



## Non-Pharmacological interventions for the delusions in patients with dementia. A cross-over RCT

BY

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### Abstract

**Objectives:** Delusional ideas include false beliefs, enduring, irrefutable, suspiciousness, misidentification, abandonment, etc. They do not only affect the caregivers' burden but also increase the cognitive decline and can lead patients with dementia to faster institutionalization and higher mortality. The current pharmacological treatment has serious side effects. The non-pharmacological interventions could be an effective alternative to reduce delusions and/or caregivers' distress because of the delusions of their dementia patients.

**Methods / Design:** The trial is a cross-over randomized controlled trial (RCT) conducted in Greece. Sixty (60) participants with several types and stages of dementia were randomly assigned to 6 different groups of 10 participants each. The three non-pharmacological interventions used are a) Validation therapy (VT) / Psycho-educational program, b) Reminiscence therapy (RT), and c) Music therapy (MT). The measurements used were MMSE, ACE-R, GDS, FRSSD, and NPI questionnaire (sub-questions for delusions). Each intervention lasted for 5 days and there was a two-day wash-out period. There was no drop-out rate.

**Results:** The most effective combination for patients' and caregivers' distress is Validation therapy/ Psychoeducational program ( $p=0.016$ )- MT ( $p=0.028$ )- RT ( $p=0.030$ ).

**Conclusions:** There is an effective combination of non-pharmacological interventions that can reduce delusions in PwD and caregivers' burden.

**Keywords:** Alzheimer's disease, BPSD, psychosis, delusions, RCT, non-pharmacological, dementia

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## 1. Introduction

Delusions is a major neurological problem in patients with dementia (PwD), and especially in patients with Lewy Body Dementia (DLB) and Parkinson's disease dementia (PDD) (Sakai et al., 2019). Delusions not only affect the cognitive abilities, illness progression, and daily activities of the PwD but also cause tremendous stress to the family caregivers, as

well (Radue et al., 2019). The term Behavioral and Psychological Symptoms in Dementia (BPSD) describes a group of different symptoms that can affect nearly 90% of PwD (Radue et al., 2019). The latest results show that the BPSD can be categorized in the following groups: psychosis, psychomotor symptoms, mood liability factor, and instinctual factor (Petrovic, 2007). By the term psychosis, the studies include delusions and hallucinations.

Delusional ideas include false beliefs, enduring, irrefutable, suspiciousness, misidentification, abandonment, etc. According to the Neuropsychiatric Inventory (NPI), PwD who suffer from delusions create stories from their own, become suspicious that their spouse is having an affair, may speak to the television figures as they were present, believe that they may be in danger or others planning to hurt them or stealing from them. Some other patients believe that his / her family members are not the ones who they say, or they generally misidentify fantasy with reality (Cummings et al., 1994). Furthermore, another critical matter in delusions is Capgras syndrome; the patient believes that a close person to him/her has been replaced by an impostor (Pereira & Oliveira, 2019). Delusions appear not only in Alzheimer's disease (AD) but also in other types of dementia. Specifically, delusions are a common symptom in Frontotemporal Degeneration (FTLD) (Gossink et al., 2017). Behavioral variant frontotemporal dementia (bvFTD) causes delusions in 10%-32% of the patients (Gossink et al., 2017). Although DLB has been associated with hallucinations, delusions have also been found, too (Tzeng et al., 2018). Capgras syndrome can affect approximately 17% of the patients with DLB (Solla et al., 2017). As DLB and PDD share the same pathophysiology (α-synuclein proteinopathies), delusions have been also found in PDD, as well (Shneider et al., 2017). Delusions in Vascular Dementia (VaD) also appear before the diagnosis (Anor, 2017). It seems that psychosis can become a very crucial matter to the family caregivers as they are strongly correlated with increasing caregivers' burden, reducing the quality of life of the patients, and leading to institutionalization (Aarsland, 2020).

The neuropathology of the delusions remains uncertain. According to a single-photon emission computed tomography study, delusions are associated with hyperperfusion of the frontal lobe (Sakai et al., 2019). Moreover, in the development of delusions, the loss of cortical cholinergic innervation seems to play a major role, as well (Sakai et al., 2019). Studies have proposed that prefrontal and parietotemporal parts of the brain are involved in delusional beliefs (Frith & Frith, 2001). Other studies claim that the amygdala, the basal frontal, diencephalic structures, and the septal region play a major role, too (Cipriani et al., 2014). According to other studies delusions of persecution are associated with dysfunction of the left hemisphere and delusions of misidentification are correlated with dysfunction of the right hemisphere (Lozupone et al., 2020).

