

The impact of COVID-19 confinement on the neurobehavioral manifestations of people with Major Neurocognitive Disorder and on the level of burden of their caregivers

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Abstract

The long-term consequences of confinement at home due to the COVID-19 pandemic are not yet known; however, an exacerbation of the neurobehavioral symptoms of patients with dementia and an increase in their caregiver burden are conceivable. The aims of this study were to investigate any changes in the neuropsychiatric symptoms of patients with Major Neurocognitive Disorder as well as in the levels of burden and distress of their caregivers due to COVID-19 confinement, and to detect any relationship between the changes in patients and their caregivers. A “pre-post” study was carried out by means of a semi-structured telephone interview, which was administered to 128 caregivers of patients with dementia. The interview included patient and caregiver demographic information, the Neuropsychiatric Inventory-Questionnaire (NPI-Q) and the Caregiver Burden Inventory (CBI). Results showed an increased risk for burning out of caregivers by about

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10%. Statistically significant differences were found between the conditions prior to lockdown (pre-lockdown) and during lockdown in both the CBI and the NPI-Q distress scale. Neuropsychiatric symptoms in patients with dementia significantly increased as well. Results have a practical implication for the organization of public and private support services.

Keywords: Caregiver burden; Caregiver distress; COVID-19; Major Neurocognitive Disorder; Neurobehavioral manifestations.

1. Introduction

The COVID-19 pandemic is having a remarkable impact on the physical and mental health of the general population (Fagiolini, Cuomo, & Frank, 2020; Wang, Li, Barbarino, Gauthier, Brodaty, Molinuevo *et al.*, 2020), and may produce a wide range of neurological and neuropsychiatric manifestations through complex mechanisms of neuroinvasion and neuroinfection (Pennisi, Lanza, Falsone, Fisicaro, Ferri, & Bella, 2020). It has changed habits, routines, and lifestyles, affecting human relationships, and has had a deep impact on the economies of countries at a global scale. In Italy at the end of July the number of people affected by SARS-CoV-2 had exceeded 245,000 and over 35,000 died (median age 80 years, interquartile range 74-88). In Sicily, the number of infected people was over 3,000 and the victims were over 280; the local government established four red zones (approximately, from March 24th to May 4th). A recent study on the Italian general population (Moccia, Janiri, Pepe, Dattoli, Molinaro, De Martin *et al.*, 2020) has indicated that a relevant proportion of the population may have experienced psychological distress during the COVID-19 outbreak. Another Italian study (Cerami, Santi, Galandra, Dodich, Cappa, Vecchi *et al.*, 2020) found that both distress and loneliness affected the perception of the severe impact of COVID-19 on health. Older adults, particularly those with dementia, were shown to be especially vulnerable during crisis times, because of their cognitive and functional impairments (Boutoleau-Bretonnière, Pouclet-Courtemanche, Gillet, Bernard, Deruet, Gouraud *et al.*, 2020; Wang *et al.*, 2020). Some measures have been put into practice by the governments of several countries, including Italy, in order to reduce the risk of SARS-CoV-2 infection: for example, social distancing, prohibition of displacement to and from certain countries, suspension of social, religious, and care activities (including outpatient visits in public and private hospitals and outpatient rehabilitation, which might potentially attenuate neuropsychiatric symptoms associated with dementia and partially reduce the speed of decline; Buschert, Bokde, & Hampel, 2010). These measures may have resulted in an increased sense of loneliness, social isolation and discomfort in frail people with dementia and their caregivers. Coping with the psychological and behavioral symptoms of dementia by the caregivers frequently produces an increase in distress (Donaldson, Tarrier, & Burns, 1998; Marvardi, Mattioli, Spazzafumo, Mastroforti, Rinaldi, Polidori *et al.*, 2005; Allegri, Sarasola, Serrano, Taragano, Arizaga, Butman *et al.*, 2006; Boutoleau-Bretonnière, & Vercelletto, 2009; Raggi, Tasca, Panerai, Neri, &

Ferri, 2015); caregivers are often alone in facing their anxiety and their burden is also frequently correlated with the onset of depressive symptoms (Sherwood, Given, Given, & von Eye, 2005). In a period of extreme discomfort, the burden and distress may increase, also due to the lack of formal and informal supports. The long-term consequences of the confinement are not known yet, but we may hypothesize an exacerbation of the neurobehavioral symptoms in patients and an increase in the self-perceived burden of caregivers.

