

## Neuropsychiatric symptoms and quality of life in Spanish patients with Alzheimer's disease during the COVID-19 lockdown

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**Background and purpose:** The COVID-19 epidemic is affecting almost all individuals worldwide, and patients with Alzheimer's disease (AD) and amnesic mild cognitive impairment (MCI) are particularly at risk due to their characteristics and age. We analysed the impact of the pandemic on these patients' neuropsychiatric symptoms and their quality of life after 5 weeks of lockdown in Spain.

**Methods:** A total of 40 patients with a diagnosis of MCI ( $n = 20$ ) or mild AD ( $n = 20$ ) from the Cognitive Stimulation Program of the Cognitive Disorders Unit were evaluated. All patients had undergone a previous evaluation during the month before the lockdown, and were re-evaluated after 5 weeks of lockdown. The Neuropsychiatric Inventory (NPI) and EuroQol-5D questionnaire (EQ-5D) were used to assess neuropsychiatric symptoms in patients and the quality of life in patients as well in caregivers.

**Results:** The mean (SD) total baseline NPI score was 33.75 (22.28), compared with 39.05 (27.96) after confinement ( $P = 0.028$ ). The most frequently affected neuropsychiatric symptoms were apathy [4.15 (3.78) vs. 5.75 (4.02);  $P = 0.002$ ] and anxiety [3.95 (3.73) vs. 5.30 (4.01);  $P = 0.006$ ] in patients with MCI, and apathy [2.35 (2.70) vs. 3.75 (3.78);  $P = 0.036$ ], agitation [0.45 (1.14) vs. 1.50 (2.66);  $P = 0.029$ ] and aberrant motor behaviour [1.25 (2.86) vs. 2.00 (2.93);  $P = 0.044$ ] in patients with AD. We did not observe differences in EQ-5D scores during the re-evaluation. The 30% of patients and 40% of caregivers reported a worsening of the patients' health status during confinement.

**Conclusions:** The results of this study show the worsening of neuropsychiatric symptoms in patients with AD and MCI during 5 weeks of lockdown, with agitation, apathy and aberrant motor activity being the most affected symptoms.

### Introduction

Coronavirus disease 2019 (COVID-19) was first described in Wuhan in December 2019 [1]. Since then, the number of cases and deaths has grown around the world, and the World Health Organization declared the COVID-19 pandemic on 11 March 2020 [2]. In Spain, the first patient with coronavirus was

diagnosed on 31 January 2020. Today, the country is nearing 219 764 cases and 22 524 deaths [3]. There has been no worldwide or standard response to the pandemic, and each country is confronting the crisis based on their own practicabilities, expertise and hypotheses [4]. Although, worldwide, the pandemic is affecting entire populations, elderly people have the highest risk of mortality, and most of the deaths have occurred in those aged over 70 years [5]. In this age group, Alzheimer's disease (AD) is highly prevalent. On 14 March, the Spanish government declared a state of emergency, prohibiting most groups of people,

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including all older people, from going out into the streets; this was accompanied by the closure of day centres and centres where cognitive stimulation is carried out. Patients with AD therefore had to remain at home for 24 hours a day, with their caregivers also remaining at home throughout the day. Given that these patients often have memory problems, they may have some difficulties understanding the situation, thus generating anxiety and nervousness for both the patients and their caregivers.

To date there have been no data assessing the effect on neuropsychiatric symptoms and on quality of life associated with this home confinement in patients with cognitive disorders and their caregivers.

## Methods

We assessed 40 patients with a diagnosis of amnesic mild cognitive impairment (MCI) or mild AD, recruited from the Cognitive Stimulation Program of the Cognitive Disorders Unit at the Hospital Universitari Santa Maria (Lleida, Spain), as well as their caregivers. Eligible patients were aged >60 years, and were diagnosed with MCI [6] or mild AD (GDS 3–4) according to the National Institute on Aging–Alzheimer's Association criteria [7]. All patients had undergone a previous evaluation as a standard procedure in the Cognitive Stimulation Program of our unit. The patient, their responsible caregiver and their legal representative (when different from the responsible caregiver) signed an informed consent form during the first evaluation and provided oral acceptance before the second evaluation.

Patients included in the Cognitive Stimulation Programme have all been diagnosed with MCI or mild AD by neurologists or geriatricians working in the unit. Exclusion criteria for the Cognitive Stimulation Programme are as follows: inability or unwillingness on the part of the patient or caregiver to come to the hospital; sensorial difficulties that could make it difficult to follow the stimulation sessions; or uncontrolled behaviour problems that could interfere with the development of the sessions. Patients with mobility problems can attend, but, given these limitations, often cannot carry out the proposed stimulation.

Our memory unit cares for patients with a wide geographical distribution, but, the majority of patients who come to the stimulation workshops live within a radius of <20 km from the memory unit.

