



Neuropsychiatric Symptoms due to the COVID-19 Pandemic in Patients with Mild Cognitive Impairment and the Impact on their Caregivers

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ABSTRACT

Objectives: The COVID-19 has a profound impact on patients and caregivers of people with Mild Cognitive Impairment (MCI) due to their cognitive and functional impairments. BPSD tend to increase with such external stressors.

Methods: A telephone-based or videoconferencing survey was administered in 43 caregivers of patients with MCI who they confined to their homes for nearly 2 months, and they were taking care from Day Care Center IASIS. The survey took place twice. We used the Neuropsychiatric Inventory-Questionnaire (NPI) and asked caregivers to report whether patients experienced any change in the Behavioral and Psychological Symptoms in Dementia (BPSD) once at the beginning of the quarantine and once at the end of it. The same measurement was used in order to evaluate the BPSD of the participants after the interventions and after the quarantine. NPI inventory also assessed the caregivers' distress.

Results: A significant increase in BPSD in MCI patients with the caregivers' burden was recorded. The intervention strategy that was found to eliminate the BPSD was occupational therapy strategies.

Conclusions: The confinement seems to impact neuropsychiatric symptomatology in dementia patients. Cognitive training, physical exercise, and occupational strategies can be an alternative model of care for the BPSD in MCI and dementia patients during the pandemic.

Keywords: Neuropsychiatric symptoms; Dementia; Mild cognitive impairment; Lockdown; COVID-19 pandemic

ABBREVIATION

(ACE-R) Addenbrooke's Cognitive Examination Revised; (AD) Alzheimer's Disease; (BPSD) Behavioural and Psychological Symptoms of Dementia; (MCI) Mild Cognitive Impairment; (MMSE) Mini Mental State Examination; (NPI) Neuropsychiatric Inventory; (PD) Parkinson's Disease; (VAD) Vascular Dementia; (VCI) Vascular Cognitive Impairment without Dementia

INTRODUCTION

The public health emergency of coronavirus disease (COVID-19) is rapidly evolving worldwide [1]. Many countries, Greece included, were forced to implement restrictive measures to cope with the spread of the outbreak. Although restrictions (such as a lockdown, confinement, isolation, social distancing, using masks) may be an effective way to limit infections, these mea-

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sures provoked behavioral changes and caused distress in the most vulnerable populations such as patients with mild cognitive impairment or dementia and their caregivers [2,3]. Except for the mortality and morbidity that the virus may cause, the “lockdown” measures also have indirect effects on families causing psychological and physical distress [4,5]. From 13th of March to 18th of May people in Greece were confined at their homes and only permitted to leave in order to buy essential goods, briefly exercise, or seek medical help. This sudden restriction at home, accompanied by social distancing measures (forbidden social and religious activities, restrictions from their regular support systems), diminished physical contact with family and the outside world and prolonged self-isolation dramatically changed most people’s daily lives, imposing a great impact on overall mental health particularly among patients with mci/dementia and their caregivers [6,7]. The accumulating stress on how to manage their needs, and the sudden changes in daily routines may have triggered the appearance of neuropsychiatric symptoms, behavioral modifications, and disruptions for MCI patients. Neuropsychiatric symptoms tend to increase with external stressors or a crisis such a sudden lockdown [8]. In the context of a rapidly evolving situation, for patients with MCI sudden changes in their living arrangements and daily routines such the above, have probably limited the use of those strategies and general rules (e.g., distraction, stimulation, and social interaction) that are routinely adopted to manage some of the dementia symptoms (e.g., neuropsychiatric symptoms) [9]. Similar mainly for those with dementia, the caregiver’s burden tends to be attenuated, because the emerging and evolving health needs and priorities of patients have not been adequately met [10].

Day Care Centre “IASIS” for Third Age is a profit organization providing care based on a holistic model to seniors with cognitive neurodegenerative disorders and their families, in Glyfada, Greece. Delivering care to this vulnerable population amidst the COVID-19 pandemic has represented a major challenge to our institution. Thus, in the context of rapidly evolving situation, we adapted our model of care from face-to-face to telephone consultations during the days of lockdown, as a potential tool to gain insight on how to rearrange the provision of care and ensure its continuity. To investigate the impact of these restrictions on MCI patients’ and their caregivers’ mental health, we evaluated neuropsychiatric symptomatology of MCI patients who were confined to their homes during the COVID-19 crisis. The aim of the current study is double: Firstly, to find interventions that are effective in order to reduce the neuropsychiatric symptoms in MCI patients during the quarantine, and secondly, to find which neuropsychiatric symptoms were affected during the quarantine, and how these symptoms influenced the caregivers.

