

Cognitive Rehabilitation combined with Neuronavigated Transcranial Magnetic Stimulation (NeuroAD System) in patients with Mild and Moderate Alzheimer's Disease

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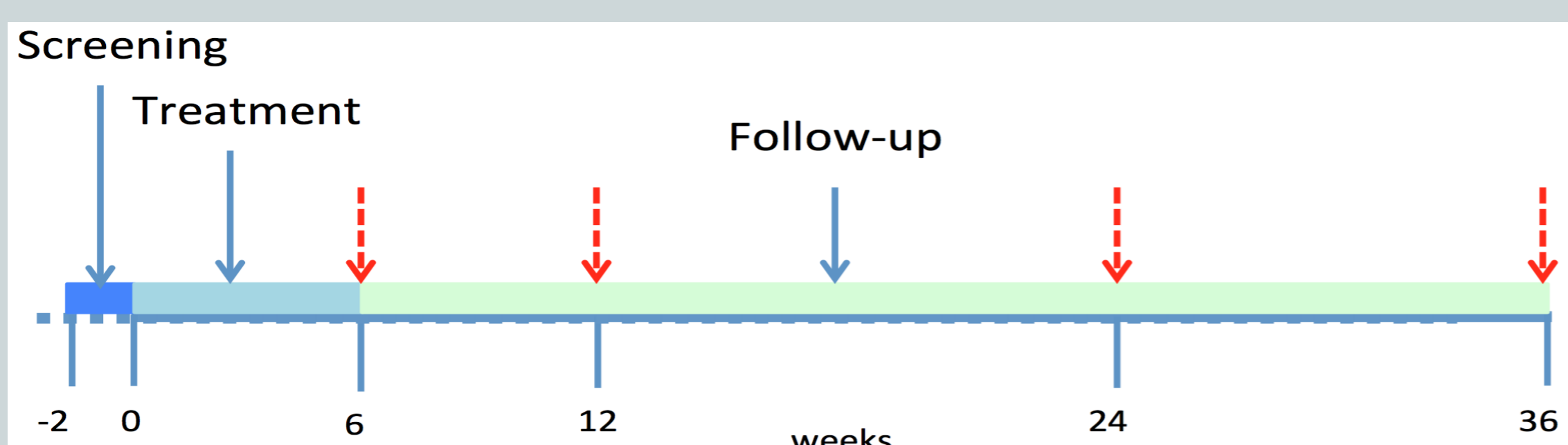
A New Treatment For Alzheimer's Disease

Objectives: We present preliminary results of a placebo-controlled randomized trial assessing the efficacy of a non-invasive and innovative therapy for AD, combining computerized cognitive rehabilitation with neuronavigated TMS of the same task-related brain areas.

