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Critically Appraised Paper for "Adaptive vs. non-adaptive cognitive training by means of a personalized App: A randomized trial in people with multiple sclerosis."

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AOTA Critically Appraised Papers Series

Evidence Exchange

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CRITICALLY APPRAISED PAPER (CAP)

Pedullà, L., Brichetto, G., Tacchino, A., Vassallo, C., Zaratin, P., Battaglia, M., . . . Bove, M. (2016). Adaptive vs. non-adaptive cognitive training by means of a personalized app: A randomized trial in people with multiple sclerosis. *Journal of NeuroEngineering and Rehabilitation,13*(1), 88. https://doi.org/10.1186/s12984-016-0193-y

CLINICAL BOTTOM LINE

The purpose of this study was to evaluate the effectiveness of a working-memory program to improve the cognitive status of people with multiple sclerosis (MS). Given the increasing use of technology in modern-day society, further research is required to provide evidence supporting working-memory training devices that are easily accessible for people with memory deficits.

In this randomized controlled trial (Level I), 28 participants received an adaptive working-memory COGNI-TRAcK program (adaptive group [ADAPT-gr]) or a nonadaptive working-memory COGNI-TRAcK program (constant group [CONST-gr]) on their home computer. The COGNI-TRAcK application is a low-cost memory-training program that can be used on off-the-shelf devices. Training, exercise types, and intensiveness were the same for both groups, with the difference being the adaptive and nonadaptive algorithms. The program was self-administered at home and consisted of five 30-minute sessions per week for 8 weeks. The adaptive program was structured so that the level of difficulty increased or decreased on the basis of the performance of the user, whereas the nonadaptive program was consistent on the level of difficulty regardless of the user's performance.

Participants in the ADAPT-gr had significantly improved verbal memory acquisition, delayed recall, verbal fluency, sustained attention, concentration, and information-processing speeds, compared with the CONST-gr. The scores obtained at postsession by the ADAPT-gr were higher than those in the CONST-gr, which further demonstrates the effectiveness of the adaptive working-memory COGNI-TRAcK program. However, because of the small sample size, training bias, medication effects, and convenience sampling, further research is required

to generalize the results to the larger population.

The results support the use of grading interventions for "just right" challenges by occupational therapists in clinical practice. Grading of interventions allows clients to experience success, helps them pace accordingly, and also provides appropriate challenges so they can gain maximal performance during therapy. This research adds to the growing body of knowledge that supports the use of occupational therapists in rehabilitation who are specifically trained to use grading to improve functioning.
Moreover, this research supports and adds to research on computerized programs that aim to improve memory among people with memory deficits. The convenience of the COGNI-TRAcK program allows clients with memory deficits to adhere to treatment at home using a computer with graded interventions to augment working memory. Therefore, for clients with MS, the COGNI-TRAcK program may enhance levels of cognition, further increasing participation in daily-life experiences.

RESEARCH OBJECTIVE(S)

Assess the effectiveness of an adaptive and intensive training using working-memory–based exercises, which were delivered through a computerized application, COGNI-TRAcK, in improving cognition for people with MS

DESIGN TYPE AND LEVEL OF EVIDENCE

Level I: Randomized controlled trial

PARTICIPANT SELECTION

Participants considered eligible for this study were outpatients chosen through snowball sampling from the Italian MS Society Rehabilitation Centre of Genoa, who complained of poor memory and attention. Each participant was screened to ensure that he or she met the inclusion criteria.

Inclusion criteria:

Participants met the MS diagnostic criteria of McDonald et al. (2001) and were in the stable phase of the disease (no relapses within the last 3 months), with complaints of memory or attention problems. The participants' cognitive status had to be at least 1.5 standard deviations below the mean normative values of one or more components of Rao's Brief Repeatable Battery of Neuropsychological Tests (BRB-NT) .

Exclusion criteria:

Participants were excluded if they were younger than 18 years; experienced one or more exacerbations 3 months prior to enrollment; had any major psychiatric disorder; were taking antidepressants or benzodiazepines; or had dyscalculia, acalculia, or severe visual loss.

PARTICIPANT CHARACTERISTICS

N=	**28**

#/ % Male:	8/28.6%	**#/ % Female:**	20/71.4%

Ethnicity:	Not reported; the study was conducted in Italy, however.

