



Introduction

Alzheimer's disease (AD) is a multi-faceted, whole brain and body illness. Combined treatment in AD and other dementias is gaining more attention among clinicians and scientists (Bragin, V., 2012, Bottino, CM., et al., 2005). There is a growing body of research related to analyzing different modifiable factors in the treatment of dementia. It is well known that cerebral blood flow (CBF) is diminished in different parts of the brain of people with dementia and this is a modifiable factor for overcoming hypoperfusion, hypoxia, mitochondria failure, and changes in protein metabolism (Daulatzai MA., 2017, de la Torre JC., 2016). Sensory stimulation and hand movements increase CBF (Ronald, PE., et al., 1982). The practical model for treatment of dementia consists of four components related to movements, memory, mood, and mitochondria, combined with pharmacological interventions (Bragin, V., 2011).

This program initially developed in 2000 was intended for people with dementia and depression among multiple medical problems with the goal of preventing physical and cognitive decline and enabling seniors to maintain quality of life for as long as possible. The results of our treatment have been shown for up to 72 months of therapy (Bragin et al., 2014).

Objective

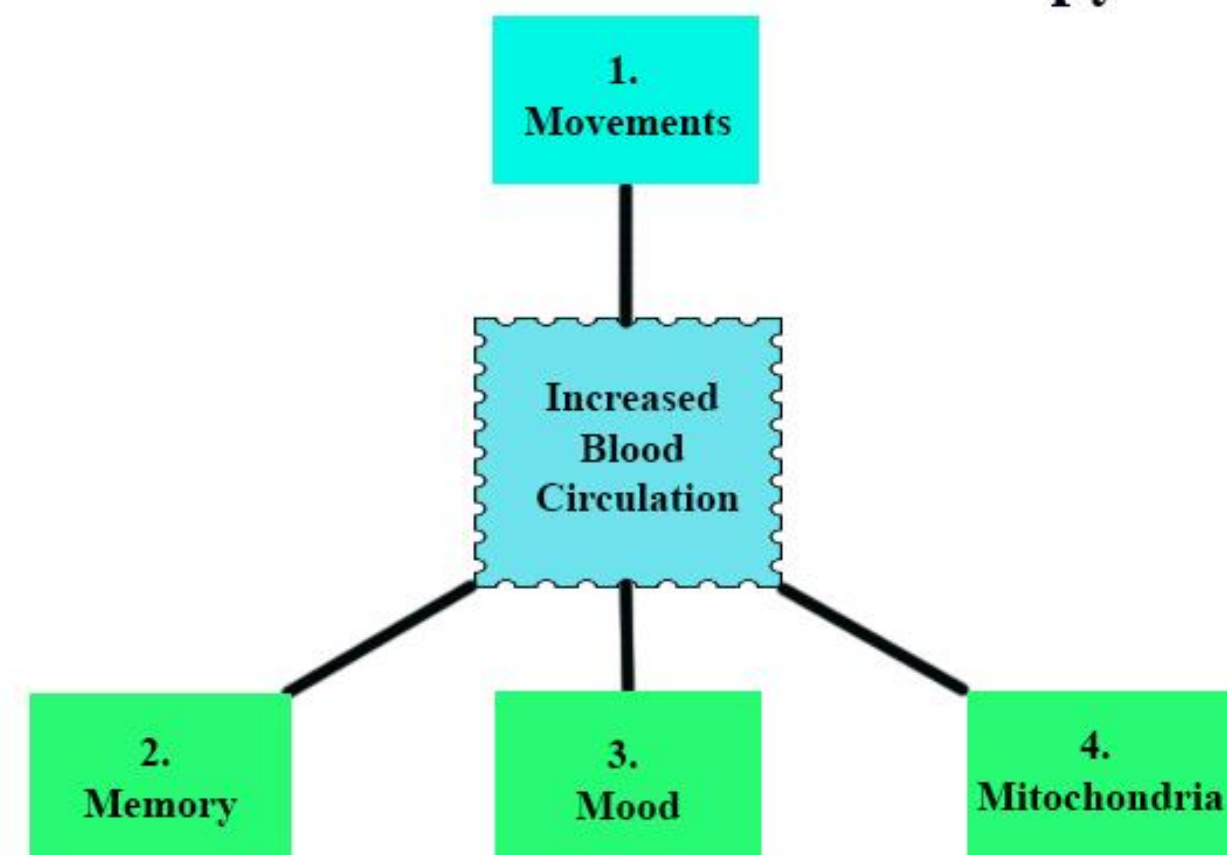
The goal of this presentation is to demonstrate the results of the treatment of a series of six patients with MCI and mild dementia for up to 15 years.