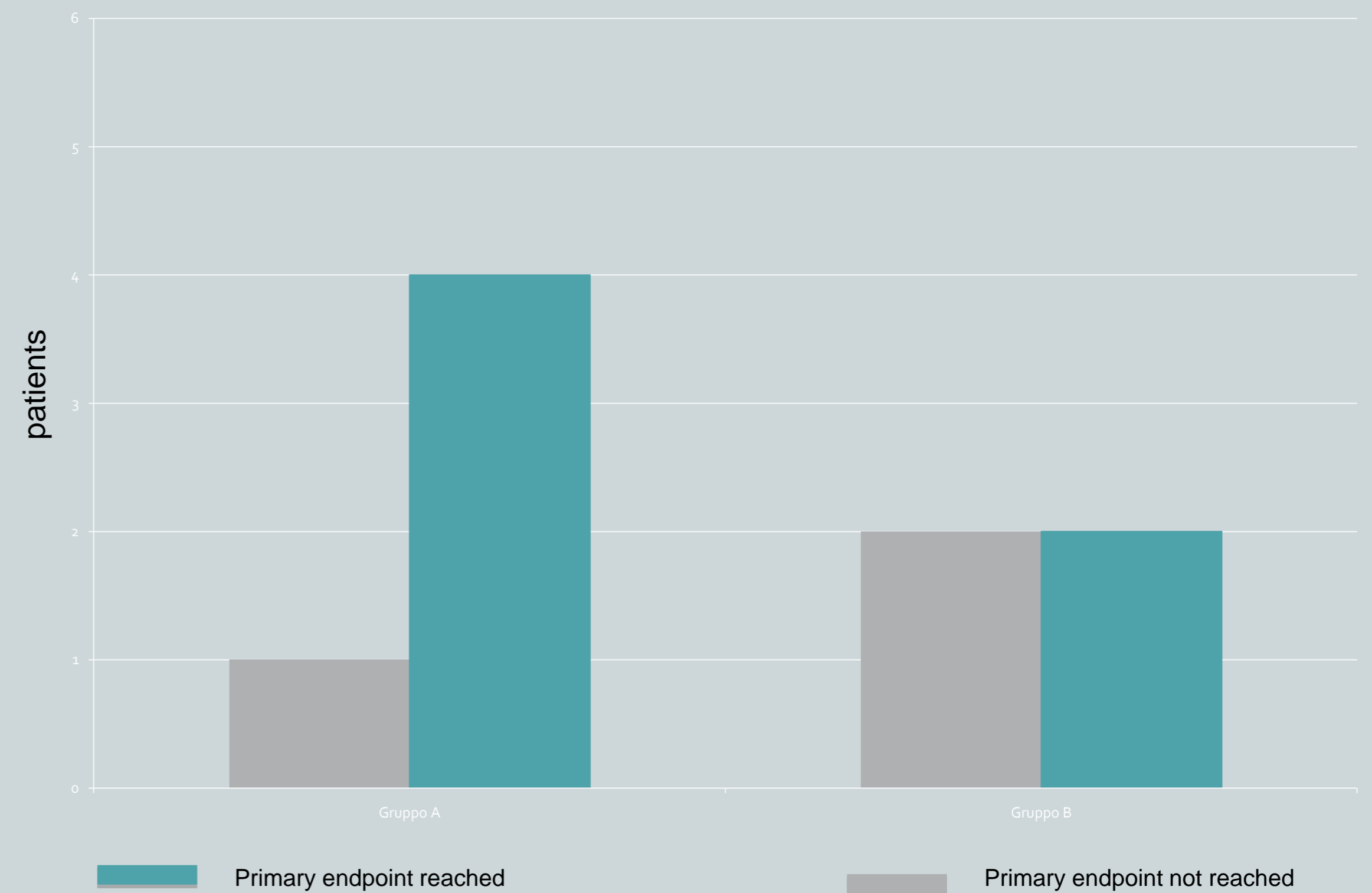
Materials: The NeuroAD system (Neuronix) delivers computerized cognitive rehabilitation combined with neuronavigated TMS. The stimulation paradigm was composed of 20-30 trains of TMS, consisting of 2 sec, 10 Hz trains (20 pulses per train) administered for each task-related brain region. TMS coil was positioned following stereotactic navigation on a personalized template extracted by individual volumetric MRI



