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Secondary impacts of COVID-19 pandemic in Fatigue, Self-Compassion, Physical and Mental Health of People with Multiple Sclerosis and Caregivers: The Teruel Study

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Abstract: The secondary impacts of the COVID-19 pandemic are distress triggers and risk factors for mental health. Conversely, self-compassion skills and compassionate thoughts/behaviors towards suffering may contribute to their alleviation. Both psychological constructs are interrelated in life-threatening diseases such as Multiple Sclerosis (MS). The Teruel Study retrospectively evaluated the impact of strict confinement in the 44 people with MS of this Spanish province and 24 caregivers on 1) fears and perceptions; 2) self-compassion (patients) and compassion (caregivers); 3) physical and mental health, and Fatigue. Despite better housing conditions, patients considered confinement very difficult to handle, more than caregivers, but they were less afraid of COVID-19 or worsening of MS. Still, they recognized worse health than before confinement. Reclusion and lack of walks were the worse of confinement. Caregivers also referred to lack of leisure and uncertainty-fear. All agreed the best was staying with the family, but some found 'nothing' positive. Self-compassion remained moderate-high and strongly correlated with their moderate levels of social function, vitality, physical role, and global health. Physical and cognitive fatigue scores were high, and self-compassion negatively correlated with them, explaining a 19% variance of global health. The high compassion of the caregivers did not correlate with any variable.

Keywords: secondary impact; COVID-19; multiple sclerosis; caregivers; fears; health; HRQoL; self-compassion; compassion; fatigue

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1. Introduction

Secondary impacts are defined as those caused by the COVID-19 pandemic indirectly, either through the effect of fear on the population or as a consequence of the measures taken to contain and control it [1]. The emergency and uncertainty associated with the COVID-19 pandemic accompanied by unsustainable economic losses and stigma have been identified as stressors and strong constraints for physical or emotional adaptation of the individuals and society [2,3]. The fear of getting infected, fear of death, or worsening of health in those already ill and their caregivers can be strong triggers of emotional distress and risk factors for mental health problems [4]. Perceived stress levels may vary in each country, partly depend on the policy adopted in each territory, and can have important implications for the health and well-being of the population, especially in those already ill [5]. Mental well-being (depression, loneliness, insomnia, daily life fatigue) during COVID-19 related home-confinement have been reported [6-8]. In the case of the Spanish population, six days after the WHO declaration of the global pandemic by COVID-19, a period of three months of strict confinement of the entire Spanish population was implemented. Afterward and still now, other governments adopt similar measures to counteract the fast spread of the pandemic despite severe confinement measures, quarantine, and social isolation exert significant psychological, societal, and economic secondary impacts [6-10].

Conversely, compassion, the process that arises from recognizing the other's suffering and in response to discomfort, contributes to alleviate and create thoughts of empathy and feelings of affability for those who suffer. Therefore, compassion is defined as the ability to establish sincere and empathetic connections with the suffering of others and to feel the desire to relieve their pain [11]. However, to connect with other people's suffering and feel compassion for the "other," it would be necessary to start with oneself, that is, with self-compassion [12]. Thus, psychology conceives self-compassion as involving the mind and allowing the development of personal skills that also translate into interpersonal relationships to promote compassionate thoughts and behaviors [13]. According to Neff [13], self-compassion is defined as the ability to understand and support oneself under challenging moments, assuming one's suffering with kindness and warmth as if it were an inward compassionate action and identifying what is needed to face this situation [14]. Compassion and self-compassion constructs are under strong feedback in those confronting a life-threatening disease or conditions such as Multiple Sclerosis (MS), and their interplay depends on many factors [14].

