Preservation of Cognitive Functioning in Depressed, Demented Geriatric Patients with Cardiovascular Risk Factors: An Ongoing 3 Year Naturalistic Study

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Background

It is well known that the majority of geriatric patients with depression and mixed dementia have cardiovascular co-morbidities, which have an additional negative impact on cognition (1). There have been no studies hitherto which have investigated the long-term effect of combined "real world" treatment (medications and non-pharmacological interventions) in this group of patients. This presentation is a part of an ongoing naturalistic study to investigate the possibility of preventing cognitive decline in demented, depressed seniors by implementing our multifaceted treatment model for a longer period of time. Previously, it was demonstrated that our integrative treatment model successfully arrests cognitive decline and even improves cognitive functions in patients with depression and dementia for 24 months (2).

Objective

To investigate the possibility of preventing cognitive decline in a real life setting for the most severely ill, depressed, demented patients with cardiovascular co-morbidities for a duration of 36 months.

Subjects / Methods

This observation study design was consistent with "real world" treatment practices, such that patient treatment was initiated upon an initial office visit and/or in the context of education programs for patients and caregivers about dementia. Clinical assessment, organic work-up and evaluation of cognitive functions were done in the first two to three office visits. An informed consent was obtained for the treatment and for cognitive testing. These patients underwent yearly cognitive retesting to assess the progress of the treatment and to make necessary corrections (to change or add medication) for next period of the treatment.

The medications included antidepressants (sertraline, citalopram, escitalopram, or venlafaxine XR, alone or in combination with bupropion XR), cholinesterase inhibitors (donepezil, rivastigmine or galantamine alone or in combination with memantine) along with their regular medications. Non-pharmacological interventions included vitamins (multivitamins, vitamin E, and Deplin or Folic acid), supplements (Alpha-Lipoic Acid, Acetyl-L-Carnitine, Omega-3 and Coenzyme Q-10), diet modification, and our unique home-based program involving mild physical exercises and cognitive training.

The program of hand movements is designed especially for this fragile population (3, 4). Movements include finger movements and rolling a tennis ball or plastic bottle, among others. Further, our patients were encouraged to use stress management tools regularly, to maintain healthy diets, to modify their lifestyle, to do memory training and to perform hands movement exercises.

This presentation is based on data collected from patients' medical records for 36 months of the treatment. Exclusion criteria for these data include patients with severe dementia (MMSE less than 15), chronic depression, psychosis, alcohol or substance abuse, severe neurological disorders, and recent major stresses (death in the family, surgery, etc.).

The study group consists of 38 patients (17 male, 21 female) with an average age of 72.34, who were diagnosed with mild dementia and depression, and had all three cardiac problems (hypertension, coronary artery disease and hyperlipidemia). Their diagnoses were probable Alzheimer's Disease (AD), Vascular Dementia (VaD), or mixed AD and VaD (5).

The assessment battery consisted of 7 tests for evaluation of attention, memory and executive functions. These included the following:

1.Mini-Mental State Examination (MMSE, a maximum score of 30). For attention assessment, serial 7 was used (6).

2.Clock drawing task

3.Word retrieval category task (animals and letters)

4.Neurobehavioral Cognitive Status Examination (Cognistat) was used along with MMSE to assess 10 cognitive domains: attention (digit span), orientation, language abilities, construction abilities, memory (four items), calculations, similarities and judgment (7)

5.Ruff Figural Fluency Test (RFFT) provides information regarding nonverbal capacity of the right frontal lobe to produce unique designs (8).

6.Ruff 2&7 Selective Attention Test (2&7 Test) is designed to measure sustained and selective attention over a short period of time (2-4 minutes) on trials of a visual search and cancellation task (9).

7. Word List Memory Learning Test (WLMLT) is used to assess verbal memory. Delayed recall of the word list is tested after a 5 minutes.

Statistical analysis was done by using SPSS-16 software and running descriptive statistics and the Wilcoxon Signed-Rank test. In this presentation, tests of significance were two-tailed.

Results

Demographics and clinical characteristics are presented in Table 1.

Table 1. Demographics and clinical characteristics

	Total	Percent
Patients	38	100.00
Women	21	55.27
Men	17	44.73
Mean age (SD)	72.34 (6.06)	-
Mean years of education (SD)	12.15 (2.64)	-
Depression	38	100.00
Length of depression (months)	31.13	19.29
Memory problems	38	100.00
Length of memory decline (mo)	40.91	19.39
Anxiety	36	94.74
Insomnia	34	89.47
Hypertension	38	100.00
Coronary Artery Disease	38	100.00
Dyslipidemia	38	100.00
Diabetes	18	47.37
Stroke	8	21.05
Head Trauma	8	21.05
Thyroid problems	5	13.16
Parkinsonism	3	7.89

Data on thirty-eight (38) patients were pulled from their medical charts. There were 21 women and 17 men (mean age = 72.34) with an education level 12.15±2.64. All the participants had depression and memory problems. The length of depression was 31.13 months. The length of memory problems was 40.91 months. There were also high percentages of anxiety (94.74%) and insomnia (89.47%) in the group. Besides the cardiac problems, patients in this group had diabetes (47.37%), history of stroke and history (21.05%), thyroid problems (13.16%) and Parkinson's disease symptoms (7.89%). Normal brain MRI was found in 13.33% of the group. The rest of the patients have cortical atrophy, lacunar infarcts, dilated ventricles and white matter microvascular changes alone or in combination with each other.

