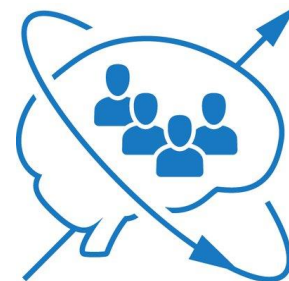




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DEPARTMENT OF NEUROSCIENCES,
REPRODUCTIVE SCIENCES AND ODONTOSTOMATOLOGY
Prof. Lucio Santoro



DRCMR

Functional and structural phenotyping of the human precentral hand knob

R. Dubbioso, K.H. Madsen, A. Thielscher, H. R. Siebner.



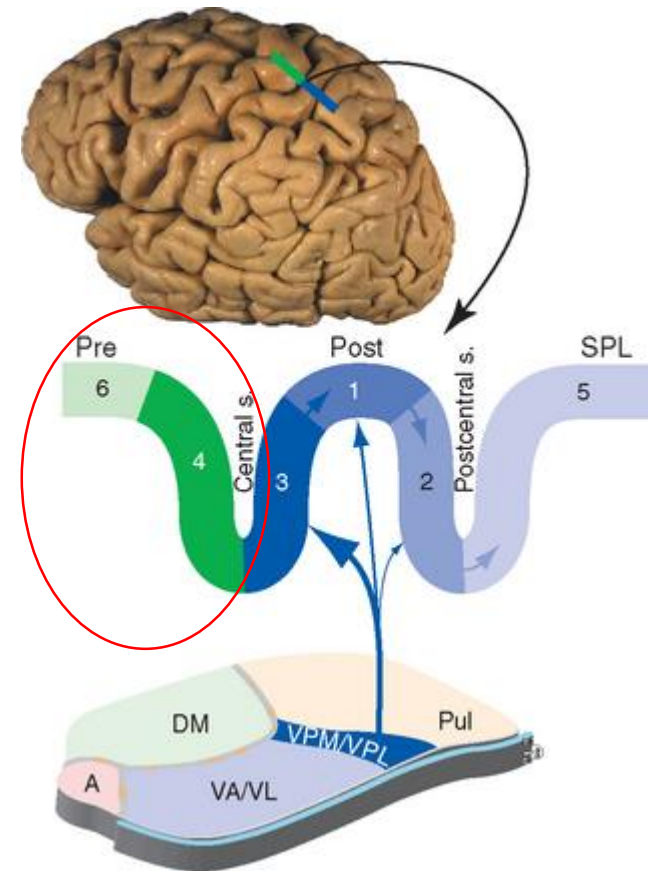
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SOCIETÀ ITALIANA DI NEUROLOGIA

Functional and structural phenotyping of the human precentral hand knob

Background

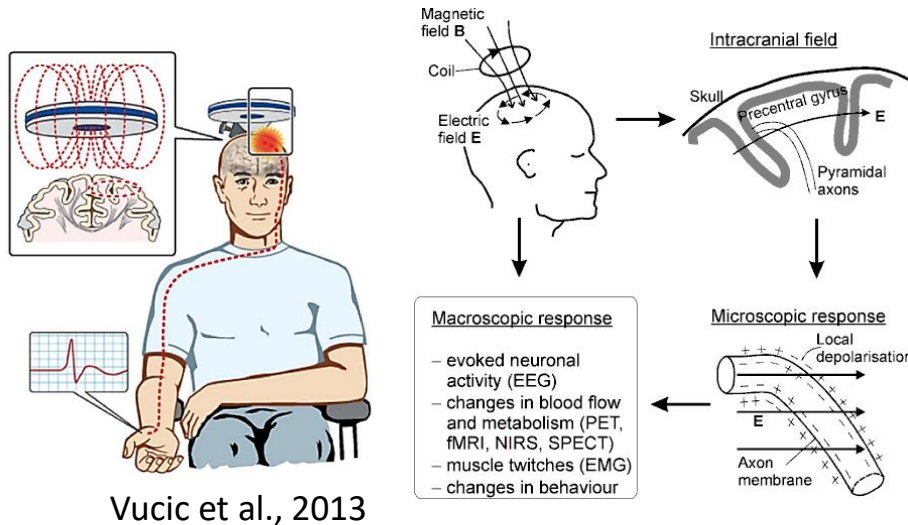
Precentral hand-knob area is crucial for fine control of hand movement; this area contains in the caudal part the primary motor cortex (M1-HAND) and in the rostral part the dorsal premotor cortex (dPMC).

M1-HAND is directly involved in the execution of independent fingers movement. The dPMC is tightly inter-connected with the M1-HAND and has been implicated in motor preparation and selection, translating visuospatial information into action plans.



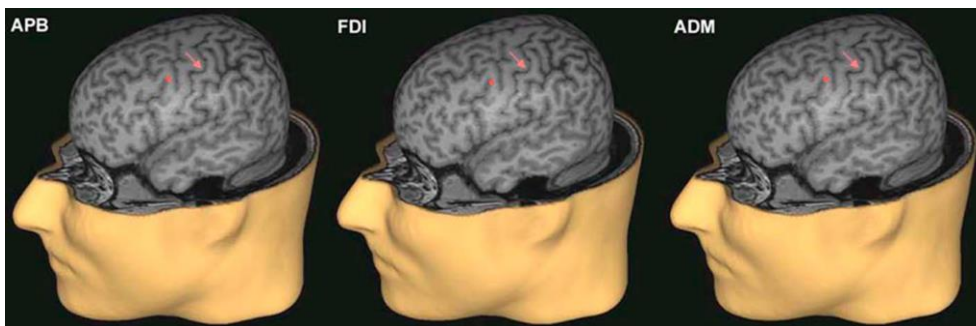
Functional and structural phenotyping of the human precentral hand knob

Background: TMS and variability of hot-spot location



Transcranial magnetic stimulation (TMS) can excite non-invasively, by generating an electric field, the axons of the pyramidal neuron in the M1 HAND.

However, the spatial peak of cortico-spinal excitability is often not located in the M1HAND but shows a huge inter-individual variability with an anterior shift towards the dPM (Teitti et al., 2008; Vaalto et al., 2011; Spieser et al., 2013; Ahdab et al., 2013; Entakli et al., 2013; Ahdab et al., 2016).



Ahdab et al., 2016

Functional and structural phenotyping of the human precentral hand knob

Aim and Hypotheses

Here we used magnetic resonance imaging (MRI) to test the hypothesis that the “hand knob” of the precentral gyrus shows different structural and microstructural properties in individuals with a dPMC representation compared to individuals with a preponderant M1-HAND representation of hand muscles.

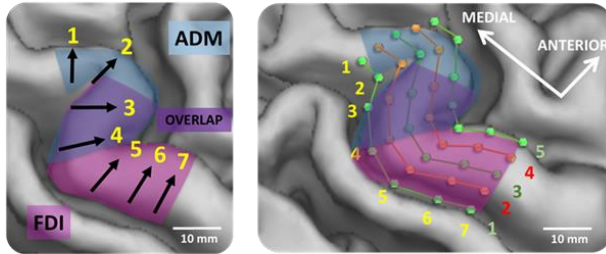
We hypothesized that a more rostral cortico-spinal peak location in precentral gyrus would be associated with longer corticomotor latencies of the MEPs, indicating that a more premotor site was targeted by TMS. We further hypothesized that a more premotor electrophysiological signature would scale with structural and functional properties of the precentral gyrus and dexterity.



