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## Non-Pharmacological Interventions for the Appetite and Eating Disorders in Patients with Dementia: A Cross-Over RCT

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## Abstract

**Objectives:** The most common appetite/ eating problems in patients with dementia (PWD) are loss or increase of appetite, loss or gain of weight, changes in eating behaviour, changes in the preferences of the food, developing specific eating behaviours, eating in an appropriate way or eating non-food items, and frequently demanding food or drinks, because they forget that they have eaten. Appetite/ eating disorder is an essential and common behavioral and psychological symptom of dementia (BPSD) that leads to poor quality of life, institutionalization, and affects the physiological function of many systems of the patient.

**Methods/ Design:** 60 patients with dementia and appetite problems and their caregivers were included. The participants were suffering from all different types and stages of dementia. The study is a cross-over randomized controlled trial. The measurements used were: Mini Mental State Examination (MMSE), Addenbrooke's Cognitive Examination Revised (ACE-R), Geriatric Scale of Depression (GDS), Functional Rating Scale for Symptoms in Dementia (FRSSD), and Neuropsychiatric Inventory (NPI). The three non-pharmacological interventions that were used: Physical Activity (PA), Music Therapy (MT), and Psycho-Educational Programme for the Caregivers (PEPC).

**Results:** The most effective combination for the reduction of appetite problems was found in group 6: PEPC (structure routine in the hours that the food is served) ( $p=0.004$ ), followed by MT ( $p=0.027$ ), followed by PA ( $p=0.036$ ). The same combination was the most effective for the reduction of caregivers' burden, as well.

**Conclusions:** There is a combination of non-pharmacological interventions (PEPC+MT+PA) that can effectively reduce the appetite/eating problems in PwD. The same combination is the most effective in reducing the caregivers' burden, as well.

### Keywords

Appetite problems; eating disorders; dementia; randomized controlled trial, BPSD; non-pharmacological interventions; Psycho educational program for Caregivers; Music Therapy; Physical Activity.

## Introduction

Even though dementia is primarily described as a cognitive neurodegenerative disorder, the non-cognitive symptoms of the disease are very important and very often. They are described by the term B behavioural and Psychological Symptoms of Dementia (BPSD) and according to the Neuropsychiatric Inventory (NPI) the most frequent behaviours are delusions, hallucinations, agitation/ aggressive behaviour, depression, anxiety, euphoria, apathy, disinhibition, irritability, wandering, sleeping problems and appetite/ eating disorders. The most common appetite/ eating problems in patients with dementia (PwD) are loss or increase of appetite, loss or gain of weight, changes in eating behaviour, changes in the preferences of the food, developing specific strange eating behaviours, eating in an appropriate way or eating non-food items, and frequently demanding food or drinks [1,2], because usually they forget that they have already eaten.

Longitudinal studies have shown that weight loss mainly occurs early in the disease and precede a diagnosis of dementia by several years. However, even though the appetite loss is an important feature of dementia, the neuroanatomical correlates remain unclear. The ventral orbitobasal frontal lobe, the

temporal lobe, the insula, the amygdala, and the orbitofrontal cortex play a major role. The hypothalamus and the oxytocin are also involved. The oxytocin is produced in the hypothalamus, and it is an important component that it is believed to decrease the appetite [3].

Appetite/ eating disorder is an essential and common BPSD that leads to poor quality of life, institutionalization, and affects the physiological functions of many systems of the patient<sup>i</sup>. Poor nutrition, and dehydration can affect independent living. It has also been reported that appetite disorders contribute to pneumonia and mortality<sup>ii</sup>. Moreover, it can be a major cause of distress for the family caregivers and nurses. PwD who suffer from appetite disorder often have also swallowing problems, as well, which lead to dysphagia and problems with their teeth. Depression frequently occurs in PwD and may be a parameter that causes also loss of appetite.

The appetite/ eating disorder is more common in patients with Alzheimer's disease (AD), and Frontotemporal Dementia (FTD), and less common in patients with vascular dementia (CVD). However, there are studies which referring to appetite problems not to be a case for AD patients, except of anorexia, but the studies, so far, have been contradictory [4-6]. AD patients with appetite problems, frequently eat fast, they are unable to feel hungry, because of brain atrophy and swallowing problems. Patients with Lewy Body Dementia (DLB) have difficulty swallowing and this causes a loss of appetite. On the other hand, FTD is a term that describes progressive focal atrophy involving anterior temporal lobes or frontal lobes or both, in connection with a spectrum of non- Alzheimer pathologies. A sub-type of an FTD syndrome, which called behavioral Frontotemporal dementia (bvFTD), causes several BPSD, such as disinhibition, impulsivity, mood changes, agitation, apathy, stereotypic behavior and poor self-care. According to recent studies FTD patients frequently experience appetite/ eating problems, such as increase of appetite, a preference for sweets, or they want to eat the same food repeatedly, as a stereotypic behavior [7]. Even though eating disorders are common in FTD patients, there are very few systematic studies comparing FTD to AD patients [4].

