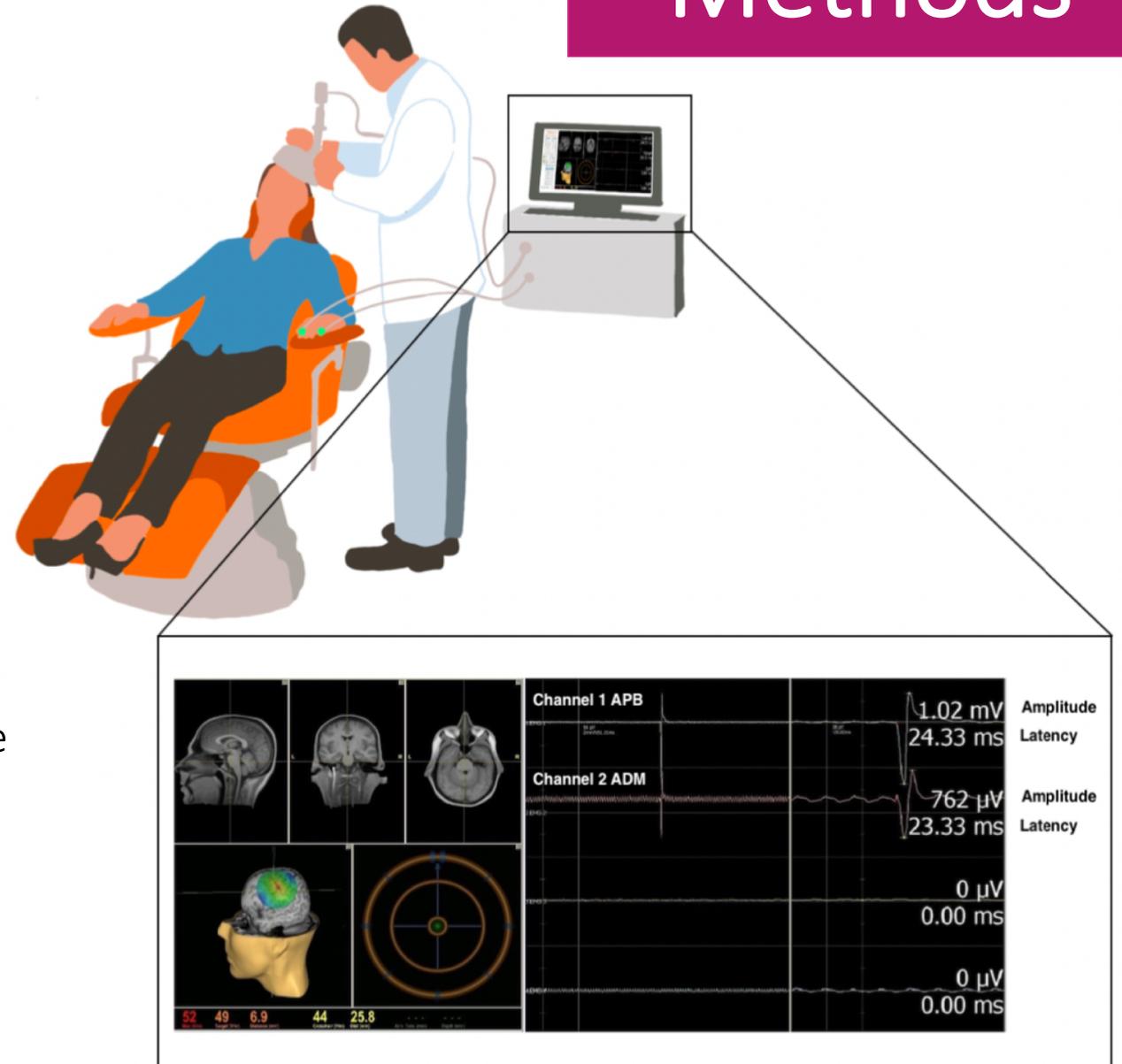
Study population:

TMS mapping of

- 26 healthy subjects (HS)
- 13 adult patients (AP) with cervical myelopathy (intramedullary or extramedullary)

Parameters studied:

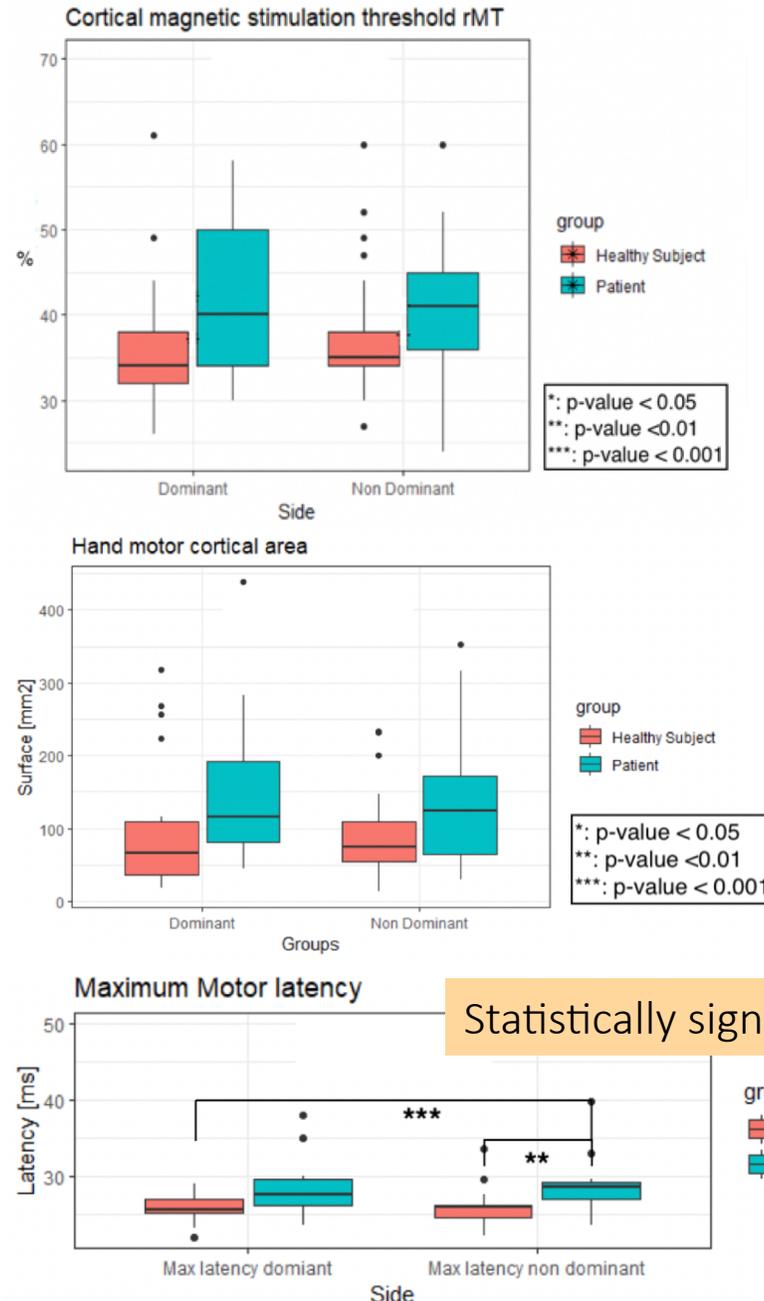
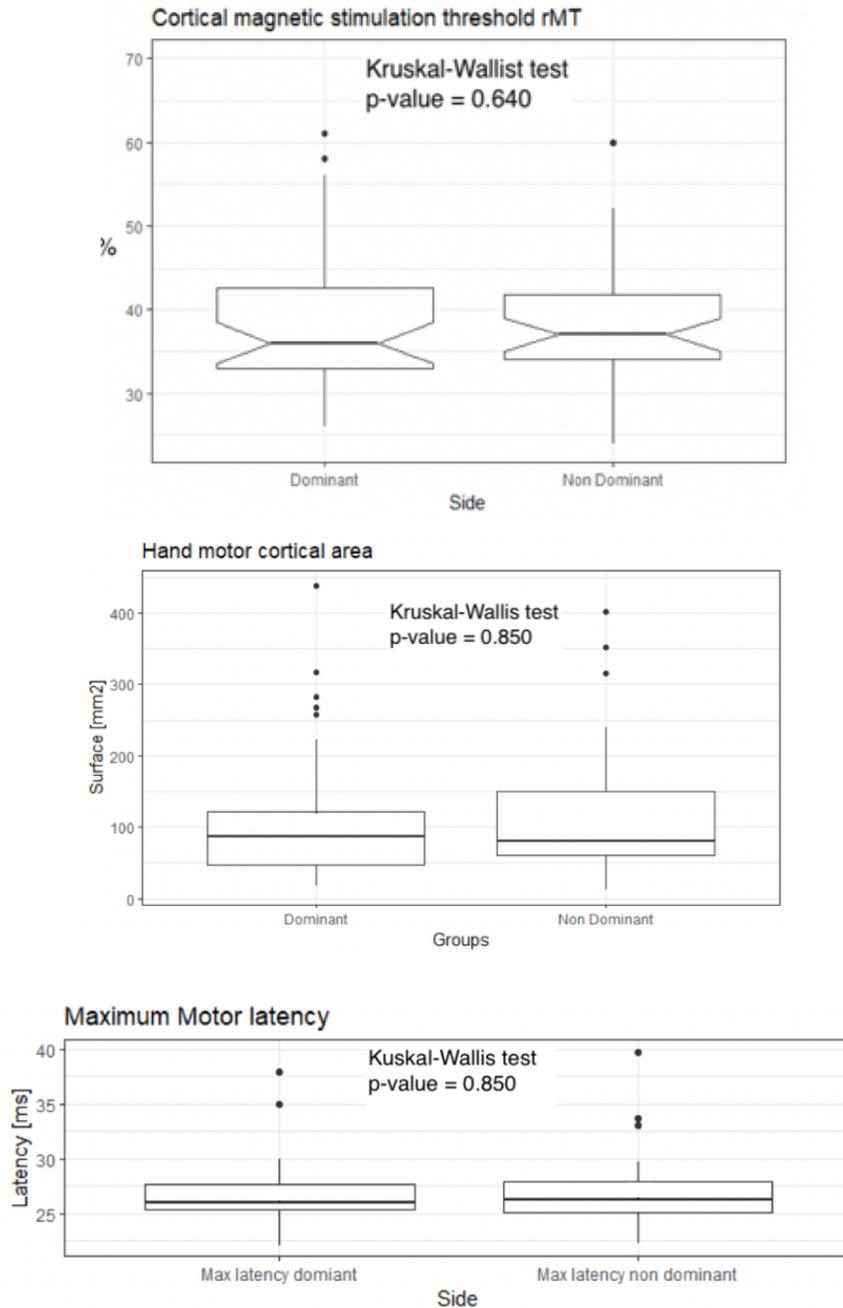
- Intensity of stimulation = 105% of the rMT
 - rMT = 50 μ V MEP (peak-to-peak) in at least 50% of the stimulations, within a latency in the range of 20 ms
- Cortical areas = including all eliciting positive stimulation in any of both muscles ($CA_{APB+ADM}$)
- Latencies