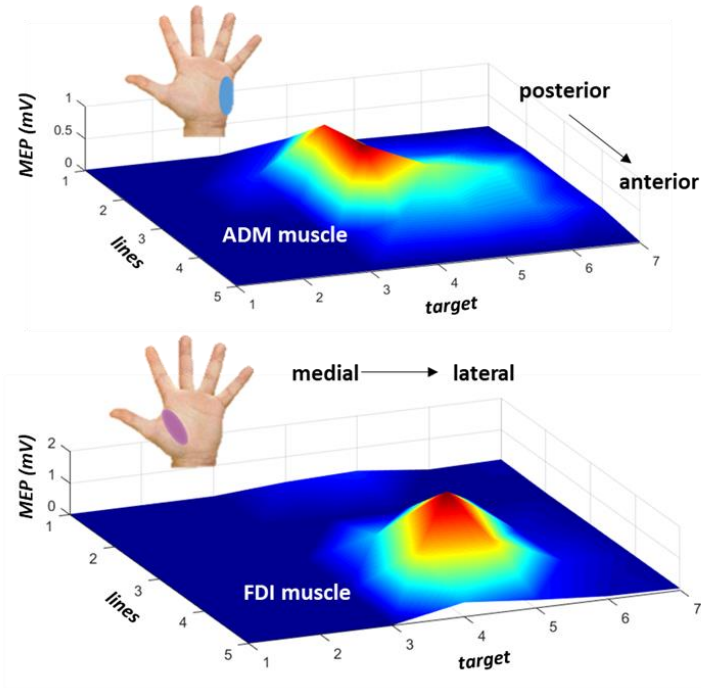
Functional and structural phenotyping of the human precentral hand knob

Methods

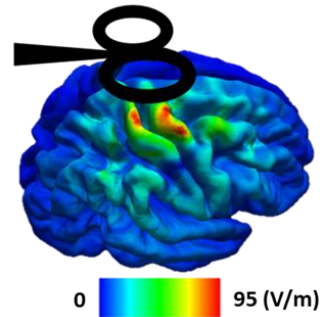
A Sulcus-shape based TMS mapping



B 3-d plot of MEPs representation

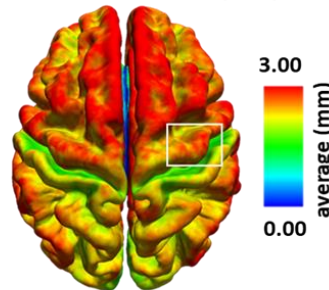


C Electric field modelling

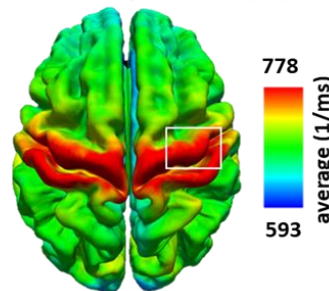


D Structural MRI

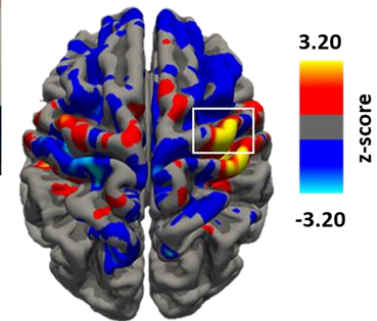
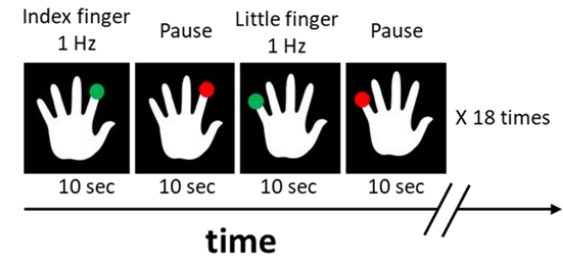
Cortical thickness (mm)



Cortical myelination (R1)



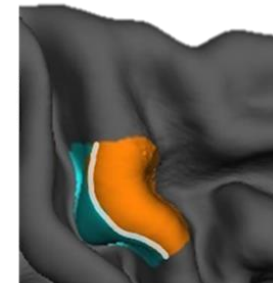
E Functional MRI during a visuo-motor synchronization task



