

## **Cognitive Impairment in Multiple Sclerosis: A Pilot Study of the Effects of Cognitive Retraining on Quality of Life and Cognitive Function.**

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## **Background**

- Approximately 45-60 % of Multiple Sclerosis (MS) patients are reported to develop some degree of cognitive impairment.
- Cognitive retraining, also referred to as cognitive rehabilitation, is a potential intervention for those who suffer from cognitive impairment.
- There are only a few studies examining the effects of cognitive rehabilitation in MS. Cognitive retraining has been studied in Alzheimer's Disease, Traumatic Brain Injury, and mild cognitive impairment.
- A review of current research reveals mixed findings on the efficacy of cognitive rehabilitation in MS.
- Some studies suggest that cognitive retraining can be beneficial and improve the quality of life of MS patients.

## Reported Benefits of Cognitive Retraining in Normal Aging

- Improves processing speed
- Improves measures of memory and attention
- Improves measures of cognitive function
- Improves performance in measures of functional independence
- Decreases risk of developing depressive symptoms
- Improves feelings of control over one's life
- Self-reported overall health improvement

## Purpose & Objectives

- **Purpose:** To determine the effects of cognitive retraining on quality of life and cognitive function in Relapsing Remitting Multiple Sclerosis patients with mild cognitive impairment.
- **Objectives:**
  - **Primary:** Improvement in quality of life after cognitive retraining.
  - **Secondary:** Improvement in cognitive function after a course of cognitive retraining as measured by short form cognitive testing.
  - The short form cognitive testing has been validated against formal neuropsychological measures (Burchette et al., 2007).



## Neurology Center of Fairfax

- The Multiple Sclerosis Center at the Neurology Center of Fairfax provides treatment to over 2,000 Multiple Sclerosis patients
  - 70 patients were recruited as possible study participants
  - 45 patients agreed to pre-screening for mild cognitive impairment
  - 22 patients were eligible based on study criteria
    - 100% of eligible patients agreed to be study participants
    - 18 Women; 4 Men
    - Average Age: 43

## Population of Interest

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> <li>• Relapsing MS patients</li> <li>• Mild cognitive impairment as determined by short form cognitive testing.</li> <li>• Ages 21-50</li> <li>• Immunomodulatory therapy for at least one year</li> <li>• No medication regimens used to treat cognitive symptoms or fatigue</li> </ul>	<ul style="list-style-type: none"> <li>• Progressive MS patients</li> <li>• &gt; Age 50</li> <li>• Moderate to severe cognitive impairment</li> <li>• Co-existing conditions which may affect cognitive function</li> <li>• Patients currently on medication regimens to treat cognitive symptoms or fatigue</li> <li>• Patients currently treated with natalizumab or administered natalizumab in the previous 12 months.</li> <li>• A documented relapse within the course of the study or within 50 days prior to enrollment.</li> <li>• Use of corticosteroids 50 days before or during the study</li> <li>• Change in immunomodulatory therapy during the study</li> </ul>

## Methods

- Each participant was tested for mild cognitive impairment using the Neurology Center of Fairfax short form cognitive testing tool.
- Eligible participants were randomly assigned into control and treatment groups. All participants completed the Perceived Deficits Questionnaire (PDQ).
- Participants in the treatment group completed 5 weeks (3 sessions/week; 30 mins each session) of computer-based cognitive retraining with the computer software program BrainHQ.
- Cognitive retraining sessions focused on memory, attention, and information processing.


## Description of Assessments

### The Perceived Deficits Questionnaire (PDQ)

- A component of the Multiple Sclerosis Quality of Life Inventory (MSQLI).
- Designed specifically for MS to provide a self-report of cognitive impairment.
- A 20-item Likert Scale
- Addresses cognitive measures that effect quality of life: retrospective memory, prospective memory, planning/organization, and attention.