2. Aims and hypothesis

Our study was aimed to: (1) investigate the presence of any changes in the neuropsychiatric symptoms of patients with dementia as well as in the levels of burden and distress of their caregivers, following the confinement decided by the local authority in order to limit the pandemic spread; (2) detect a potential relationship between the changes in patients and caregivers. The long-term consequences of the confinement are not known yet, but we may hypothesize an exacerbation of the neurobehavioral symptoms in patients and an increase in the self-perceived burden of caregivers.

3. Methods

3.1. *Study Design*

A “pre-post” study was carried out between April 14th and May 16th 2020 in which the impact of the confinement during the Covid-19 pandemic on the neurobehavioral manifestations of patients with Major Neurocognitive Disorders (M-NCD; American Psychiatric Association, 2013) as well as in the levels of distress and burden of their caregivers was investigated.

3.2. *Sample*

A convenience sampling was chosen to facilitate the recruitment of available caregivers; patients were identified among those living in Sicily and diagnosed in our Institute during the six months preceding the national quarantine imposed on March 9th 2020 by the Italian Government. Diagnoses were made by a multidisciplinary team on the basis of the DSM 5 (American Psychiatric Association, 2013) criteria for M-NCD. During the

diagnostic process, dementia was staged using the Clinical Dementia Rating Scale (CDR) (Hughes, Berg, Danziger, Coben, & Martin, 1982); any comorbidities were identified using the Cumulative Illness Rating Scale (CIRS index; Parmelee, Thuras, Katz, & Lawton, 1995).

Among all potential participants ($N = 134$), 128 accepted to participate in the study. The socio-demographic characteristics of caregivers ($N = 128$) are shown in Table 1. The clinical and socio-demographic characteristics of patients with M-NCD ($N = 128$) are shown in Table 2.

Table 1 – Socio-demographic characteristics of caregivers

Variables	Median (IQR), or N
Sex, <i>males/females</i>	34/94
Chronological age, <i>years</i>	57.5 (47-70)
Level of instruction, <i>years</i>	8 (8-13)
Marital status, <i>married/cohabiting/single/separated</i>	102/2/20/4
Relationship degree with relatives with dementia	
- children/spouses/other	62/57/9
Medical pathology	
- hypertension	26
- headache, pain	13
- cardiovascular disorders	11
- endocrinological pathologies	7
- infected by Covid 19	0
- other pathologies	29
Pre-Covid occupational status	
- employed/unemployed/retired	39/56/33
Dismissal during pandemic	8

IQR = Interquartile range

Table 2 – *Clinical and socio-demographic characteristics of patients with M-NCD*

Variables	Median (IQR), or N
Sex, <i>males/females</i>	61/67
Chronological age, years	76 (68.75-82)
Clinical Dementia Rating scale (CDR)	
- 1 = mild/2 = moderate/3-4 = severe	59/47/22
Dementia type	
- AD/FTD/VD/PD/Mixed/Other	31/8/42/5/7/35
Patient infected by Covid-19	0
Drug assumption	128
Cumulative Illness Rating Scale, Comorbidity index	2 (1-3)
Cumulative Illness Rating Scale, Severity index	1.3 (1.15-1.46)
Decrease of memory skills during confinement*	50 (39%)
Decrease of self-care skills during confinement*	39 (30,5%)
Living conditions during confinement	
- maintained routines (daily habits, mealtimes, bedtime)	111 (86.7%)
- planned day	66 (51.6%)
- possibility to go out (backyard, home garden)	54 (42.2%)
- maintained formal and informal support for assistance	92 (71.9%)

* Data based on information from the caregivers.

