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# An Innovative Framework for Integrative Rehabilitation in Dementia

*Valentin Bragin and Ilya Bragin*

## Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder with multiple pathophysiological mechanisms affecting every organ and system in the body. Cerebral hypoperfusion, hypoxia, mitochondrial failure, abnormal protein deposition, multiple neurotransmitters and synaptic failures, white matter lesions, and inflammation, along with sensory-motor system dysfunctions, hypodynamia, sarcopenia, muscle spasticity, muscle hypoxia, digestive problems, weight loss, and immune system alterations. Rehabilitation of AD patients is an emerging concept aimed at achieving optimum levels of physical and psychological functioning in the presence of aging, neurodegenerative processes, and progression of chronic medical illnesses. We hypothesize that the simultaneous implementation of multiple rehabilitation modalities can delay the progression of mild into moderate dementia. This chapter highlights recent research related to a novel treatment model aimed at modifying the natural course of AD and delaying cognitive decline for medically ill community-dwelling patients with dementia. For practical implementation of rehabilitation in AD, the standardized treatment protocols are warranted.

**Keywords:** dementia, Alzheimer's disease, vascular dementia, cerebrovascular disease, rehabilitation, physical exercises, nutrition, cognitive training, integrative treatment, pharmacological and non-pharmacological interventions

## 1. Introduction

Alzheimer's disease (AD) is a chronic and progressive neurodegenerative disorder, with multiple pathophysiological mechanisms. It currently affects more than 5 million individuals in the United States, and this number is growing daily. It is a whole-body disease, manifested by brain and body function changes during its progression. Clinically, people progressing through dementia demonstrate different manifestations of brain and body functions, including psychiatric manifestations, sensory-motor system disabilities, digestion insufficiency, and multiple bodily system involvement. A diverse combination of symptoms reflects the complexity of vascular, biochemical, physiological, and morphological changes in the brain and body during the development and progression of dementia. The amyloid cascade hypothesis has dominated the field of AD for many years. The intensive research concerning amelioration of the protein abnormalities in AD, based on the amyloid hypothesis, does not have practical value yet despite a very controversial,

accelerated FDA approval of Aducanumab, an amyloid monoclonal antibody [1]. Conventional therapies—monotherapy or combinations of multiple medications—are not able to stop the progression of the disease and have very limited modifying effects. Our present understanding of the pathogenesis of AD goes far beyond brain dysfunction and pathology. Clinical and epidemiological studies have helped to identify modifiable factors in the onset and treatment of AD. Among these, hemodynamics, muscle health, and nutritional factors have been researched in animal and clinical studies for many years. The hemodynamic factor is related to vasculature, cerebral blood flow (CBF), and structural changes in the brain. A decrease in CBF is well documented during the progression of dementia. Sensory muscle status, changes in gait, balance, and fine dexterous motor skills are all strongly connected to the initiation and progression of dementia [2].

Nutritional deficiencies begin in the early stages of AD with a loss of taste and smell, which interferes with normal digestive processes. This disruption progresses to digestive disorders, malnutrition, and weight loss in advanced stages of dementia [3].

Rehabilitation is an important part of any treatment and has gained attention from the World Health Organization (WHO). In February 2017, there was a meeting hosted by the WHO, “Rehabilitation 2030: A Call for Action.” At the event, WHO issued a call for action towards “concerted and coordinated global action to scale up rehabilitation.” Rehabilitation is very important for people living on the wide spectrum of our world’s economies and should thus be available for all medical conditions that require it, including dementia [4].

The rehabilitation of patients with dementia is an emerging concept aimed at achieving the optimum level of physical and psychological functioning in the progression of aging, neurodegenerative processes, and chronic medical illnesses. The general hypothesis for this combined therapy is based on the suggestion that every modality has a unique influence on brain functions in AD, and a combination of these modalities could have a synergistic effect, significantly slowing the rate of cognitive decline, improving quality of life, and delaying institutionalization. Nutrition and other non-pharmacological interventions, especially physical and cognitive activities, have shown promising results in delaying the onset of dementia and could potentially improve the outcome of dementia treatment. Research related to simultaneous implementation of medication and multiple non-pharmacological interventions is very limited [5, 6].

Studies relating to cognitive rehabilitation, physical exercises, and nutrition alone have shown a positive effect on cognition in animals and humans in time frames ranging from several months to several years [7–10].

Since 2000, we have developed a working rehabilitation model, utilizing all available resources, most of which are accessible to the average individual in the hopes of delaying the progression of dementia and possibly improving function in certain cognitive and physical domains. The objectives of this rehabilitation model are the activation of brain functions through the alteration of neurotransmitter activities and the increase of muscle activity, sensory input to the brain, CBF, and nutrients and oxygen supply.