Multiple Sclerosis is an autoimmune, neuroinflammatory, demyelinating, and neurodegenerative disease of unknown etiology, chronic in nature, and unpredictable course that affects the central nervous system and the immune system [15,16]. Present throughout the world, MS can affect each person in a heterogeneous way, but it is ranked as the second leading cause of neurological disability in young adults, causing greater functional and cognitive disability and detriment to their quality of life [15,16]. MS usually appears between the ages of 20-45 years and occasionally begins in childhood or later in life, with three-quarters of the patients being women. There is a large latitudinal difference in the distribution of MS, with higher figures in areas distant from the equator, so sun exposure and vitamin D deficiency are some of the most studied environmental risk factors [17]. Tobacco use, childhood obesity, diet, intestinal microbiota also increase the risk of MS. A wide variety of viruses have been associated with MS, although no direct relationship has been demonstrated with any of them [15]. Symptoms of MS vary depending on the size and location of central nervous system damage. They include mental (cognitive impairment, mood, emotional and affective disorders) and physical health problems (decreased limb function, impaired bowel or bladder control, spasticity, sexual dysfunctions, vision disturbances, impaired balance, pain, and debilitating fatigue). Most importantly, the physical and mental affectations can be synergistic. Thus, MS-associated fatigue can affect 87% of patients and cause significant physical, psychological, emotional, work, and social limitations. 40% of these patients consider fatigue as the most disabling symptom, and it constitutes one of the main causes of unemployment among people with MS. In fact, fatigue is defined as a subjective feeling of tiredness or lack of energy, disproportionate to the effort made or the degree of disability that significantly interferes [18]. The pathophysiology of fatigue in MS is currently unknown. However, different hypotheses are proposed, and a multifactorial origin is postulated, combining different factors and a different specific weight in each of them [18]. It is important to emphasize that there are difficulties in understanding its pathophysiology, quantifying it, and treating it. In addition, many modifying MS treatments are based on suppressing or modifying the immune system, and therefore worries about some predisposition, MS medications increasing the chance of developing complications from a COVID-19 infection, as well as clinical characteristics and outcomes in patients with COVID-19 and MS, raised during the pandemic [19-24].

The Teruel Study aimed to evaluate retrospectively, during June-July 2020, the physical and psychological impact of the COVID-19 pandemic in the 44 people with MS of this central-eastern area of the Iberian Peninsula and 24 caregivers. First, we questioned them about the features of their confinement, fears of worsening the disease, being infected and ill of COVID-19, and the best/worse of that situation. After that, the study aimed to assess self-compassion (people with MS) and compassion (caregivers) and relate to physical and emotional health variables, specifically to fatigue. Questionnaires validated to the Spanish population that measure compassionate abilities and physical and mental health were used. To determine the relationships and the predictive and explanatory validity of the psychological and emotional factors that make up self-compassion with states of general health, physical function, physical role, emotional role, social function, body pain, vitality, mental health, as well as physical, cognitive and psychosocial fatigue.

2. Materials and Methods

2.1. Sample and Experimental design

The sample population was constituted of 44 people with MS and 24 caregivers. It was a cross-sectional, naturalistic design with consecutive cases diagnosed of MS according to the McDonald criteria [25,26] that requests objective evidence in at least two areas of myelin loss or demyelinating lesions appearing in two distinct and time-spaced neurological areas and a differential diagnosis with similar neurological diseases.

MS sample population- The inclusion criteria were: Adults over 18 years from Teruel with a diagnosis of MS by the Specialized Health Service of Neurology by the Neurological Units and belonging to the Turolense Association of Multiple Sclerosis (ATUEM) or the Spanish Multiple Sclerosis Association (EME); Sustained attention and verbal understanding of the language; Participation and informed consent. The exclusion criteria were: Refusal to participate in the study, Severe cognitive and/or physical impairment or disorder.

Caregiver sample population - The inclusion criteria were: Adults over 18 years caregivers of a person with MS participant in the Teruel Study, Participation, and informed consent. The exclusion criteria were: Refusal to participate in the study.

2.2. Procedures and Variables of Study

The research protocol, informed consent, and information collection instruments were reviewed and approved by the ethics committee of ATUEM. All participants were informed of the objectives of the present study and signed the informed consent before participating in the study. They also confirmed in writing the policy of the General Data Protection Regulation (GDPR).

The variables of the study were as follows:

Sociodemographic: age, sex, educational level, employment situation, type of coexistence, place of residence.

Personal survey on coexistence, positive and negative aspects, fears of getting sick or getting infected and personal reflections in times of the COVID-19 pandemic.

Psychological and emotional variables related to compassion and self-compassion.

Quality of life related to general health, physical function, physical role, emotional role (anxiety and depression), social function, body pain, vitality, and mental health.

Symptoms of physical fatigue, cognitive and psychosocial fatigue.