IQR = Interquartile range; AD = Alzheimer's Disease; FTD = Fronto-Temporal Dementia; VD = Vascular Dementia; PD = Parkinson's Dementia

3.3. Instruments

The semi-structured interview consisted of three parts: (1) the collection of personal data of patients and their caregivers and information about their living conditions during the lockdown; (2) how caregivers judged the impact of confinement on the cognitive and adaptive skills of their relatives (patients) with dementia, and (3) the administration of two questionnaires, the Neuropsychiatric Inventory-Questionnaire (NPI-Q; Kaufer, Cummings, Ketchel, Smith, MacMillan, Shelley *et al.*, 2000) and the Caregiver Burden Inventory (CBI; Novak, & Guest, 1989).

The NPI-Q is used to detect the presence or absence of neuropsychiatric symptoms and their severity in patients with dementia. It assesses 12

behavioral symptoms (delusions, hallucinations, dysphoria, anxiety, agitation/aggression, euphoria, disinhibition, irritability/lability, apathy, aberrant motor activity, sleep and night time behavior disorder, appetite and eating disorder); the severity scores range from 1 to 3 points (mild-to-severe), whereas the associated caregiver distress from 0 to 5 points (from “no distress” to “extreme distress”). Test-retest correlations between the symptoms and distress scores are .80 and .94, respectively ($p < .0001$ for both). The interscale correlation between the Neuropsychiatric Inventory total score and the NPI-Q severity total score is .91, while the interscale correlation between caregiver distress ratings is .92 (Cummings, Mega, Gray, Rosenberg-Thompson, Carusi, & Gornbein, 1994).

The CBI includes a total of 24 items divided into five subscales: Time Dependence, describing the restriction of the caregivers personal time; Developmental burden, referred to the caregivers sense of failure about the expected life-course, hopes and intentions, with respect to their peers; Physical, referred to the caregivers sense of fatigue and damage to their own physical health; Social, referring to family relationship and job performance, and Emotional, describing caregivers negative feelings due to the patient’s inappropriate behaviors. Each item is scored on the basis of a Likert-type scale ranging from 0 (strongly disagree) to 4 (strongly agree). A total score of 36 indicates a risk for burning out, whereas scores near or slightly above 24 indicate the need to take a break and rest (Raggi *et al.*, 2015). The alpha factor of internal consistency is .73 - .86. The high internal consistency of the test ($\alpha = .80$) has also been validated in the Italian context by the study conducted by Marvardi and colleagues (2005).

3.4. Procedure

The semi-structured telephone interview was administered to the caregivers by clinical psychologists working at the Brain Aging Department of our Institute, specifically devoted to people with dementia and acquired cognitive impairment. Caregivers were given a first phone call in order to be informed about the purpose and characteristics of the interview and the tasks required by the study protocol, the probable duration of the phone call, the confidentiality of data to be collected, the risk and benefits of the study, the invitation to decide whether to participate or not, the researcher contact information. After obtaining an informed consent by clicking a box, a second phone call was scheduled to carry out the proper interview to each participant. For the NPI-Q and the CBI, caregivers were required to score

the items in relation to the pre-lockdown period (four weeks) and during the lockdown (four weeks). Questionnaires were administered in the time interval April 14th - May 16th 2020, i.e. between lockdown phase 1 and the beginning of phase 2 (that started in Italy on May 4th 2020). During phase 2, displacements and access to public places for elderly and frail people were rather limited as well. Approval was obtained from the Local Ethics Committee “Comitato Etico IRCCS Sicilia–Oasi Maria SS.” and was done in accordance with the Helsinki Declaration of 1975.