The pharmacological treatment of delusions includes quetiapine, olanzapine and risperidone. The side effects of these anti-psychotic drugs should be well-considered; dizziness, extrapyramidal reactions, hyperkinesia, akinesia, dyspepsia, mask-like face, xerostomia, back pain, fever, orthostatic hypotension, myoclonus, weight gain, headache, diarrhea, insomnia, lack of concentration, paresthesia, dystonia, tachycardia, and personality disorders (Smeets et al., 2018). Therefore, there is a need for non-pharmacological interventions to reduce delusions in PwD. The present study aims to find a combination of non-pharmacological

interventions that can reduce delusions in PwD and caregivers' burden.

## 2. MATERIALS AND METHODS

### 2.1 Subjects

Sixty (60) patients with different types and stages of dementia, with delusions, and their caregivers were included in this study. The 61.7% in this study were females (N=37), with average age 74.6 years old (Mean 74.6, SD 7.7), and their average years of education were 9.1 years old (SD 3.9). The sample was taken from the Neurological Department of the General Hospital of Thessaloniki "G. Papanikolaou" and the General Hospital of Athens "G. Gennimatas". The study was running according the ethical principles (Declaration of Helsinki). The subjects were living in their homes and their caregivers were family members. We included the dementia patient who have been prescribed stable dosage of antipsychotics/antidepressants/anxiolytics or not for the study duration. The caregivers have given consent. No ethical issues occurred. The 63.3% of the patients suffered from AD, the 5% from VAD, the 6.7% from DLB, the 2.2% from PDD, the 6.7% from FTD, and the 11.7% had MCI. Table 1 shows the baseline characteristics of the sample.

### 2.2 Procedure

A cross-over randomized controlled trial was applied. The participants were randomly assigned in 6 different groups of 10 patients each. Three non-pharmacological interventions were applied. Each group received the same interventions but in a different sequence. The sequence of the interventions is shown on table 2. At the beginning of the process, we recorded the scores of following questionnaires: Mini-Mental State Examination (MMSE), Addenbrooke's Cognitive Examination Revised (ACE-R), Geriatric Depression Scale (GDS), Functional Rating Scale for Symptoms in Dementia (FRSSD) and NPI (only the questions and sub-questions that refer to delusions). Each intervention took place for five days and at the morning of the 6<sup>th</sup> day the results of NPI questionnaire were also recorded.

### 2.3 Interventions

#### a) Validation Therapy (VT) / Psycho-educational program

This treatment is a cognitive non-pharmacological intervention. It is centered around the patient's needs. The guideline for the caregivers was to "agree" with the patient, whatever the patient says. The caregiver does not ignore or attempt to explain the illogical or irrational behavior of the patient. The aim of this therapy is to accept the patient without asking why (Scales et al., 2018). VT is rooted in Rogerian humanistic psychology (Berg-Weger & Stewart, 2017). VT focuses on accepting the reality of the patient empathically and aims to enhance positive feelings. It includes non-threatening words, rephrasing the patient's words, maintaining eye contact, speaking with a gentle tone of voice, responding in general terms when meanings are confusing, and, in some cases, avoiding touch (Scales et al., 2018). For the caregivers to be educated in this therapy, a psycho-education program took place. It was administrated to all family caregivers either in face-to-face meetings in General Hospitals, or online

(skype meetings). The educational seminars took place before the beginning of every intervention. The duration of the psycho-educational program was 12 weeks and included 24 seminars. Every seminar lasted approximately 2 hours. The seminars were referring to general knowledge about dementia, its progress, BPSD, non-pharmacological interventions, and daily challenges. One private personal counseling session (60min.), and one group counseling session (90min.), were also included. The instruction in the “Psycho-educational therapy” was to apply the Validation theories, such as “do not try to convince the patient that his/ her believes are false”, “accept his/ her reality and speak to him/ her with a gentle and kind tone of voice”. Additionally, the caregivers should maintain the visual contact with their patient and if it was necessary ignore completely the delusional symptoms.

#### b) Reminiscence therapy (RT)

It is a cognitive-based intervention. It is used to recall past memorable events of the patient’s life. The caregiver aims to include the patient in discussions of past experiences and events. The intervention also uses photos, music, books, and letters. In accordance with previous studies (Woods et al., 2018; Scales et al., 2018), the current trial used photo albums to recall past experiences. The intervention applied by the caregiver for 60min. per session once a day, every morning after breakfast.

#### c) Music Therapy (MT)

The treatment belongs to Stimulant Based Interventions. MT has shown positive results in reducing several BPSD (Trainor, 2019). It remains unknown which type of music and which is the duration of the MT which has the most effective results (Ueda, 2013). Therefore, the caregivers used CDs with patients’ preferred music for 45min., five times a week, once a day, every morning after breakfast.