### Short form Cognitive Testing (COG1)

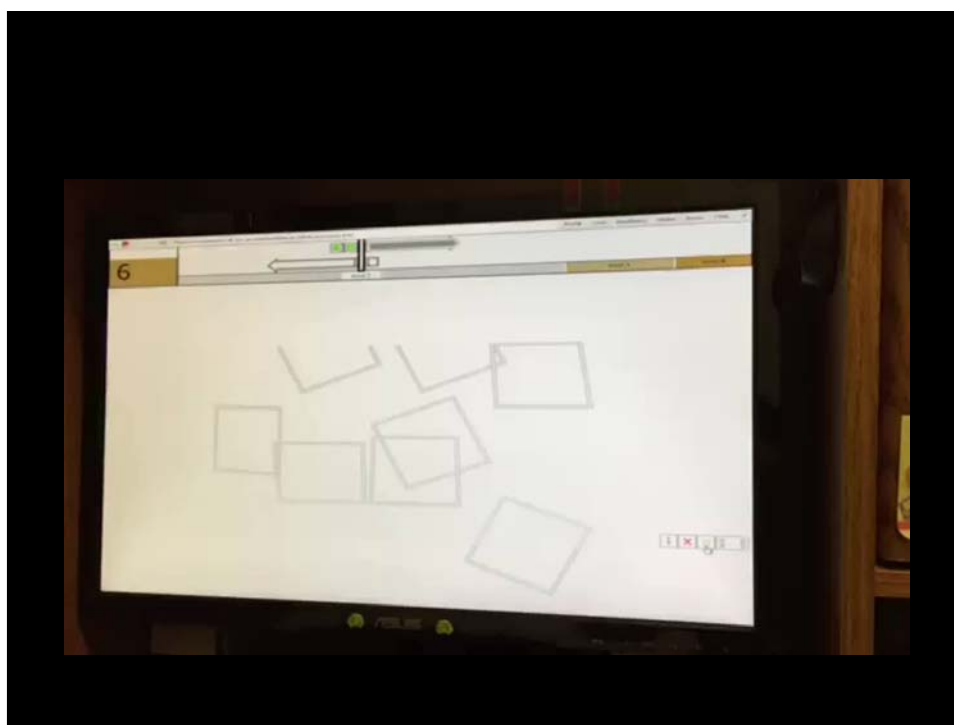
- Verbal Category Fluency
- Boston Naming
- Mini-Mental State Examination
- Hopkins Verbal Learning
- Digit Span (Forward, Backward, and Sequential)
- Hopkins Verbal Learning Recall
- Hopkins Verbal Learning Recognition
- Trails A & B
- Beck Depression Inventory.



# Cognitive Retraining Intervention

**Based on the Science of Brain Plasticity**  
The ability of the brain to change functionally, physically, and chemically throughout life.

- >20 randomized controlled trials
- >75 peer-reviewed published studies
- >10,000 participants involved in clinical trials
- Published studies in schizophrenia, chemobrain, HIV-associated neurocognitive disorder, mild cognitive impairment, and traumatic brain injury



## Study Design & Duration

### Study Design

- Pretest/post test experimental design with random assignment of control and treatment groups

### Study Duration

- A total of 10 weeks was allowed for pretesting, cognitive retraining (treatment group), post testing, and data collection