Disease/disability diagnosis:	MS

INTERVENTION AND CONTROL GROUPS

Group 1: Intervention group (ADAPT-gr)

Brief description of the intervention	Participants in the intervention group (ADAPT-gr) used COGNI-TRAcK, a customized application software that provided working-memory–based exercises. COGNI-TRAcK implemented three 10-minute sessions that included three different types of exercises: a visuospatial working-memory task, an operation N-back task, and a dual N-back task. The intervention group's application was set to an adaptive training feature that graded the level of difficulty of the exercises on the basis of the participant's performance.
How many participants in the group?	14
Where did the intervention take place?	Participant's home
Who delivered?	Self-administered

How often?	Five 30-minute sessions per week
For how long?	8 weeks

Group 2: Control group (CONST-gr)

Brief description of the intervention	Participants in the control group (CONST-gr) used COGNI-TRAcK, a customized application software that provided working-memory–based exercises. COGNI-TRAcK implemented three 10-minute sessions that included three different types of exercises: a visuospatial working-memory task, an operation N-back task, and a dual N-back task. The control group received a nonadaptive training feature that implemented two low-difficulty-level sessions that alternated every day, regardless of the participant's performance.
How many participants in the group?	14
Where did the intervention take place?	Participant's home
Who delivered?	Self-administered
How often?	Five 30-minute sessions per week
For how long?	8 weeks

INTERVENTION BIASES

Contamination:

YES ☐ NO ☒	It is not likely that there was cross-contamination in the intervention, because the participants performed the intervention in their own home on their personal computer.

Co-intervention:

YES ☒ NO ☐	Although the authors did not note any cointervention biases, it is possible that some of the participants had changes in their medications related to MS symptoms during the study. It is also possible that the participants

	were receiving other outside interventions to help manage cognitive symptoms related to MS.

Timing of intervention:

YES ☒ NO ☐	The intervention took place over a period of 8 weeks, which is adequate time to note change in function. Given the progressive nature of MS, however, it is possible that some of the participants experienced a decline in their condition during the 8-week period.

Site of intervention:

YES ☒ NO ☐	Interventions took place in different home environments. These were not controlled environments, so participants could have received outside help from family members or had different levels of noise or distractions in their household, which might have affected the outcome of the results.

Use of different therapists to provide intervention:

YES ☐ NO ☒	The intervention was self-administered at home. No other information was provided in terms of who trained the participants on the intervention software initially.

Baseline equality:

YES ☐ NO ☒	The two groups did not differ in any demographic. Cognitive performance at baseline was equal in all neuropsychological domains except the Selective Reminding Test—Consistent Long-Term Retrieval subset of the BRB-NT. The CONST-gr scored significantly higher on the BRB-NT than did the ADAPT-gr, $t = 2.10$, $p = .045$.

MEASURES AND OUTCOMES

Measure 1: BRB-NT

Name/type of measure used:	BRB-NT
What outcome is measured?	Cognitive status Subtests used: • Selective Reminding Test, for verbal memory acquisition (Selective Reminding Test—Long-Term Storage; Selective

	Reminding Test—Consistent Long-Term Retrieval) and delayed recall (Selective Reminding Test–D); • 10/36 Spatial Recall Test, for visual memory acquisition and delayed recall (Spatial Recall Test—Delayed); • Paced Auditory Serial Addition Test (PASAT-2 and PASAT-3) and Symbol Digit Modalities Test (SDMT), for sustained attention, concentration, and information-processing speed; • Word List Generation, for verbal fluency on semantic stimuli
Is the measure reliable (as reported in the article)?	YES ☒ NO ☐ Not Reported ☐ Reliability of the normative values and correction factors was based on the Italian validation of the BRB-NT (Amato et al., 2006).
Is the measure valid (as reported in the article)?	YES ☒ NO ☐ Not Reported ☐ The PASAT-3 and SDMT evaluate for processing speed, which is the first cognitive domain to emerge and the most affected by MS. The SDMT has been used as a screening tool to measure cognitive intelligence because of its high sensitivity (López-Góngora, Querol, & Escartín, 2015; Van Schependom et al., 2014).
When is the measure used?	At baseline (before rehabilitative treatment) and posttreatment Follow-up measures: PASAT-3 and SDMT

Measure 2: Wisconsin Card Sorting Test

Name/type of measure used:	Wisconsin Card Sorting Test		
What outcome is measured?	Frontal-lobe executive functioning		
Is the measure reliable as reported in the article?	YES ☐	NO ☐	Not Reported ☒
Is the measure valid as reported in the article?	YES ☐	NO ☐	Not Reported ☒
When is the	At baseline (before rehabilitative treatment) and posttreatment		

measure used?	