To the best of our knowledge, there is no rehabilitation model related to the simultaneous implementation of multiple available modalities (medications, physical and cognitive exercises, nutrition, and sensory stimulations) for AD patients living at home. We hypothesize that the simultaneous implementation of all possible rehabilitation modalities could delay the progression of dementia significantly, when compared to the utilization of a single modality. Here, we present the key elements of this working rehabilitation model for patients living at home.

## **2. Pathophysiology of dementia in context of rehabilitation**

### **2.1 Several factors in the pathogenesis of dementia**

Our understanding of pathophysiology in dementia has shifted in focus from amyloid accumulation to hemodynamic and energetic metabolism changes in the brain. It is a chronic, progressive disorder that affects the entire body [11]. Amyloid accumulation in the brain is a dynamic process in response to different etiological factors: stress, hypoxia, loss of subcortical nuclei (the nucleus basalis of Meynert, the locus coeruleus, and the raphe nucleus) [12–14].

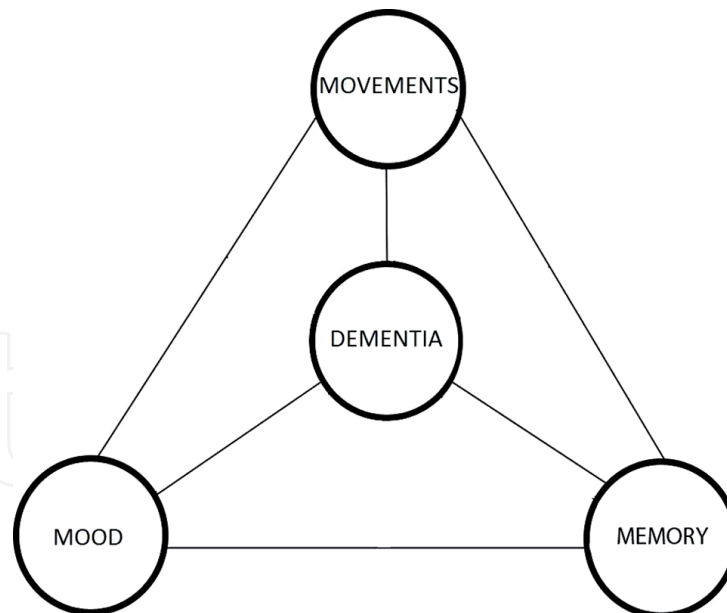
The hemodynamic factor is related to the development of hypoxia- and hypoxia-related metabolic and structural changes in the brain. Hypoperfusion affects white matter, subcortical nuclei, and the cortex of the brain in people with dementia. Chronic hypoxia decreases energy production in the brain, affecting protein synthesis pathways, which cause the development of reversible and irreversible morphological changes in the brain structure. During dementia progression, there are cerebral cortex and cortical corpus callosum atrophy, white matter damage, and dysfunction of subcortical nuclei. Alzheimer's dementia often begins as a disease of small blood vessels that are damaged by oxidation-induced inflammation and dysregulated amyloid metabolism, which may be seen as implications for early detection and therapy [15]. Today, there is an overlap between Alzheimer's disease and cerebral vascular dementia. Vast evidence from epidemiological, neural, physiological, clinical, and pharmacological studies suggests common pathogenic pathways between these two types of dementia and highlights the vital roles of vascular pathways in dementia development and pathology. The deficiency of cerebral blood flow could be a reason for neuronal dysfunction, white matter damage, and death of brain cells in both types of dementia.

The course of dementia is associated with progressive changes in cardiovascular pathology in the brain, increased numbers of micro and lacunar infarcts, cerebral atrophy, white matter changes, and signs of demyelination [16, 17]. CBF changes have been well documented in normal aging, MCI, and dementia by using different imaging techniques, such as single-photon emission computed tomography (SPECT), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), among others. On an rCBF—SPECT test, people with mild AD showed a significant reduction in rCBF in the left parietal cortex during an episodic memory task [18]. The conversion from MCI to AD, as well as the progression of AD, is associated with CBF changes. The lower the patient's CBF, the faster and more drastic is their decline of Mini-Mental Status Exam (MMSE) scores [19].

The first notable changes in CBF start in the entorhinal and hippocampal areas of the brain, eventually expanding into the temporal and parietal lobes until finally reaching the frontal lobes [20]. In some places of the brain such as the sensory-motor strip areas and the cerebellum, CBF is relatively well-preserved in dementia [21]. This fact helps our understanding and explanation of the preservation of procedural memory in dementia, which is initiated in sensory-motor areas of the brain [22].

Moreover, judging from the same studies, it is quite possible to suggest that regulation of CBF is preserved as well, at least in the sensory-motor strip and cerebellum in moderate stages of the disease. Another example of preserved CBF in dementia is the report concerning increased CBF in frontal-occipital cortex in mild–moderate AD patients (7 affected people), compared to the control group (8 healthy individuals) during a visual face-matching task [23].