Results

Dominant vs non dominant hand

Regarding the three parameters studied, potential differences between dominant and non-dominant hand within the two populations, and by mixing them, were below our detection threshold



Results

Healthy subjects vs patients

Overall (dominant and non-dominant together) intensities of stimulation bigger for the patients' group

The intensity of stimulation increased from 37.5 ± 8.1 % in HS to 41.7 ± 9.2 % in AP

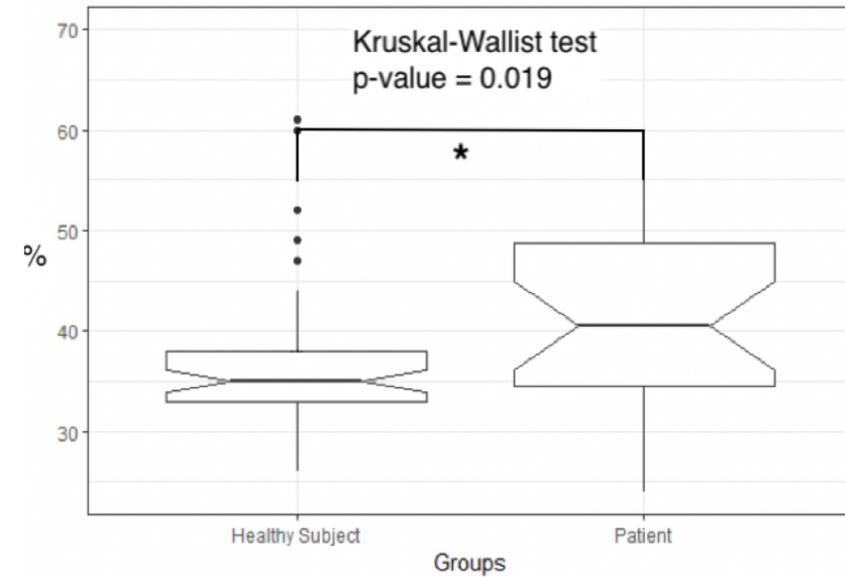
Overall patients' areas bigger than HS

The area increased from 96.9 ± 82.8 mm² in HS to 148.2 ± 104.7 mm² in AP

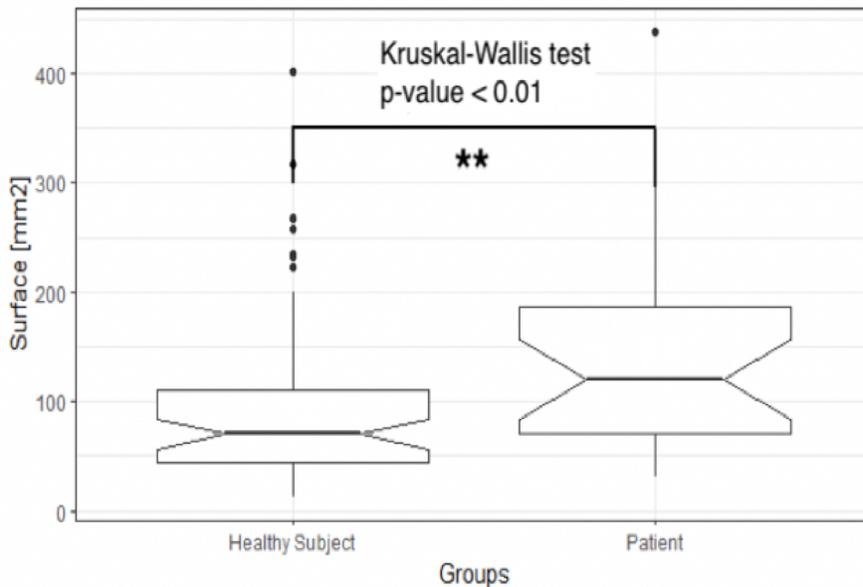
Overall patients' maximal latency bigger than HS

The maximal latency increased from 25.9 ± 1.9 ms in HS to 28.8 ± 3.9 ms in AP

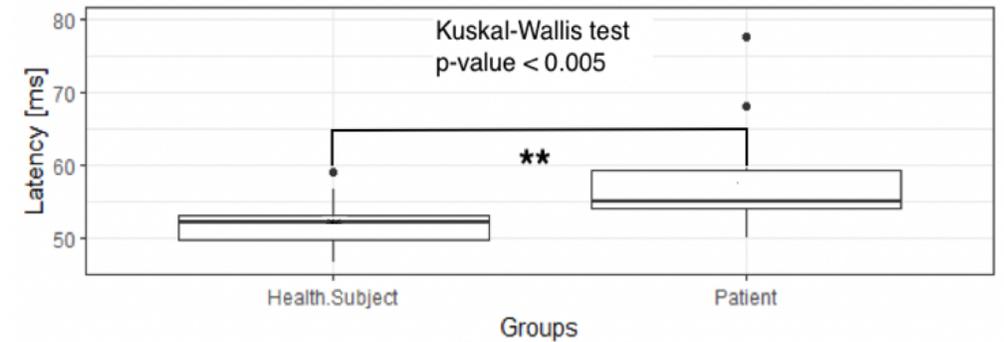
Cortical magnetic stimulation threshold rMT