F

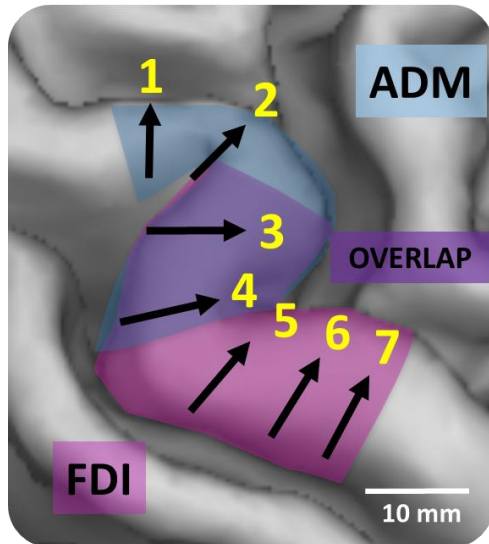
REGION OF INTERESTS

Right M1-HAND Right dPMC

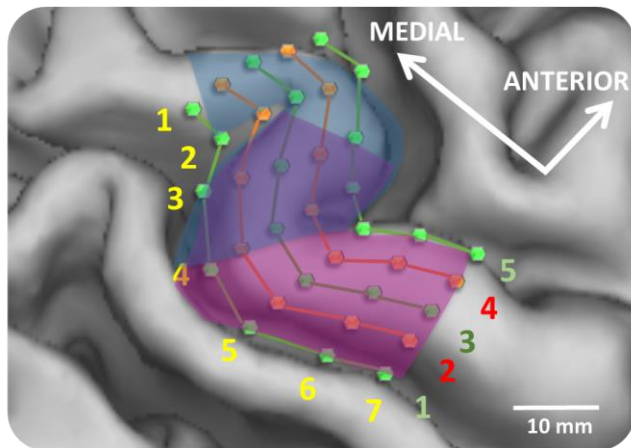
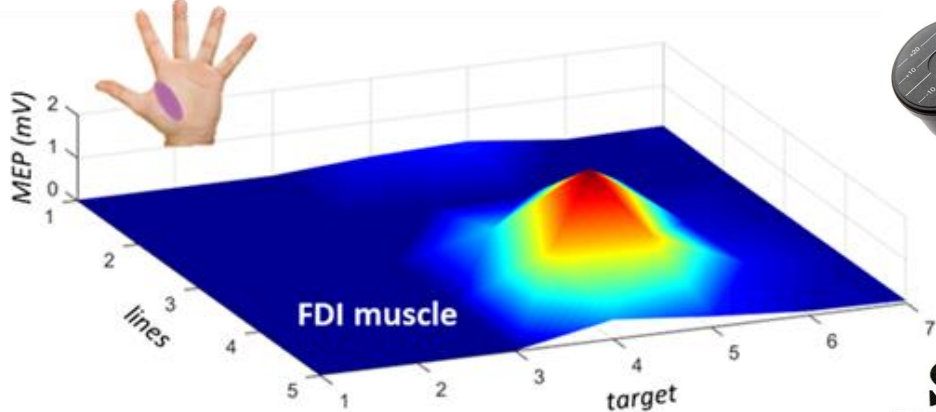
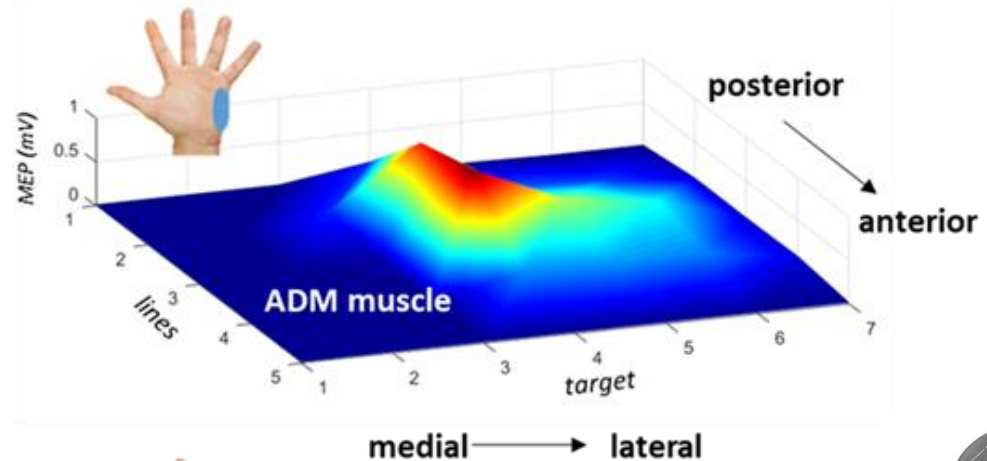


Functional and structural phenotyping of the human precentral hand knob

Methods: TMS mapping



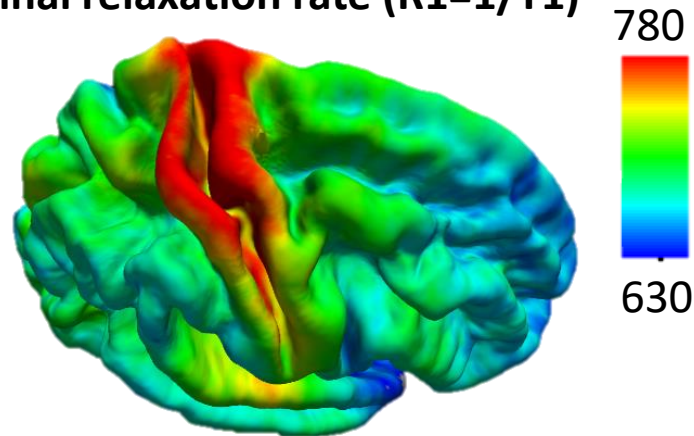
- Intensity of TMS stimulation: 120% of RMT-FDI muscle
- Biphasic pulse
- Left FDI and ADM muscle



Functional and structural phenotyping of the human precentral hand knob

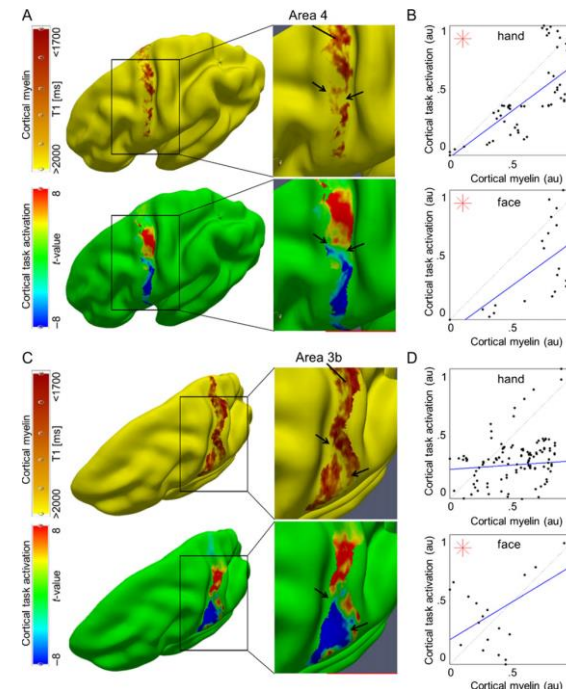
Background: Cortical myelination and fMRI

Longitudinal relaxation rate ($R1=1/T1$)



Cortical myelination is closely linked to intrinsic functional activity in unimodal areas and with task-related functional activity within visual cortex, auditory cortex and sensory-motor cortex.

In vivo MRI-based myelin maps provide an initial window into the architectonics of cerebral cortex in living brains that can also be studied with functional methods.

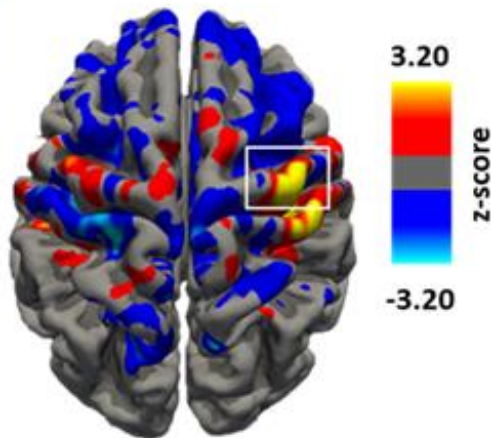
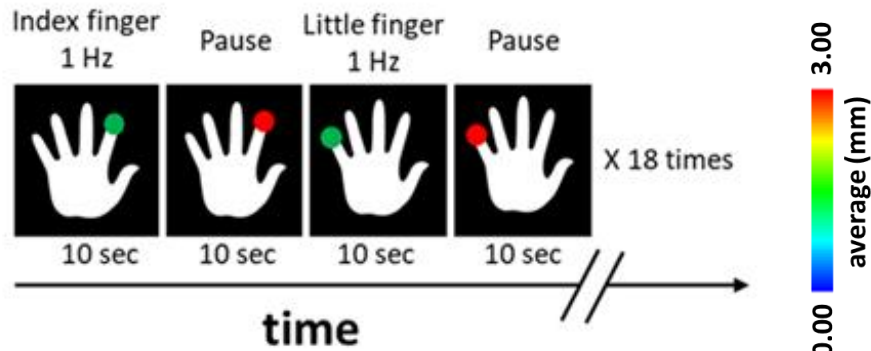


Kuehn et al., 2017

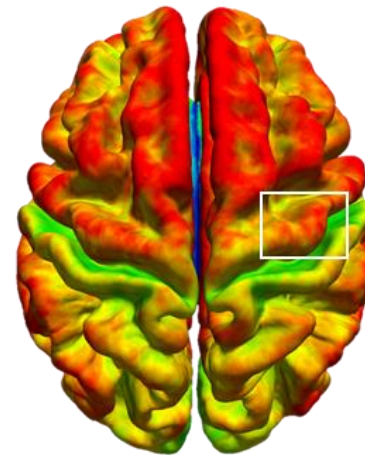
Functional and structural phenotyping of the human precentral hand knob