Energetic crises include mitochondrial failure and a decrease in the flow of substrate in brain neurons. A decrease in energy production in the central nervous



**Figure 1.**  
*3M's dementia assessment model™ for dementia.*

system is one of the key factors in pathogenesis of dementia, which profoundly changes neuron function.

On the peripheral level, there are well-documented changes in sensory-motor system; decrease in feelings of taste, smell, and number of proprioceptive receptors; changes in mobility of joints and spine; increase in muscle spasticity; and decrease in muscles blood flow. Chronic muscles hypoxia is associated with muscle atrophy and sarcopenia. The decreased number of receptors and their functions result in diminished sensory input to the brain, and compromised CBF and neurotransmitters activities.

## 2.2 The 3M's dementia assessment model™ for dementia

Dementia has a progressive course of cognitive decline and physical disability, negatively affecting the quality of life, the capacity to socialize, and the ability to perform everyday activities. From a practical point of view, we developed the 3M's dementia assessment model™ for dementia evaluation, which includes assessing memory, mood, and movements. It is displayed in **Figure 1**.

Dementia can start from any of them, alone or in combination with each other. All factors could be affected at different speeds, and all of them have to be taken into consideration during dementia evaluation [24, 25]. Movements, general slowness, and fine motor skills could start before the development of the cognitive problems in dementia [26].

## 3. Modifiable factors in context of rehabilitation

Each of these modifiable factors could affect disease progression and treatment.

### 3.1 Stress

Acute and chronic stresses can affect brain and bodily functions by mobilization of sympathetic nervous system and activation of hypothalamic–pituitary–adrenal (HPA) axis on different stages of stress. Since Hans Selye's discovery of the general



adaptation syndrome, countless publications demonstrate relationships between stressors, stress response, and diseases in animal and clinical studies [27]. Stress affects physiological and biochemical processes in every organ in the body during dementia initiation and progression [28]. Sensitivity to stress events increases with aging and may accelerate cognitive and physical decline in dementia [29]. Acute stress affects attention and memory [30]. Chronic stress could play a role in development and progression of dementia by persistent activation of fundamental surviving pathophysiological mechanisms [31, 32]. There are links between chronic stress and level of memory loss in MCI and dementia [33]. Stress-related hormones mobilization is manifested in failures of homeostasis, thus leading to various diseases, including dementia [34]. Stress affects physiological and biochemical processes in every organ and system in the body during dementia initiation and progression [28].

They may be bidirectional relationships between stress and dementia. Stress is associated with CBF redistribution, mitochondrial and multiple neural pathways changes, and decreased attention and memory [35]. However, during dementia progression, loss of memory, behavior, and social communications could be stressors and evoke stress response by themselves.

There is related data utilization of different interventions aimed at modulation of stress response; the practical recommendations are in the early stages of research [36]. Effective stress management activities could be helpful for patients with dementia and their caregivers and need to be included in dementia treatment strategy [36, 37].

### **3.2 Depression and other emotional problems**

Depression like dementia is a whole-body disease, affecting brain metabolism, sensory systems, muscle health, and nutrition. Depression could share common pathophysiological mechanisms with dementia, such as hypoperfusion, hypoxia, oxidative stress, and energetic and neurotransmitters failure and stress. Depression is one of the risk factors for developing dementia [24].

Depression could precede dementia and accompany dementia progression. The “vascular depression” hypothesis has been proposed, based on clinical, physiological, and morphological changes in seniors, suffering from persistent depression [38]. Clinical and radiology data and epidemiological studies demonstrate the changes in brain structure in dementia in old-old patients [39]. Treatment of late-life depression with vascular pathology is a challenging task for clinicians.

Apathy and anxiety may be seen in depression and dementia affecting the course of these diseases and associated with detrimental effects on activities of daily living [40–43].

### **3.3 CBF and vascular pathology**

The fact that cardiovascular pathology occurs in multiple neurodegenerative processes in dementia is well documented. However, it remains necessary to investigate the interconnections and order of occurrence of these two factors [44, 45]. The course of dementia is associated with progressive changes in cardiovascular pathology, increased numbers of microbleeds and lacunar infarcts, cerebral atrophy, white matter changes, and signs of demyelination [17].

Vascular pathology and decrease of CBF contribute to progression of clinical manifestations, improving cognitive and physical functions, and developing morphological changes in dementia. Changes in CBF, cerebral ischemia, and hypoxia negatively affect substrate delivery, necessary for energy production and protein synthesis and essential neuronal activities [46].

### **3.4 Digestive system**

In epidemiological studies, nutrition has been under investigation for many years as an important factor contributing to healthy aging and prevention of dementia and multiple chronic diseases.

For the purposes of this discussion, the nutritional aspect in the treatment of dementia can be separated into four components.