Total hand motor cortical area



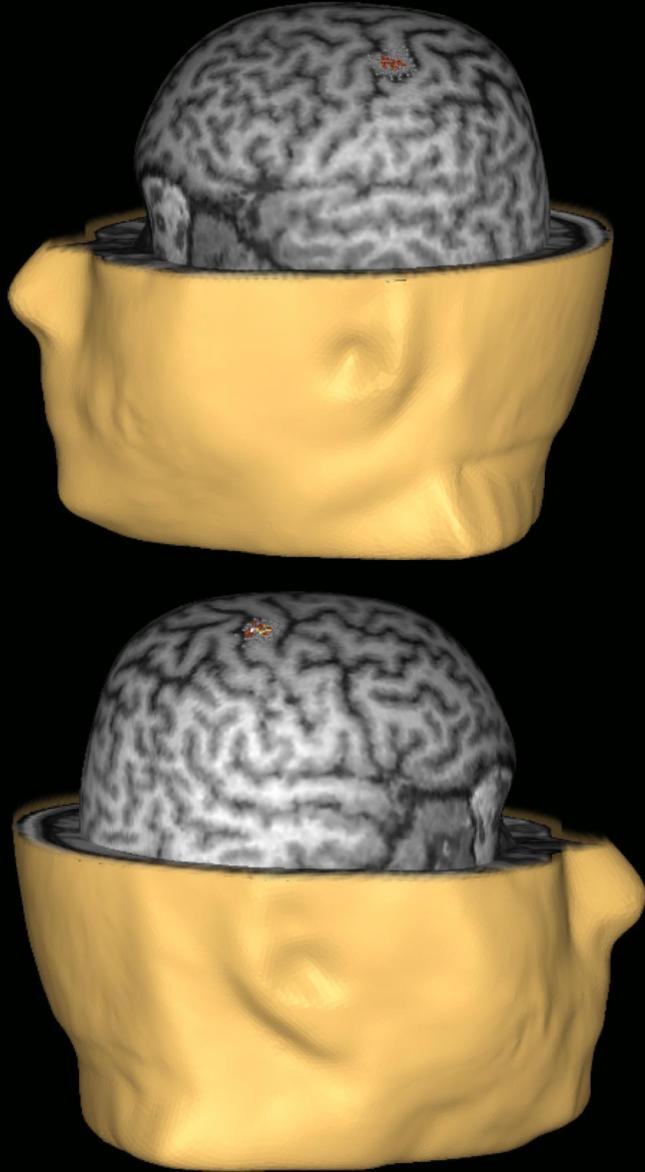
Maximum motor latency



Results

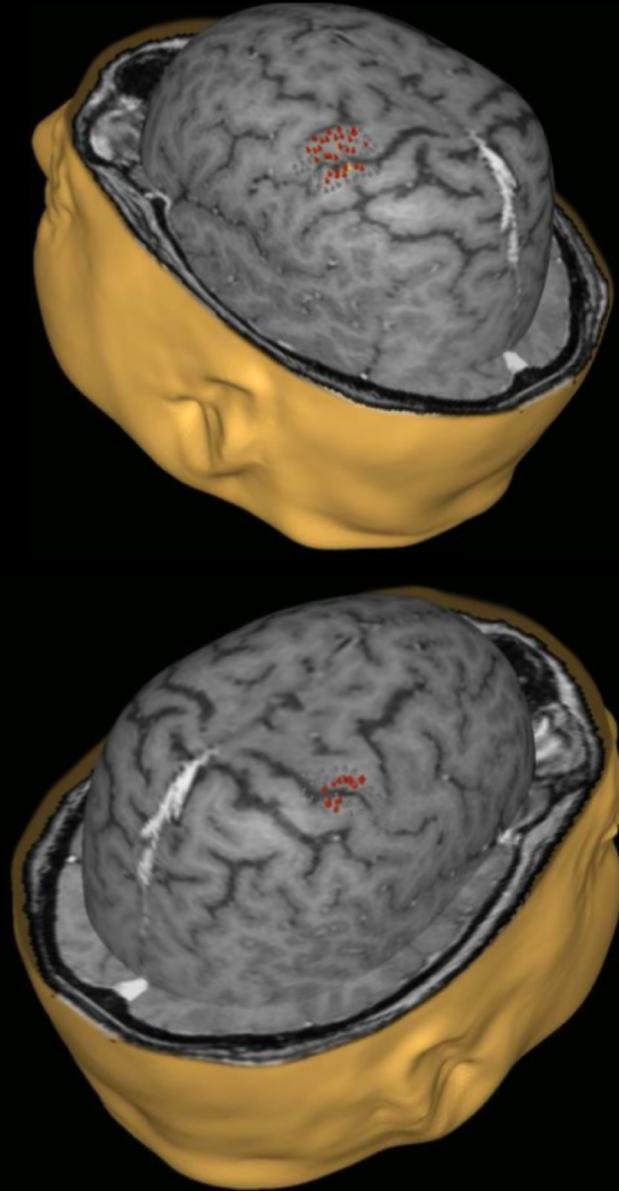
a)

HS



b)

