Intermittent Theta Burst Stimulation Enhances Brain Network Connectivity in a patient with Posterior Cortical Atrophy

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BACKGROUND

- Posterior cortical atrophy (PCA) is a rare syndrome characterized by progressive visuoperceptual and visuospatial symptoms arising from neurodegeneration of the posterior parieto-temporal and occipital cortices[1]. PCA is usually an early-onset (<65 years old) dementia caused by Alzheimer's disease (AD) neuropathologic changes. Though management strategies exist, there is currently no treatment that can slow or stop the progression of the disease[2]. Recently, repetitive transcranial magnetic stimulation (rTMS) has emerged as a potential treatment option in AD[3], providing a new intervention method to explore for PCA treatment.
- In this case report, we studied a PCA patient with visuospatial and memory deficits, who underwent rTMS.
- **Goal:** To investigate whether rTMS of the memory circuit (Default Mode Network, DMN) can modulate brain network functional connectivity (FC) within the DMN and improve memory symptoms in a patient with PCA.

METHODS

Case presentation: The patient is a 76-year-old female right-handed retired English professor diagnosed with PCA. Symptom onset began at age 69 with difficulty reading out loud and retrieving names of familiar writers. Visuospatial symptoms progressed to include impaired depth perception, simultagnosia, and a right lower quadrant visual field defect. In 2023, she reported increasing concern about memory loss, and her amnestic symptoms have since progressed. At the time of her participation in the study in the summer of 2024, the patient's cognitive-functional status was consistent with mild dementia.

rTMS protocol: A double-blinded, sham controlled design (Figure 1) was used to administer intermittent theta burst stimulation (iTBS) over a left caudal middle frontal gyrus (cMFG) target connected to DMN. Stimulation was delivered at 110% of motor threshold in three sessions of 20 trains per day, for a total of 1800 pulses per day over a 10-day block. The stimulation target was individually defined based on the FC of the five bilateral regions of interest (ROIs) within the DMN: the angular gyrus, posterior cingulate cortex, lateral temporal cortex, hippocampus, and anterior medial prefrontal cortex[4] (Figure 2).

Figure 1. A schematic of the experimental protocol

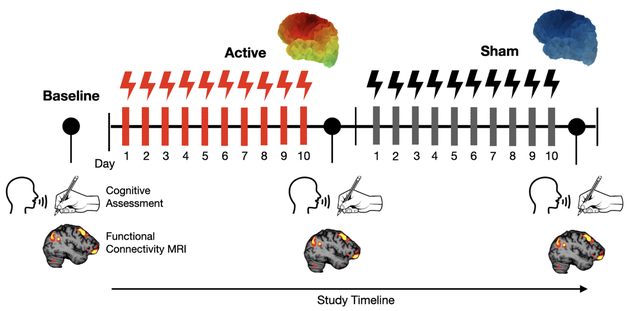
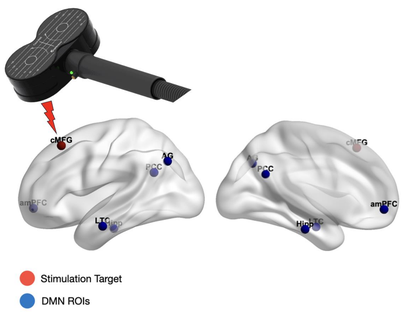


Figure 2. Stimulation site and DMN nodes

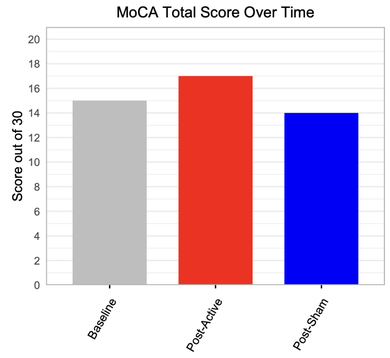


Clinical outcome measures: Neuropsychological testing was administered to measure the effects of iTBS on general cognitive functioning (Montreal Cognitive Assessment, MoCA) and memory.

Imaging outcome measures: We examined changes in the intrinsic FC of the left cMFG target between the active and sham iTBS conditions using a vertex-wise approach.

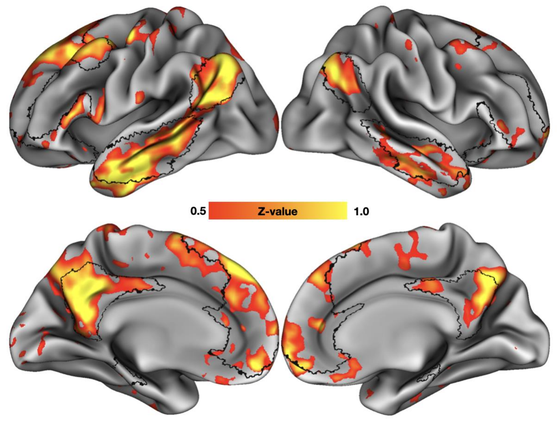
RESULTS

A Behavioral Results



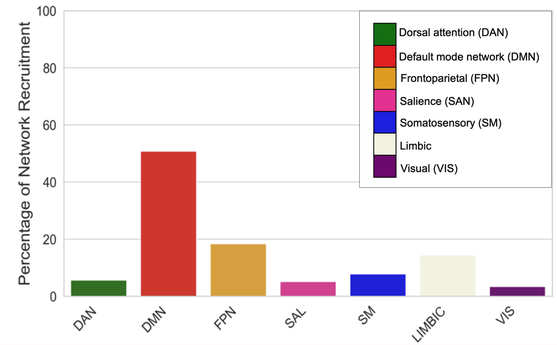
(A) On the MoCA, a general test of multiple cognitive domains (memory, executive function, attention, language, visuospatial, and orientation), the patient demonstrated a 2-point improvement, corresponding to the attention and abstraction tasks. This improvement was selective to the active iTBS condition.

B Stimulation Site (cMFG) Functional Connectivity in Active vs Sham



(B) Colored vertices identify areas of the cerebral cortex showing positive functional connectivity with the left cMFG target in the Active-Sham contrast surface map (thresholded at $Z > 0.5$). The default mode network is outlined in black.

C Functional Connectivity Increases by Functional Network



(C) The functional networks[5] with highest percentage of suprathreshold vertices were the default mode network (50.8%) the frontoparietal network (18.4%), and the limbic network (14.4%).

CONCLUSIONS

- This report presents novel evidence that personalized FC-guided iTBS targeting the left cMFG increased FC of the DMN, as well as the FPN, and improved some aspects of cognitive function in a patient with PCA.
- Future studies should evaluate the durability of the effects of iTBS on FC and cognitive performance over time, as well as the clinical significance of any imaging or neuropsychological findings.
- These findings are limited in being a single case report. Larger controlled trials with PCA patients with testing batteries catered towards this atypical phenotype are needed.

REFERENCES & ACKNOWLEDGEMENTS

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