The microstructural changes in human brain induced by intermittent theta burst stimulation

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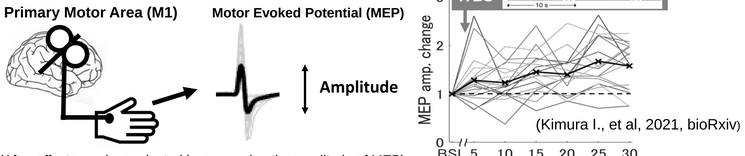
BACKGROUND

iTBS after-effect has substantial inter-individual variability

- Intermittent theta-burst stimulation (iTBS) can facilitate neural activity for 30–60 mins. (Huang Y.Z., et al., 2006, Neuron)
- iTBS has been used widely for neuroscientific research and clinical trials. (Rounis E., et al., 2020, Exp. Brain Research)
- A major concern in iTBS is its inter-individual variability in the after-effect. (Lopez-Alonso V. et al., 2014, Brain Stimulation)
- This variability can be predicted by the microstructural properties of the brain (Kimura I., et al., bioRxiv)



TBS can modulate microstructural properties in the human brain

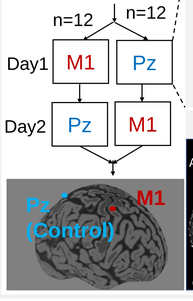
- Structural changes were also observed right after cTBS (Jung J., et al., 2021, NeuroImage)
- Animal studies also revealed the microstructural changes after iTBS (Benali. A., et al., 2011, JNS)
- **Currently, the relationship between iTBS-after effect and the microstructural modulations on the stimulated region is unknown**

QUESTION

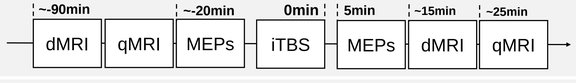
Is the inter-individual variability of **the iTBS after-effect** is related to **the microstructural modulations induced by iTBS**?

METHOD

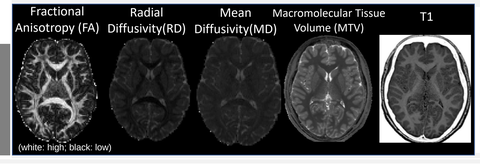
PROCEDURES



We collected **diffusion/quantitative MRI data** to evaluate **microstructural property** **MEPs** to evaluate **iTBS after-effect**



FA / RD / MD were calculated from dMRI and **MTV / T1** from qMRI



High FA/Low RD
= High Myelination or Large Axon Diameter
Low MD
= High activity of glial cells or large cell-number
High MTV
= High density of non-water tissue
Low T1
= High myelin content

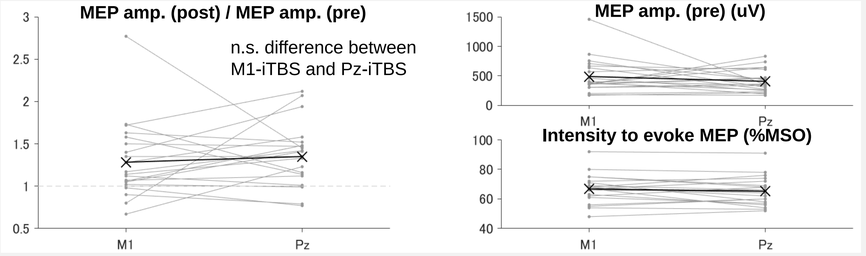
METHOD-continued

STATISTICS

STEP1: Detect microstructurally modulated regions
Run **paired t-test** comparing **post-iTBS and pre-iTBS** in each property (FA, RD, MD, MTV, and T1) in M1-iTBS and Pz-iTBS

STEP2: Correlations between the modulation in MEP and microstructural properties
Run regression analysis to search for the significant correlation with **the modulation in MEP-amplitude** (MEP-amp. (post-iTBS) / MEP-amp. (pre-iTBS)) in **microstructurally modulated areas** in M1-iTBS (FWE-P<0.1 in STEP1)