The criteria in order to use the above-mentioned interventions were a) are pleasurable, b) do not have side-effects, c) can be easily applied by unprofessional caregivers, and d) they belong to different non-pharmacological interventions: Psychoeducational program belongs to behavioral interventions, RT belongs to cognitive interventions and MT belongs to sensory interventions.

### 2.4 Measures

Two measurements were used to identify the severity of the cognitive decline :

- a) **Mini-Mental State Examination (MMSE)** (Folstein, 1983), (Fountoulakis, 2000): MMSE is a 30-point short questionnaire that is used to evaluate global cognitive status. It is used to estimate the severity of cognitive decline. The questionnaire examines registration, attention, recall, language, and orientation. Higher scores indicate better cognitive performance and lower scores mean severe cognitive decline.
- b) **Addenbrooke’s Cognitive Examination Revised (ACE-R)**(Mathuranath, 2000), (Konstantinopoulou, 2011): ACE is a 100-point questionnaire that is used to evaluate global cognitive impairment. It includes

MMSE. It is highly sensitive and can be used in the procedure of diagnosis of dementia. It includes questions about orientation, registration, attention, concentration, recall, verbal fluency, memory, language, spatial abilities, perceptual abilities, and recognition. Higher scores indicate better cognitive performance.

The following measurement was used to identify the depressive symptoms of the PwD:

- c) **Geriatric Scale of Depression (GDS)**<sup>(Yesavage, 1983), (Fountoulakis et al., 1999)</sup>: This scale is a questionnaire of 30 questions that examines if the patient has depression. The patient answers with a YES / NO. Higher score indicates higher level of depression.

The following measurement was used to identify the daily functionality of the sample:

- d) **Functional Rating Scale for Symptoms in Dementia (FRSSD)** (Hutton et al., 1998; Tsolaki, 1997): 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).

The following measurement was used to identify the BPSD of the sample:

- e) **Neuropsychiatric Inventory (NPI)** (Cummings et al., 1994; Politis et al., 2004) The questionnaire is administered to the caregiver. It includes questions for 12 behavioral and psychological symptoms in dementia with 7-8 sub-questions for each. These are delusions, hallucinations, aggressive behavior, depression, anxiety, euphoria, apathy, disinhibition, agitation, wandering, sleeping disturbances, and eating problems. The questionnaire evaluates the frequency and severity of the symptom and the impact that each behavior has on the caregiver. Frequency is scored from 0-4 (0= rarely happens, 4= happens every day), severity from 1-3 (1=mild severity, 3=severe), and the distress is scored from 0-5 (0= not at all, 5= extremely). The domain total score is the product of; a) frequency X severity score and b) the total score of caregivers’ distress. A total score is obtained by summing all the domain total scores. The questions of NPI for delusions are:
  - Does the resident believe that he/she is in danger? Other are planning to hurt him/her or have been hurting him/ her?
  - Does the resident believe that others are stealing from him/her?
  - Does the resident believe that his/her spouse is having an affair?
  - Does the resident believe that his/her family, staff members, or others are not who they say they are?

- Does the resident believe that television or magazine figures are actually present in the room? Does he/she try to talk or interact with them?
- Does he/she believe any other unusual things that I haven't asked about?

### 2.5 Data Analysis

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

## 3. RESULTS

The Mean scores from all the patients were MMSE (Mean 18.6, SD 4.5), ACE-R (Mean 55.2, SD 16.2), GDS (Mean 8.4, SD 4.9), FRSSD (Mean 18.2, SD 8.8) and NPI Result (Mean 7.6, SD 1.7) and NPI Distress of the caregiver (Mean 3.6, SD 0.7). No differences were found between males and females between the six categories defined by the sequence schemes ( $p=0.715$ ). In addition, no differences were found on age ( $p=0.431$ ), years of education ( $p=0.143$ ), MMSE ( $p=0.078$ ), ACE-R ( $p=0.096$ ), GDS ( $p=0.103$ ), NPI Result ( $p=0.233$ ) and NPI Distress ( $p=0.562$ ) between the six categories defined by the sequence at the baseline assessment. There was no relationship between the six categories and the different types and severity of dementia ( $p=0.191$ ). The Mean score of the age of the 6 groups was 74.6 (SD 2.61). Chi-square was used to find if there is a difference between genders among groups. According to the statistics chi-square test was  $p=0.350$ , which means that there was no statistically significant difference. Z value score was used to examine the type of dementia among groups (diagnosis): group 1 had Mean score 3.10 (SD 3.69), group 2 4.40 (SD 4.06), group 3 2.40 (SD 1.89), group 4 1.10 (SD 0.31), group 5 3 (SD 2.82) and finally group 6 2.20 (SD 2.89).

