

# An Adaptive Computer-Based Cognitive Training Program Accessed from Home Improves Cognitive Functioning in Multiple Sclerosis (MS): Results of a Double-Blind Randomized Active-Placebo-Controlled 12-Week Trial

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## Objective

We completed a double-blind, randomized, active-placebo controlled trial to determine the cognitive benefits of an adaptive computer-based cognitive training program accessed from home in individuals with MS.

## Background

Cognitive impairment affects more than half of all individuals living with MS and treatment options remain limited.

Cognitive remediation has potential benefits, but typically requires frequent outpatient visits to receive services.

Computer-based adaptive cognitive training programs can provide intensive remediation that adjusts to the individual user's level of performance in real-time for consistent levels of engagement and effort. As an additional benefit, the programs can be accessed by the individual from home.

## Methods

Study eligibility included diagnosis of MS (any subtype) with cognitive impairment determined by scoring at least 1 SD below published norms on the Symbol Digit Modalities Test (SDMT).

Participants were assigned to either the adaptive training program (Posit Science's BrainHQ) or the active placebo (Hoyle Puzzle and Board Games) using stratified permuted block randomization. Training was completed on study-provided laptops equipped with remote monitoring software, used to monitor compliance, with a goal of one hour per day, five days per week, over 12 weeks (target 60 hours). Technical support and weekly coaching sessions were delivered by a study technician.

A baseline and study end visit were coordinated to both administer neuropsychological testing and to deliver and instruct use of the study-provided laptops. Cognitive performance was represented by a composite z-score of the neuropsychological tests.

## Results

There were a total of 135 participants enrolled (n=71 in the adaptive training group and n=64 in the active placebo comparison). All but n=5 completed the study: n=1 due to a clinical relapse, n=4 for personal reasons. The groups were balanced in age (mean=50 years), disability (median EDSS=3.5), and baseline cognitive functioning (mean SDMT z-score=-2.1).

Demographic Characteristics	Full Sample (n=135)	Adaptive Condition (n=74)	Active Placebo Condition (n=61)	p value
Sex (% Female)	77.04%	67.57%	88.52%	0.0040*
Age (mean years)	49.80±12.45	47.99±13.07	52.00±11.38	0.0588
Education (Years)	14.93±2.45	14.82±2.37	15.05±2.55	0.5999
Race (%):	-	-	-	0.6088
White	84.44%	85.14%	83.61%	-
Black/African American	8.15%	9.75%	6.56%	-
Unknown or unreported	7.41%	5.41%	9.84%	-
Ethnicity – Hispanic or Latino (%)	7.81%	9.86%	5.26%	0.3356
Clinical Characteristics	Full Sample (n=135)	Adaptive Condition (n=74)	Active Placebo Condition (n=61)	p value
Disease Duration (mean years)	12.62±10.46	11.9±10.9	13.5±10.0	0.4567
EDSS (median score with IQR)	3.50±4.00	3.50±4.00	3.50±4.00	0.3041
25 Foot Timed Walk (mean seconds)	7.09±3.99	7.01±4.10	7.18±3.89	0.8090
Screening SDMT z score (mean score)	-2.10±0.99	-2.10±0.99	-2.10±1.01	0.9989

\* = statistically significant p value corresponding to a 95% confidence interval.

