TMS-EEG unveils network dysfunction in early Multiple Sclerosis patients

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INTRODUCTION

Transcranial magnetic stimulation (TMS) has revealed synaptic dysfunction and altered cortical excitability in advanced Multiple Sclerosis patients (pwMS), but data in early, non-disabled patients are lacking. Indeed, subtle cortical dysfunction in early pwMS may elude traditional clinical and evoked potential measures.

AIM

We investigated whether TMS-EEG–derived indices, specifically Perturbational Complexity Index (PCI), could reveal early cortical network alterations in minimally disabled relapsing pwMS.

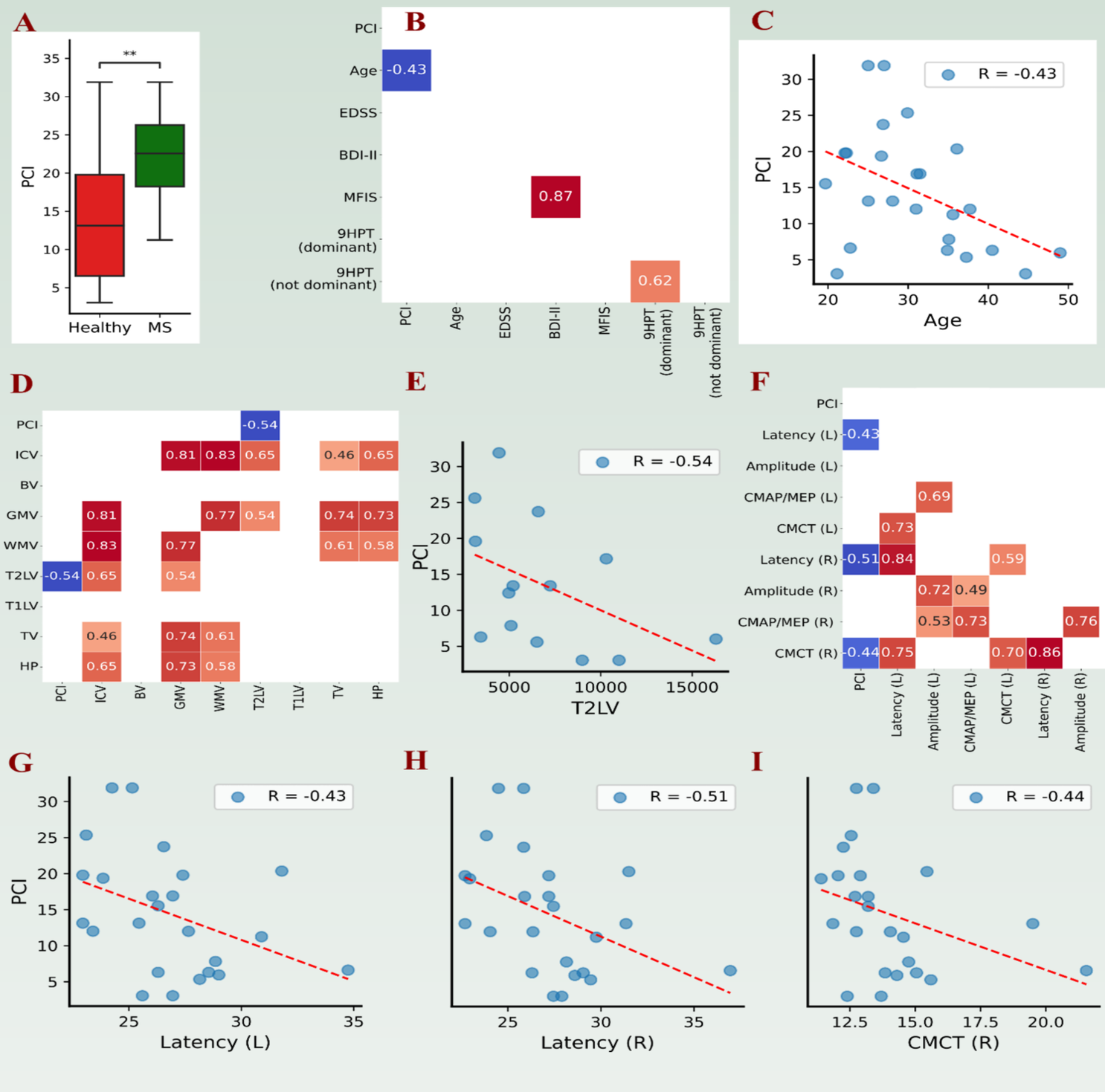
METHOD

We prospectively recruited 28 early relapsing pwMS (disease duration <3 years, Expanded Disability Status Scale <2.0) and 25 demographically matched healthy controls (HCs).

All underwent single-pulse TMS over the left motor cortex with simultaneous 32-channel electroencephalography (EEG), as well as MEP-related features. EEG data were filtered and TMS-evoked potentials (TEPs: N45, P60, N100, P180), Global Field Power (GFP), and PCI were extracted. Mann-Whitney tests were then used to compare these features between pwMS and HCs.

Clinical data and brain magnetic resonance imaging (MRI) volumes were also collected and correlated to TMS-EEG metrics.

RESULTS



Amplitude and latencies of conventional TEPs (N45, P60, N100, P180) and GFP were not significantly different between pwMS and HCs.

Conversely, ***PCI was markedly reduced in pwMS*** *(median 13 [IQR 10–20])* ***relative to controls*** *(18 [13–26], p<0.01).* ***Among MRI-derived volumes T2 lesion volume was found to be strongly inversely related with PCI*** *(R=-0.54, p=0.047).*

Furthermore, it was found an inverse relationship between PCI and right (R =-0.51, p= 0.009) and left (R =-0.43, p=0.036) latency, as well as between PCI and right central motor conduction time (CMCT) (R =-0.44, p=0.032).

Table 1. PCI comparison between healthy and MS patients (A) with correlational analysis with clinical (B), MRI (D), and MEP (F) parameters. Significant correlations were also represented in a scatterplot. In particular, from the clinical data, age (C) was reported. From the MRI-data, the correlation between PCI and T2LV was reported (E), while from the MEP-data the correlation with latency (L/R) and CMCT (R) were reported respectively in panel G, H, I.

CONCLUSIONS

- The PCI is sensitive to subtle cortical network alterations in early MS prior to overt clinical and neurophysiological abnormalities. PCI offers a single quantitative index capturing reduced global spatiotemporal complexity, related to synaptic dysfunction.
- Cortical connectivity alterations seem present in early pwMS, before clinical disability emerges. TMS-EEG appears to be a feasible, sensitive diagnostic tool for detecting early synaptic dysfunction, linked to overt demyelination, but also neuroinflammation, causing a disorder of network integrity.
- Longitudinal studies are underway to assess whether early PCI reductions might flag silent disease progression, allowing for closer monitoring or earlier therapeutic intervention.

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