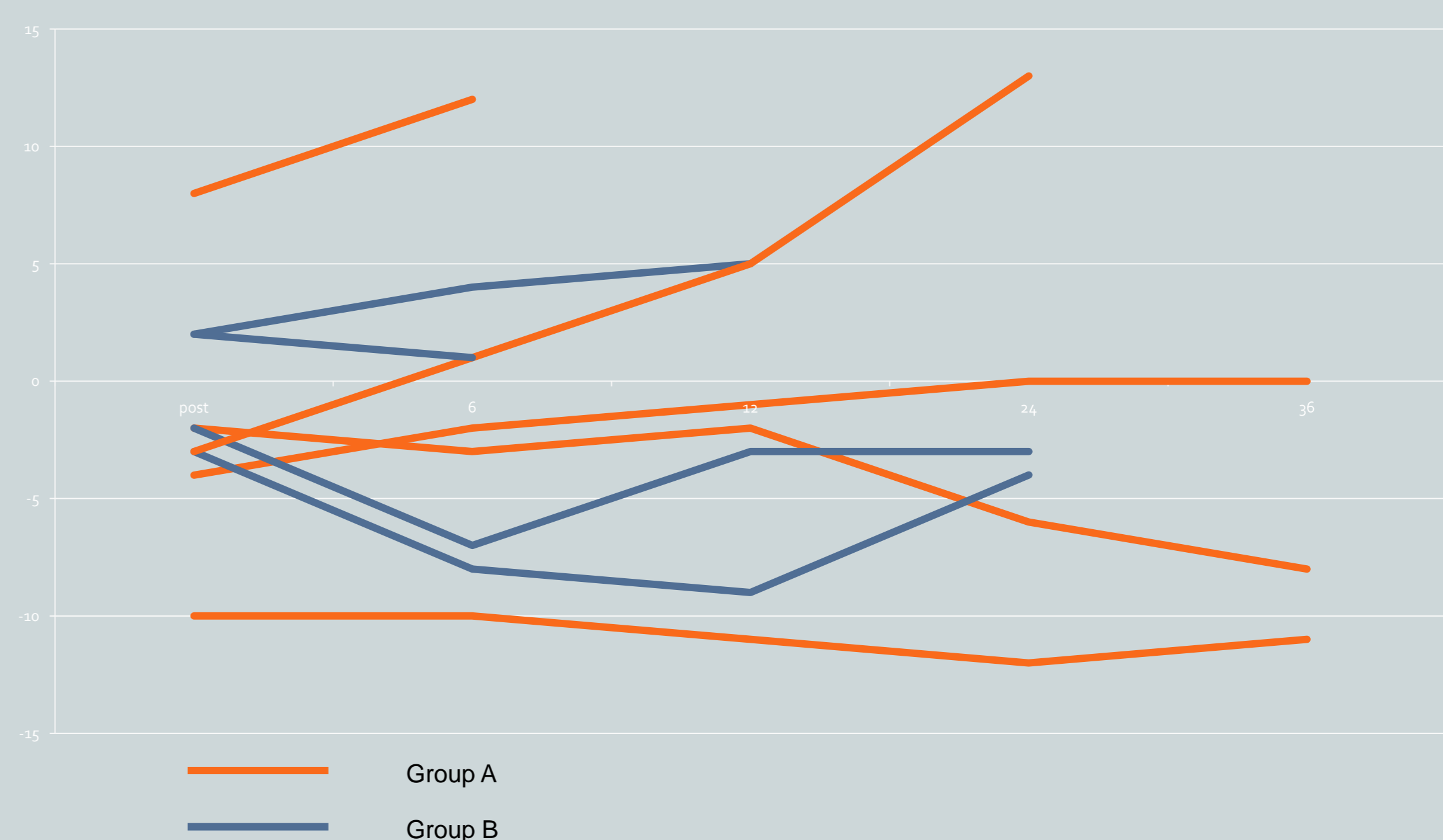
Methods: To date, 11 mild-moderate AD patients were recruited and assigned to 3 groups: 5 to Group A= TMS stimulation + cognitive training; 4 to Group B= sham TMS + cognitive training; 2 to group C= sham TMS + pseudo-cognitive training. Each Group underwent 30 sessions of treatment (1 session/day x 5 days/week x 6 weeks). TMS was applied on 3 cortical areas per day (total 45-60 min) concurrently followed by cognitive rehabilitation. The cortical area stimulated by TMS matched the cognitive domain trained soon afterwards with several cognitive paradigms including syntax and grammar tasks (Broca region), words comprehension and categorization tasks (Wernicke region), actions and objects naming and spatial memory tasks (R- and L-dIPFC regions), spatial attention tasks (R- and L-pSAC regions). The primary endpoints were the changes in the ADAS-Cog, ADCS and CDR-SB scales at the end of treatment with a follow-up at 6-12-24-36 weeks.



Results: To date, available data only allow the comparison between Group A and Group B soon after treatment. An ANOVA for repeated measures was carried out, setting group (A vs B) as categorical predictor, and pre-post treatment as levels of repeated measures. There was not effect of group ($p=0.901$), pre-post condition ($p=0.126$) or group x pre-post ($p=0.103$). Post-hoc comparisons in group A showed a statistical trend for changes in both ADCS (pre: 41.0 ± 9.85 ; post: 38.0 ± 13.05 ; $p=0.09$) and CDR-SB (pre: 1.2 ± 0.44 ; post: 1.0 ± 0.61 ; $p=0.07$) but not in ADAS-cog (pre: 21.4 ± 3.13 ; post: 19.2 ± 9.30 ; $p=0.37$). The scores obtained in Group B at the baseline did not differ from scores after treatment



Discussion: The preliminary results are encouraging; the benefit of treatment seems to be, at least in some subjects, long-lasting. In the future more robust evidence will be available with a larger sample of subjects and a prolonged follow-up period.



Conclusions: Our findings suggest that cognitive rehabilitation combined with neuronavigated TMS in mild-moderate AD patients has the potential to be considered a promising treatment for the disease.