Table 3 shows the percentages of the different types of dementia of the sample. Results of Wilcoxon test are on Table 4. Group 2 reduced delusions and caregivers' distress, as well. Its combination was: the first week applied VT in combination with Psychoeducational program, the second week MT and the third week RT. The same combination was the most effective for the reduction of caregivers' distress, as well. The other groups did not show statistically significant results.

## 4. DISCUSSION

This study shows that there is a combination of non-pharmacological interventions that can reduce statistically significant delusions. This combination is: "VT / Psycho-educational program- MT- RT". The same combination reduced caregivers' burden, as well.

The literature so far lacks studies on the current matter. Most non-pharmacological interventions refer to other BPSD. However, it is crucial to mention the ones that refer to delusions: One pilot RCT study with one psychologist (60min./visit) and an occupational therapist (90min./visit) who gave information to the caregivers. The study also had a control group, which received casual counseling. The intervention lasted for 6-12 months and there was also a follow-up after 12 months (N=39 families). According to the results, the study found significant reduction of delusional symptoms in all 39 families (Nobili, 2004).

Another single-blind cross-over RCT study with 15 participants in Canada found that Cognitive Rehabilitation showed significant positive results on the reduction of delusions (Brunelle- Hamann, 2015). The intervention was to learn and re-learn an instrumental activity of daily living. It lasted for 6 months, and it was taken place four times a week. However, the small sample size of the trial is an important limitation of the study.

Furthermore, according to other reviews, VT has shown beneficial results for the reduction of depression, anxiety, sleeping problems, and apathy, but does not mention any benefit on the reduction of the delusional symptoms (Scales et al, 2018; Abraha et al., 2017). However, the review claims that VT does not affect the negative emotions that the patient may feel. According to the review, the studies so far have important limitations methodologically. According to these reviews, VT is a well-accepted intervention, and it is not harmful, but there is small evidence. It seems that VT can be a promising non-pharmacological intervention, but there is a strong need for further research.

The psycho-educational programs seem to have positive results. Families and clinicians need to collaborate more. Caregivers need support to know the prognosis of the BPSD and how to deal with them in daily life (Waxman, 2018). Caregivers' burden is a crucial problem in dementia and should not remain unsolved. Approximately 30-55% of the caregivers suffer from depression and anxiety symptoms (Youngran, 2019). Psycho-educational programs for the caregivers are economically beneficial because may delay the institutionalization (Youngran, 2019). It is very important to find alternatives that can reduce caregivers' burden. It seems that the prognosis and institutionalization of the patients depends on the physical and mental health of the caregiver (Garcia-Ptacek, 2019). Psycho-educational programs help caregivers to be socialized and get confident. They offer the opportunity of socialization to dementia caregivers. Thus, it is an alternative that should be well-considered.

Additionally, another critical conclusion is that there is a relevance between the intervention that reduced the unwanted behavior and the intervention that reduced caregivers' burden. An explanation is that caregivers' psychology is directly affected by the behavior of their patients. Therefore, an intervention that can control an unwanted behavior it is, at the same moment, possibly to reduce the caregivers' burden, too. In particular, the current instruction of the Psycho-educational

program was “to do nothing” when the delusions appear. This intervention was effective for the reduction of the caregivers’ distress, as well. A possible explanation is that many caregivers feel the obligation to do something when an unwanted behavior occurs and act. The intervention, however, asked them to do the exact opposite. Hence, the caregivers may experience relief because they are not in charge of doing anything to control the delusions. An interesting finding is that delusions seemed to be reduced in PwD when their caregivers do not pay attention to them. The literature so far has not found a valid explanation about that.

Furthermore, according to previous studies MT has shown positive results in decreasing many BPSD (anxiety, apathy, aggressive behaviors) but there is no evidence that MT can be helpful in delusions (Abraha, 2017). In the current study, MT was suggested because it is a pleasurable intervention and previous studies have shown that has no side effects (Abraha, 2017). RT was also used because has no side effects and has shown some promising evidence as an effective non-pharmacological intervention for other BPSD, such as apathy and depression (Bohlmeijer, 2007). Nevertheless, the literature lacks evidence on the impact of RT on the delusional symptoms in dementia (Park, 2019). Therefore, there is also a need for further research.