Methods: Functional e structural MRI

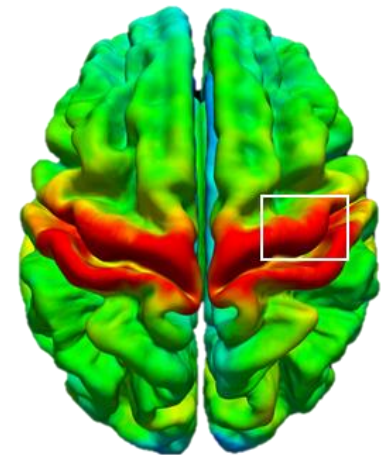
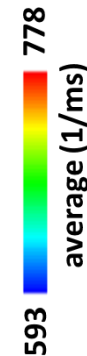
Functional MRI during a visuo-motor synchronization task



Cortical thickness



Cortical myelination



REGION OF INTERESTS

Right M1-HAND



Right dPMC



Functional and structural phenotyping of the human precentral hand knob

Subjects

- Twenty-four volunteers
- Right handed as assessed by Edinburgh Handedness Inventory
- Age (mean \pm SD): 24.25 \pm 0.91
- Male/Female: 12/12
- No musician nor video-gamer



Functional and structural phenotyping of the human precentral hand knob

Data Analysis

- IBM SPSS Statistics software (Version 22 for Windows, New York City, USA).
- Group-based surface analysis and average of cortical thickness and myelination maps across subjects were computed by using FreeSurfer software package (Fischl et al. 1999).