3.5. Data analysis

Asymmetry and kurtosis calculations did not show any normal distribution for most of the variables considered in the study so that non-parametric statistics were used. The significance level was set at $p < .05$. Differences between the conditions of pre-lockdown and during lockdown in the neurobehavioral manifestations of patients, as well as in distress and burden of family caregivers, were analyzed by means of the Wilcoxon matched pairs test. Effect sizes were calculated by using the $r = z/\sqrt{N}$ formula, where N is the total number of participants ($r = .1$, small effect size; $r = .3$, medium effect size; $r = .5$, large effect size). The Chi square test was used to evaluate differences between the number of worsened and stable patients or caregivers, grouped on the basis of opposite conditions experienced during the confinement, for example maintenance/non-maintenance of cognitive and self-care skills by patients, or cessation/maintenance of formal and informal support for assistance, cessation/maintenance of daily routines. The effect sizes were calculated by using the Cramer’s V test, where scores $\leq .2$ indicate a small effect size, scores between $.2$ and $\leq .6$ a moderate effect size, and $> .6$ a strong effect size. Correlation analysis of differences between the phases of pre- and during lockdown on the CBI (total and subsection scores) and the NPI-Q (severity and distress scales) were carried out with the Spearman’s test.

4. Results

As far as caregivers are concerned, CBI scores indicated a risk for burning out (score ≥ 36) in 12.5% of individuals ($N = 16$) in the pre-lockdown condition and in 21.9% ($N = 28$) during lockdown, with an increase of about 10%. Statistically significant differences (Tab. 3) were found between pre-and during lockdown CBI total and subsection scores,

with a large effect size in total scores and Physical burden and a medium effect size in Time Dependence and Developmental burden.

Table 3 – *Caregiver Burden Inventory (CBI) and Neuropsychiatric Inventory-Questionnaire (NPI-Q) scores in the conditions of pre- and during lockdown and statistically significant differences in the whole sample*

	Pre-lockdown	During-lockdown	Wilcoxon's test		
	Median (IQR)	Median (IQR)	<i>z</i>	<i>p</i> ≤	effect size, <i>r</i>
Caregivers (<i>N</i> = 128)					
CBI					
- Time dependence	10 (5-15)	11 (6-16)	5.51	.000001	.49
- Developmental burden	4.5 (1-9)	5 (1-10)	4.56	.000005	.4
- Physical burden	2 (0-5)	4 (0-6.5)	6.16	.000001	.545
- Social burden	0 (0-1)	0 (0-2)	2.60	.009	.23
- Emotional burden	0 (0-1)	1 (0-2)	2.97	.003	.26
- Total scores	18.5 (9-28)	21 (11-34)	6.97	.000001	.61
NPI-Q					
- Distress	4 (1-8)	5 (2-9)	2.66	.008	.23
Patients (<i>N</i> = 128)					
NPI-Q					
- Symptoms	3 (1-4)	3 (2-5)	4.83	.000001	.43
- Severity	3 (1-6)	5 (2.75-8)	4.94	.000001	.44

IQR = Interquartile range; CBI = Caregiver Burden Inventory; NPI-Q = Neuropsychiatric Inventory-Questionnaire

Social and emotional burden also significantly increased, as well as the NPI-Q distress; however, the relative effect sizes were small. The statistical analysis (Chi Square test) carried out on the differences between the number of worsened and stable caregivers, grouped into opposite categories based on opposite life conditions experienced during confinement, showed the following results (Tab. 4): the CDR 2 severity dementia condition was associated with increased distress (NPI-Q distress) in a larger number of caregivers when compared to CDR 1 and CDR 3-4; the condition of decreased memory skills in the patients produced an increase in both distress

(NPI-Q distress) and psychophysical burden (CBI) in a larger number of caregivers when compared with the condition of stable memory skills.

The patients' condition of decreased self-care skills, the cessation of formal and informal support, the inability to maintain daily routines, as well as the non-planned days all brought about to an increased psychophysical burden (CBI) in a higher number of caregivers when compared with the opposite conditions (stable self-care skills, maintenance of formal and informal support, maintenance of daily routines and planned days, respectively). In the condition regarding the possibility/impossibility to go out, no statistically significant difference was found between the number of worsened and stable caregivers in terms of burden and distress scores.

The severity of the neuropsychiatric symptoms of patients significantly increased (Tab. 3), with a medium effect size. The amount of symptoms, as detected in the conditions of pre- and during lockdown, significantly increased as well, showing a p value of .000001, and a medium effect size ($r = .43$). The same statistical test applied to subgroups on the basis of the rating of dementia severity showed significantly increased neuropsychiatric symptoms in CDR 1 (symptoms amount: $p = .0011$, $r = .42$; symptoms severity: $p = .0016$, $r = .41$), and CDR 2 subgroups (symptoms amount: $p = .002$, $r = .44$; symptoms severity: $p = .00019$, $r = .54$).