Measure 3: Adherence to treatment

Name/type of measure used:	Adherence to treatment		
What outcome is measured?	Participants' percentage of completed training sessions out of the total number of scheduled sessions		
Is the measure reliable as reported in the article?	YES ☐	NO ☐	Not Reported ☒
Is the measure valid as reported in the article?	YES ☐	NO ☐	Not Reported ☒
When is the measure used?	COGNI-TRAcK automatically recorded the percentage of correctly executed exercises and the mean difficulty level maintained during the training.		

MEASUREMENT BIASES

Were the evaluators blind to treatment status?

YES ☐ NO ☒	It is unknown whether the evaluators of the research data were blind to the participants. No data were provided.

Was there recall or memory bias?

YES ☐ NO ☒	Adherence to treatment was calculated and recorded by the COGNI-TRAcK program. Adherence was calculated as a percentage of the completed training sessions out of the total 40 scheduled sessions. The BRB-NT and Wisconsin Card Sorting Test do not require personal reporting.

Other measurement biases:

RESULTS

Neuropsychological Effects

Post hoc analysis showed a significant improvement in the ADAPT-gr after the intervention of the COGNI-TRAcK in 6 out of the 10 tests. The analysis of variance showed an effect of time (pretreatment vs. posttreatment) for all the tests given. In particular, verbal memory acquisition ($F = 4.40$, $p < .05$); delayed recall ($F = 12.01$, $p = .001$); verbal fluency ($F = 6.67$, $p = .01$); and sustained attention, concentration, and information-processing speed ($F = 8.92$, $p < .01$) all had significantly higher scores after the intervention in the ADAPT-gr with respect to baseline. The participants in the ADAPT-gr also performed better on the Selective Reminding Test—Consistent Long Term Retrieval than the CONST-gr ($p = .003$), even though they initially had statistically significantly lower scores at baseline.

Follow-Up

Twenty participants concluded the follow-up assessments on the PASAT-3 and SDMT. The ADAPT-gr scored higher on both the PASAT-3 ($F = 9.69$, $p < .001$) and the SDMT ($F = 3.50$ $p < .05$), which thus reveals that there was a lasting effect maintained after 6 months of treatment. The CONST-gr's performance did not change across time.

Participants adhered to the intervention at a rate of 87%, for a 13% rate of noncompliance with the program over the span of 8 weeks. No difference was found between the two groups ($t = 0.24$, $p = .81$). All participants completed the intervention.

Was this study adequately powered (large enough to show a difference)?

YES ☐ NO ☒	*Explanation:* A power analysis was not documented; therefore it is unknown whether the study was adequately powered. The sample size might not have been large enough to adequately power the study, however.

Were the analysis methods appropriate?

YES ☒ NO ☐	*Explanation:* The researchers used a *t* test for independent samples for the continuous data, and they compared categorical variables using a Pearson's chi-square test to analyze the differences between groups regarding demographic data. The results of the cognitive rehabilitation intervention were analyzed with a two-way analysis of variance. For the missing data due to dropouts, a "last observation carried forward" analysis was an appropriate method to document missing information.

Were statistics appropriately reported (in written or table format)?

YES ☒ NO ☐	*Explanation:* Statistics included tables, figures, charts, and graphs to represent the results of COGNI-TRAcK and participant data. Written

	results of the intervention and control group analysis were organized into three different categories: training results comparing the mean percentages of performance, neuropsychological assessment results comparing time differences, and follow-up results.

Was participant dropout less than 20% in total sample and balanced between groups?

YES ☐ NO ☒	*Explanation:* All 28 participants completed the assessments at baseline and posttreatment. Eight participants were lost from posttreatment to follow-up, which resulted in a 28% dropout rate. The authors used intention-to-treat analysis, however, so the dropout rate did not diminish the power of the study.

What are the overall study limitations?

The present study used a convenience sample from one rehabilitation center in Italy and therefore lacks generalizability. Larger sample sizes would allow for greater statistical power and the ability to make greater inferences about the effects of the intervention.
The study did not include information about who trained the participants to use the COGNI-TRAcK app, which might have caused a training bias. Follow-up assessments consisted of only two measurements from the battery of assessments. A complete neurological evaluation in the follow-up assessment would have given a better picture of the effects of the intervention.
Medication effects and the effect of the concurrent treatment of MS might have had an effect on the cognitive intervention as a result of the medications' interactions.

CONCLUSIONS

The results of the research study suggest that adaptive cognitive exercises with COGNI-TRAcK were an effective treatment method for improving cognitive deficits among people with MS, particularly in the domains of attention, information-processing speed, new learning, verbal memory, and verbal fluency. Moreover, COGNI-TRAcK is personalizable to each participant's cognitive weaknesses and needs.

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