The strength of the current study is its strong methodology. The cross-over randomized designed reduces risk of bias. The sequence of the interventions does not interfere with the results. In addition, apart from the heterogeneity of the sample, it seems that our results affect both genders, different types, and stages of dementia. Moreover, the psycho-educational program that applied was very well-organized and covered in detail all the important issues that dementia raises. NPI is an effective, valid, and reliable questionnaire (Lai, 2014). NPI can evaluate a wide range of psychopathology including delusions and it can be used across different ethnic groups (Lai, 2014). It is also flexible and easy to use. The limitations of the current study are the interventions lasted for only five days and there was no follow-up. However, since the caregivers needed rapid solutions to their problems, the short length of the interventions can be justified. Additionally, the interventions were administrated by the caregivers. This could also be a limitation, but the caregivers were educated in the psycho-educational program and have been guided with detail, illustrative and strict way. Future studies should focus on non-pharmacological interventions of the reduction of the delusions in dementia. There is a strong need for evidence, well-designed trials with methodological quality, and large sample size. Pharmacological treatments are important and sometimes inevitable; however, their side effects should be well-considered.

In conclusion, the treatment of delusions seems critical. The study found that there is a promising combination of non-

pharmacological interventions that can reduce delusions and caregivers’ burden, too. However, the literature so far lacks valid studies that have examined the non-pharmacological interventions for the reduction of delusions in PwD and their caregivers.

**CONFLICT OF INTEREST**

The authors report no conflict of interest.

**FUNDING**

None

**Tables**

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

	Mean (SD) or N (%)
<b>Females, N(%)</b>	61.7% (37)
<b>Age</b>	74.6 (7.7)
<b>Years of education</b>	9.1 (3.9)
<b>MMSE</b>	18.6 (4.5)
<b>ACE-R</b>	55.2 (16.2)
<b>GDS</b>	8.4 (4.9)
<b>FRSSD</b>	18.2 (8.8)
<b>NPI Results</b>	7.6 (1.7)
<b>NPI Distress</b>	3.6 (0.7)

**Table 2: The sequence of the interventions based on the 6 different groups. A: VT/ Psychoeducational Program, B: RT, C: MT**

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

**Table 3: Percentages of the different types of dementia of the sample (N=60)**

AD	VAD	LBD	PDD	FTD	MCI
63.3 %	5%	6.7%	6.7%	6.7%	11.7%

**Table 4: a) Wilcoxon results (patients)**

group 1	Baseline NPI	NPI before A	A-B	B-C
Mean score± SD	8± 1.83	8± 1.83 - 5± 1.63	5 ± 1.63 - 6± 1.85	6± 1.85 - 6± 1.71

Percentile		6-8, 3.75-6	3.75-6, 5.25-6.50	5.25-6.50, 6-8
p		0.007	0.257	0.196
<b>group 2</b>	<b>Baseline NPI</b>	<b>NPI before A</b>	<b>A-C</b>	<b>C-B</b>
Mean score± SD	7± 1.63	7± 1.63 - 5± 1.64	5 ± 1.64 - 4± 1.64	4± 1.64 - 3± 1.10
Percentile		6-8.25,4-6.50	4-6.50, 4-6	4-6, 2-2
p		0.016	0.028	0.030
<b>group 3</b>	<b>Baseline NPI</b>	<b>NPI before B</b>	<b>B-A</b>	<b>A-C</b>
Mean score± SD	8± 1.68	8± 1.68 - 6± 1.91	6± 1.91 - 6± 1.81	6± 1.81 - 7± 1.63
Percentile		7.50-9, 4-6	6-8, 4-6.50	6-8, 6-8.25
p		0.039	0.206	0.660
<b>group 4</b>	<b>Baseline NPI</b>	<b>NPI before B</b>	<b>B-C</b>	<b>C-A</b>
Mean score± SD	7± 1.75	7± 1.75 - 6± 1.81	6± 1.81 - 6± 1.89	6± 1.89 - 5± 1.19
Percentile		6-8, 5.50-8	5.50-8, 5.50-8	5.50-8, 4-6
p		0.083	0.564	0.024
<b>group 5</b>	<b>Baseline NPI</b>	<b>NPI before C</b>	<b>C-A</b>	<b>A-B</b>
Mean score± SD	8± 1.85	8± 1.85 - 7± 1.41	7± 1.41 - 6± 1.79	6± 1.79-7± 1.19
Percentile		6-9, 6-9	6-9, 4-8	4-8, 6-8
p		0.102	0.061	0.666
<b>group 6</b>	<b>Baseline NPI</b>	<b>NPI before C</b>	<b>C-B</b>	<b>B-A</b>
Mean score± SD	8± 1.82	8± 1.82 - 7± 2.05	7± 2.05 - 8± 2.16	8± 2.16 - 6± 1.19
Percentile		6-9, 5.50-8.25	5.50-9.25,	5.50-9, 4-6
p		0.039	0.140	0.016