The current treatment for the appetite/ eating disorders in PwD includes pharmacological interventions with rivastigmine, and non-pharmacological interventions, such as ketogenic diet. Rivastigmine has an advantage of improving appetite compared to donepezil, by increasing the acyl/des-acyl ghrelin ratio and cortisol levels [10]. On the other hand, the ketogenic diet has been used successfully in other neurological disorders, such as epilepsy, and it is now under examination if it has positive results on PwD, as well [11]. The current pharmacological treatments have severe side-effects, such as: low blood pressure, nausea, muscle weakness, bradycardia, breathing problems, vomiting, stomach pain, loss of appetite, diarrhoea etc [12].

Therefore, the aim of the current study is to find a combination of effective non-pharmacological interventions that can reduce the appetite/ eating disorders in PwD and decrease the caregivers' burden.

## Methods and Materials

### Participants

Sixty (60) patients suffering from all different types and stages of dementia were included in the current study. Their caregivers were also included. The sample was recruited from the Neurological Department of the General Hospitals of Thessaloniki and Athens. The patients were diagnosed in accordance with the ethical principles (declaration of Helsinki). All participants have been informed and have given consent. The sample was diagnosed with the following: AD, Vascular Dementia (VAD), Lewy Body Dementia (LBD), Dementia in Parkinson's disease (PDD), Frontotemporal Dementia (FTD), and Mild Cognitive Impairment (MCI). Twenty-nine (29) participants were males (48.3%) and the average age of the sample was 73.4 (SD 7.99) years old, and the average years of education is 10.1 (SD 4.67). The baseline characteristics of the sample are shown in (Table 1).

	Mean (SD) or N (%)
Males, N (%)	48.3% (N=29)
Age	73.4 (7.99)
Years of education	10.1 (4.67)
MMSE	19.6 (4.86)
ACE-R	59.6 (1.7)
GDS	7.8 (5.53)
FRSSD	16.2 (9.15)
NPI Results	7.2 (1.98)
NPI Distress	3 (0.75)

**Table 1:** Baseline characteristics of the sample.

### Procedure

The trial is a cross-over randomized controlled trial. The sample was assigned to 6 different groups, randomly. Each group included 10 participants. There were three non-pharmacological interventions used in a cross-over way, as shown in (Table 2,3). There was no dropout rate. At the beginning of the process the NPI questionnaire for appetite disorders was applied to the family caregivers. The results were recorded. Each treatment was taken place for five days, there was two days wash-out period and at the morning of the 6<sup>th</sup> day NPI questionnaire (only appetite questions and sub-questions) were applied again, to record the results.

### Interventions

The interventions were chosen based on four factors: a) they should be easily performed by the unprofessional caregivers, b) the literature so far has pointed promising results from these interventions, c) they are pleasurable and d) they have no known side-effects.

### **a) Physical activity/ exercise**

Physical activity (PA) has been shown several promising results on the reduction of some BPSD (such as agitation, depression, anxiety, wandering and sleeping problems) [13-15]. Our intervention in accordance with the literature so far was administrated every day for 30 min. All the family caregivers chose walking, as the easiest PA for their patients. The intervention was taken place every morning after breakfast.

### **b) Music therapy (MT)**

MT is a pleasurable and effective non-pharmacological intervention for some BPSD. Literature so far points some promising results; however there are no evidence for its impact on the reduction of the appetite/ eating problems in dementia. In the current study we followed the example of other randomized controlled trials [17]. We administrated 45min.of MT every day. The intervention was taken place while the patient was eating. The caregivers chose the favorite music of their patient.

### **c) Psycho-educational programme for the caregivers: structured routine**

Our psycho-educational programme for the caregivers aimed to educate them about dementia, BPSD and other matters related to the disease. The program took place in face to face and online meetings for caregivers who had other obligations the same time of the program. The program included 24 seminars, lasted for 12 weeks and the duration of each seminar was approximately 2 hours. Our intervention was administrated accordingly to the daily program of every family caregiver. All family caregivers chose a specific time for serving breakfast, lunch, and dinner to their patients. This routine was structured by the caregivers and kept strict.