2.3. Evaluation Instruments

Five scales validated in the Spanish population were used:

[1] *Quality of Life Scale SF-36* [27] It is a generic scale that provides a health status profile, and it applies to both patients and the general user population. It is made up of 36 items that analyze the 8 dimensions of health status. Briefly, 1.Physical function; 2.Physical role; 3.Body pain; 4.General health; 5.Vitality; 6.Social function; 7.Emotional role; 8.Mental

health. The questionnaire allows the calculation of two summary scores, the physical component summary (PCS) and the mental component (MCS). It is useful for evaluating health-related quality of life (HRQoL) in the general population and specific subgroups, comparing the burden of various diseases, detecting health benefits produced by a wide range of treatments, and assessing the individual health status of patients. It has good psychometric properties that have been evaluated in numerous articles and allow the comparison of results; therefore, it is considered one of the instruments with the greatest potential in HRQoL that has been validated in the Spanish population [27].

[2] *Self-Compassion Scale (SCS)* [28]. The questionnaire SCS has 26 items and assesses six factors, the three main factors of compassion and their respective opposite constructs: kindness and self-judgment, common humanity and isolation, and mindfulness and over-identification. This questionnaire offers both a separate score of each component and a total score. It evaluates the extent to which the participants show they are self-compassion, how they accept that suffering, failure, and defects are inherent to the human condition. Thus, it analyzes the openness towards their suffering, experiencing feelings of kindness towards oneself, with a position free of negative judgments in the face of suffering. The Spanish version [29] of its short form, *Self-Compassion Scale-short form (*SCS-SF) [30] reduced to the 12 items was also used in this study. The SCS-SF presents appropriate psychometric properties as Cronbach’s alpha of 0.85, test-retest reliability of 0.89, and high correlations with the long-form.

[3] *Compassion Scale* (CS) [31]. The Compassion Scale has 24 items self-report, and it is based on Neff’s Self Compassion Scale [28] in the structure of compassion toward oneself (self-compassion) to compassion toward others. The SCS and the CS have the same three main components (kindness, common humanity and mindfulness), but they differ in their opposites. Thus, in the questionnaire CS, the opposite of kindness is indifference, the common humanity is separation, and mindfulness is the opposite of disengagement. The CS scale was not significantly correlated with Neff’s SCS. The Spanish version of CS [32] has adequate validity and internal consistency (Cronbach’s Alpha = 0.89).

[4] *Modified Fatigue Impact Scale (MFIS)* [33,34]. The MFIS is a multidimensional scale, a method widely used to assess fatigue in patients with MS. It is a modified version of the Fatigue Impact Scale (FIS 8) [35]. It has been shown to be an adequate measure of response to change and presents validity for the subjective daily experience of fatigue, originally developed to assess the effects of fatigue on the quality of life of patients with chronic diseases. It has shown reliability and validity in application to different populations of different cultures [36]. It comprises 21 items with high inter-element correlations and distributed in 3 subscales: physical, cognitive, and psychosocial. It contains 9 items that measure the physical factor, 10 items, the cognitive factor, and 2 items, the psychosocial factor. The global score ranges from 0 to 84. A cut-off point (38) has been established to define the presence or absence of fatigue. Higher scores indicate a greater impact of fatigue on the disease and the patient's quality of life.

2.4. Statistics

Statistical analysis was performed with SPSS 25.0 software (IBM Corp., Armonk, NY, USA). First, sample descriptives were made using relative and absolute frequencies, dispersion, and central tendency: mean, median, standard deviation, minimum, maximum, confidence interval (CI), and the number valid of cases. To determine the relationship between categorical variables with two levels and quantitative variables, the Student *t*-test or analysis of variance was used if the quantitative variable assumed normality. The normality of the contrasted variables was evaluated with the Kolmogorov-Smirnoff test. In another case, the non-parametric Mann-Whitney U or Kruskal-Wallis H tests were used. In a second stage, to analyze the correlations between the different quantitative constructs, a Spearman Rho non-parametric correlation matrix was calculated, which included the constructs or psychological variables of self-compassion and the variables related to general health and fatigue. In a third stage, to determine the weight of the constructs of self-compassion and compassion related to physical and emotional health in the measured prognostic variables, a logistic regression analysis was used to control general health and fatigue variables.