**b) Wilcoxon results (caregivers)**

<b>group 1</b>	<b>Baseline NPI</b>	<b>NPI before A</b>	<b>A-B</b>	<b>B-C</b>
Mean score ± SD	5± 1.63	5± 1.63 - 2± 0.56	2± 0.56 - 3± 0.84	3± 0.84 - 3± 0.63
Percentile		3.75-6, 2-2.25	2-2.25,	2-3, 2-3
p		0.005	0.509	0.317
<b>group 2</b>	<b>Baseline NPI</b>	<b>NPI before A</b>	<b>A-C</b>	<b>C-B</b>
Mean score ± SD	5± 1.63	5± 1.63 - 2.5± 0.82	2.5± 0.82 - 1.50± 0.96	3.50± 0.96 - 1± 0.86
Percentile		4-6.50,2-3.25	2-3.25, 1.25-2	1.25-2, 1-1
p		0.007	0.024	0.042
<b>group 3</b>	<b>Baseline NPI</b>	<b>NPI before B</b>	<b>B-A</b>	<b>A-C</b>
Mean score± SD	6± 1.81	6± 1.81 - 3± 0.73	3± 0.73 - 2± 0.42	2± 0.42 - 3± 0.73
Percentile		7.50-9, 2-3.25	2-3.25, 2-2.25	2-2.25, 2.75-4
p		0.007	0.014	0.310
<b>group 4</b>	<b>Baseline NPI</b>	<b>NPI before B</b>	<b>B-C</b>	<b>C-A</b>
Mean score± SD	5± 1.19	5± 1.19 - 3± 0.99	3± 0.99 - 2± 0.42	6± 1.89 - 2± 0.42
Percentile		4-6, 2-3.25	2-3.25,3-4	3-4, 2-2.25
p		0.004	0.102	0.009

group 5	Baseline NPI	NPI beforeC	C-A	A-B
Mean score± SD	6± 1.79	6± 1.79 - 3± 0.87	3± 0.87 - 2± 0.48	2± 0.48, 3± 0.67
Εύρος		4-8, 2-4	2-4, 2-3	2-3, 3-4
p		0.008	0.150	0.460
group 6	Baseline NPI	NPI beforeC	C-B	B-A
Mean score± SD	6± 1.19	6± 1.19 - 3± 0.73	3± 0.73 - 3.5± 1.17	3.5± 1.17 - 2± 0.31
Percentile		4-6, 2.75-4	2.75-4, 2-4.25	2-4.25, 2-2
p		0.005	0.276	0.016

