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# Effect of cognitive improvement by high or low frequency rTMS treatment in Alzheimer-induced mouse

Jong Moon Kim[1,2*], Jinseung Choung[2], MinYoung Kim[1,1†]

CHA Bundang Medical Center, CHA University School of Medicine, Department of Rehabilitation Medicine[1], CHA University, Rehabilitation and Regeneration Research Center[2]

## Introduction

Previous studies of repetitive transcranial magnetic stimulation (rTMS) has been shown possibility of efficacy to relieve cognitive dysfunction from Alzheimer dementia. However, because the rTMS protocols used in each study are different, there are no objective data that reveal most effective protocol. And frequency of the stimulation is still on debate in protocols of rTMS. Therefore, we conducted an experiment to determine more effective stimulation between high and low frequencies in cognitive function improvement when rTMS was applied in Alzheimer-induced mouse model.

## Methods

Thirty-six mouse were included in this research and those were divided into three groups: control group with no experiment, control group with saline injection in cerebral ventricle and Alzheimer-induced mouse group with amyloid beta injection in the ventricle. Each group was divided into high frequency rTMS, low frequency rTMS, and no treatment subgroups. The rTMS treated groups were stimulated for 2 weeks, 5 days a week (Figure 1). High frequency rTMS group received rTMS with 20 Hz, 2s, 40 trains, 28s interstimulus interval, with total 1,600 pulses; and low frequency rTMS group received rTMS of continuous 1 Hz and 1,600 pulses in total. Both rTMS applied to the whole brain of the mouse and the intensity was 1.26 tesla. Y Maze test and novel object recognition task (NORT) were used for assessment of cognitive function and measured before rTMS and 1st and 2nd week after the rTMS.

## Results

Before rTMS, the Alzheimer-induced mouse group showed lower Y maze and NORT scores than the other control groups, and there was no difference among the subgroups in each group. After initiation of rTMS, Alzheimer-induced mouse group showed increments of spontaneous alteration in Y Maze and recognition of novel objects in NORT in both high and low frequencies of rTMS compared to non-stimulated subgroup at 1st and 2nd week (Figure 2, 3). There was no statistical differences in scores of Y Maze and NORT between high and low frequency at 1st and 2nd week after the rTMS.

## Conclusions

Both high and low frequency rTMS in Alzheimer-induced mouse brought improvement of cognitive function, which may be used as a therapeutic method to treat Alzheimer's disease. Studies on the pathophysiology of rTMS effect and long term follow up are needed.

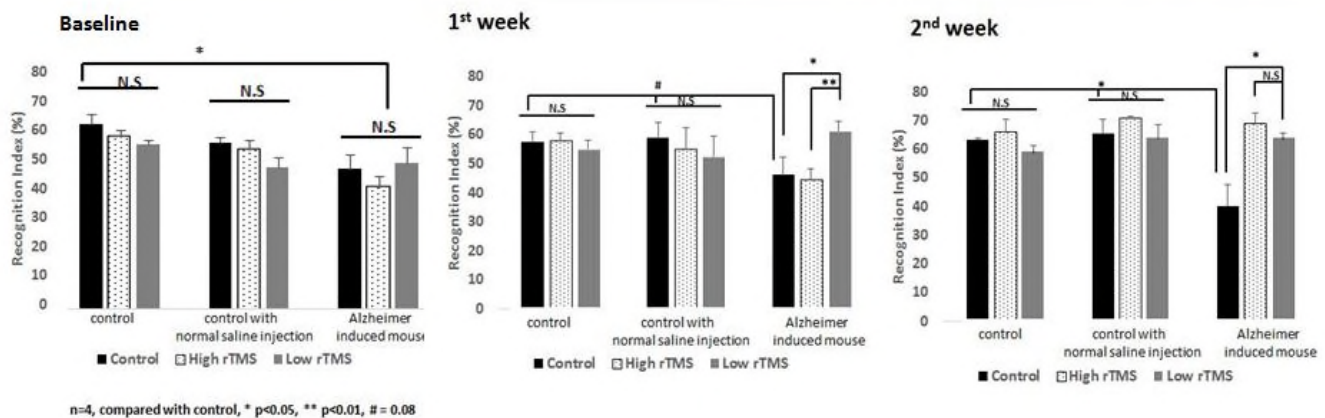| | MON | TUE | WED | THU | FRI | SAT |
|---|---|---|---|---|---|---|
| | | | Experimental mouse modeling | | Adaptive training: Y maze, NORT | |
| 1st week | rTMS | rTMS | rTMS | rTMS | rTMS, Y maze test, NORT training | NORT test |
| 2nd week | rTMS | rTMS | rTMS | rTMS | rTMS, Y maze test, NORT training | NORT test |

**Flow chart of experiment**

# Y maze



**Changes of Y maze test score**

n=4, compared with control, * p<0.05, ** p<0.01, $ = 0.06

# Novel object recognition task



n=4, compared with control, * p<0.05, ** p<0.01, # = 0.08

**Changes of novel object recognition task test score**