A total of 42 patients underwent evaluation in the previous month, which formed the baseline assessment. Two patients could not be contacted by telephone. All patients who were contacted ( $n = 40$ ) agreed to participate in the follow-up study.

Neuropsychiatric Inventory (NPI) and EuroQol-5D questionnaire (EQ-5D) scores were obtained via telephone interview after 5 weeks of home confinement, and the results were compared with those obtained during the first evaluation.

The EQ-5D instrument includes questions to assess different domains, such as mobility, personal self-care, instrumental activities of daily living, pain and depression. The caregiver answered in regard to themselves and the patient [8]. The NPI is used to assess the severity and frequency of the following 12 domains of behavioural functioning: delusions; hallucinations; agitation/aggression; dysphoria; anxiety; euphoria; apathy; disinhibition; irritability/lability; aberrant motor activity; night-time behavioural disturbances; and appetite and eating abnormalities [9].

## Statistical analyses

Mean (SD) or median (interquartile range) values were the descriptive statistics used for estimates of quantitative variables with a normal or non-normal distribution, respectively. Absolute and relative frequencies were used for qualitative variables. The normality of the distribution was analysed using the Shapiro–Wilk test. Mean values were compared using paired-samples Student's *t*-tests. Comparison between categorical variables was performed using the chi-squared test, Pearson's test and Fisher's exact test. The statistical analysis was performed using the SPSS 19.0 program (SPSS, Chicago, IL, USA). Significance was set at  $P < 0.05$  for all analyses.

## Results

We evaluated 40 patients: 20 with MCI and 20 with AD. The baseline characteristics of the sample are shown in Table 1. Most ( $n = 24$ ) were living with a partner/spouse (60%), while nine (22.5%) were living alone with an occasional caregiver. Six (15%) had changed address in relation to confinement. The patients showed a significant worsening in neuropsychiatric symptoms: the mean (SD) preconfinement NPI score was 33.75 (22.28), compared with 39.05 (27.96) after 5 weeks of domiciliary confinement ( $P = 0.028$ ).

Table 2 shows that agitation, apathy and aberrant motor activity were the most affected neuropsychiatric symptoms in our patients. Other symptoms, such as depression, also worsened, but were not statistically significantly different. Mean (SD) neuropsychiatric symptom scores worsened, to a similar extent, in patients with MCI [35.40 (21.15) vs. 39.95 (24.62), difference 4.5;  $P = 0.103$ ] and those with AD [32.10

**Table 1** Descriptive characteristics of patients with mild cognitive impairment and moderate Alzheimer's disease

	Total	MCI	AD	<i>P</i>
Mean (SD) age, years	77.4 (5.25)	77.3 (4.05)	77.5 (6.33)	0.049
Women, <i>n</i> (%)	24 (60.0)	10 (50.5)	14 (70.0)	0.167
Mean (SD) MMSE score	23.1 (3.76)	25.3 (2.77)	20.9 (3.37)	0.433
Married, <i>n</i> (%)	25 (62.5)	13 (65.0)	8 (40.0)	0.596
Non-professional caregiver, <i>n</i> (%)	39 (97.5)	19 (95.0)	20 (100)	0.503
Hypertension, <i>n</i> (%)	24 (60.0)	9 (45.0)	15 (75.0)	0.053
Diabetes, <i>n</i> (%)	12 (30.0)	7 (35.0)	5 (25.0)	0.366
Dislipidemia, <i>n</i> (%)	21 (52.5)	10 (50.5)	11 (55.0)	0.514
Psychiatric treatment, <i>n</i> (%)	22 (55.0)	12 (60.0)	10 (50.0)	0.376
Acetylcholinesterase inhibitors, <i>n</i> (%)	21 (52.5)	5 (25.0)	16 (80.0)	0.001

AD, Alzheimer's disease; MCI, mild cognitive impairment.

**Table 2** Changes in neuropsychiatric symptoms included in the Neuropsychiatric Inventory from baseline to 5 weeks of lockdown due to the COVID-19 pandemic

	Mean (SD) NPI score pre-lockdown	Mean (SD) NPI score after 5 weeks of lockdown	<i>P</i>
Stress	9.85 (7.75)	10.33 (8.29)	0.554
Delusions	0.63 (1.90)	0.75 (2.20)	0.565
Hallucinations	0.20 (0.72)	0.15 (0.70)	0.700
Agitation/aggression	0.68 (1.50)	1.50 (2.58)	0.020
Depression/dysphoria	2.25 (3.06)	2.50 (3.49)	0.602
Anxiety	4.73 (3.92)	5.18 (4.34)	0.458
Euphoria	0.53 (1.24)	0.43 (1.48)	0.514
Apathy	3.25 (3.37)	4.75 (3.98)	0.000
Desinhibition	0.85 (1.62)	0.82 (1.55)	0.852
Irritability/lability	3.33 (3.14)	3.83 (3.80)	0.278
Aberrant motor behaviour	1.15 (2.58)	1.83 (2.84)	0.019
Night-time behavioral disturbances	2.45 (3.57)	2.80 (3.40)	0.548
Appetite/eating disorders	3.88 (4.88)	4.20 (4.93)	0.537

NPI, Neuropsychiatric Inventory.