MATERIALS AND METHODS

Participants

Forty-three (N=43) subjects at the stage of MCI were recruited from the IASIS-Day Care Center for Mental Disorders of Third Age. The inclusion criteria were:

- Patients and their caregivers who were diagnosed with MCI according to the Petersen’s criteria [11] and DSM-5 criteria

[12], as well

- A previous month cognitive evaluation available
- Written informed consent from patients, caregivers, and the legal representative (when different from the responsible caregiver)
- Participation in all the phases of the study (baseline and follow-up evaluation).

Patients or caregivers were excluded from the study if they were negative to participate in the study or had difficulty to follow the instructions of the study. The study was conducted in compliance with the regulations of the local ethics committee and in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Procedures

Patients and caregivers were contacted twice *via* phone or viber (viber is a free application on smart phones, which gives the opportunity to audio or video call anyone for free), once at the begging and once after the end of the lockdown. During the procedures there was another telephone or viber call in order to ensure that the caregivers and or the patients did not need any further help. The caregiver answered for themselves and on behalf of the patient. All patients who contacted were evaluated with the Addenbrook’s Cognitive Examination Revised (ACE-R), which has become a daily routine of the IASIS Center of the 3rd Age, in order to assess their cognitive capacity. ACE-R is a highly sensitive measurement that includes Mini Mental State Examination (MMSE) and assesses all cognitive abilities: Memory, concentration, attention, language, and visual ability. Its highest score is 100 points. Higher scores indicate a better performance.

Minor impairments on daily functioning were mentioned for the MCI and dementia patients according to ADCS-ADL questionnaire (ADCS Activities of Daily Living Inventory (ADL)) [13]. Those concerned mainly social participation routines, contacting others through telephone, going to supermarket, walking around the neighbourhood, dressing, and participating in a hobby. Moreover, cognitive impairments were mentioned after unstructured interview to the caregiver for patient’s memory problems, and executive domains in comparison with the previous month. During the lockdown, a series of interventions in order to relief the observed neuropsychiatric symptoms took place, including environmental modification, cognitive training, physical exercise, strengthening relationships, creative activities, psychoeducation, occupational therapy and pharmacological treatment.

Assessment of Neuropsychiatric Symptoms

The Neuropsychiatric Inventory (NPI) was used for the neuropsychiatric assessment at the begging of the procedure and after 8 weeks of home confinement *via* phone/viber interview. The NPI is a validated caregiver-based behavioral rating inventory for the assessment of the behavioral deficits in dementia. It includes 12 domains: Delusions, hallucinations, agitation/aggressive behavior, depression, anxiety, euphoria, apathy, disinhibition, irritability/lability, aberrant motor activity/wandering, sleeping disorders and eating problems. An index of severity is

created for each behavioral variable by multiplying the frequency and severity scores.

The ADCS-ADL evaluates the competence of the AD patients in daily activities. It is a questionnaire that can be completed by the caregiver. All responses refer to the 4 weeks prior to the time of the evaluation [14]. There are 6 daily-activities items and the questionnaire provides descriptions of level of competence [15]. There are also versions of the questionnaire suitable for people with MCI (ADCSMCIADL) [16]. Higher scores reflect greater competence. ADCSADL is a useful tool because its careful selection of items suggests that is suitable for use in clinical trials because it can successfully discriminate MCI patients from healthy subjects [17]. Addenbrooke's Cognitive Examination Revised (ACE-R) was also used for the cognitive evaluation of the subjects. ACE-R includes Mini Mental State Examination (MMSE). It is a highly sensitive scale that assesses all cognitive domains: Concentration, attention, memory, language, words' production, and visual spatial ability. Higher scores indicate a better performance.