The first component is related to the diet. There is currently no consensus regarding a diet geared towards at least partially normalizing brain metabolism in dementia. Along with the well-known Mediterranean diet, calorie-restrictive diets, as well as ketogenic diets, may have a beneficial neuroprotective effect in aging and multiple neurodegenerative diseases [47]. The diet close to that used for cardiovascular pathology and diabetes with some modification geared towards very low carbohydrate products is probably the most suitable diet to be offered for dementia patients.

The second component is a number of vitamins and nutraceuticals, which have been known to affect critical biochemical pathways involved in the pathophysiology of dementia. Among them are vitamins and nutrients that are a part of the normal metabolic processes and become deficient during stress, lack of exercises, hypoxia, and many other clinical conditions. In a controlled study on institutionalized, moderate-to-severe dementia patients taking a vitamin/nutraceutical combination for 9 months demonstrated a significant delay in decline on the Dementia Rating Scale and clock-drawing test, compared to those receiving placebo. The vitamin-nutraceutical combination in this study was designed to support antioxidant activities, energy production, and protein synthesis. This small study supports the notion that even in severe dementia, there is still room for stabilization of disease progression [48]. The specific research data related to different nutritional substances and vitamins is out of scope of this chapter.

General recommendations include products that are rich in antioxidants and include dietary precursors for mitochondria function, protein metabolism, and membrane phosphatide synthesis [6, 49].

The third component is associated with changes in gastrointestinal functions in every part of the GI system. These begin in the early stages of dementia and worsen with disease progression, frequently manifested as nutritional disorders such as anorexia, poor digestion, malnutrition, and weight loss. The loss of taste and smell develops in the early stages of dementia, results in the loss of appetite, and negatively impacts all stages of digestion. Even in the early stages of AD, community-dwelling patients display poor nutritional consumption [50]. Patients with dementia often forget to eat or drink on time. In the advanced stages of dementia, progressive GI malfunctions occur simultaneously with chewing and swallowing problems, dysphagia, and a decreased feeling of thirst, all of which are connected to poor food digestion and absorption, vitamin deficiencies, decreased immunity, loss of muscle mass, increased frequency of infection, poor balance, and falls [3]. Weight loss is associated with severity and mortality in AD and is an indicator of protein, energy, vitamin, and nutrient deficiency [51]. According to these authors, in the middle stage of AD (MMSE— $16.6 \pm 4.9$ ), significant weight loss is observed in more than 40% of patients living at home.

The presence of malnutrition in dementia could be a result of GI system dysregulation: changes in appetite, weight, and GI motility, and the probable development of exocrine pancreatic insufficiency.

An indicator of pancreatic exocrine insufficiency is the level of fecal elastase-1 in stool, the concentration of which decreases progressively with age. Pancreatic exocrine insufficiency was seen in 21.7% of people over 65 years without

gastrointestinal disorders, surgery, or diabetes [52]. Pancreatic exocrine insufficiency is more prominent in patients with insulin-dependent diabetes [53].

The existence of pancreatic insufficiency during the aging process and in diabetes, as well as changes in glucose metabolism in dementia, makes it quite possible that exocrine pancreatic insufficiency plays an important role in the digestive malfunctions in dementia.

The fourth component is the microbiome. Imbalance in gut flora can negatively affect general health. The first connection between intestinal microbiome and longevity was described over a century ago by Elie Metchnikoff [54]. Research about the gut-brain axis demonstrates the strong bidirectional connections between gut-body health. Gut flora participates in production of serotonin, dopamine, and GABA—neurotransmitters, actively affected in many neurodegenerative illnesses and medical diseases as well. Stress, depression, and dementia negatively influence the health of the gut. A practical recommendation about using probiotics, prebiotics, and postbiotics for depression and dementia is on the horizon [55–57].

### **3.5 Medical illnesses**

Medical illnesses (cardiac problems, diabetes, etc.) are risk factors for dementia development and progression. In recent years, accumulating evidence of research has suggested that cardiovascular pathology, especially irregular pulse, could be associated with dementia progression. In diabetes mellitus (type 2), there are metabolic changes, which affect vasculature and cell functions in every organ in the body. The cognitive and physical decline in dementia became worse with progression of diabetes.

The treatment and stabilization of these medical illnesses and disorders have a positive effect on people with dementia. The same approach could be applied to diseases related to the transport of oxygen to the organs (anemia, pulmonary pathology, and renal problems).

### **3.6 Cognitive activities**

Mental activities have a positive effect on CBF in healthy individuals and have been shown to delay the onset of dementia [58]. Research related to improving CBF in AD patients through the use of cognitive activities is slowly growing. Recently a program of mental exercises for nursing home residents with mild AD showed an improvement in cognitive function after being implemented for 6 months. This program was based on extensive previous research done by the same research team relating to increased CBF during various mental tasks [59].

### **3.7 Physical activities**

The connections between physical activities and rCBF are well established and done on healthy seniors, patients with MCI, and animal dementia models [60]. Physical exercise is considered a preventative or disease-modifying intervention, as it has shown a neuroprotective effect in brain aging [61]. Physical activities increase level of BDNF, which is responsible for brain health [62].