Descriptive statistics are shown in Table 2.

Table 2. Descriptive statistics

Tests	Baseline			12 months				24 months				36 months			
	n	Mean	STD	n	Mean	STD	p 12 - 0*	n	Mean	STD	p 24 - 0**	n	Mean	STD	p 36 - 0***
MMSE	38	26.03	3.39	30	25.56	3.22	0.427	29	27.41	2.57	**0.002**	25	26.84	2.87	0.177
Clock drawing score	38	2.92	1.15	30	3.35	1.02	0.18	29	3.54	0.88	**0.023**	25	3.52	0.77	**0.005**
Category animals	38	10.79	3.73	30	12.23	5.11	0.203	29	13.41	4.15	**0.001**	25	12.08	4.97	0.585
Category letters	38	9.65	4.19	30	10.03	4	0.42	29	11.34	4.43	**0.014**	25	10.80	5.14	0.213
Cognistat Orientation	38	11.26	1.29	30	11.39	1.48	0.312	29	11.83	0.6	**0.001**	24	11.63	0.82	**0.07**
Cognistat Attention	38	5.34	2.47	30	6.18	2.31	**0.011**	29	6.97	1.74	**0.000**	24	7.29	1.37	**0.001**
Cognistat Comprehension	38	5.76	0.68	30	5.82	0.73	0.854	29	5.86	0.52	0.276	24	6.00	0.00	0.102
Cognistat Repetition	38	10.95	2.05	30	11.39	1.52	0.067	29	11.69	1.14	**0.009**	24	11.75	0.90	**0.049**
Cognistat Naming	38	6.97	1.38	30	7.61	0.97	**0.007**	29	7.55	1.12	**0.048**	24	7.67	1.01	0.052
Cognistat Construction	38	3.16	1.57	30	3.48	1.97	0.237	29	4.31	1.51	**0.001**	24	3.96	1.71	**0.009**
Cognistat Memory	38	6.74	3.26	30	7.82	2.66	0.174	29	8.69	2.63	**0.009**	24	7.96	2.85	0.067
Cognistat Calculation	38	3.66	0.81	30	3.55	1.03	0.596	29	3.55	0.91	0.279	24	3.75	0.61	0.167
Cognistat Similarities	38	6.74	1.81	30	6.91	1.53	0.214	29	7.14	1.38	0.108	24	6.92	1.56	0.498
Cognistat Judgment	38	5.34	1.07	30	5.76	0.61	**0.005**	29	5.59	1.18	0.07	24	5.71	1.08	**0.012**
RFFT Total Unique Designs	31	44.35	12.90	24	49.50	13.62	**0.044**	27	49.48	18.20	**0.02**	22	50.00	15.60	0.573
RFFT Total Perseveration Errors	31	11.45	10.17	24	15.17	22.64	0.986	27	9.15	7.67	0.858	22	9.14	6.69	0.679
Automatic detection speed	20	95.95	23.74	17	97.88	28.11	0.917	15	110.53	32.60	**0.034**	15	104.27	25.11	0.286
Automatic detection errors	20	7.35	7.05	17	10.12	12.20	0.247	15	5.33	3.79	0.529	15	7.47	7.47	0.674
Automatic detection accuracy	20	92.55	7.24	17	90.42	11.28	0.311	15	95.07	4.28	0.600	15	92.96	7.99	0.450
Controlled search speed	20	85.70	19.74	17	86.29	19.40	0.666	15	95.27	25.60	0.075	15	89.53	15.64	0.533
Controlled search errors	20	9.85	8.98	17	10.76	7.72	0.753	15	7.53	5.72	0.666	15	10.93	7.39	0.447
Controlled search accuracy	20	90.01	7.24	17	88.43	8.45	0.382	15	92.34	6.49	0.463	15	88.68	8.64	0.859
WMT trial 1 correct	11	4.36	0.92	11	3.36	1.29	0.180	10	3.60	0.70	0.058	8	4.13	1.36	0.564
WMT 5 minute recall correct	11	6.27	2.45	11	7.27	1.68	0.056	10	7.60	2.22	0.516	8	6.25	3.92	0.893

*p value between 12 months and baseline.
**p value between 24 months and baseline.
***p value between 36 months and baseline.

By the end of 12 months, there were no signs of cognitive functions decline on all parameters. The MMSE, the verbal fluency letter task, 2&7 test and WLMLT remained the same. The clock drawing and verbal fluency category task performance had a tendency to be improved. On Cognistat, most subtests showed signs of improvement, with significant difference evident only on attention (digit span), naming and judgment. Unique design (RFFT) was significantly increased by the end of 12 months ($p < 0.044$), and at the same time, perseverative errors increased without statistical significance.