Recommended Interventions/Strategies

At Day Care Centre IASIS patients and their caregivers are attending variable psychosocial intervention programs in groups. We proposed to MCI patients and caregivers some of the intervention strategies to support them at their home. The MCI patients were suggested to apply the program that they were following in IASIS center: Light physical exercise, solving Sudoku, crosswords, maintain their daily routine of dressing (dressing like they are going to leave the house), maintain daily communication *via* telephone with their loved ones and the other patients of IASIS center. Additionally, we reformed and organized a new care plan based on mainly counselling through technological assistive methods (telephone, mail, internet), and gave specific directions on how to adapt and tailor these strategies to patient's functional and cognitive status. These are referred to:

Environmental modification: Ergonomics and safety at home for people with dementia: Due to extended staying at home because of the quarantine, we recommended to the caregivers several home modifications for a safer and more supportive environment at home. These recommendations included at bathroom installing a detachable, handheld showerhead, an adjustable shower chair and grab rails intended to provide more stability and control in the shower. For a safer transportation inside the home, we recommended removing throw rugs to reduce the potential for a fall, and using only the necessary furniture, simple clothes, and personal objects for patient's daily living. In addition, we asked for adjustments to be done in the light safer transportation at night (from bedroom to bathroom). Visual cues were also proposed to be used in order to name rooms and objects for better space orientation. We advised on keeping away dangerous chemical and medical products in safe place and covering sockets.

Cognitive training: In order to keep patients mentally and cognitive stimulated there were given a series of adaptive cognitive exercises on language, memory, attention, spatial and time orientation such as writing diary/word lists/naming specific objects/persons in photos, playing mind/memory games, solving crosswords/Sudoku/puzzles.

Physical activity exercises: Due to the positive association between physical activity participation and improved cognitive function and emotional levels across various states of cognitive decline, we proposed to MCI patients and their caregivers to adjust easy exercise participation/work out in their daily routines as an attractive strategy to address the challenge of remaining at home. These exercises refer to daily activities at home. The participants watched on youtube light programs of physical exercise for the elderly, music and dancing classes and it was suggested to apply these activities in their daily life. Moreover, structured and semi structured activities, such as walking small distances around their residence, stretching movements, light work out and dancing were also included.

Strengthening relationships: Especially those living alone in the community complained to suffer from loneliness due to increased isolation and disruption of group activities. We increased support in the form of more frequent contact by telephone or video chat and we reminded caregivers to provide vital interaction with their family and friends through telephone, technology and internet.

Recreational activities: Recreational activities are highly recommended for seniors to spend creatively their time. They seem to have a great effect on the management of their neuropsychiatric symptoms. We proposed structured participation (once or twice a day) in activities such as drawing, reading, knitting, gardening, cooking, playing cards to keep their mind distracted in an entertaining and creative way.

Psychoeducation for the caregivers: Our support to the caregivers included training regarding the symptoms of the disease. Furthermore, the psychoeducation included optimal care, using strategies such as: Encouraging vital communication/interaction/keep daily contact with the patient, and supporting the communication with other members of the group through telephone/internet, in order to reduce social distancing. Safeguard procedures (e.g., washing hands and wearing masks), and keeping a daily routine with maintained sleeping habits was highly recommended [18].

Occupational therapy strategies: The MCI patients were asked to create and maintain safe daily routines at home. We focused on problem-solving, errorless learning, and habit/memory training strategies to optimize performance in activities of daily living, home management, maintenance, and leisure/interest activities to fulfil their day. We asked them to plan each day on a steady/regular plan where they will focus on executing specific basic and instrumental activities of daily living (such as cooking, cleaning the house, dressing), deal with recreational and reminiscence activities, keeping frequent contact with relatives and friends, *via* telephone or internet, rest systematically and sleep well. Moreover, where possible, we asked caregivers to perform grocery and pharmacy outings for patients. Further, we also proposed environmental modifications in the patient's living residence, such as visual signs for orientation, removal of physical restraints and safety precautions (fall and door exit alarms, closing electricity in specific devices), in order to facilitate more independent and safe transportation inside the house [19].

Medication: Caregivers were asked to pay special attention to pharmacological management of their patients, and directions were given, when necessary, by licensed doctors.

Statistical Analyses

Quantitative variables are presented with mean and standard deviation (SD) and/or with median (interquartile range=IQR). Qualitative variables are presented with absolute and relative frequencies. The normality assumption was evaluated using Kolmogorov-Smirnov test. Wilcoxon signed rank tests were used for the comparison of continuous variables among the two time points. Differences in changes of study variables during the follow up period between different groups as defined from the different interventions were evaluated using repeated measurements analysis of variance (ANOVA). Logarithmic transformations were used in case of not normal distribution for repeated measurements analyses. All p values reported are two-tailed. Statistical significance was set at 0.05 and analyses were conducted using SPSS statistical software (version 22.0).