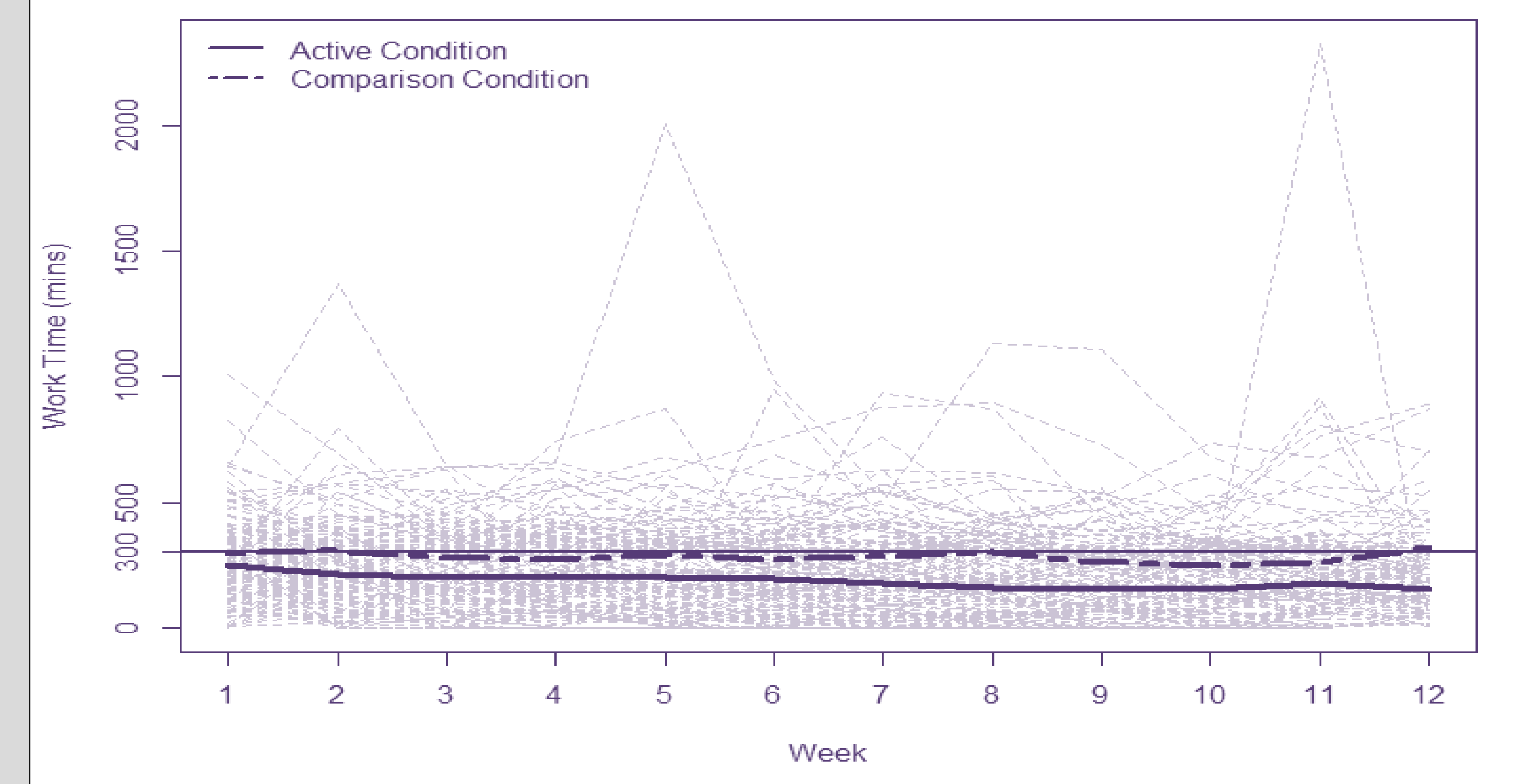
Program compliance was defined in two ways, total training hours and the number of weeks a subject was consecutively compliant (defined as one hour each day, five days per week). The comparison condition had a higher degree of compliance (n=48, 78.69% vs. n=43, 58.11%, or n=48, 78.69% vs. n=44, 59.46%).

Change in the composite z-score from baseline to study end showed that the adaptive training program resulted in significantly greater improvement in cognitive functioning (See Table 2), with marked treatment response observed in some individuals. This improvement occurred despite longer playing time in the placebo vs. active condition (56.95±34.53 vs. 37.74 ±23.78 hours played, p=0.0056, as seen in Figure 1).

	Mean ± SD	Minimum	Median	Maximum
Adaptive Training Condition (n=60)	0.25 ± 0.45	-1.39	0.33	1.34
Active Placebo Condition (n=70)	0.09 ± 0.37	-0.79	0.10	0.81

\*stratified nonparametric test (van Elteren test) p=0.0073, linear mixed model adjusted by covariates of age, Wide Range Achievement Test-III reading standard score, and SDMT z-score p=0.0286.

Figure 1. Time Spent Training by Week



## Conclusions

- Adaptive, computer-based cognitive remediation significantly improves cognitive functioning in MS.
- Remotely-supervised cognitive training can be successfully provided to individuals with MS accessing treatment from home.

## References

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