The effects of resistance training and aerobic exercises are connected to increased activity of the entire cardiovascular system and CBF simultaneously. These physical activities increase level of BDNF, which actively participate in learning, memory, and mood [63].

Hand exercises are more suitable and safer for fragile medically ill patients with all stages of AD because they can be done in a seated or laying position and appear to be a practical model for a home-based exercise regimen [11].



Simple hand movements have been shown to increase CBF in contralateral hemisphere of healthy subjects [64]. An increase in CBF during meditation, with simultaneous chanting and finger movements (dual tasks), has been observed by SPECT in healthy volunteers [65].

Physical activities have positive effect on neuropsychiatric symptoms in dementia [37].

Physical and mental exercises alone, as well as a combination of the both, could modify CBF and improve cerebral metabolism, decrease hypoxia, increase availability of oxygen and nutrients to brain cells and structures, increase brain vitality and prolong an active life for patients with dementia.

#### 4. Rehabilitation model for dementia

Rehabilitation of AD patients is an emerging concept aimed at achieving optimum levels of physical cognitive and psychological functioning in the presence of neurodegenerative processes, aging, and progression of chronic medical illnesses.

Given the complexity regarding the pathogenesis of AD, we hypothesize that the simultaneous implementation of multiple rehabilitation modalities could delay the progression of dementia. To the best of our knowledge, there is no rehabilitation model designed for the treatment at home for many years. This program starts in the doctor's office and continues in the home indefinitely.

##### 4.1 4M's dementia rehabilitation model™ for dementia

From a practical point of view, we approach dementia rehabilitation with the 4M's dementia rehabilitation model™, which includes treating memory, mood, movements, and mitochondria to increase the vitality of neurons and their connections by increasing CBF, as shown in Figure 2.

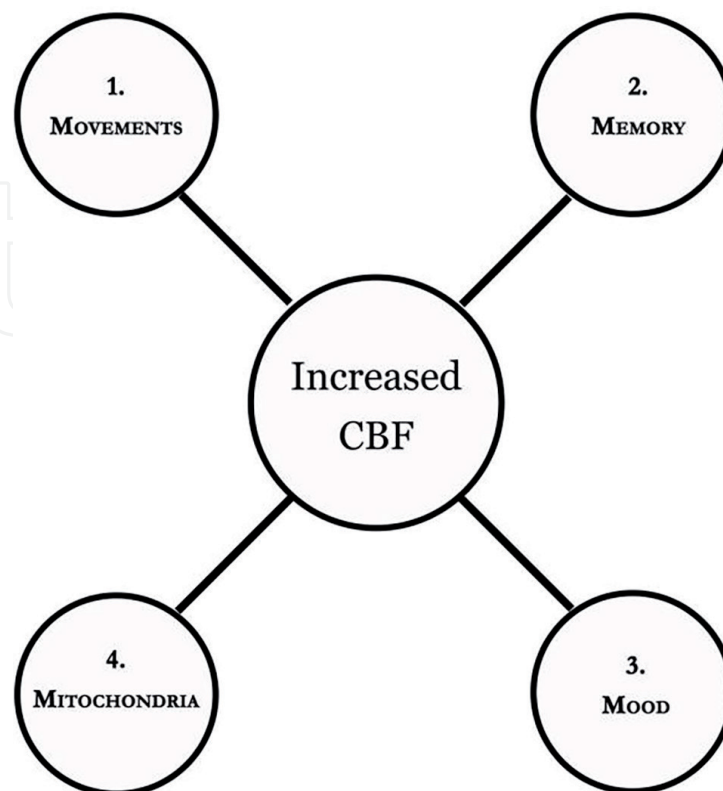


Figure 2.  
4M's dementia rehabilitation model™.

## 4.2 Office and home parts of the program

The in-office part of the model includes (a) an assessment of cognitive functions and movements, with special attention paid to preserved areas in cognition and motor system; (b) education about AD, modifiable factors, which needs to be used; (c) teaching patients and caregivers stress reduction techniques, as well as appropriate physical and cognitive exercises, based on patient's level of dementia; (d) physical and cognitive training during office visits; and (e) monitoring of treatment progress during subsequent office visits.

The home part of the model includes (a) physical exercises, cognitive training, and stress management techniques practiced as per the workbook and videos (which are given to each patient); (b) sensory activation (light, sound, relaxation videos with tranquil nature scenery; and (c) nutrition.

The physical and cognitive aspects of the rehabilitation program have been developed based on the physiological, real-life interplay between physical activity, attention, and procedural memory. Physical activities require attention and help with procedural memory. All of them have a direct effect on CBF [64–66]. During the progression of AD, all three components deteriorate at different rates over time. However, they are relatively preserved, compared to other cognitive functions until the late stages of AD.