Subject/Methods

Patients (4 females, 2 males, mean age of 71.2±2.56 years upon initiation of therapy, mean education 14.7±1.63) multiple chronic medical comorbidities (cardiovascular pathology, diabetes, osteoarthritis etc.). Non-pharmacological intervention modalities include office and home-based physical and cognitive exercises. (Bragin, V., 2012) Cognitive testing (MMSE, clock drawing test, semantic and phonemic verbal fluency) was performed yearly.

Figure 1.

4 M's Combination of Four Modalities for Dementia Therapy



The non-pharmacological intervention part of the therapy program we named the "Four M's™," which consists of simultaneous interventions relating to movements, memory, mood, and the mitochondria (Figure 1). Movements are directly connected to increasing blood circulation and take up about 40% of treatment efforts. Memory, mood, and mitochondria functions positively respond to blood circulation improvement.

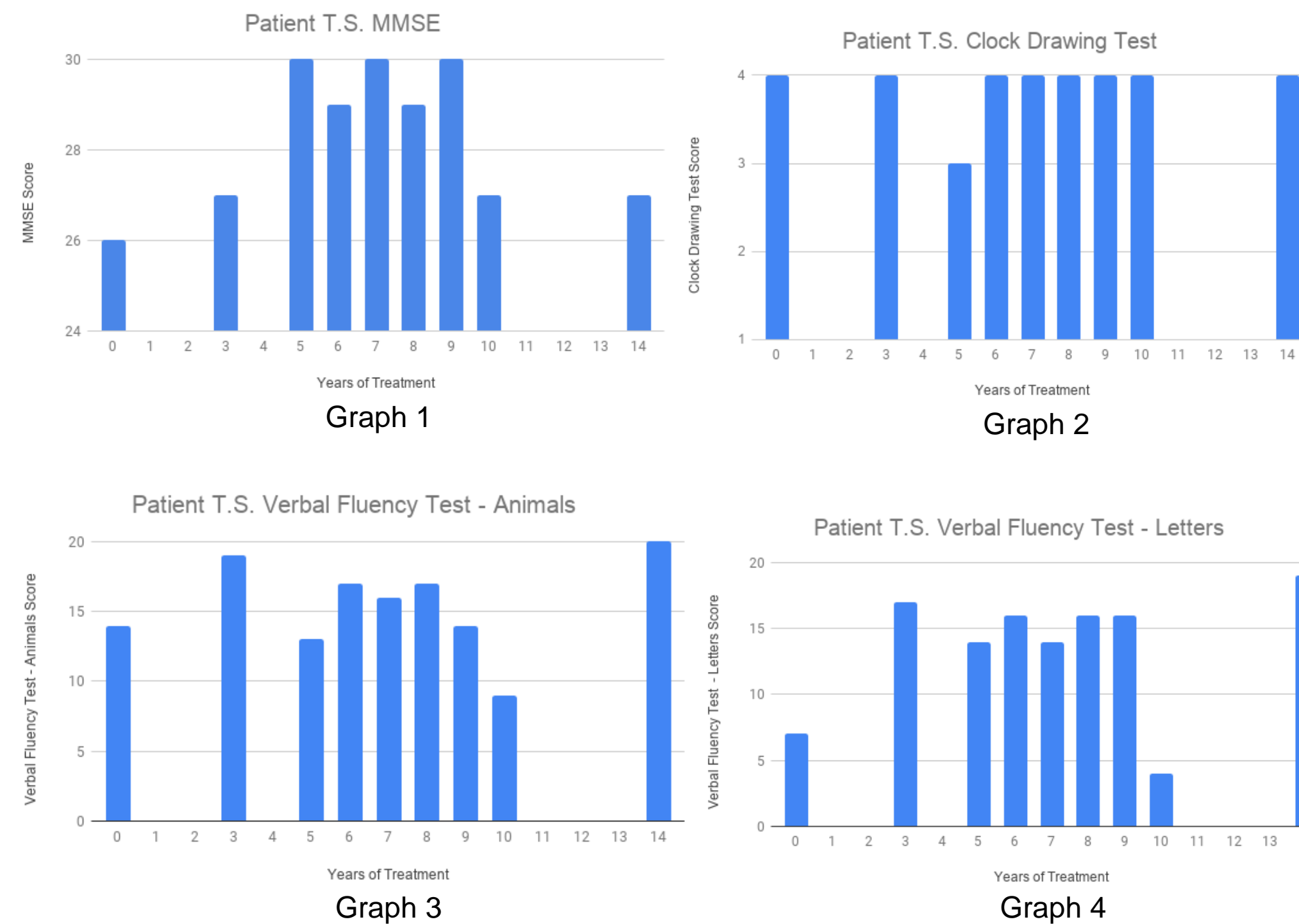
Results

Tests	Patient R.S.		Patient E.S.		Patient E.K.		Patient T.S.		Patient V.S.		Patient M.Z.	
	Baseline	15 Years	Baseline	15 Years	Baseline	15 Years	Baseline	14 Years	Baseline	13 Years	Baseline	10 Years
MMSE	28	27	23	28	25	26	26	27	28	27	27	27
CDT	3	3	3	3	2	4	4	4	4	4	4	4
VFA	18	12	8	6	8	15	14	20	12	13	25	20
VFL	12	13	4	10	n/a	12	7	19	17	16	25	17

By the end of the treatment period, all 6 patients had the same MMSE score (± 1 point), as seen in Table 1. The clock drawing task scores remained stable as well. Semantic (Animals) verbal fluency scores were stable in half of the patients. Phonemic verbal fluency (Letters) was stable in 3 of 5 patients.

Patient T.S., one of the six patients, was chosen to demonstrate her yearly cognitive performance.

Patient T.S. was a 74 year old female, college graduate, with a history of depression, progressive memory loss, anxiety, insomnia, osteoarthritis, gait problems, diabetes, and coronary artery disease, angiography, stroke (2014), and glaucoma, when she began treatment 14 years ago. Her MMSE score was 26 at the start of her treatment, and after 6 years of treatment she achieved the maximum score of 29-30 which remained until her 12th year of treatment, when her medical problems became worse (stroke) and her score declined to 27, one point above her initial score (Graph 1). Her Clock Drawing Test score was stable for all 14 years of treatment (Graph 2). Her Verbal Fluency Test – Animals was better by the end of year 14 (initial score 14 with the end score being 20) (Graph 3). Her Verbal Fluency Test – Letters demonstrated the same trend (initial score 7 with the end score being 18) (Graph 4).



Discussion