Patients



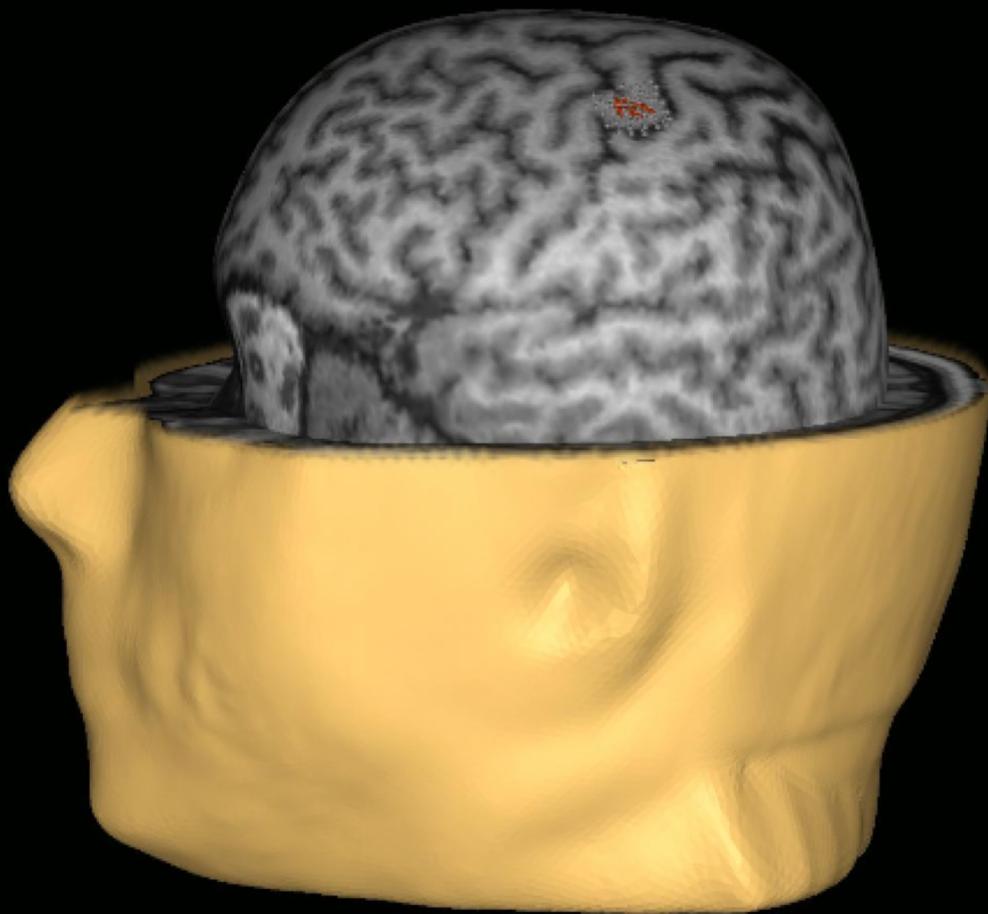
Cortical area

Posterior shift in the axial plane → an overlap with the post-central gyrus in at least one of the two hands, in 10/13 patients versus 5/26 healthy subjects