RESULTS

Sample consisted of 43 cases (41 with AD_MCI, 1 with VCI (Vascular cognitive impairment without dementia) and 1 with PD (Parkinson's disease without dementia)). The mean age was 79

years (SD=6.0) and 67.4% were women. Sample characteristics are presented in **Tables 1 and 2** shows description of interventions that were performed during the study period. Comparison of distress items and total score between 1st and 2nd period (**Table 3**) showed significant increase for aggression, aberrant motor behavior, sleeping disorders, eating problems and total score. Additionally, comparison of NPI items and total score between 1st and 2nd period (**Table 4**) showed significant increase for aggression, anxiety, apathy, aberrant motor behavior, sleeping disorders and total score. Changes in distress score between 1st and 2nd period according to different interventions was investigated and presented in **Table 5**. It was found that distress was increased in most cases (with or without intervention) but in those that cognitive training, physical activity, and occupational strategies were applied a lower degree of change was found, indicating that the aforementioned interventions were effective in distress control. Similarly, when repeated measurements analysis was applied for NPI total score, it was indicated from the interaction effect, that the degree of change was lower in subjects where cognitive training, physical activity, and occupational strategies were applied (**Table 6**).

Table 1: Sample characteristics.

Sex	N (%)
Males	14 (32.6)
Females	29 (67.4)
Age, mean (SD)	79.0 (6.0)
Diagnosis	N (%)
AD_MCI	41 (95.4)
VCI	1 (2.3)
PD	1 (2.3)
Years of education, mean (SD)	10.2 (4.9)
MMSE, mean (SD)	26.7 (1.7)
ACE_R, mean (SD)	80.0 (7.8)
ADCS, mean (SD)	69.3 (10.1)

Table 2: Description of interventions.

	N (%)
Environmental modification	15 (34.9)
Cognitive training	37 (86)
Physical activity	33 (76.7)
Strengthening relationship	38 (88.4)
Recreational activities	36 (83.7)
Psychoeducation caregivers	33 (76.7)
Occupational strategies	38 (88.4)
Medication modification	13 (30.2)

Table 3: Comparison of caregivers' distress items and total score between 1st and 2nd period.

DISTRESS	1 st period		2 nd period		P Wilcoxon test
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Delusions	0.00 (0.00)	0 (0-0)	0.14 (0.77)	0 (0-0)	0.18
Hallucinations	0.00 (0.00)	0 (0-0)	0.00 (0.00)	0 (0-0)	>.999
Aggression	0.37 (0.87)	0 (0-0)	1.19 (1.59)	0 (0-2)	0.001
Depression	1.42 (1.59)	1 (0-2)	1.65 (1.62)	2 (0-3)	0.596
Anxiety	1.40 (1.24)	1 (0-2)	1.53 (1.37)	1 (0-2)	0.568
Euphoria	0.05 (0.3)	0 (0-0)	0.09 (0.43)	0 (0-0)	0.564

Apathy	0.44 (1.18)	0 (0-0)	0.81 (1.53)	0 (0-1)	0.184
Disinhibition	0.21 (0.97)	0 (0-0)	0.49 (1.33)	0 (0 0)	0.123
Irritability	0.79 (1.55)	0 (0-1)	0.86 (1.55)	0 (0 1)	0.774
Aberrant motor	0.07 (0.34)	0 (0-0)	0.53 (1.26)	0 (0-0)	0.017
Sleep_Disord	0.33 (0.68)	0 (0-0)	1.12 (1.18)	1 (0-2)	<.001
Eating_Disord	0.40 (1.00)	0 (0-0)	0.84 (1.00)	1 (0-1)	0.008
TOTAL score	5.47 (5.23)	3 (2-8)	9.26 (8.36)	6 (4-12)	0.002

Table 4: Comparison of NPI items and total score of the patients between 1st and 2nd period.