The maximum significant cognitive improvement in all cognitive domains was seen by the end of 24 months of the treatment in MMSE, clock drawing and verbal fluency tasks, in Cognistat (orientation, attention, repetition, naming, memory, naming, construction), RFFT (unique design only), Automatic detection speed (2&7 Test) compared to baseline. The rest of the tests did not show signs of decline.

By the end of 36 months of the treatment, overall cognitive performance was slightly decline in comparison with previous year. The significant improvements were still observed on clock drawing, Cognistat (orientation, attention, repetition, and construction).

Test performance dynamics are presented in the following figures.

Figure 1. Mini Mental Status Exam

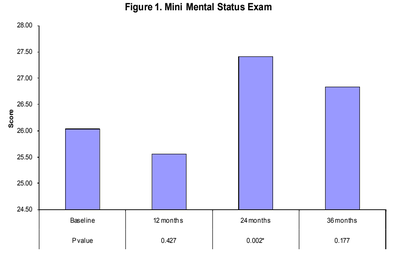


Figure 2. Clock Drawing Task

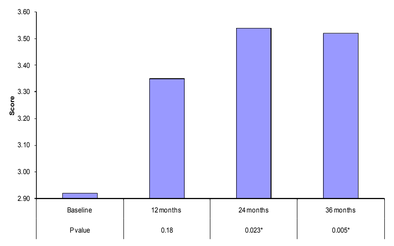


Figure 3. Verbal Fluency Tasks

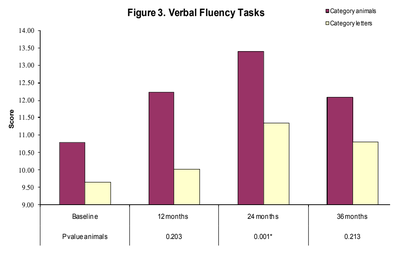


Figure 4. Ruff Figural Fluency Test

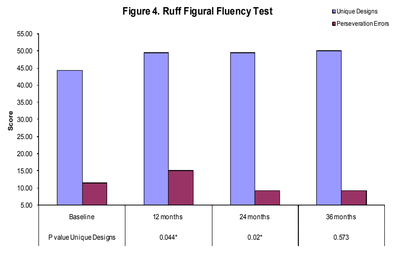
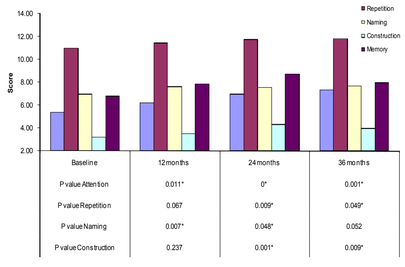


Figure 5. The Neurobehavioral Cognitive Status Examination (Cognistat)



Discussion

Integrative therapy for the Alzheimer's patients is a novel model based on emerging knowledge about neuroplasticity, increasing brain circulation with movements, and mitochondrial involvement in dementia (10, 11, 12, 13, 14). This treatment is in the earliest stage of its development. There are still open questions about the possibility of arresting cognitive decline in people with dementia for a period of time.

Since 2000 we have been developing a "real life," integrative treatment model based on pharmacological and non pharmacological interventions (Amarilis Acevedo). For individually customized treatment protocols, special attention was paid to preserved areas of brain functions.

The physical part of the treatment protocol was developed based on research related to gait and hand movement problems in dementia and the connection between hand movements and regional cerebral blood flow (15, 16, 17, 18, 19). The computerized training part of the program was developed and implemented in 2006-2008 (20).

This presentation is part of an ongoing naturalistic study about the possibility of preventing cognitive decline in mild to moderately demented patients using an integrative treatment approach. Results after 2 years of integrative treatment demonstrated preservation and improvement of cognitive functions in people with depression and dementia (2). In this presentation we looked at one of our most severely ill cohorts, cardiac patients.

Here we demonstrate preservation and even improvement of cognition in cardiac patients with depression and dementia for a period of three years. These results are in sync with our 2 years treatment results. The main difference in results is the time period when these cognitive improvements were observed. In the two-year study, maximum improvement in cognitive functions was seen after 6 months which persisted for the whole period of observation. In three-year study, the maximum cognitive improvement was observed by 24 months. By 36 months, performance of some tasks (MMSE, Verbal Fluency Test, some tasks from the Cognistat) decreased, but remained above the baseline. Performance on the 2&7 and the word list memory task was preserved throughout the whole 3 years.

We postulate that this difference in timing between the general group and the cardiac group was associated with an increase in latency in cognitive response in the cardiac cohort. This suggestion needs to be investigated further.

The presented "real life" treatment results may serve as a foundation for future research related to preservation of cognitive and physical disability in dementia. Our group wants to collaborate with other researchers and clinicians. We are open to providing expertise to any interested parties.

Conclusion

Our integrative treatment model for depressed, demented patients with cardiovascular co-morbidities was effective in delaying cognitive decline for 36 months of the therapy.

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