It is well known that besides the progression of dementia, there are two other processes occurring in the body simultaneously: natural aging (hypodynamia, sarcopenia, and decreased activities in all sensory channels) and the progression of medical diseases (hypertension, cardiac problems, high cholesterol, irregular pulse, diabetes, thyroid dysfunctions, arthritis, etc.).

Given the complexity and uncertainty of the pathogenesis of AD, aging process, and medical illnesses, our integrative rehabilitation program has been developed based on the assumptions that modifiable factors could change the course of AD. Among all modifiable factors special attention is given to CBF, which could be increased by sensory activation, movements, and cognitive training.

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Discussion (continued)

The long-term treatment, annual testing, and data analysis gives us a unique opportunity to see the dementia progression or regression.

In this presentation, we were able to demonstrate the long term effects of integrative treatment, when all available therapeutic modalities were used simultaneously.

The results that we obtained after 15 years of treatment were unexpected, as each of the patients showed stability in cognitive functions. These positive results demonstrate that the brain as an organ has the capacity to stabilize its functions by sensory-motor input and an increase in blood, oxygen and nutrient supply. In addition, diet modifications and vitamin support helped the brain to stabilize cognitive performance as well.

In presenting the case of patient T.S, her yearly performance on MMSE was consistently better, reaching her maximum score by her sixth year of treatment and then dropping after she had a stroke, but still remaining above her baseline. Take into consideration that the MMSE test consists of small subtests, each of which activates certain neural networks in the brain. It would be possible to suggest that these networks are still active even after a stroke.

Performance on the clock-drawing was stable for all 14 years of treatment. Although it is a very simple task, it provides quick and simple information of frontal lobe functioning. It is highly correlated with the verbal fluency task (verbal hemisphere) and Ruff Figural Fluency Test (non-verbal hemisphere) (Bragin, V., et al., 2003).

Scores on the verbal fluency tasks (Animals and Letters) show significant improvement by the end of the fourteen years of treatment with a brief decline in her twelfth year of treatment related to a stroke.

Conclusion

For the first time we have demonstrated the stabilization of cognitive function in MCI and mild Dementia for up to 15 years of combined therapy. Combined therapy is a viable treatment option for medically ill people with dementia until new effective medications become available.

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