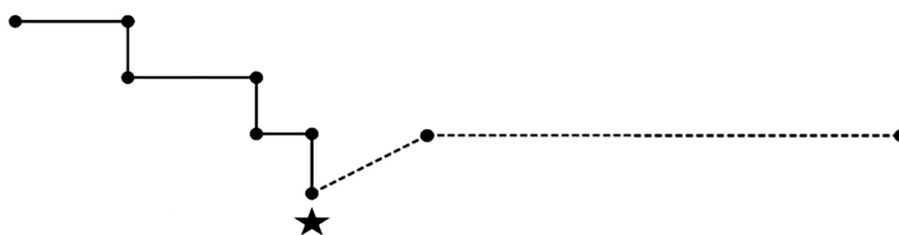
Over the years, preservation of cognitive function has been demonstrated up to 72 months of treatment. Remaining at the same level of cognitive function at the initial visit is a significant treatment achievement [67, 68].

Even though the progression of dementia is going along with development of chronic hypoxia, there is still room for developing neuroplastic changes in response to sensory-motor stimulation [69]. In recent review, ischemic damages evoke an initiation of network reorganization in spared areas of the brain [70].

## 4.3 Rehabilitation in chronic versus acute brain diseases

There are different goals for rehabilitation for chronic and acute brain diseases; even all available rehabilitation modalities are implemented simultaneously in both types of rehabilitation. The goal of rehabilitation in dementia is to prevent cognitive and physical decline and to preserve the level of functioning and the quality of life for as long as possible. Rehabilitation activities for people living at home have to continue without time limits, for many years. Home program refers to activities designed for joint patient and caregivers, which increase patient–caregiver connections. The office staff get training, related to interaction with patients and their caregivers. Much attention is placed on education and support of caregivers as well. Elements of physical, occupational, and speech therapy in outpatient clinics could be provided by office staff in the office and by caregivers at home. Cognitive and physical stabilization is expected, as demonstrated in **Figure 3**.

In stroke and head trauma (acute brain catastrophes), the goal of rehabilitation is to return to the premorbid level as close as possible. Rehabilitation in this case is



**Figure 3.**  
*Rehabilitation in chronic brain disease.*



**Figure 4.**  
*Rehabilitation in acute brain trauma/stroke.*

a time-limited process, lasting from several months to several years. Cognitive and physical improvement is expected, as shown in **Figure 4**.

#### 4.4 Six pillars of rehabilitation

The six pillars of the program consist of pharmacological interventions, mild physical exercises, multisensory stimulation, cognitive training, nutrition, and emotional support. Each pillar has direct and indirect effects on the elements of the 4M's Dementia Rehabilitation Model™.

Medications and supplements comprise the first pillar in this model. Cholinesterase inhibitors, NMDA receptor antagonists, antidepressants, neuroleptics, and mood stabilizers, along with medication for sleep and pain, are used when clinically appropriate. Supplements include vitamin D3, B-complex, fish oil, folic acid, alpha-lipoic acid, acetyl-L-carnitine, inositol, Ribose, and other vitamins.

Mild physical exercises are the second pillar in this rehabilitation. Muscle activities couple with increasing brain blood flow and simultaneously attention and procedural memory training. Exercises are designed for people with extremely limited physical capacities and problems with gait and ambulation. The physical exercises are safe and done in sitting positions and can be performed in the doctor's office or at home.

Physical exercises mainly consist of simple, coordinated hand and leg exercises performed both with and without the use of simple objects, such as a tennis ball. Dual-task exercises consist of hand movements, coupled with counting and breathing. Special exercises have been developed for balance training and include eye movements for decreasing visual fields and working with neck movements.

Multisensory stimulations include pleasurable activities related to auditory, visual, and tactile and other sensory channels. For example, patients work on pegboards to increase finger mobility and right-left coordination, or patients read tongue twisters loudly, sing songs, or watch comedians.

Attention and memory training consist of computerized attention ("go, no-go") and working memory exercises ("N-back" paradigm), tasks that are performed in the doctor's office with different objects (words, numbers, shapes, pictures, textures) plus pen and paper cognitive exercises, performed at home.

Nutrition includes diet and digestive support for microbiome and pancreatic enzymes, if clinically indicated (loss of weight).

Emotional support consists of implementation of stress management tools, brief educational sessions, related to family relationships, psychotherapy for patient's emotional reactions in response to decline of cognitive and physical functions. For caregivers, there are psychotherapy sessions for developing coping strategies to manage behavior problems in dementia and to recognize symptoms of burnout syndrome. The family understanding and support help dementia victims stay at home for a long period of time.