### Intervention

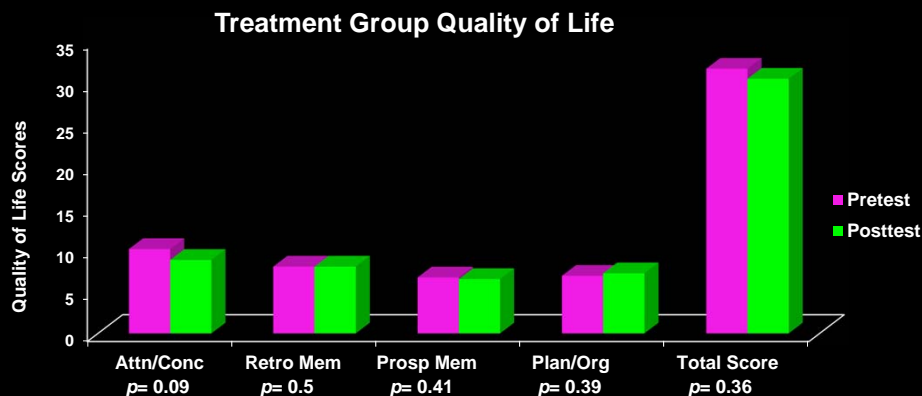
- The treatment group received 5 Weeks (Three 30 minute sessions/per week) of cognitive retraining.
- The control and treatment groups completed post testing 5-8 weeks after pretesting.

## Data Analysis

- Results were obtained from the pretest and post test short form cognitive testing and Perceived Deficits Questionnaire scores.
- Paired t-test statistical analysis was used to evaluate the differences between pretest and post test scores of each group.
- Independent t-test statistical analysis was used to evaluate differences in post test scores between control and treatment groups.

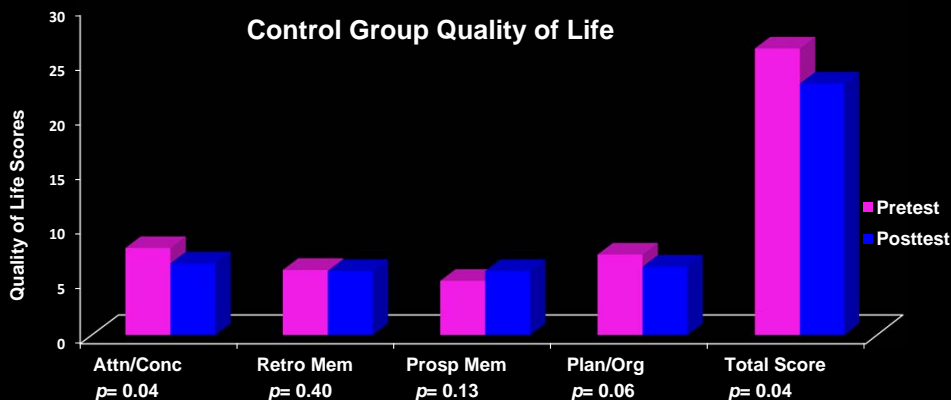
## Treatment Group: Quality of Life

- A comparison of pretest and post test results for the treatment group did not identify any statistically significant difference for any of the quality of life measures



## Control Group: Quality of Life

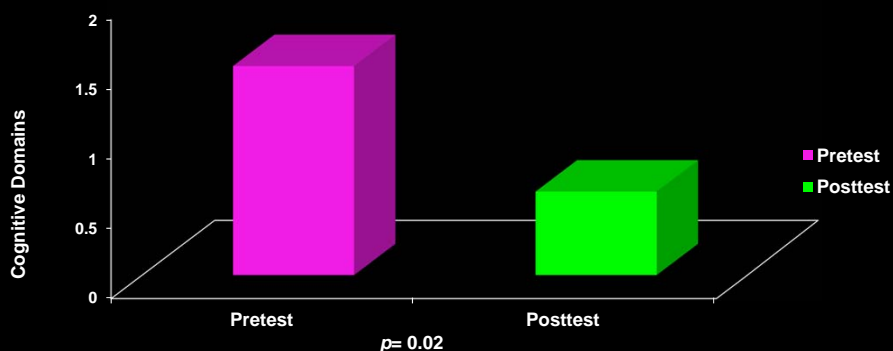
- A comparison of pretest and post test results for the control group identified a statistically significant improvement in the attention/concentration quality of life measure, as well as total quality of life score.



## Treatment Group: Cognitive Function

- Comparing pre and post test cognitive function scores for the treatment group indicated a statistically significant improvement after treatment.