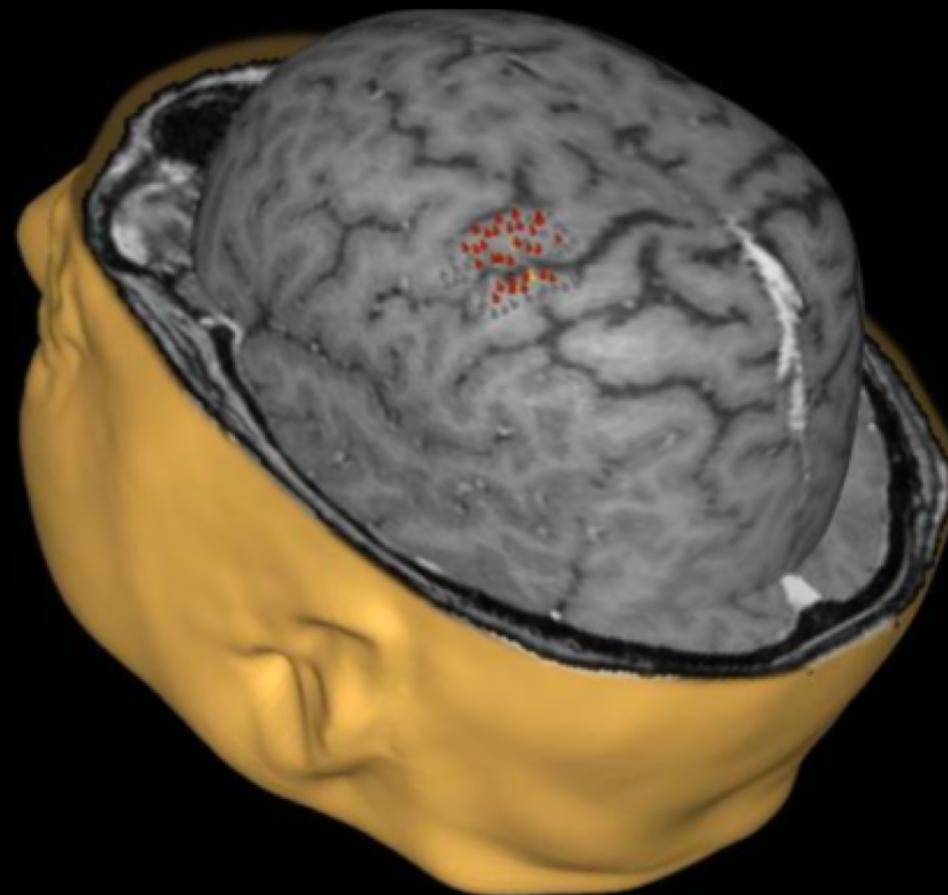
Results

Cortical area

a) HS



b) Patients



1. The dominant hand:

- smaller area
- lower intensities of stimulation
- lower latencies



The effect of dominance is small and requires a rigorous approach...

2. Patients with cervical myelopathy:

- posterior extension reorganization
- bigger intensities of stimulation
- bigger latencies



Are the symptoms proportional to this cortical reorganization?

Are these differences found reversible with effective surgical treatment?

Aknowledgement

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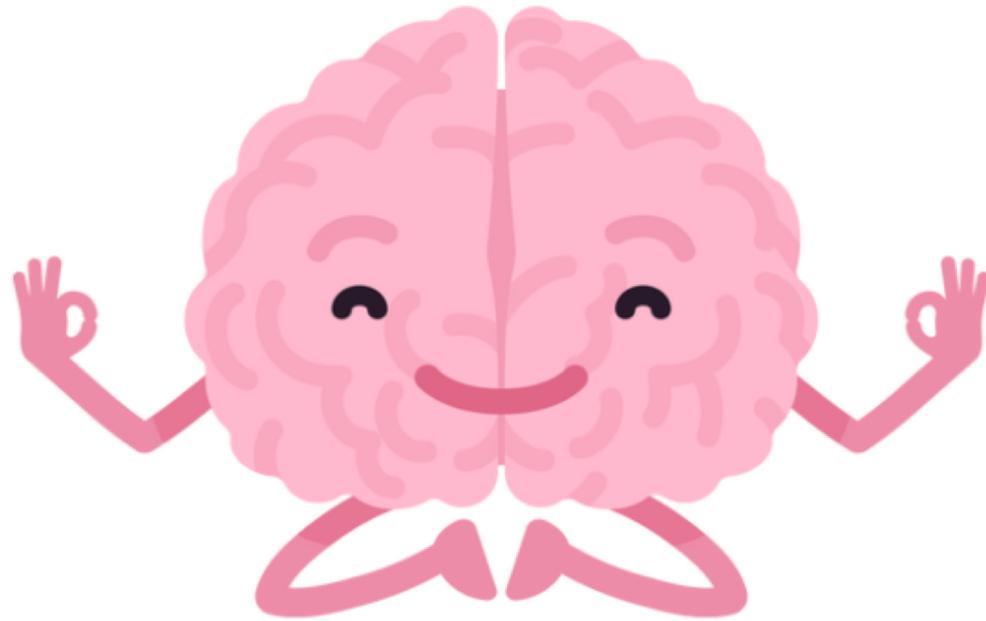


Prof. Shahan Momjian



Prof. Karl Schaller

Questions?