The symptom severity turned out to be increased in a large number of patients, but only among those who showed decreased memory skills, when compared to those who maintained stable memory skills (Tab. 4). No statistically significant differences were found between the number of worsened and stable patients regarding any of the other conditions.

Statistically significant positive correlations (Spearman's test; $p < .05$) were found between the periods of pre- and during lockdown in the NPI-Q distress scale and in the CBI total scores, as well as in the Physical and Emotional subsections ($R = .23$, $.24$ and $.27$, respectively). The NPI-Q distress scale and the CBI Physical burden subsection showed a statistically significant correlation also with the NPI-Q severity scale ($R = .42$ and $R = .19$, respectively).

Table 4 – Comparison between worsened and stable caregivers and patients, grouped into categories based on some personal and living variables during confinement (Chi square test)

	Caregiver CBI total score			Caregiver NPI-Q distress			Patient NPI-Q severity		
	worsened, %	χ^2 test $p \leq$	Cramer's V	worsened, %	χ^2 test $p \leq$	Cramer's V	worsened, %	χ^2 test $p \leq$	Cramer's V
CDR 1/2/3-4	40.7/57.4/59.1	NS		42.4/63.8/36.4	.037*	.23	57.6/57.4/36.4	NS	
Memory decreased/stable	84.0/33.3	.00001	.495	64.0/39.7	.007	.24	66.0/46.2	.028	.19
Self-care decreased/stable	79.5/39.3	.000029	.37	46.2/50.6	NS		56.4/52.8	NS	
Support maintained/cessation	44.6/75.0	.0019	.27	47.8/50.0	NS		51.1/58.3	NS	
Routines maintained/non-maintained	49.5/82.4	.011	.22	50.5/35.3	NS		55.9/41.2	NS	
Day planned/non-planned	37.9/67.7	.00072	.3	50.0/46.8	NS		53.0/54.8	NS	
Going out possible/impossible	42.6/59.5	NS		50.0/48.6	NS		55.6/52.7	NS	

CBI = Caregiver Burden Inventory; NPI-Q = Neuropsychiatric Inventory-Questionnaire; CDR = Clinical Dementia Rating

5. Discussion

To the best of our knowledge, this is the first study in which the caregiver's emotional condition has been analyzed during a pandemic by means of a multidimensional scale (CBI) and the NPI-Q distress scale; moreover, other characterizing aspects of the family life during the pandemic have been also taken into account.

The results presented here are suggestive of the fact that the confinement during the COVID-19 outbreak brought about an increase in the amount and severity of neuropsychiatric symptoms in people with dementia, with subsequently higher levels of burden and distress in their caregivers. Caregivers at risk for burning-out increased by 10%. Unlike results by Boutoleau-Bretonnière and co-workers (2020), a statistically significant increase in neuropsychiatric symptoms was found especially in patients with a mild or moderate dementia (CDR 1 and CDR 2, respectively). Patients with more severe stages of dementia (CDR 3 and 4) hardly showed any worsening in cognitive and daily-living skills, probably due to their being almost unaware of what was happening around them. As a consequence, their behaviors appeared to be more as an effect of the degenerative process, than a response to environmental stimuli. The difference between our results and those reported by Boutoleau-Bretonnière and colleagues (2020) is probably due to the measures used: indeed, we used the Clinical Dementia Rating (CDR) scale, whereas Boutoleau-Bretonnière and co-workers (2020) used the Mini-Mental State Examination scores, as obtained during the last visits in person prior to the pandemic. Moreover, our sample included patients with M-NCD with different etiologies, whereas the sample selected by Boutoleau-Bretonnière and others (2020) only included patients with Alzheimer's type dementia.