NPI	1 st period		2 nd period		P Wilcoxon test
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Delusions	0.00 (0.00)	0 (0-0)	0.47 (2.46)	0 (0-0)	0.102
Hallucinations	0.00 (0.00)	0 (0-0)	0.00 (0.00)	0 (0-0)	>.999
Aggression	0.49 (1.42)	0 (0-0)	2.86 (3.88)	1 (0-6)	<.001
Depression	2.88 (3.94)	1 (0-4)	4.09 (4.52)	4 (0-6)	0.108
Anxiety	2.02 (2.35)	1 (0-3)	3.63 (3.69)	4 (0-6)	0.01
Euphoria	0.05 (0.30)	0 (0-0)	0.26 (1.09)	0 (0-0)	0.273
Apathy	0.67 (1.92)	0 (0-0)	2.16 (3.77)	0 (0-4)	0.005
Disinhibition	0.14 (0.68)	0 (0-0)	1.02 (3.29)	0 (0-0)	0.089
Irritability	1.26 (2.69)	0 (0-1)	1.86 (3.73)	0 (0-2)	0.395
Aberrant motor	0.07 (0.34)	0 (0-0)	0.84 (2.17)	0 (0-0)	0.011
Sleep_Disord	0.51 (1.24)	0 (0-1)	2.47 (2.68)	1 (0-4)	<.001
Eating_Disord	1.16 (2.83)	0 (0-0)	2.07 (2.88)	1 (0-4)	0.006
TOTAL score	9.26 (10.77)	5 (2-14)	21.72 (21.43)	14 (6-28)	<.001

Table 5: Changes in caregivers' distress score between 1st and 2nd period according to different interventions 1p-value for group effect; 2p-value for time effect; Effects reported include differences between the groups in the degree of change (repeated measurements ANOVA) after logarithmic transformation.

		Distress total						P2	P3
		1 st period		2 nd period		Change			
		Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		
Environmental Modification	No	5.11 (5.44)	2.5 (1-8)	9.71 (8.68)	8 (4-11.5)	4.61 (7.59)	4.5 (-0.5-7.5)	0.003	0.32
	Yes	6.13 (4.93)	6 (2-11)	8.4 (7.94)	6 (4-13)	2.27 (7.76)	2 (-3-7)	0.291	
	P1	0.395		0.794					
Cognitive training	No	3.83 (3.97)	3 (0-7)	16.17 (10.36)	13 (10-22)	12.33 (9.46)	9.5 (7-12)	<.001	0.009
	Yes	5.73 (5.4)	4 (2-8)	8.14 (7.57)	6 (4-9)	2.41 (6.44)	3 (-2-6)	0.037	
	P1	0.409		0.036					
Physical activity	No	4.4 (3.63)	3 (2-7)	12.4 (7.9)	10.5 (9-12)	8 (9.37)	7 (6-9)	0.002	0.042
	Yes	5.79 (5.63)	4 (1-10)	8.3 (8.37)	5 (3-9)	2.52 (6.69)	3 (-2-5)	0.068	
	P1	0.906		0.041					
Strengthening relationship	No	3.4 (3.13)	2 (2-5)	10.2 (8.98)	11 (5-11)	6.8 (6.53)	6 (5-9)	0.107	0.549
	Yes	5.74 (5.42)	3.5 (2-10)	9.13 (8.39)	6 (4-12)	3.39 (7.76)	3 (-1-7)	0.008	
	P1	0.503		0.996					
Recreational activities	No	5.43 (4.96)	5 (1-8)	12.29 (7.83)	11 (5-22)	6.86 (4.88)	6 (3-9)	0.023	0.252
	Yes	5.47 (5.35)	3 (2-9)	8.67 (8.43)	6 (3.5-11)	3.19 (7.98)	3 (-2-7)	0.018	
	P1	0.937		0.156					
Psychoeducation caregiver	No	4.5 (4.58)	2.5 (2-8)	11 (9.94)	8.5 (4-12)	6.5 (9.38)	4.5 (1-8)	0.019	0.31
	Yes	5.76 (5.44)	5 (2-8)	8.73 (7.91)	6 (4-11)	2.97 (6.99)	4 (-2-7)	0.027	
	P1	0.716		0.428					

Occupational strategies	No	5.6 (4.04)	7 (3-8)	20.8 (9.34)	22 (14-24)	15.2 (9.42)	12 (10-16)	0.003	0.036
	Yes	5.45 (5.41)	3 (2-8)	7.74 (7.04)	6 (4-9)	2.29 (6.06)	3 (-2-6)	0.022	
	P1	0.778		0.005					
Medication modification	No	5.13 (5.58)	2.5 (1-8)	8.37 (8.2)	5.5 (3-11)	3.23 (7.75)	3 (-1-7)	0.013	0.945
	Yes	6.23 (4.44)	6 (2-10)	11.31 (8.69)	9 (6-14)	5.08 (7.52)	4 (1-10)	0.081	
	P1	0.288		0.233					

Table 6: Changes on NPI score of the patients between 1st and 2nd period according to different interventions 1p-value for group effect; 2p-value for time effect; Effects reported include differences between the groups in the degree of change (repeated measurements ANOVA) after logarithmic transformation.