## REFERENCES

- Aarsland D. (2020). Impact of Dementia-Related Psychosis on Patients and Caregivers: The Treatment Imperative. *The Journal of clinical psychiatry*, 81(6), AD19038BR2C. <https://doi.org/10.4088/JCP.AD19038BR2C>
- Abraha, I., Rimland, J. M., Trotta, F. M., Dell'Aquila, G., Cruz-Jentoft, A., Petrovic, M., Gudmundsson, A., Soiza, R., O'Mahony, D., Guaita, A., & Cherubini, A. (2017). Systematic review of systematic reviews of non-pharmacological interventions to treat behavioural disturbances in older patients with dementia. The SENATOR-OnTop series. *BMJ open*, 7(3), e012759. <https://doi.org/10.1136/bmjopen-2016-012759>
- Anderson CA, Camp J, Filley CM. Erotomania after aneurysmal subarachnoid hemorrhage: case report and literature review. *J Neuropsychiatry Clin Neurosci*1998;10:330–337.
- Anor C, J, O'Connor S, Saund A, Tang-Wai D, F, Keren R, Tartaglia M, C: Neuropsychiatric Symptoms in Alzheimer Disease, Vascular Dementia, and Mixed Dementia. *Neurodegener Dis* 2017;17:127-134. doi: 10.1159/000455127
- Berg-Weger, M., & Stewart, D. B. (2017). Non-pharmacologic Interventions for Persons with Dementia. *Missouri Medicine*, 114(2), 116–119.
- Bohlmeijer E. Reminiscence and depression in later life (Dissertation). Amsterdam: Faculty of Psychology and Education, Vrije Universiteit, 2007.
- Brunelle-Hamann, L., Thivierge, S., & Simard, M. (2015). Impact of a cognitive rehabilitation intervention on neuropsychiatric symptoms in mild to moderate Alzheimer's disease. *Neuropsychological rehabilitation*, 25(5), 677–707. <https://doi.org/10.1080/09602011.2014.964731>
- Cipriani, G., Danti, S., Vedovello, M., Nuti, A., & Lucetti, C. (2014). Understanding delusion in dementia: a review. *Geriatrics & gerontology international*, 14(1), 32–39. <https://doi.org/10.1111/ggi.12105>
- Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. (1994). The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology*, 44(12), 2308–2314. <https://doi.org/10.1212/wnl.44.12.2308>
- Folstein, M. F., Robins, L. N., & Helzer, J. E. (1983). The Mini-Mental State Examination. *Archives of general psychiatry*, 40(7), 812. <https://doi.org/10.1001/archpsyc.1983.01790060110016>
- Fountoulakis, K. N., Tsolaki, M., Chantzi, H., & Kazis, A. (2000). Mini-Mental State Examination (MMSE): A validation study in Greece. *American Journal of Alzheimer's Disease & Other Dementias*, 342–345. <https://doi.org/10.1177/153331750001500604>
- Fountoulakis, K. N., Tsolaki, M., Iacovides, A., Yesavage, J., O'Hara, R., Kazis, A., & Ierodiakonou, C. (1999). The validation of the short form of the Geriatric Depression Scale (GDS) in Greece. *Aging (Milan, Italy)*, 11(6), 367–372. <https://doi.org/10.1007/BF03339814>
- Frith U, Frith C. The biological basis of social interaction. *Curr Dir Psychol Sci*2001;10: 151–155.
- Garcia-Ptacek, S., Dahlrup, B., Edlund, A. K., Wijk, H., & Eriksdotter, M. (2019). The caregiving phenomenon and caregiver participation in dementia. *Scandinavian Journal of caring sciences*, 33(2), 255–265. <https://doi.org/10.1111/scs.12627>
- Gossink, F. T., Vijverberg, E. G., Krudop, W., Scheltens, P., Stek, M. L., Pijnenburg, Y. A., & Dols, A. (2017). Psychosis in behavioral variant frontotemporal dementia. *Neuropsychiatric disease and treatment*, 13, 1099–1106. <https://doi.org/10.2147/NDT.S127863>
- Hutton, J.T., Dippel, R.L., Loewenson, R.B. Functional rating scale for the symptoms of dementia. In J. J. Gallo, W, Reichel and L, Andersen (Eds.) Handbook of geriatric assessment. Rockville, MD: Aspen Publishers 77-80, 1998.
- Konstantinopoulou, E., Kosmidis, M. H., Ioannidis, P., Kiosseoglou, G., Karacostas, D., & Taskos, N. (2011). Adaptation of Addenbrooke's Cognitive Examination-Revised for the Greek population. *European journal of Neurology*, 18(3), 442–447. <https://doi.org/10.1111/j.1468-1331.2010.03173.x>
- Lai C. K. (2014). The merits and problems of Neuropsychiatric Inventory as an assessment tool in people with dementia and other neurological disorders. *Clinical interventions in aging*, 9, 1051–