## 5. Clinical cases

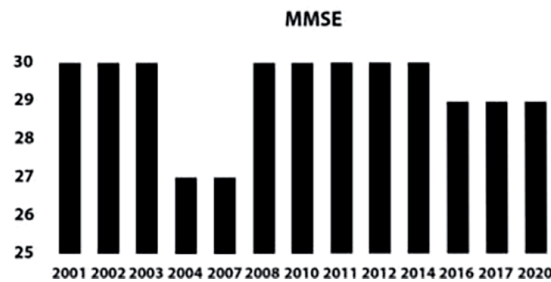
Here, we present two cases with mild dementia stabilized over years with an integrative treatment approach.

### 5.1 Case 1

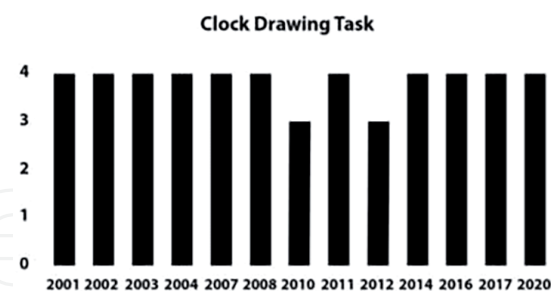
Patient was an 87-year-old, retired engineer, who first came to our office at age 68. Her diagnosis was mild dementia with episodes of depression, anxiety, insomnia, HTN, diabetes, neuropathy, arthritis, dizziness, and gait problems. Her current psychiatric medications are memantine, gabapentin, clonazepam, zolpidem, bupropion SR, donepezil, vitamin D, lovaza, magnesium oxide, B-complex, and folic acid.

This patient has been treated for 19 years (2001–2020). Cognitive assessments include the MMSE, clock-drawing task, verbal fluency animals, and verbal fluency letters tests. She was doing full rehabilitation protocol with any new modifications, which had been developed during this time interval in our office.

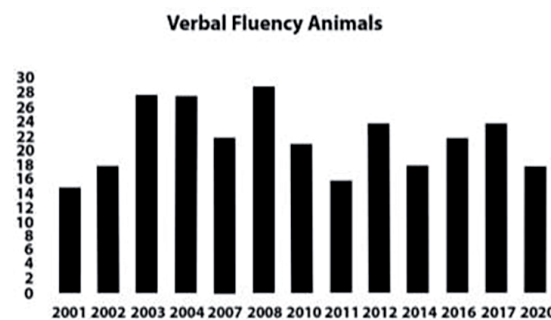
As you can see in **Figures 5–8**, this patient has been stable for the whole period of treatment based on the results of these 4 tests.



**Figure 5.**  
*MMSE stabilization.*



**Figure 6.**  
*Clock-drawing task stabilization.*



**Figure 7.**  
*Verbal fluency animals.*



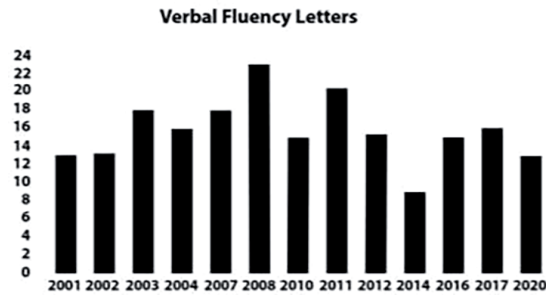


Figure 8.  
Verbal fluency letters.

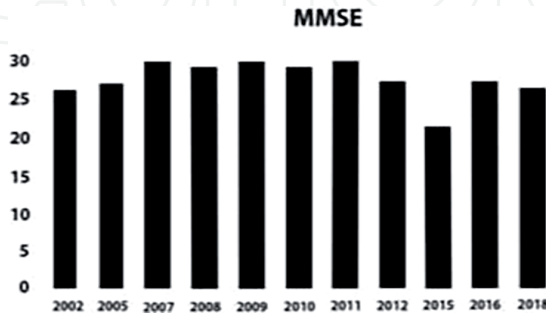


Figure 9  
MMSE stabilization.

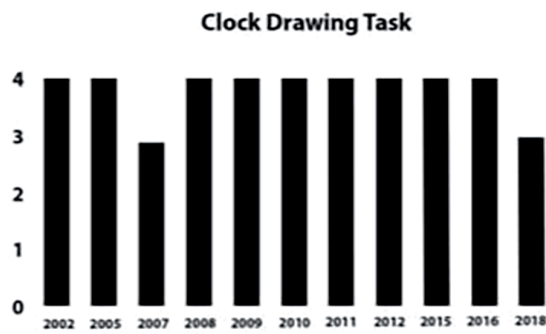


Figure 10.  
Clock-drawing task stabilization.