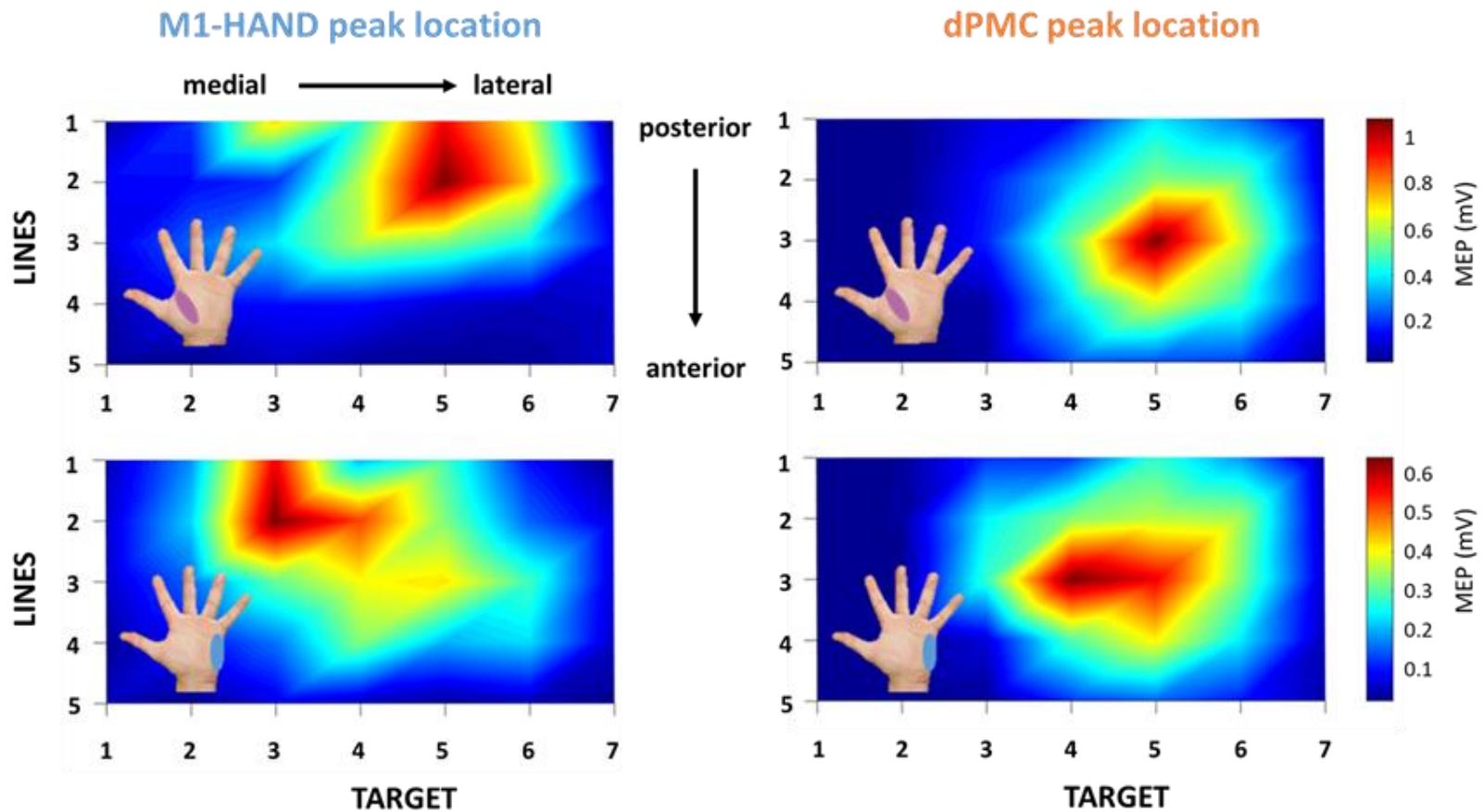


FreeSurfer

Functional and structural phenotyping of the human precentral hand knob

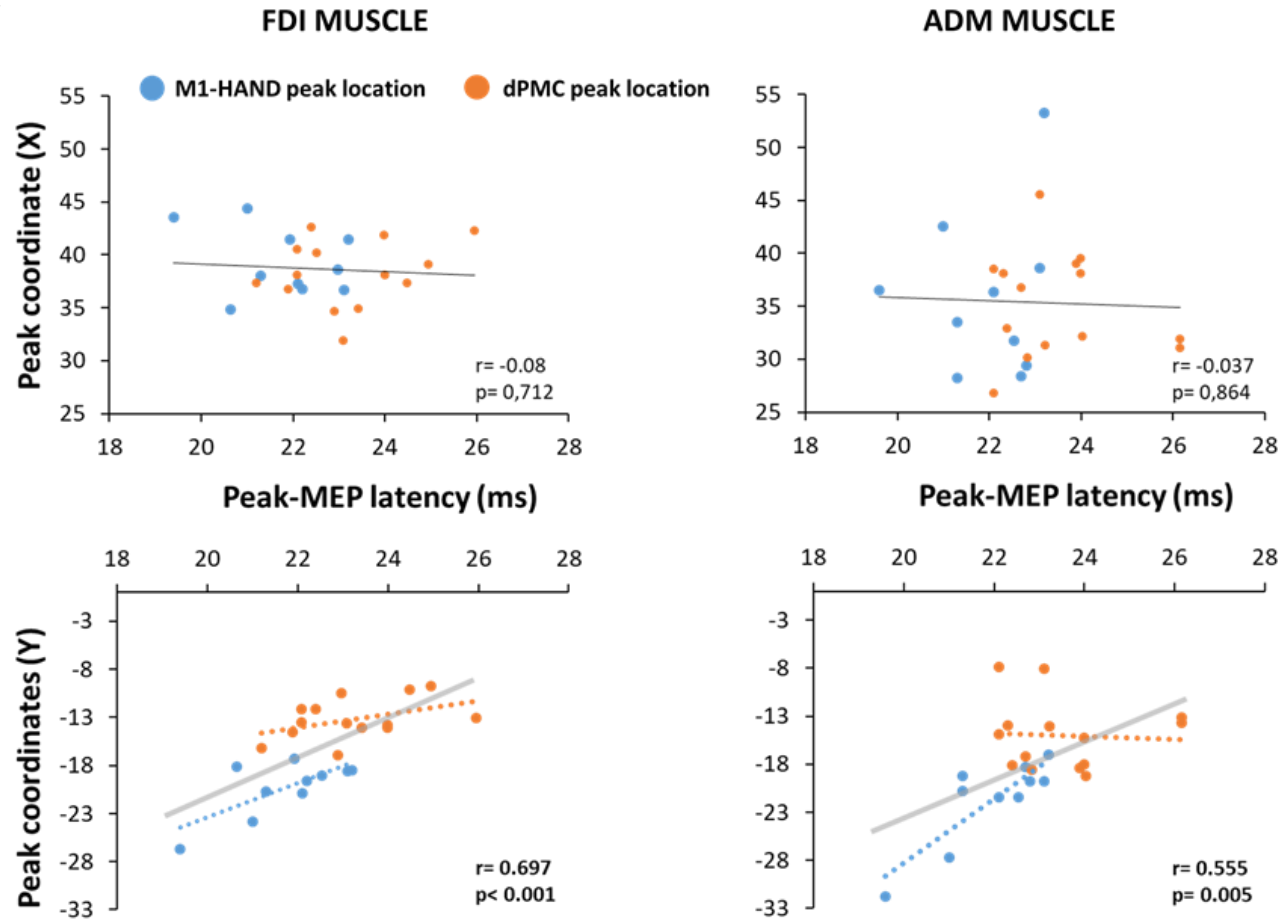
Results: TMS cortico-motor maps

A



Functional and structural phenotyping of the human precentral hand knob

Results: Relationship between peak excitability and MEP latency

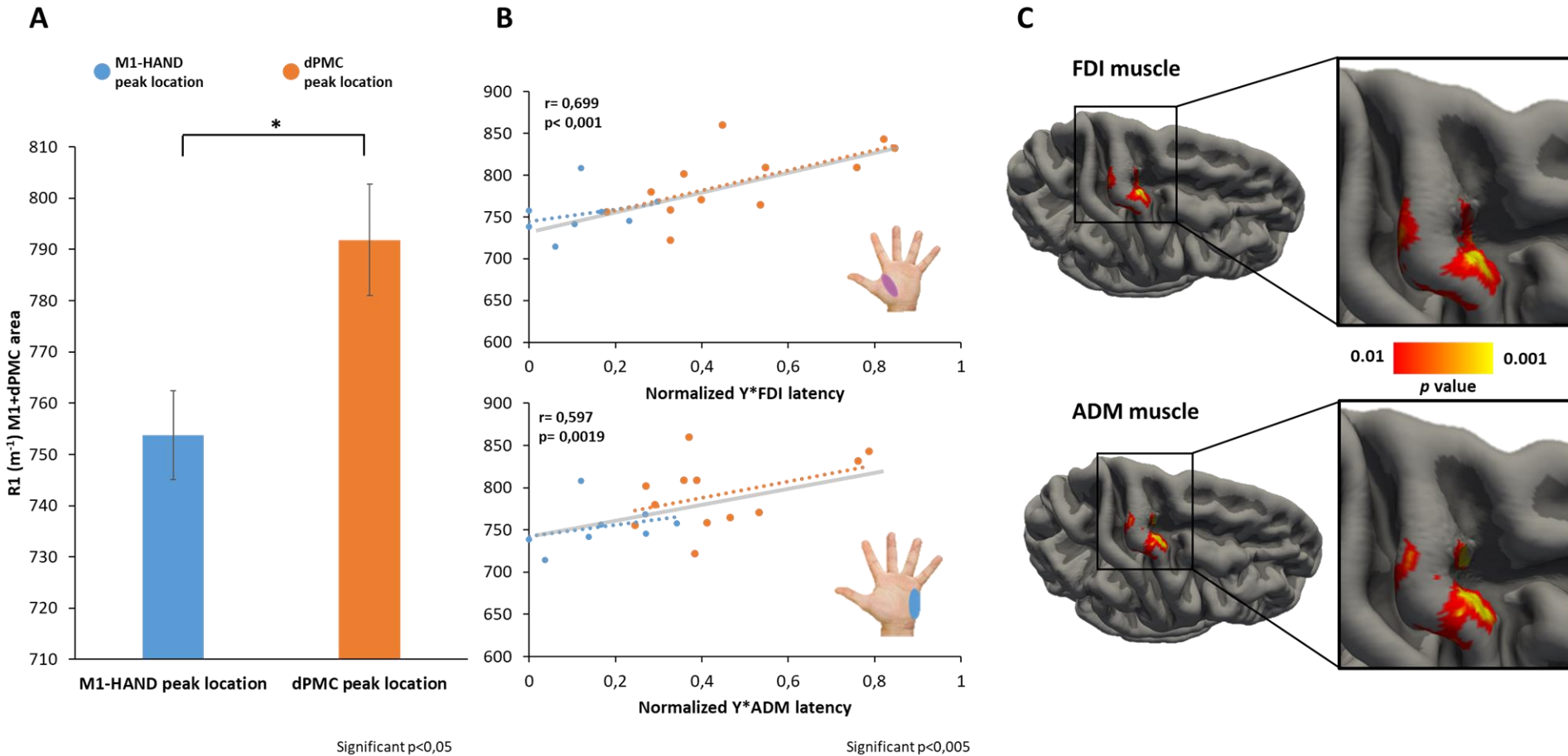


ROSTRALITY INDEX

Peak-MEP latency * Y coordinate

Functional and structural phenotyping of the human precentral hand knob

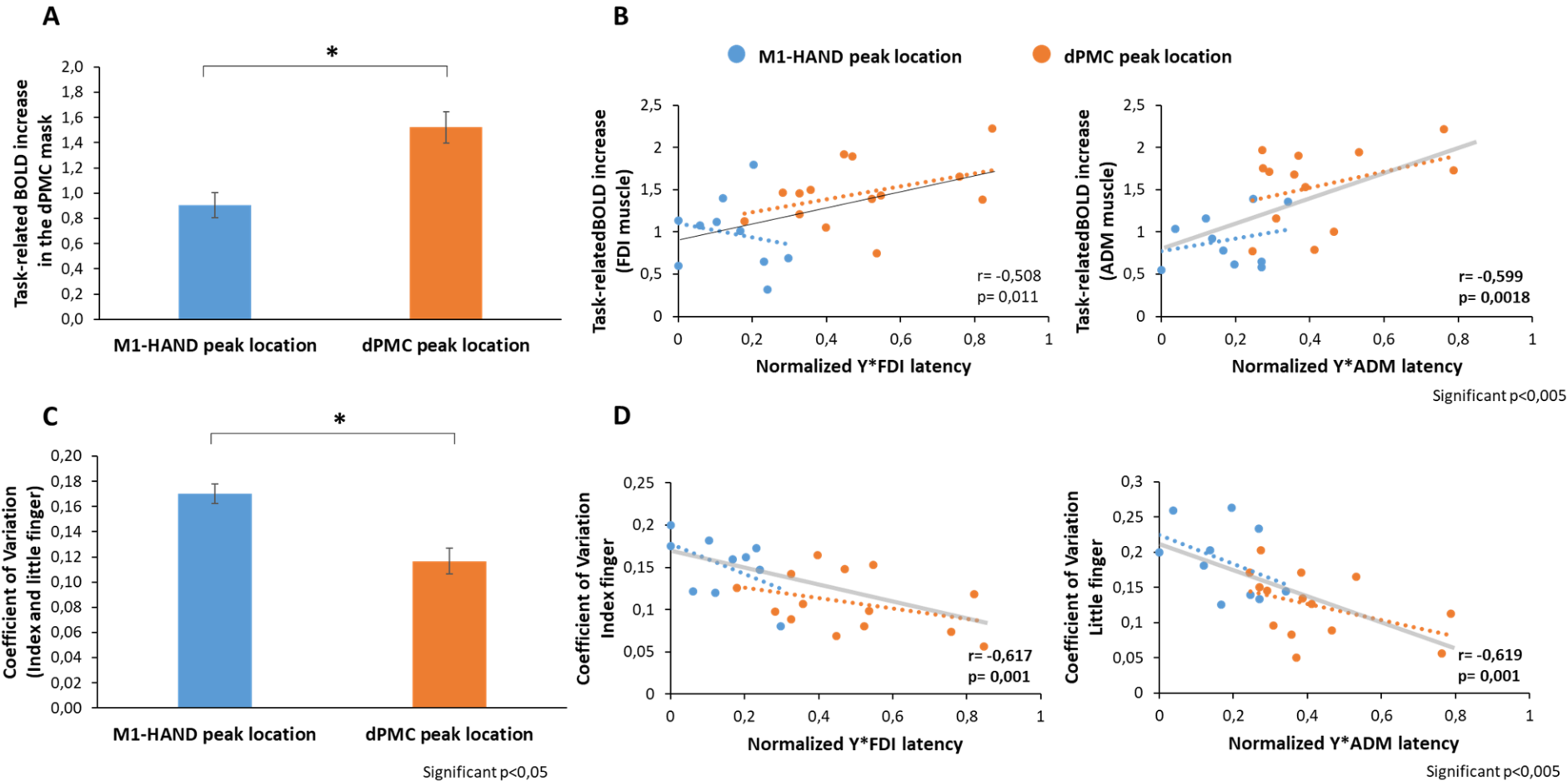
Results: Cortical Myelination in the precentral gyrus



Participants with dPMC peak location have an overall higher cortical myelination