## **Measures**

### **Mini mental state examination (MMSE)**

MMSE is a 30-point questionnaire that is used to evaluate the cognitive status. The test is used to evaluate the severity of the cognitive decline. The questionnaire examines the following: registration, attention, recall, language, and orientation. Higher scores indicate better cognitive performance and lower scores severe cognitive decline [18,19].

### **Addenbrooke's cognitive examination revised (ACE-R)**

ACE is a 100-point questionnaire that is used to evaluate the cognitive impairment. It includes MMSE. It is a reliable scale that can be used for the diagnosis of dementia. The following areas are examined: orientation, registration, attention, concentration, recall, verbal fluency, memory, language, spatial abilities, perceptual abilities, and recognition. Higher scores indicate better cognitive performance [20,21].

### **Geriatric scale of depression (GDS)**

This scale is a questionnaire of 30 questions that examines if the patient has depression. The patient answers with a YES / NO. Higher scores indicate higher level of depression [22,23].

### Functional rating scale for symptoms in dementia (FRSSD)

It is a scale to assess the Activities of Daily Living. The scale is a questionnaire to the caregiver and includes 14 different daily activities, such as eating, dressing, incontinent, speaking, sleeping, faces' recognition, personal hygiene, name memory, fact memory, alertness, agitation, space orientation, emotional status, socializing. The scale is scored from 0-3 (whereas 0= fully independence and 3= fully dependence) [24,25].

### Neuropsychiatric inventory (NPI)

The questionnaire is administrated to the caregiver. The questionnaire evaluates the frequency and severity of the symptom if the impact that each behaviour has on the caregiver. A total score is obtained by summing all the domain total scores [26,27]. The questions of NPI for appetite disorders are.

- Does he/ she have a poor appetite?
- Does he/she have an unusual good appetite?
- Has he/she lost weight?
- Has he/she gained weight?
- Does he/she have unusual eating behavior such as putting too much food in his/her mouth at once?
- Has he/she had a change in the kind of food he/she likes such as wanting too many sweets or other specific type of food?
- Has he/she developed eating behaviors such as eating exactly the same types of food each day or eating the food in exactly same order?
- Have there been any changes in appetite or eating that I haven't asked about?

### Data Analysis

Categorical variables were presented as percentages while continuous variables were presented as Mean value and Standard Deviation (SD). Because the distribution of the differences between the samples cannot be assumed to be normally distributed Wilcoxon signed-rank test was used. In order to find the differences in gender in the 6 groups the Chi-square test was used. Finally, in order to find the type of dementia in each group the z value score was also used. P values less than 0.05 were considered statistically significant. For the statistical analysis the SPSS 25.0 (IBM Inc., Armonk, NY) was used.

### Results

The 58.3% of our sample suffered from AD, the 8.3% from VAD, the 5% from LBD, the 10% from PDD, the 5% from FTD and the 13.3% from MCI. The Mean scores of all the patients were MMSE 19.6 (SD 4.86), ACE-R 56.9 (SD 1.7), GDS 7.8 (SD 5.53), FRSSD 16.2 (SD 9.15), NPI Result 7.2 (SD 1.98) and NPI Distress 3 (SD 0.75). The most effective combination for the reduction of appetite problems was found in group 6. Specifically, the most effective combination was: PEPC (structure routine in the hours that the food is served) ( $p=0.004$ ), followed by MT ( $p=0.027$ ), followed by PA ( $p=0.036$ ). The same combination was found as the most effective for the reduction of caregivers' distress, as well. Specifically, PEPC ( $p=0.004$ ), followed by MT ( $p=0.014$ ), followed by PA ( $p=0.017$ ) reduced caregivers' distress statistically significant. All results are shown in (Table 4).

Group	Sequence	1 <sup>nd</sup> week	2 <sup>nd</sup> week	3 <sup>rd</sup> week
1	ABC	A	B	C
2	ACB	A	C	B
3	BAC	B	A	C
4	BCA	B	C	A
5	CAB	C	A	B
6	CBA	C	B	A