As far as the burden dimensions are concerned (CBI subscales), Time Dependence and Developmental and Physical burden showed the largest increases, while Social and Emotional burden, together with the NPI-Q distress scores, showed lower increases (i.e. small effect sizes). Therefore, despite the general framework of worsened burden conditions, the emotional manifestations and social relationships of caregivers appeared to be slightly less affected than other variables. Which are the elements that more specifically influence these domains cannot be deduced from the results of this study; however, we can hypothesize that they reside in both personal and family educational variables, for example, in the value of the family, as is strongly felt by the Sicilian general population, especially by the older

generations. In our sample, certain conditions seemed to be more directly related to increased levels of distress and burden due to the lack of daily routines and formal and informal support, the severity of dementia (especially CDR 2 stage), the loss of cognitive and daily living skills of patients as well as the lack of planned days. Some of these factors can be interpreted as coping strategies, especially the ability to organize the day and to maintain the daily routines, in order to guarantee stable life conditions to patients with dementia, or to face the lack of support by way of seeking strategies. Adaptive coping strategies might contribute to mitigate any difficulties in controlling psychological and behavioral symptoms of patients, thus promoting the well-being of caregivers. Results from our study are consistent with those from a previous study by Raggi and colleagues (2015), which was conducted on a mixed sample of Northern and Southern Italian caregivers: these authors found that increased caregiver distress was correlated with a lack of specific coping strategies, such as seeking for social support, and a marked focus on problem and avoiding behaviors.

Other studies (Donaldson *et al.*, 1998; Marvardi *et al.*, 2005; Allegri *et al.*, 2006; Raggi *et al.*, 2015) found a significantly positive correlation between neurobehavioral manifestations of patients and increased distress and burden in caregivers; the same positive correlation was found in our study. The caregiver distress in our sample appeared to be especially related to emotional burden. Consequently, we may interpret the distress as being more related to internal (negative feelings and thoughts, and emotional conflicts) than to external environmental factors.

In conclusion, our study suggests that the confinement of M-NCD patients due to the COVID-19 pandemic had a negative impact on the neurobehavioral manifestations of patients with dementia, as well as on the distress and burden of their caregivers. These results have a practical implication for the organization of public and private support services based on telehealth, in order to protect this frail population and their caregivers, by monitoring patients potentially affected by COVID 19 and by mitigating the adverse effects seen in non-infected patients and caregivers forced to confinement. An Italian study (Capozzo, Zoccolella, Frisullo, Barone, Dell'Abate, Barulli *et al.*, 2020) described the efficacy of the telehealth service, based on phone calls, in a sample of patients with frontotemporal dementia and their caregivers. In the case of non-infected people, as in our sample, services might be addressed to both patients with dementia and their caregivers, by means of videoconferences, e-mail, apps, and also simple telephone calls. Services for patients might allow the continuation of care

and rehabilitation interventions, including psychological therapies (Choi, Hegel, Marti, Marinucci, Sirrianni, & Bruce, 2014; Zamir, Hennessy, Taylor, & Jones, 2018) as well as cognitive stimulation programs (García-Betances, Jiménez-Mixco, Arredondo, & Cabrera-Umpiérrez, 2015; Arlati, Colombo, Spoladore, Greci, Pedrolì, Serino *et al.*, 2019; Dobkin, Mann, Gara, Interian, Rodriguez, & Menza, 2020), such as the Telephone-Reality Orientation Therapy and daily living skills rehabilitation (Panerai, Catania, Rundo, Bevilacqua, Brunetti, De Meo *et al.*, 2019) by using apps installed on tablets or PCs. These teleservices will be an anchorage in order to avoid patient and caregiver withdrawal, due to the prolonged period of loneliness and social distancing, and to prevent depressive disorders and the worsening of both patient neurobehavioral symptoms and distress and burden of caregivers.

The strength of our study lies in the use of a multidimensional approach to investigate caregivers' personal conditions during a pandemic, together with the fact that this is the first Italian study on this topic with a fairly large sample, as far as we know. The weakness of this study, however, is its limitation of using only one source of information provided by the caregivers.

The development of telemedicine interventions could allow the collection of data also from tests administered directly to patients, thus providing a more exhaustive and enriched clinical picture on which to deepen research hypotheses.

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