Repetitive transcranial magnetic stimulation combined with cognitive training in Alzheimer's disease

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BACKGROUND

Repetitive transcranial magnetic stimulation (rTMS) has been examined as a potential treatment for many neurological disorders. High-frequency rTMS in particular improves cognitive functions such as verbal fluency and memory. In the previous study, we reported that rTMS combined with cognitive training (rTMS-CT) showed cognitive improvement with Alzheimer's disease (AD), especially, in the mild stage of the disease. We analyzed the effect of initial and booster rTMS-CT in patients with AD.

METHODS

Study population (n=26)

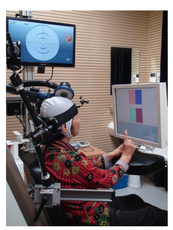
Inclusion criteria

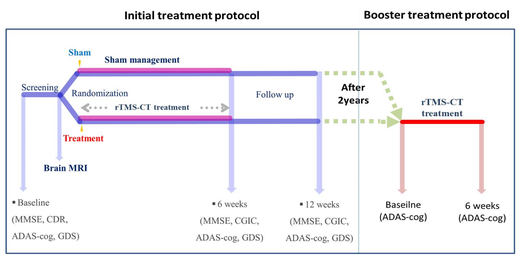
- ❖ Age : 60-90 years
- ❖ Mild or moderate stage of AD (DSM-IV)
- ❖ MMSE : 18 to 26
- ❖ ADAS-cog : above 17
- ❖ stable AD medication at least 6 month without changes

Exclusion criteria

- ❖ CDR : 0, 0.5 or 3
- ❖ Unstable medical condition
- ❖ History of epilepsy
- ❖ Patients with metal in the head except the mouth
- ❖ Cardiac pacemakers, medication pumps, intracardiac lines

Study design





Cognitive training

- Broca area – syntax and grammar tasks
- Wernicke area – comprehension of lexical meaning and categorization tasks
- dlPFC – action naming, object naming and memory tasks
- pSAC - spatial attention(shapes and letters) tasks

rTMS protocol

- 1 session/day, 5 day/week, total 30 sessions during 6 weeks
- 20 trains of rTMS (2 seconds of 10 Hz/train, 20 pulses/train)
- 6 areas - Broca, R-/L-dlPFC (90%)Wernicke, R-/L-pSAC (110%)
- Stimulation 3 areas/day, max 1500 pulses/day
- Each trains followed by 2-4 cognitive tasks (20~40 seconds)

RESULTS

Initial treatment results

Table 1. Characteristics of the participants

	Total (n=26)	Treatment (n=18)	Sham (n=8)	*p* value
Age (mean)	71.6 ± 6.8	72.1 ± 7.6	70.3 ± 4.8	0.531
Female (%)	57.7	55.6	62.5	1.000
Education (years)	9.9 ± 3.9	9.9 ± 4.8	9.9 ± 3.7	0.978
ADAS-cog (mean)	23.4 ± 6.2	23.7 ± 6.4	22.9 ± 6.2	0.892
MMSE (mean)	22.5 ± 2.7	22.4 ± 2.9	22.8 ± 2.5	0.807
GDS (mean)	10.9 ± 6.9	10.5 ± 6.2	11.6 ± 8.9	0.807

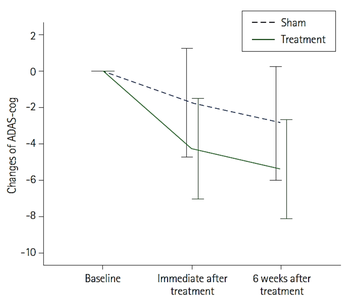


Fig 1. Differences in ADAS-cog score at each measurement time point (immediate after, 6 weeks after treatment) from baseline. There was no significant difference between group, although significant improvements were found in the treatment group during 12 weeks.

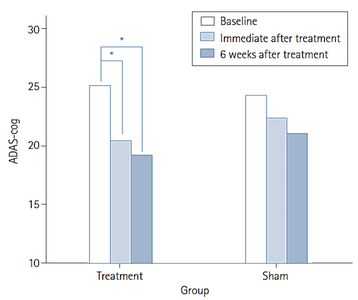


Fig 2. Significantly improved ADAS-cog scores were found following treatment compared with baseline (immediately after treatment, improved by 4.28 points, p=0.014; 6 weeks after treatment, improved by 5.39 points, p=0.002). *p<0.05.

Booster treatment results

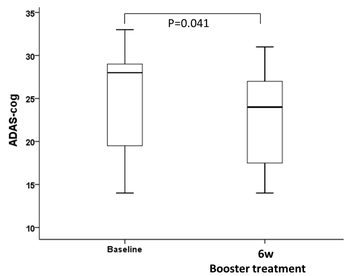


Fig 3. Changes of ADAS-cog scores in the booster treatment groups (n=8).

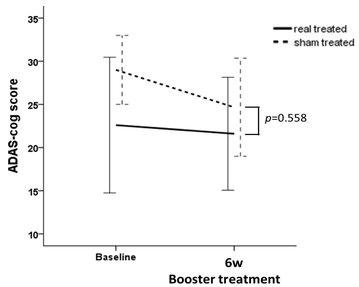


Fig 4. Comparison of ADAS-cog scores between first-ever and booster treatment groups.

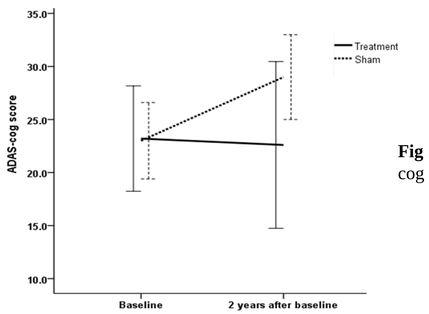


Fig 5. Two-year changes of baseline ADAS-cog scores between treated & sham groups.

CONCLUSIONS

rTMS-CT shows significant effect on cognitive function in AD, therefore rTMS-CT might be useful adjuvant therapy of cholinesterase inhibitors in AD. Cognitive function in the rTMS-CT treated group retains in 2 years, so booster rTMS-CT treatment might be useful to maintain cognitive function in AD though the treatment interval has not been determined.