**Table 2:** The sequence of the procedure.

AD	VAD	LBD	PDD	FTD	MCI
58.3%	8.3%	5%	10%	5%	13.3%

**Table 3:** Percentages of the different types of dementia of the sample.

group 1	NPI baseline	NPI before A	A-B	B-C	NPI baseline- NPI final
Mean score ± SD	7± 2.14	7± 2.14 - 7± 2.14	7± 2.14 - 7± 2.35	7± 2.35 - 6± 1.68	7± 2.14- 6± 1.68
Percentile		6-8, 6-8	6-8, 5.50-8	5.50-8, 3.50-6	6-8, 3.50-6
p		1	0.961	0.038	0.04
group 2	NPI baseline	NPI before A	A-C	C-B	NPI baseline- NPI final
Mean score ± SD	8± 0.94	8± 0.94 - 8± 0.94	8± 0.94 - 5± 1.05	5± 1.05 - 8± 1.43	8± 0.94-8± 1.43
Percentile		7.50-8, 7.50-8	7.50-8, 4-6	4-6, 7.50-8	7.50-8, 7.50-8
p		1	0.04	0.636	1
group 3	NPI baseline	NPI before B	B-A	A-C	NPI baseline- NPI final
Mean score ± SD	8± 1.83	8± 1.83 - 8± 1.03	8± 1.03 - 8± 1.83	8± 1.83 - 4± 1.47	8± 1.83 - 4± 1.47

Percentile		6-8, 6-8	6-8, 6-8	6-8, 3.50-6	6-8, 3.50-6
p		0.883	0.968	0.004	0.004
<b>group 4</b>	NPI baseline	NPI before B	B-C	C-A	NPI baseline- NPI final
Mean score ± SD	6± 1.26	6± 1.26- 6± 1.26	6± 1.26 - 4± 1.26	4± 1.26 - 6± 1.26	6± 1.26- 6± 1.26
Percentile		6-8, 6-8	6-8, 4-6	4-6, 6-8	6-8, 6-8
p		1	0.002	0.262	1
<b>group 5</b>	NPI baseline	NPI before C	C-A	A-B	NPI baseline- NPI final
Mean score ± SD	6± 3.01	6± 3.01 - 4± 1.57	4± 1.57- 6± 3.01	6± 3.01- 6± 3.01	6± 3.01- 6± 3.01
Percentile		4-9, 2-4.50	2-4.50, 4-9	4-9, 4-9	4-9, 4-9
p		0.004	0.4	1	1
<b>group 6</b>	NPI baseline	NPI before C	C-B	B-A	
Mean score ± SD	8± 2.17	8± 2.17 - 4± 1.57	4± 1.57 – 3± 2.17	3± 2.17 – 2.5± 0.69	
Percentile		6-8.25, 3.50-6	3.50-6, 2-4	2-4, 2-2	
p		0.004	0.027	0.036	
<b>Results (caregivers)</b>					
<b>group 1</b>	NPI baseline	NPI before A	A-B	B-C	NPI baseline- NPI final
Mean score ± SD	3± 0.63	3± 0.63- 3± 0.63	3± 0.63 - 3± 0.87	3± 0.87- 2± 0.48	3± 0.63-2± 0.48
Percentile		3-4, 3-4	3-4, 3-4	3-4, 1-2	3-4, 1-2
p		1	0.387	0.032	0.03



<b>group 2</b>	NPI baseline	NPI before A	A-C	C-B	NPI baseline- NPI final
Mean score ± SD	3.5± 0.84	3.5± 0.84 – 3.5± 0.84	3.5± 0.84 – 2± 0.31	2± 0.31 – 3.5± 0.84	3.5± 0.84- 3.5± 0.84
Percentile		3-4, 3-4	3-4, 2-2	2-2, 3-4	3-4, 3-4
p		1	0.004	0.404	1
<b>group 3</b>	NPI baseline	NPI before B	B-A	A-C	NPI baseline- NPI final
Mean score ± SD	3± 0.56	3± 0.56- 3± 0.56	3± 0.56 - 3± 0.56-	3± 0.56- 1.5 ± 0.52	3± 0.56- 1.5 ± 0.52
Percentile		2.75-3, 2.75-3	2.75-3, 2.75-3	2.75-3, 1-2	2.75-3, 1-2
p		1	1	0.006	0.006
<b>group 4</b>	NPI baseline	NPI before B	B-C	C-A	NPI baseline- NPI final
Mean score ± SD	2.5 ± 0.84	2.5 ± 0.84 – 2.5 ± 0.84	2.5 ± 0.84 – 1± 0.48	1± 0.48–2.5 ± 0.84	2.5 ± 0.84- 2.5 ± 0.84
Percentile		2-3, 2-3	2-3, 1-2	1-2, 2-3	2-3, 2-3
p		1	0.036	0.606	1
<b>group 5</b>	NPI baseline	NPI before C	C-A	A-B	NPI baseline- NPI final
Mean score ± SD	3± 0.63	3± 0.63 - 2± 0.48	2± 0.48 – 3± 0.63	3± 0.63-3± 0.63	3± 0.63-3± 0.63
Percentile		2-3, 1-2	1-2, 2-3	2-3, 2-3	2-3, 2-3
p		0.015	0.15	1	1
<b>group 6</b>	NPI baseline	NPI before C	C-B	B-A	