1061. <https://doi.org/10.2147/CIA.S63504>
19. Lozupone, M., La Montagna, M., Bellomo, A., Battista, P., Seripa, D., Daniele, A. & Panza, F. (2020). Delusions in dementias. In *Genetics, Neurology, Behavior, and Diet in Dementia* (pp. 647-664). Academic Press.
  20. Mathuranath, P. S., Nestor, P. J., Berrios, G. E., Rakowicz, W., & Hodges, J. R. (2000). A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology*, 55(11), 1613–1620. <https://doi.org/10.1212/01.wnl.0000434309.85312.19>
  21. Nobili, A., Riva, E., Tettamanti, M., Lucca, U., Liscio, M., Petrucci, B., & Porro, G. S. (2004). The effect of a structured intervention on caregivers of patients with dementia and problem behaviors: a randomized controlled pilot study. *Alzheimer disease and associated disorders*, 18(2), 75–82. <https://doi.org/10.1097/01.wad.0000126618.98867.fc>
  22. Park, J., Cohen, I. (2019). ) Effects of Exercise Interventions in Older Adults with Various Types of Dementia: Systematic Review, Activities, Adaptation & Aging, 43:2, 83-117, DOI: 10.1080/01924788.2018.1493897
  23. Pereira, G., & de Oliveira, G. C. (2019). Prevalence of Capgras syndrome in Alzheimer's patients: A systematic review and meta-analysis. *Dementia & neuropsychologia*, 13(4), 463–468. <https://doi.org/10.1590/1980-57642018dn13-040014>
  24. Petrovic M., Hurt, C., Collins, D., Burns, A., Camus, R., Liperoti, A., et al. (2007). Clustering of Behavioural and Psychological symptoms in dementia (BPSD): A European Alzheimer's Disease Consortium (EADC) study, *Acta Clinica Belgica*, 62:6, 426-432, Doi: [10.1179/acb.2007.062](https://doi.org/10.1179/acb.2007.062)
  25. Politis, A. M., Mayer, L. S., Passa, M., Maillis, A., & Lyketsos, C. G. (2004). Validity and reliability of the newly translated Hellenic Neuropsychiatric Inventory (H-NPI) applied to Greek outpatients with Alzheimer's disease: a study of disturbing behaviors among referrals to a memory clinic. *International Journal of geriatric psychiatry*, 19(3), 203–208. <https://doi.org/10.1002/gps.1045>
  26. Radue, R., Walaszek, A., & Asthana, S. (2019). Neuropsychiatric symptoms in dementia. *Handbook of clinical neurology*, 167, 437–454. <https://doi.org/10.1016/B978-0-12-804766-8.00024-8>
  27. Sakai, K., Ikeda, T., Ishida, C., Komai, K., & Yamada, M. (2019). Delusions and visual hallucinations in a patient with Parkinson's disease with dementia showing pronounced Lewy body pathology in the nucleus basalis of Meynert. *Neuropathology: official journal of the Japanese Society of Neuropathology*, 39(4), 319–323. <https://doi.org/10.1111/neup.12581>
  28. Scales, K., Zimmerman, S., & Miller, S. J. (2018). Evidence-Based Nonpharmacological Practices to Address Behavioral and Psychological Symptoms of Dementia. *The Gerontologist*, 58(suppl\_1), S88–S102. <https://doi.org/10.1093/geront/gnx167>
  29. Schneider, R. B., Iourinets, J., & Richard, I. H. (2017). Parkinson's disease psychosis: presentation, diagnosis, and management. *Neurodegenerative disease management*, 7(6), 365–376. <https://doi.org/10.2217/nmt-2017-0028>
  30. Smeets, C., Zuidema, S. U., Hulshof, T. A., Smalbrugge, M., Gerritsen, D. L., Koopmans, R., & Luijendijk, H. J. (2018). Efficacy of antipsychotics in dementia depended on the definition of patients and outcomes: a meta-epidemiological study. *Journal of clinical epidemiology*, 101, 17–27. <https://doi.org/10.1016/j.jclinepi.2018.05.004>
  31. Solla, P., Mura, G., Cannas, A., Floris, G., Fonti, D., Orofino, G., Carta, M. G., & Marrosu, F. (2017). An unusual delusion of duplication in a patient affected by Dementia with Lewy bodies. *BMC neurology*, 17(1), 78. <https://doi.org/10.1186/s12883-017-0842-1>
  32. Trainor H. (2019). Effects of Using Music Therapy for Patients Suffering From Dementia. *The health care manager*, 38(3), 206–210. <https://doi.org/10.1097/HCM.0000000000000276>
  33. Tsolaki M. Neuropsychological Evaluation of the Elderly. Melissa, Thessaloniki, 1997.
  34. Tzeng, R. C., Tsai, C. F., Wang, C. T., Wang, T. Y., & Chiu, P. Y. (2018). Delusions in Patients with Dementia with Lewy Bodies and the Associated Factors. *Behavioural neurology*, 2018, 6707291. <https://doi.org/10.1155/2018/6707291>
  35. Ueda, T., Suzukamo, Y., Sato, M., & Izumi, S. (2013). Effects of music therapy on behavioral and psychological symptoms of dementia: a systematic review and meta-analysis. *Ageing research reviews*, 12(2), 628–641. <https://doi.org/10.1016/j.arr.2013.02.003>
  36. Waxman, R., Russell, B., Iu, O., & Mulsant, B. (2018). Impact of brief education on healthy seniors' attitudes and healthcare choices about Alzheimer's disease and associated symptoms. *International Psychogeriatrics*, 30(12), 1889-1897. doi:10.1017/S1041610218000479
  37. Woods, B., O'Philbin, L., Farrell, E. M., Spector, A. E., & Orrell, M. (2018). Reminiscence therapy for dementia. *The Cochrane Database of systematic reviews*, 3(3), CD001120. <https://doi.org/10.1002/14651858.CD001120.pub3>
  38. Yesavage, J. A., Brink, T. L., Rose, T. L., Lum, O., Huang, V., Adey, M., & Leirer, V. O. (1982). Development and validation of a geriatric depression screening scale: a preliminary report. *Journal of psychiatric research*, 17(1), 37–49.



[https://doi.org/10.1016/0022-3956\(82\)90033-4](https://doi.org/10.1016/0022-3956(82)90033-4)  
39. Youngran, T., Junghee, S., Haeyoung, W., Jiyeon  
An. (2019). Realist Review: Understanding  
Effectiveness of Intervention Programs for

Dementia Caregivers, Asian Nursing Research,13  
(1); 11-19, ISSN 1976-1317,  
<https://doi.org/10.1016/j.anr.2019.01.002>.