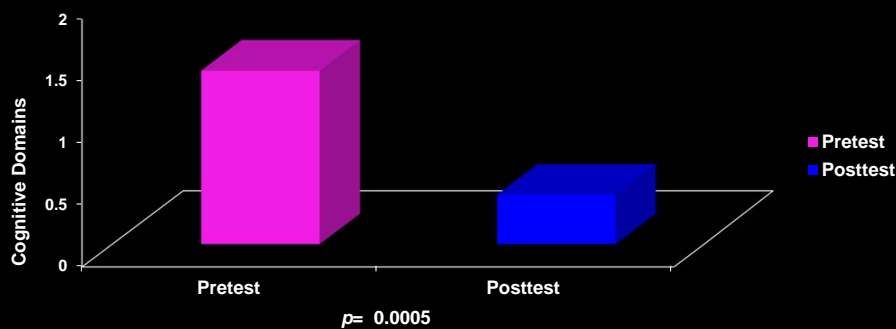
Treatment Group Cognitive Function



## Control Group: Cognitive Function

- Comparison of pre and post test cognitive function scores in the control group indicated a statistically significant improvement. This may be due to practice effect.

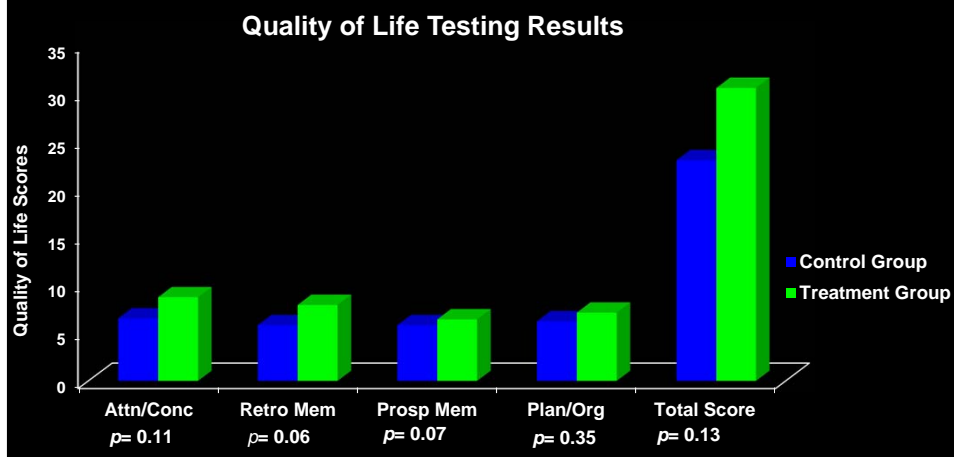
Control Group Cognitive Function





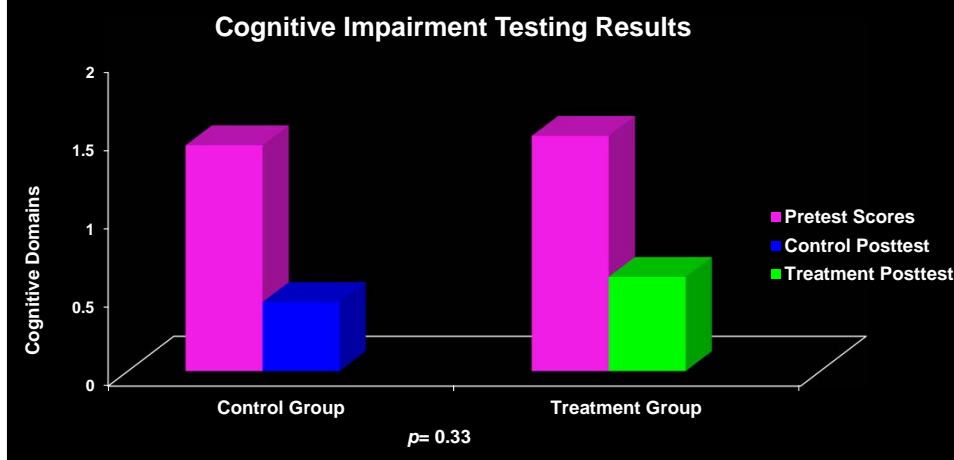
## Comparative Quality of Life Scores

- post test quality of life scores did not yield a statistically significant difference between control and treatment groups.