		NPI total						P2	P3
		Pre		Post		Change			
		Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		
Environmental modification	No	8.96 (11.57)	2.5 (1-15.5)	22.93 (23.49)	15 (6-25.5)	13.96 (21.4)	8.5 (1.5-18.5)	<.001	0.291
	Yes	9.8 (9.44)	6 (2-14)	19.47 (17.45)	13 (4-32)	9.67 (14.24)	7 (-1-23)	0.065	
	P1	0.406		0.729					
Cognitive training	No	4.67 (5.65)	2.5 (0-9)	34 (27.02)	24.5 (14-42)	29.33 (28.21)	14 (14-39)	<.001	0.009
	Yes	10 (11.26)	5 (2-15)	19.73 (20.13)	14 (6-25)	9.73 (16.17)	5 (0-22)	0.001	
	P1	0.239		0.089					
Physical activity	No	6.3 (6.95)	2.5 (2-9)	27.6 (22.64)	18.5 (14-36)	21.3 (25.46)	14 (7-34)	<.001	0.049
	Yes	10.15 (11.62)	5 (1-14)	19.94 (21.08)	13 (4-26)	9.79 (16.33)	5 (0-22)	0.002	
	P1	0.609		0.099					
Strengthening relationship	No	4.4 (4.28)	3 (2-6)	28 (24.42)	17 (14-36)	23.6 (21.41)	14 (11-34)	0.004	0.132
	Yes	9.89 (11.22)	5 (2-15)	20.89 (21.23)	14 (6-26)	11 (18.63)	6 (0-22)	<.001	
	P1	0.436		0.361					
Recreational activities	No	8.71 (9.09)	6 (1-17)	32.29 (23.15)	20 (14-61)	23.57 (19.14)	14 (10-37)	0.002	0.14
	Yes	9.36 (11.17)	5 (2-14)	19.67 (20.8)	14 (5-25.5)	1.31 (18.63)	5 (0-18)	0.001	
	P1	0.996		0.085					
Psychoeducation caregiver	No	7.7 (9.86)	2 (2-17)	27.4 (27.2)	18 (9-42)	19.7 (26.39)	8.5 (3-37)	0.002	0.231
	Yes	9.73 (11.13)	6 (2-14)	20 (19.53)	14 (6-26)	1.27 (16.23)	7 (1-22)	0.001	
	P1	0.574		0.43					
Occupational strategies	No	7.2 (5.97)	9 (2-11)	43 (31.1)	26 (23-67)	35.8 (32.22)	14 (14-56)	0.002	0.048
	Yes	9.53 (11.27)	5 (2-15)	18.92 (18.64)	14 (6-25)	9.39 (14.84)	5 (0-22)	<.001	
	P1	0.933		0.042					
Medication Modification	No	8.17 (10.73)	2.5 (1-14)	19.07 (21.78)	12.5 (4-23)	1.9 (19.74)	6 (1-14)	<.001	0.996
	Yes	11.77 (10.84)	6 (5-20)	27.85 (20.05)	24 (14-38)	16.08 (17.89)	14 (3-25)	0.015	
	P1	0.182		0.164					

DISCUSSION

In the present study we aimed the following:

- To find interventions that help the neuropsychiatric symptoms in MCI patients during the lockdown due to COVID-19, and
- To find which neuropsychiatric symptoms gotten worse or better during the lockdown and what was the impact of the changes in the behavior of the patients to the caregiver.

The current study shows that the most effective interventions

are cognitive training, physical exercise, and occupational strategies. MCI patients suffer from neuropsychiatric symptoms that affect their cognitive ability, quality of life and they are a burden for the caregivers, as well. The lockdown affected the activities of the patients and forced them to be inside their houses all day. This has as a result to stop some activities, and the caregivers were forced to provide care all day. The limitation of the activities and the changes in the daily routine of the patients had as a result a worsening of their neuropsychiatric symptoms. According to the results the neuropsychiatric symptoms that seemed to be aggravated are aggression, aberrant motor be-

havior, sleeping problems and eating disorders. Moreover, the total score of the NPI questionnaire has been affected due to the lockdown, as well.