References

- [1] Ahdab R, Ayache SS, Brugières P, Farhat WH, Lefaucheur JP. The Hand Motor Hotspot is not Always Located in the Hand Knob: A Neuronavigated Transcranial Magnetic Stimulation Study. *Brain Topogr*. 2016 Jul;29(4):590–7.
- [2] Dubbioso R, Raffin E, Karabanov A, Thielscher A, Siebner HR. Centre-surround organization of fast sensorimotor integration in human motor hand area. *NeuroImage*. 2017 Sep;158:37–47.
- [3] Dubbioso R, Madsen KH, Thielscher A, Siebner HR. The Myelin Content of the Human Precentral Hand Knob Reflects Interindividual Differences in Manual Motor Control at the Physiological and Behavioral Level. *J Neurosci Off J Soc Neurosci*. 2021 Apr 7;41(14):3163–79.
- [4] Raffin E, Pellegrino G, Di Lazzaro V, Thielscher A, Siebner HR. Bringing transcranial mapping into shape: Sulcus-aligned mapping captures motor somatotopy in human primary motor hand area. *NeuroImage*. 2015 Oct 15;120:164–75.
- [5] Raffin E, Siebner HR. Use-Dependent Plasticity in Human Primary Motor Hand Area: Synergistic Interplay Between Training and Immobilization. *Cereb Cortex N Y N 1991*. 2019 Jan 1;29(1):356–71.
- [6] Numssen O, Zier AL, Thielscher A, Hartwigsen G, Knösche TR, Weise K. Efficient high-resolution TMS mapping of the human motor cortex by nonlinear regression. *NeuroImage*. 2021 Dec 15;245:118654.

References

- [7] Cantello R, Gianelli M, Bettucci D, Civardi C, De Angelis MS, Mutani R. Parkinson's disease rigidity: magnetic motor evoked potentials in a small hand muscle. *Neurology*. 1991 Sep;41(9):1449–56.
- [8] Macdonell RA, Shapiro BE, Chiappa KH, Helmers SL, Cros D, Day BJ, et al. Hemispheric threshold differences for motor evoked potentials produced by magnetic coil stimulation. *Neurology*. 1991 Sep;41(9):1441–4.
- [9] Triggs WJ, Calvanio R, Macdonell RA, Cros D, Chiappa KH. Physiological motor asymmetry in human handedness: evidence from transcranial magnetic stimulation. *Brain Res*. 1994 Feb 14;636(2):270–6.
- [10] Cicinelli P, Traversa R, Oliveri M, Palmieri MG, Filippi MM, Pasqualetti P, et al. Intracortical excitatory and inhibitory phenomena to paired transcranial magnetic stimulation in healthy human subjects: differences between the right and left hemisphere. *Neurosci Lett*. 2000 Jul 21;288(3):171–4.
- [11] Civardi C, Cavalli A, Naldi P, Varrasi C, Cantello R. Hemispheric asymmetries of cortico-cortical connections in human hand motor areas. *Clin Neurophysiol Off J Int Fed Clin Neurophysiol*. 2000 Apr;111(4):624–9.
- [12] Netz J, Ziemann U, Hömberg V. Hemispheric asymmetry of transcallosal inhibition in man. *Exp Brain Res*. 1995;104(3):527–33.

References

- [13] Triggs WJ, Subramaniam B, Rossi F. Hand preference and transcranial magnetic stimulation asymmetry of cortical motor representation. *Brain Res.* 1999 Jul 24;835(2):324– 9.
- [14] Nicolini C, Harasym D, Turco CV, Nelson AJ. Human motor cortical organization is influenced by handedness. *Cortex J Devoted Study Nerv Syst Behav.* 2019 Jun;115:172– 83.
- [15] Hammond G. Correlates of human handedness in primary motor cortex: a review and hypothesis. *Neurosci Biobehav Rev.* 2002 May;26(3):285–92.
- [16] Kokotilo KJ, Eng JJ, Curt A. Reorganization and preservation of motor control of the brain in spinal cord injury: a systematic review. *J Neurotrauma.* 2009 Nov;26(11):2113–26.
- [17] Nardone R, Höller Y, Brigo F, Orioli A, Tezzon F, Schwenker K, et al. Descending motor pathways and cortical physiology after spinal cord injury assessed by transcranial magnetic stimulation: a systematic review. *Brain Res.* 2015 Sep 4;1619:139–54.
- [18] Solstrand Dahlberg L, Becerra L, Borsook D, Linnman C. Brain changes after spinal cord injury, a quantitative meta-analysis and review. *Neurosci Biobehav Rev.* 2018 Jul;90:272–93.