Functional and structural phenotyping of the human precentral hand knob

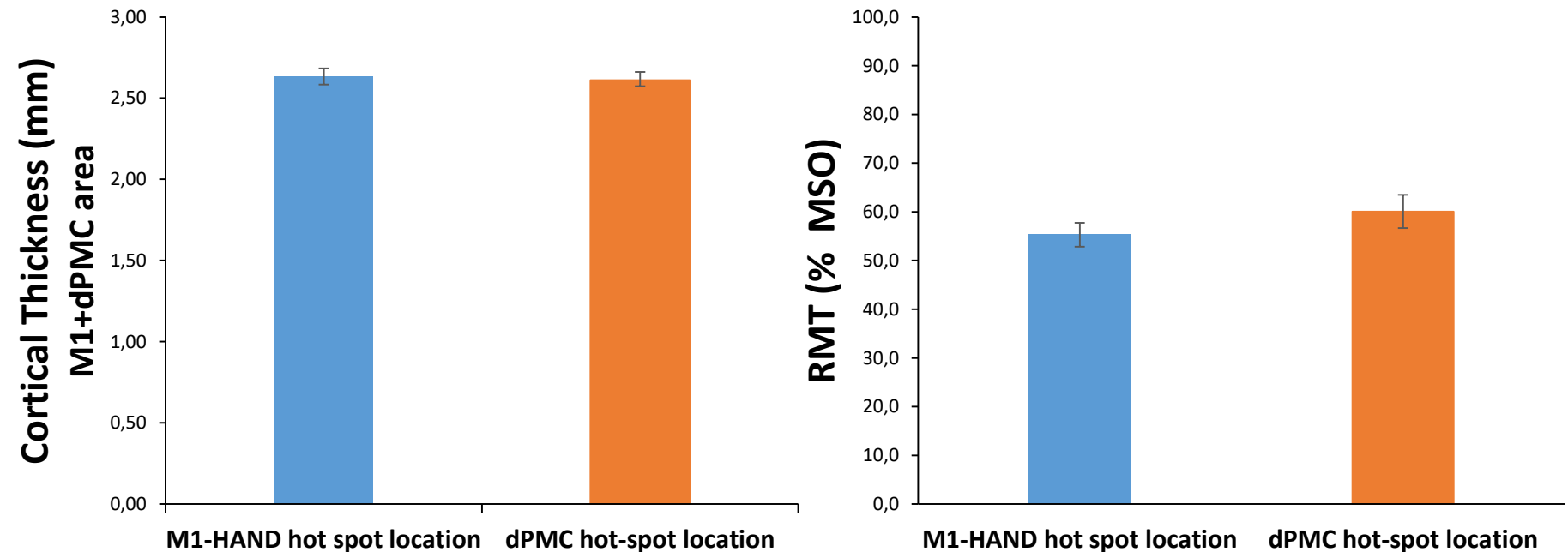
Results: Electric Field simulation in the precentral gyrus



Participants with dPMC peak location have a higher task-related functional activity and higher hand dexterity

Functional and structural phenotyping of the human precentral hand knob

Results



No significant difference between two groups for cortical thickness and RMT

Functional and structural phenotyping of the human precentral hand knob

Conclusion

Substantial posterior-anterior variability of the CS peak excitability localization within the precentral gyrus.