(23.79) vs. 38.15 (31.58), difference 6.0;  $P = 0.135$ ]. The most affected symptoms were apathy [4.15 (3.78) vs. 5.75 (4.02);  $P = 0.002$ ] and anxiety [3.95 (3.73) vs. 5.30 (4.01);  $P = 0.006$ ] for patients with MCI. Apathy [2.35 (2.70) vs. 3.75 (3.78);  $P = 0.036$ ], along with agitation [0.45 (1.14) vs. 1.50 (2.66);  $P = 0.029$ ] and aberrant motor behaviour [1.25 (2.86) vs. 2.00 (2.93);  $P = 0.044$ ], were the most commonly affected symptoms in patients with AD.

There were no differences in median (interquartile range) quality-of-life scores across the 5 weeks of lockdown in patients [0.66 (0.60; 0.72) vs. 0.62 (0.56; 0.69), differences  $-0.03$  ( $-0.08$ ; 0.01);  $P = 0.456$ ] or caregivers [0.74 (0.68; 0.80) vs. 0.72 (0.65; 0.79), differences  $-0.02$  ( $-0.06$ ; 0.02);  $P = 0.387$ ]. In terms to the EQ-5D about if the patient's health condition had worsened after 5 weeks of confinement, 30% (12) of the patients and 40% (16) of the caregivers reported worse scores. However, no differences were observed in visual analogue scale scores, either for the caregivers [69.88 (19.23) vs. 65.50 (23.66);  $P = 0.101$ ] or for the caregivers their own behalf with regard to their caregiving [55.63 (16, 49) vs. 52.88 (20.28);  $P = 0.123$ ].

## Discussion

In the present study, we investigated the impact of 5 weeks of lockdown in patients with MCI and AD during the COVID-19 epidemic in Spain. There was a statistically significant increase in levels of agitation, apathy and aberrant motor activity. We did not observe a decrease in quality of life in either patients or caregivers.

The COVID-19 pandemic is an unprecedented disaster and a significant psychological stressor, in addition to having a tremendous impact on every facet of individuals' lives and of organizations in virtually all social and economic sectors worldwide [10]. In the general population, the increasing burden of the epidemic has led to a global atmosphere of anxiety and depression [11].

Patients with AD are a particularly vulnerable population. Most have memory problems that can make it difficult for them to understand what is happening around them. As for most of the population, the patients' routines have been altered, and their environment may be more chaotic as a result of the uncertainties caused by the pandemic. Furthermore, their stimulation programmes have been interrupted or severely modified. All these circumstances can generate important alterations in such patients [12].

A longitudinal study of the general population showed that depression, anxiety and stress increased during the pandemic in China. We observed that neuropsychiatric symptoms and quality of life in patients with cognitive impairment and in their caregivers were affected.

Patients included in the Cognitive Stimulation Program attend the hospital three times a week to perform physical and cognitive stimulation tasks. The works according to their cognitive statement, so

patients included in the study were in two different groups.

Our results showed worsening agitation, apathy and aberrant motor activity after 5 weeks of lockdown in a Spanish population with MCI or AD. No previous study has evaluated these changes in patients with memory problems. We did not observe significant differences in quality of life, but many patients and caregivers said that their health condition had worsened after confinement.

Several strategies to try to improve the situation of patients with AD during the COVID-19 pandemic have been published by different associations or Alzheimer's Health Organizations [12–14]. Based on the results of the present study, there is an urgent need for this information to be acted on and disseminated throughout the AD patient community.

Despite the limited range of tests used in the present study, it is the first study to report information on patients with AD and MCI in these exceptional circumstances. However, some limitations need to be considered. One is the fact that the first evaluation was carried out by personal interview whilst the second was by telephone interview. This could explain some of the differences, however, the interview was conducted by the same professional in both cases to try to reduce possible bias. Another limitation is that our patients usually attend the memory unit 3 days a week. This change of routine could have affected these patients and could explain the worse neuropsychiatric symptoms. However, these patients began the program and were evaluated only 1 month before the lockdown; therefore, they may not yet have acquired this routine.

In conclusion, the present study underlines the need to take into account the particular characteristics of patients with cognitive impairment when developing measures of de-escalation during confinement to try to minimize the effects on neuropsychiatric symptoms and quality of life in patients.

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### Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

### Data availability statement

The data that support the findings of this study are available from the corresponding author on reasonable request.

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