Our results are in accordance with previous studies. Specifically, two Greek studies have shown that the quarantine increased the caregivers' burden due to the neuropsychiatric problems of their MCI patients [20,21]. Furthermore, a study from Brazil shows that the neuropsychiatric symptoms worsen during the pandemic and used telemedicine in order to address the problems of the patients and their caregivers [22]. The caregivers should be supported by the specialists and telemedicine allows easy access to the professional and can help the patient in maintaining clinical stability. In addition, it provides sufficient guidance to the caregivers to deal with the neuropsychiatric symptoms, which is a burden for the caregivers. The study also found that telemedicine can be a helpful way in order to control the neuropsychiatric symptoms of dementia during the quarantine. According to a review most of the studies were person-centered strategies and included psychosocial and psycho-educational interventions based on the cognitive-behavioral therapy [23]. Most studies found positive results in controlling the neuropsychiatric symptoms and anxiety of the caregivers, contributing to an improvement in the quality of life. Another study named WeCareAdvisor provides caregivers with information, tips, strategies and evaluating of the effectiveness of these techniques [24]. The trial included 326 caregivers randomly assigned into groups: The first group was receiving the WeCareAdvisor treatment, the second group was the control group. The study found positive results in controlling the neuropsychiatric symptoms.

A challenging thing is the environmental modification due to the quarantine. It is suggested that technology could help the dementia patients and their caregivers being in touch with the outside world [25]. This can reduce boredom and the feeling of isolation. Moreover, the online activities could help the patients reduce their neuropsychiatric symptoms. In addition, activities in and around the home could be also very helpful. In particular, gardening, reading, listening to music, physical exercise and cooking may be beneficial for the patients. Developing a daily routine that resembles the "real life" and the activities that the patients used to do, can be calming. In that way, this routine can decrease anxiety symptoms. The coronavirus presents an opportunity to enhance techniques that could remain in time and help the MCI caregivers. The study appointed effective strategies that help the MCI patients and their caregivers to reduce the neuropsychiatric symptoms in cost-effective ways. The pandemic underlines the importance of finding effective solutions and design plans for future crisis, in order to be totally prepared to support the patients and their caregivers. Telephone and viber can be effective for helping the patient and the caregiver, as well. The present study has several limitations: The sample size is small, the study design is not a randomized controlled trial, and the sample does not include a large number of patients with different types of dementia, such as vascular dementia, Parkinson dementia and frontotemporal dementia. Future studies should focus on finding effective ways in order to help the dementia patients and their caregivers controlling the neuropsychiatric symptoms of the disease [26,27].

CONCLUSION

In conclusion, according to some studies prolonged periods of quarantine in dementia patients could become chronic and this is crucial. Furthermore, some neuropsychiatric symptoms (such as aggressive behavior), can be extremely challenging for the caregivers, as well. Additionally, it seems that the pandemic is disproportionately impacting the MCI patients and mostly the ones who suffer from neuropsychiatric symptoms. The patients and their caregivers are facing severe challenges due to the changes of their daily routine. Certain neuropsychiatric symptoms may lead to a higher risk of infection, and this is crucial, because it leads to higher mortality rates. Therefore, it is important to find effective interventions for the neuropsychiatric symptoms.

STATEMENT OF ETHICS

All the authors mentioned in the manuscript have agreed for authorship, read, and approved the manuscript, and given consent for submission and subsequent publication of the manuscript. The manuscript in part or in full has not been submitted or published anywhere. The manuscript will not be submitted elsewhere until the editorial process is completed. The study protocol was reviewed and approved by the ethics committee of the center. All participants (or their legal representative) have completed a written informed consent to participate in the study.

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AUTHOR CONTRIBUTIONS

T. Dimitriou: Writing original article and review; M. Koustimpi: Writing original article; V. Kamtsiadeli: Project execution; M. Hatzopoulou: Project execution; A. Zagka: Project execution; A. Grigoriou: Project execution; K. Siarkos: Supervision; J. Papatriantafyllou: Conceptualization, supervision, methodology, formal analysis, resources.

DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

DATA STATEMENT

The data has not been previously presented orally or by poster at scientific meetings

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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