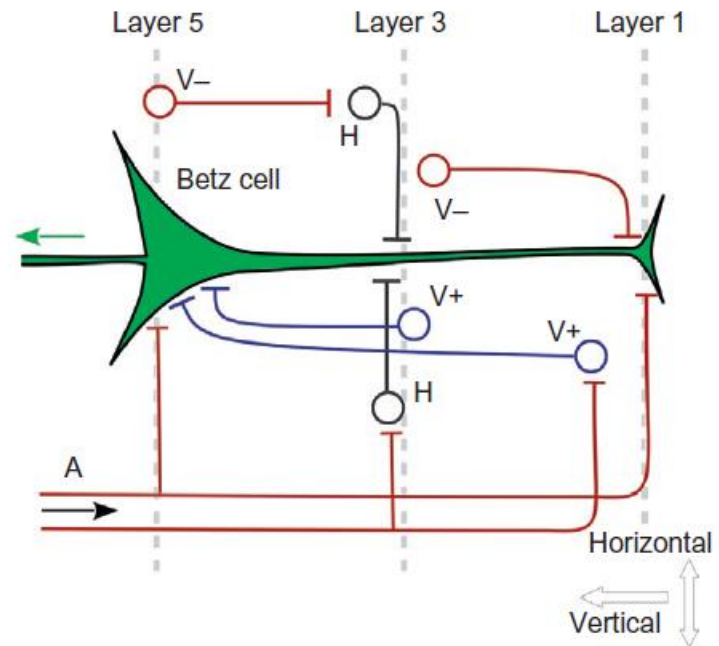
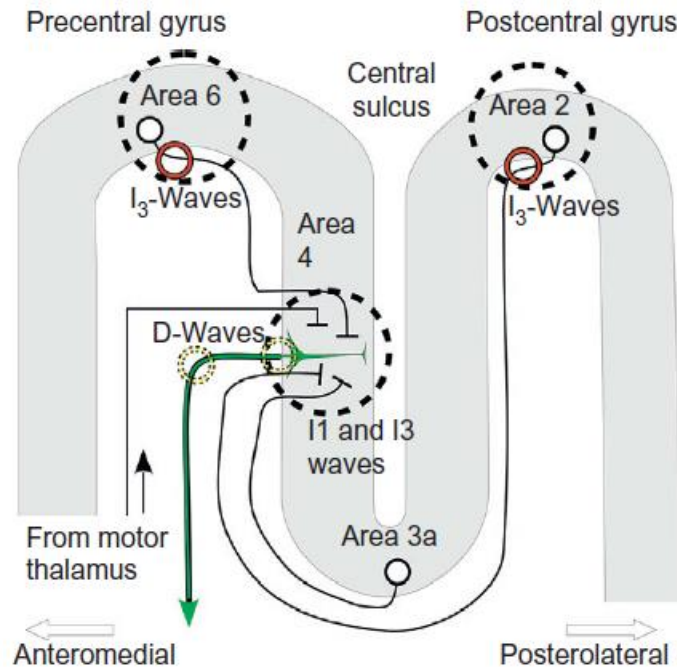
First evidence showing a continuum in terms of microstructure-function along the motor-premotor area in the precentral gyrus.

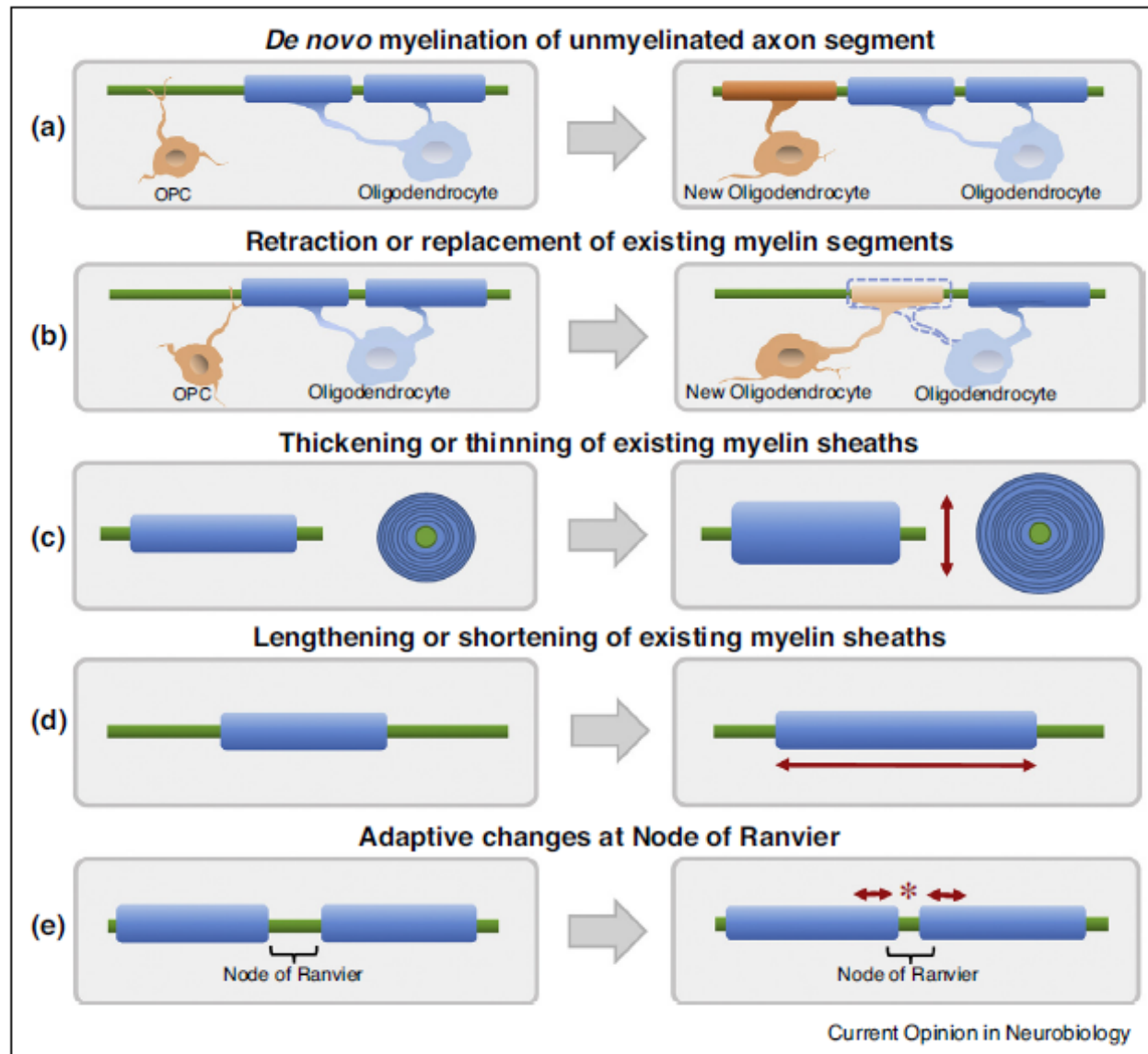
Participants with dPMC hot-spot localization have an overall higher cortical myelination associated to a higher functional activity and hand dexterity

Such motor-premotor phenotypic spectrum is relevant to understand the variability of response and replicability of Non-invasive brain stimulation techniques.