## Comparative Cognitive Function Scores

- post test cognitive function scores improved in both the control and treatment groups, but did not reach statistical significance.



## Discussion Points

- One treatment patient was excluded due to inactivity on the training schedule.
- One control patient was removed due to a clinical relapse.
- Three treatment patients reported an increased perceived deficit in the planning/organization quality of life measure.
- Two treatment patients reported a perceived decline in at least three of the quality of life measures; thus influencing the average total scores.
- One treatment patient's cognitive function post test scores increased to 4 impaired domains compared to 2 impaired cognitive domains on pretesting.

## Discussion Points

- Mood was excluded as a cognitive measure in the determination of mild cognitive impairment
  - Cognitive function pretesting indicated mood was impaired in 3 of 10 control patients.
    - **2 of 3** patients continued to have impaired mood on post test cognitive function scores.
  - Cognitive function pretesting indicated mood was impaired in 3 of 10 treatment patients.
    - **1 of 3** patients continued to have impaired mood on post testing cognitive function scores

## Patient Responses

- Patient 110: “ I had so much fun...”
- Patient 105: “ I needed to break after 10 minutes...”
- Patient 111: “ I enjoyed it, but I couldn’t always understand the computer program...”
- Patient 121: “ On the days I was tired, I could tell I didn’t do well...”

## Limitations

- Small sample size
  - Inclusion and Exclusion Criteria Limits
- Practice Effect
- Short study Duration
- Methodology (computer-based versus 1:1 training)
- Computer Literacy of patients

## Future Research

- More studies directly comparing methods of cognitive retraining.
- Studies accounting for more variables that can contribute to cognitive function and quality of life.
- Longer duration of training periods.
- Larger sample sizes
- Studies addressing the best age and disease duration at which to begin cognitive retraining.
- Studies on whether cognitive retraining can reduce disability.
- Standardized definition of cognitive impairment.
- The need for more standardized cognitive batteries.

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## Acknowledgements

- Patients of the Neurology Center of Fairfax
  - James P. Simsarian, MD
  - Tatjana Lyons, CHES
- Joan M. Ohayon, NP-C
- Neuropsychology Associates of Fairfax
  - Mary Elizabeth Quig, PhD
  - Allison Logemann, MA
- Joanna Luzzi
- Sharaya Testa

Investigator Initiated Trial  
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## Current Evidence

<u>Literature</u>	<u>Evidence</u>
Glanz et al. (2009)	Cross sectional design; 92 patients; Linkage between QOL and information processing after accounting for depression
Baumstarck-Barrau et al. (2011)	Cross sectional design; 124 patients; No links between quality of life measures and cognitive testing.
Anhoque et al. (2012)	18 CIS patients; Correlational study; Cognition, but not disability, anxiety, or depression was associated with reduced QOL.
das Nair et al (2011)	Systemic Review (8 studies, 521 participants). No association between QOL and cognitive retraining.

## Current Evidence

<u>Literature</u>	<u>Evidence</u>
Stuifbergen et al (2012)	Single blind RCT; 61 patients; Computer-based and group session; Improvements in verbal memory.
Flavia et al (2010)	Double blind control; 150 patients; Computer-based retraining; Improvements in depression, information processing, and executive function.
Edgar et al (2010)	Longitudinal design; 43 patients; computer-based retraining; Improvements in attention and information processing
Chiaravalloti et al (2013)	Double Blind Placebo Controlled; 86 patients; Imagery technique; Improvements in encoding, learning, and memory. Booster sessions little benefit. CLASS I EVIDENCE