Mean score ± SD	3± 0.66	3± 0.66 - 2± 0.51	2± 0.51 – 1.5± 0.56	1.5± 0.56 - 1± 0.26	
Percentile		2.75-3.25, 2-3	2-3, 2-2	2-2, 1-2	
p		0.004	0.014	0.017	

**Table 4:** Results (patients).

## Discussion

The literature lacks evidence on the reduction of the appetite/ eating disorders in dementia. The current pharmacological treatments are useful in order to decrease the depression, agitation, irritability, anxiety and apathy of the PwD, which in many cases affect eating. However, there are no pharmacological treatments that can manage the eating disorders in PwD. Hence, non-pharmacological management could be a first line solution. According to our results there is a combination of non-pharmacological interventions that can reduce appetite problems and caregivers' distress, too.

The “structure routine” aimed to create a scheduled program of eating every day. The caregivers chose their preferable time to eat, to be convenient with their other activities. This could be a factor of the statistically significant reduction of their burden. Furthermore, with the “structure routine” it is easier to balance the quantity of the meals. For patients who have bulimia and eat uncontrolled, this intervention was helpful. Moreover, the fact that the same hour both the caregiver and the patient were eating together, helped the patients with anorexia to eat more. An explanation is that people with anorexia seem to be more willing to eat when someone else is also eating at the same time. In addition, the structure routine can help the patients who eat specific kind of food (such as too many sweets) to have a balanced nutrition. However, it is crucial to mention that the study could not identify if structure routine can change “unusual eating behaviors such as putting too much food in the mouth at once”, that NPI refers to. Our experience showed that if the caregiver put small pieces of food on the patient's plate, this abnormal behavior is reduced.

MT is an enjoyable non-pharmacological intervention that has no side-effects. It has shown promising results [28,29], however there are no trials that confirm that MT can have an impact on appetite disturbances. It is a matter of fact that MT is a useful non-pharmacological intervention for the reduction of anxiety, depression, agitation, and apathy symptoms in PwD [30,31]. These factors may affect eating problems. Therefore, as it seems there is a connection between those symptoms and appetite problems, MT can be beneficial for eating disturbances, as well. PA has shown some promising results so far [32], but there is no evidence that claim that it can be beneficial for appetite/ eating problems. Possibly, for patients who have anorexia, exercise could arise their appetite levels, but there is no clear evidence for that, so far. It is very important to know about it.

An interesting finding of our study is that the same intervention that reduces the unwanted behavior is the same intervention that reduces the caregivers' burden, as well. A possible explanation is that the

caregivers' burden is in dependence with the behavioral disorder. Therefore, finding an effective combination that can reduce the appetite disorders, we can also reduce the Distress of the caregivers. Another finding is that comparing the baseline NPI to the final NPI it seems that there are statistically significant results when other combinations occur, too. Specifically, PEPC when combined either with MT or PA, can reduce appetite problems effectively. Therefore, it seems that when PRPC applies first, has promising results.

Strengths of the study include the design methodology. It is a cross-over randomized controlled trial. The sequence does not interfere with the results. Risk of bias has been avoided. The sample had heterogeneity, because we included patients with all different types and stages of dementia (MCI to severe dementia). However, despite this, the results apply to both genders, stages, and different types of dementia. Moreover, NPI is a valid and reliable tool that can be used across different ethnic groups, different forms of dementia and it is comprehensive, easy to use and flexible<sup>iii</sup>. Furthermore, the PEPC was very well-organized and detailed. Strict and understandable instructions have been given to all caregivers.

The limitations of our study are the short period of the interventions. However, since the caregivers needed effective and rapid solutions, the short length of the interventions can be justified. Furthermore, not having the same music for all the patients, may occur to a risk of bias. Additionally, another limitation is that the interventions were administrated by the caregivers. However, the clinician, who gave the guidelines, kept a strict schedule and was in communication with the caregivers, if any problem occurred.

According to NPI questionnaire there are contradictory symptoms of eating disorders (eating less or eating too much, anorexia or bulimia). This seems to be an essential problem on the management of this BPSD. Future research should focus on specific problems of eating disorders, to come to safe conclusions for each kind of eating disorders. The literature lacks evidence and there is a strong need for further research.

## Conflict of Interest

None.

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