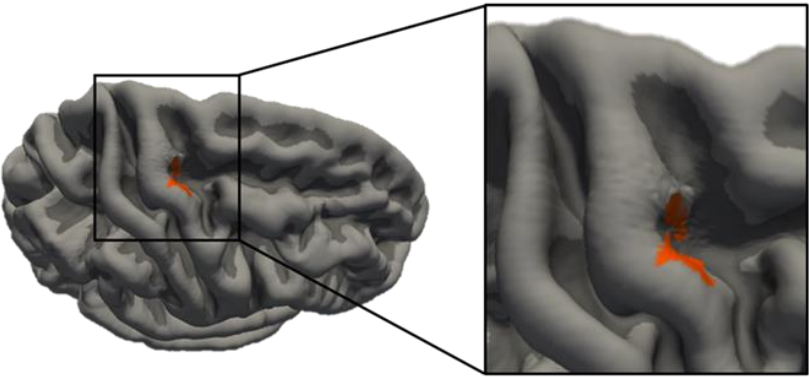
GRAZIE

5 Extension 2: Modeling the effects of pulse waveform and direction

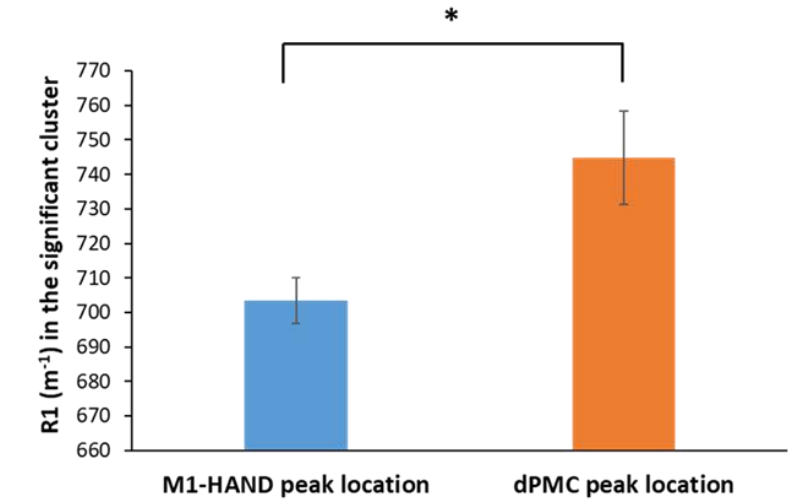




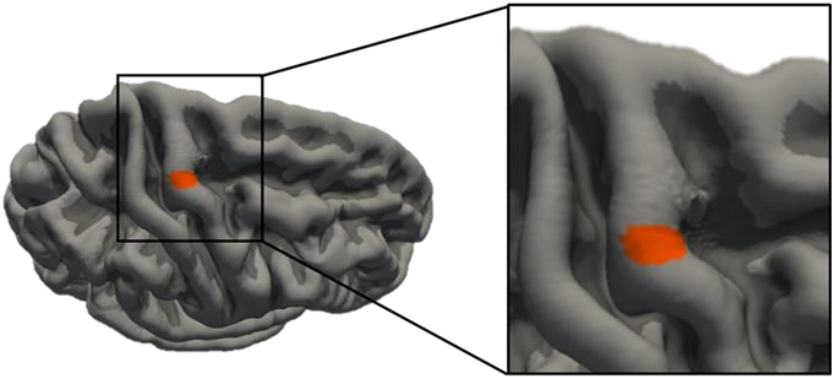
A



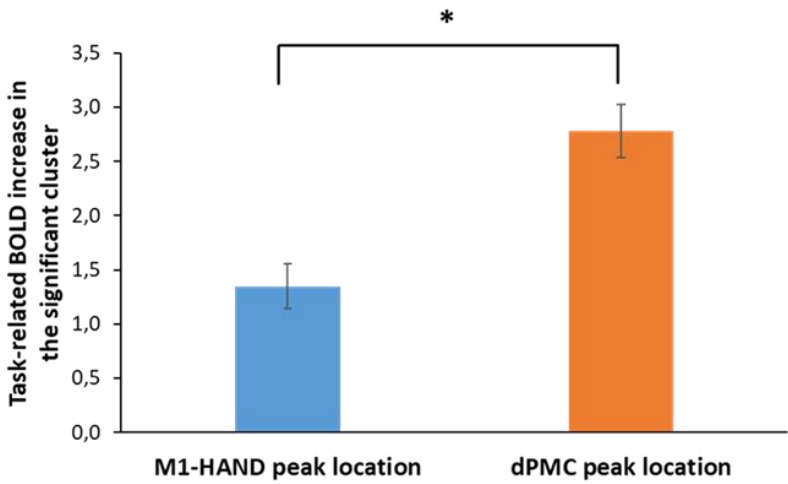
B



C

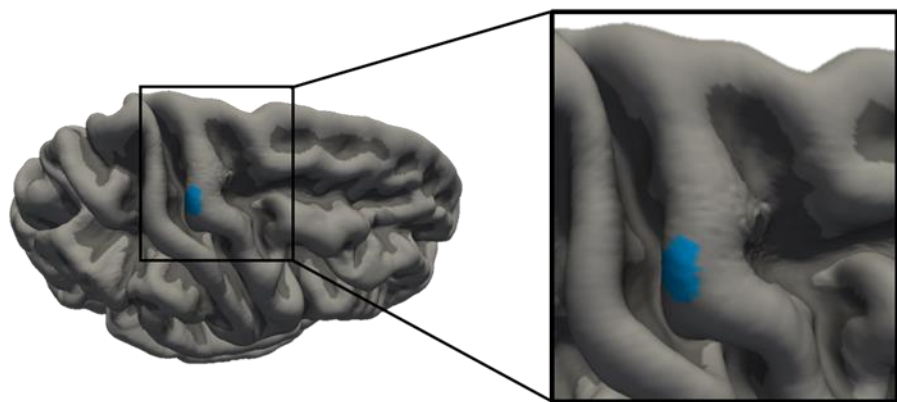


D



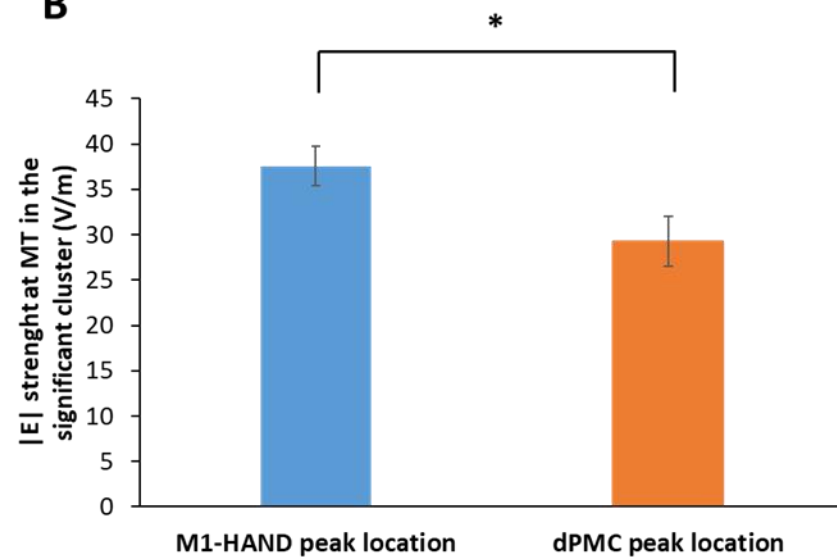
dPMC group > M1-HAND group

Significant $p < 0,05$

A

M1-HAND group > dPMC group

Cluster-forming threshold $p=0.01$

B

* = $p < 0.05$