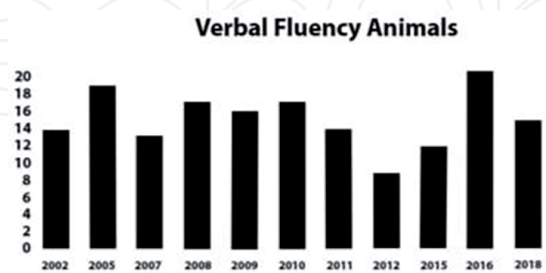
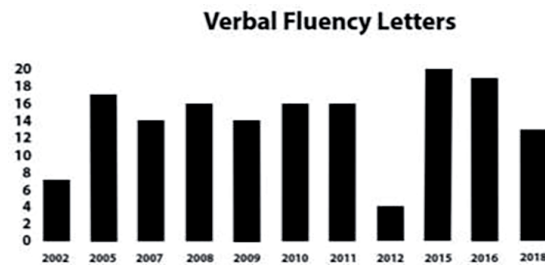


Figure 11.  
Verbal fluency animals.

## 5.2 Case 2

This patient was a 92-year-old female, retired clerk, who came for treatment at age 74. Her diagnosis was mild dementia with episodes of depression, anxiety, insomnia, HTN, CAD, diabetes, arthritis, dizziness, and gait problems. She had a mini-stroke in 2015. Current medications are Namenda, Trintellix, B-complex, folic acid, and magnesium oxide.



**Figure 12.**  
*Verbal fluency letters.*

This patient has been treated for 16 years (2002–2020). Cognitive assessments include Mini-Mental Status Examination (MMSE), clock-drawing task, verbal fluency animals, and verbal fluency letters tests. She was doing full rehabilitation protocol with any new modifications as in the previous case 1.

After mini-stroke (2014–2015), her MMSE dropped to 22 and then returned to 25.

As you see in **Figures 9–12**, this patient has been stable for the whole period of treatment.

## 6. Discussion

The theoretical basis of this rehabilitation model is rooted in emerging research related to neuroplasticity data. Other well-known facts regarding AD pathogenesis—including chronic hypoperfusion and hypoxia, oxidative stress, and mitochondrial and bioenergetics failure—also provide a solid theoretical foundation upon which to effectively design and test different treatment modalities available for rehabilitation in AD [69–71]. Additionally, modifiable risk factors for AD development and progression continue to be identified [72].

In a broader sense, rehabilitation in AD could include medications that are available today (and those that will become available in the future), in addition to all possible non-pharmacological modalities that are aimed at stabilizing brain and body functions, with special attention to physical and cognitive exercises, sensory stimulations, and dietary modifications.

The rehabilitation of AD has to be seen as an ongoing treatment approach not limited by time constraints. It can be adapted to the different stages of this illness, including even the preclinical stage.

Not all motor and cognitive functions are equally affected in AD. At various levels of dementia and in each cognitive domain, there is a time-related evolution of brain disability. Meanwhile, there is a growing body of data related to the preservation of some of the brain functions in AD, including certain learning and procedural memory capacities, emotional and movement controls, and the ability to use external memory aids [72–76].

The multifaceted rehabilitation model for home usage presented here demonstrates strategies that go beyond the prescribing of medications to alleviate AD progression alone. It is a dynamic framework that is open to the addition of any newfound medications or innovations in nonpharmacological interventions. This model is based on a proactive, 24/7 approach to battling AD—starting with doctor's office visits and continuing into the patient's home for an indefinite period of time.

These rehabilitation strategies become meaningful only with ongoing support from caregivers who help the patients at home with nutrition and everyday physical and cognitive activities. This model is flexible, and the key to it is to use all the five

elements of the program simultaneously. This kind of simultaneous approach is already commonly used in the treatment of many other progressive chronic ailments, such as cardiac problems, dyslipidemia, hypertension, and diabetes.

The cost for implementation of this home-based rehabilitation model is minimal (workbook, videos, and tennis ball). In addition, this model may ease the financial burden of this deadly disease on the health care system as a whole by reducing secondary medical problems from progressive dementia and delaying nursing home placement.

## **7. Conclusion**

A multifaceted rehabilitation model for dementia at home offers a promising strategy for postponing cognitive and physical decline in dementia. Modifiable factors in dementia could be implemented at low cost.

The development of comprehensive therapy models for rehabilitation in dementia is a matter of time. There is an urgent need for the designing of long-term studies, in which all available modalities will be simultaneously implemented and for as long as possible. Further research is needed to assess the efficacy and economic impact of this multifaceted rehabilitation model.

## **8. Summary points**

- Epidemiological studies have identified a number of modifiable factors in the onset and progression of dementia.
- A new understanding of the pathogenesis of dementia has revealed that protein changes in the brain develop simultaneously with cerebrovascular pathology.
- Progression of clinical dementia depends on the stress, emotional reactions, CBF, digestive system, medical illnesses profile, cognitive activities, and muscle health.
- Physical and mental activities may contribute to the delay of the onset of dementia and slow down the disease progression.
- A novel treatment model for dementia patients is the simultaneous use of nonpharmacological modifiable factors and pharmacological interventions for many years.

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## **Conflict of interest**

The authors declare that they have no competing interests. The authors have no financial interests in this project.

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