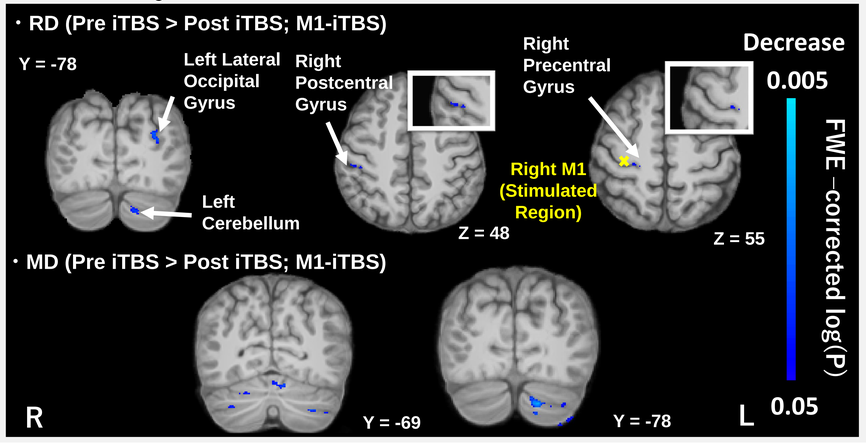
RESULT-1 (Behavioral Data)



Thick black line with cross indicates mean

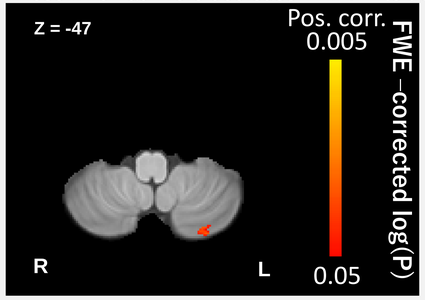
RESULT-2 (microstructurally modulated areas in M1-iTBS)

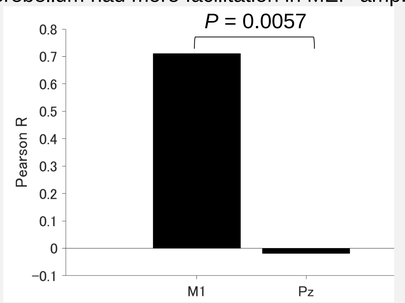
iTBS induced significant decrease in MD/RD but not in MTV/T1



RESULT-3 (correlation with MEP-amplitude change)

Those who had more decrease in MD in left cerebellum had more facilitation in MEP-amp.



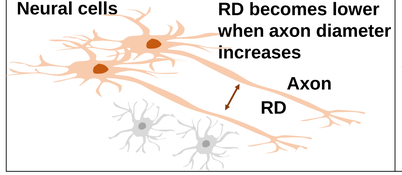


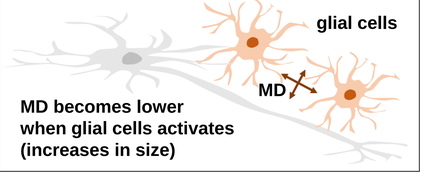
Comparing the Pearson's correlation between the mean decrease of MD in significant clusters and MEP-amplitude change in M1-iTBS and Pz-iTBS, we found the significant difference (Bootstrap Testing)

DISCUSSION

#1. iTBS decreased RD in right post/pre-central gyrus and left cerebellum MD in bilateral cerebellum

Decrease of RD	Decrease of MD
・increase of **axon diameter** ・increase of myelin (but T1(myelin) was unchanged)	・activation of **glial cells** ・increase of cell-density (but MTV(cell-density) was unchanged)





#2. increase in MEP was reflected in the decrease of MD in the left cerebellum

Right M1 is connected to the left cerebellum (Spampinato D., et al., 2020, JNS)

⇒**Glial cells in left cerebellum** might be associated with the **M1-iTBS after-effect**

CONCLUSION

The activity of glial cells in remote regions might be related to **the iTBS after-effect** on the stimulated region