The IMPACT Study: A Randomized Controlled Trial of a Brain Plasticity-Based Training Program for Age-Related Cognitive Decline

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Abstract

Introduction: Previous interventions for normal age-related cognitive declines have shown limited generalizability beyond the skills directly trained.

Purpose: We report results from a large-scale randomized controlled clinical trial designed to evaluate whether improvements from training can extend to untrained measures of memory performance and to self-perceived everyday cognition.

Methods: The IMPACT Study was a multi-site double-blind trial in adults ≥65 with normal cognition (MMSE ≥ 26) of the Post Stroke Brain Fitness Program (BF). Each had an average of 12 weeks of training. BFP targets the speed/accuracy of auditory and language processing, and neuremodulatory systems associated with learning and memory. 480 individuals were randomized to the BFP intervention(s), or a 2 x 2 computer-based learning program matched for novelty/intensity (control). Prebaseline endpoints did not differ in content from training exercises included standardized neuropsychological assessments of memory and participant-reported outcome (PRO) assessments measuring perceptions of everyday cognition.

Results: The participants’ mean age was 75.1 (±4.6), education: 15.7 (±2.4, estimated IQ: 113.9. After 10 weeks of training, significant group by time interactions (p < 0.05) favoring the experimental group were seen on the primary endpoint measures (RBANS Auditory Memory and multiple within-modality (RAVLT total 1-5, WMS-III digits backwards, WMS-III letter-number) but not cross-modality (RBANS Visual Memory) secondary endpoint measures. PRO measures of everyday cognitive function were significant on pre-post (p < 0.002) and post-only (p < 0.001) assessments.

Conclusion: These results demonstrate the training program studied produces significantly superior improvements in generalized measures of memory and perception of cognitive performance in everyday life, compared to a treatment-as-usual control.

Background

• Normal, healthy aging adults may experience declines in memory and other cognitive abilities, including information processing, executive function, and working memory.

• Prevalence of memory complaints in community-based samples of older adults varies between 25% and 50% (Koeck, Gervais & Schmand, 2000).

• Predictors of negative frequency of forgetting ratings include: higher depression, lower conscientiousness, poorer performance on list recall, female gender, and increased age (Zelinski & Gilewski, 2004).

Problem

Numerous interventions for improving cognitive and memory performance are available. However, the effectiveness of most interventions has not been extensively evaluated, especially in regard to the generalizability of improvements beyond directly trained skills (see Woiznecky et al., 2006; Wills et al., 2004).

Objective

To evaluate whether improvements from a training program based on brain plasticity extend to untrained measures of memory performance and self-perceived everyday cognition.

Methods

Participants

Recruitment: Direct mail, radio, newspaper ads, flyers, presentations

Inclusion criteria

• Age ≥65
• Mini-Mental Status Examination (MMSE) score ≥26
• Able to read 1 point type
• Adequate learning capacity
• Willing to commit to 6-month time requirement of the study period

Methods (continued)

Procedure

• Multi-site double-blind randomized clinical trial using test re-test treatment control design

• Participants randomized into treatment (ET) and active control (AC) groups

• Clinicians administering neuropsychological examinations blinded as to randomization

• Follow-up on all outcome measures at 6-month intervals

Outcome Measures

Primary

Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): Global Auditory Memory Score, derived from six sub-tests (list learning, story memory, digit span forward, delayed list recall, delayed list recognition, delayed free story recall).

Secondary

• Rey Auditory Verbal Learning Test (RAVLT): Trials 1-5 and Delayed Recall

• Wechsler Memory Scale (WMS-III): Digit Span Backwards and Letter-Number Sequencing

• Rey Auditory-Motor Behavior Test (RBMT): Story Memory Delayed

RBANS Visual Function Score, derived from four sub-tests (figure copy, line orientation, copying, figure recall)

Participant Reported Outcome (PRO) assessments

• Cognitive Self-Report Questionnaire: CSQ-25

• CSQ-6

Analysis Groups

• Intent to Treat (ITT) Participants randomized into the study

• Fully Evaluable: Participants who completed the study

• Fully Trained: ET Participants who completed 85% of training on principal exercises

Interventions

ET: The Brain Fitness Program (BFP, Post Stroke) is intended to improve memory performance by increasing the speed and accuracy of aural information processing, and the production of neuremodulatory improvements in learning and memory. Training consisted of:

• Six adaptive, challenging computerized listening exercises

• Stimuli span acoustic and organizational structure of language, from simple sounds to complex sentences

• Neuromodulators important for learning and memory. Training consisted of:

• 60 minutes/day, 5 days/week, for 8–10 weeks

• No baseline group differences distinguished ET (n=232) and AC (n=236) groups

• No significant interactions were found for two within-modality (RBMT Story Memory Immediate and Delayed) and one cross-modality (RBANS Visual Memory) measures

• PRO measures of everyday cognitive function were significant on pre-post (p < 0.002) and post-only (p < 0.001) assessments.

Discussion

Compared to a treatment-as-usual control, the experimental treatment yielded significant improvements in:

• Speed of processing

• Generalized measures of memory

• Self-reported cognitive benefits

No significant interactions were found for two within-modality (RBMT Story Memory Immediate and Delayed) and one cross-modality (RBANS Visual Memory) measures. PRO measures of everyday cognitive performance were significant on pre-post (p < 0.002) and post-only (p < 0.001) assessments.

Results

Table 2. Baseline Characteristics (ITT)

<table>
<thead>
<tr>
<th>Age</th>
<th>Education</th>
<th>Gender</th>
<th>Predicted IQ</th>
<th>Overall Memory Composite</th>
<th>RBANS Auditory Memory Score</th>
<th>ET Baseline</th>
<th>ET Post-Training</th>
<th>AC Baseline</th>
<th>AC Post-Training</th>
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</thead>
<tbody>
<tr>
<td>75.3</td>
<td>15.7</td>
<td>52.5%</td>
<td>114.0</td>
<td>28.1</td>
<td>74.9</td>
<td>&lt; 0.001</td>
<td>&lt; 0.05</td>
<td>&lt; 0.001</td>
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Table 3. Mean Change in Scores (ITT)

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>ITT (N = 468)</th>
<th>ET (N = 389)</th>
<th>AC (N = 28)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speed of Processing</td>
<td>-0.001</td>
<td>0.002</td>
<td>-0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Table 4. ITT Versus Fully Trained Effect Sizes (Cohen’s d)

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>ITT</th>
<th>ET</th>
<th>AC</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBANS Auditory Memory Score</td>
<td>0.24</td>
<td>0.28</td>
<td>0.25</td>
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<table>
<thead>
<tr>
<th>Correlation Coefficient</th>
<th>ET</th>
<th>Post-Training Assessment</th>
<th>AC</th>
<th>Post-Training Assessment</th>
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<tr>
<td>Pearson</td>
<td>0.30</td>
<td>0.43</td>
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References