3. Results

3.1. Sociodemographic Descriptives of people with MS and Caregivers

The descriptives of a total sample of the 68 participants (44 people with MS and 24 caregivers) in this study are detailed in Table 1.

Table 1. Distribution of the samples of people with MS and their caregivers according to sociodemographic variables.

		People with MS		Caregivers	
		N = 44		N = 24	
		Frequencies	%	Frequencies	%
Gender	Female	31	70.45	16	66.67
	Male	13	29.55	8	33.34
Age	<36 years	2	4.55	7	29.16
	de 36 a 45	10	22.73	2	8.34
	de 46 a 55	21	47.73	9	37.5
	>55 years	11	25.00	6	25
Marital status	Married/ living with partner	35	79.55	17	70.83
	Single	6	13.64	7	29.17
	Separated/ Divorced	3	6.82	-	-
Living arrangements	Lives alone	4	9.09	3	12.5
	Lives with partner/spouse	15	34.09	11	45.84
	Lives with partner/spouse and children	19	43.18	8	33.34
	Lives with other family	6	13.64	1	4.16
	Other	-	-	1	4.16
Education	No qualifications	1	2.27		
	Primary school	8	18.18	5	20.83
	Secundary school	13	29.55	9	37.5
	University	22	50.00	10	41.67
Employment situation	Students			4	16.67
	Homemarker	2	4.55	1	4.17
	Unemployed	1	2.27	-	-
	Employed	10	22.73	11	45.83
	Temporary unemployed	1	2.27	3	12.5
	Retired	13	29.55	3	12.5
	Permanent disability	12	27.27	1	4.17
	Other	5	11.36	1	4.17

Gender and Age: Forty-four people with MS voluntarily participated in this study, in a female:male ratio of 70:30 (31 women, 13 men), with a mean age of 49.98 years (95% CI: 47.31-52.65; SD: 8.78, Minimum and maximum value of 27 and 70 years, respectively). By age ranges, the highest percentage appeared in the age group between 46 and 55 years. Twenty-four caregivers voluntarily participated, in a female:male ratio of 67:33 (16 women, 8 men), with a mean age of 45.90 years (95% CI: 39.53-52.30, SD: 14.76, Minimum and maximum value of 23 and 67 years, respectively). By age ranges, the highest percentage also appeared in the age group between 46 and 55 years. The distribution by age bands of the samples of MS patients and MS caregivers is shown in Table 1.

Marital Status: Almost 80% of the MS patients were married or with a partner. The rest of the sample was distributed among singles (13.6%), separated and/or divorced (6.8%). These last two categories accounted for approximately 20% of the sample. 70.8 % of the MS caregivers were married or with a partner, and the rest were single (29.1%).

Living arrangements: Regarding residence, 98% of the MS patients and MS caregivers resided in Teruel and the province and 2% in Zaragoza. About half of the MS patients (43.2%) lived in their own home with a partner and/or children, followed by those who lived with a partner without children (34.1%). 13.6% lived in the home of relatives, and 9.1% lived alone in their own home. Practically, half of the MS caregivers (45.8%) lived in their own home with their partner, and 33.3% lived with their partner and children. 8.2% lived at the home of relatives and neighbors.

Education: Regarding the academic level of MS patients, 50% had higher university studies, almost 30% studied until secondary school, 18.2% had primary studies, and only 2.3% had no studies. Almost 80% of MS caregivers attended secondary and/or university studies, and 20.8% studied until primary education.

Employment Situation: 29.5% of the MS patients were retired. The next largest group was people with permanent disabilities (27.3%), and 22.7% were working. 11.4% of the MS patients were self-employed and/or entrepreneurs, 4.5% corresponded to housewives or dedicated to caring for the family, and 4.6% were unemployed with temporary leave. The employment situation of MS caregivers was as follows: 45.8% were working. 16.6% were students, and 12.5% had sick leave and retired, respectively.

3.2. COVID-19, Confinement and Fears

Figures 1, 2, and 3 illustrate the features of the confinement for the sample population. During the confinement, MS patients were living in a home (Figure 1A) with a 2 to 4 people structure (22% with another person, 20% with 2 people, 29.55% with 3 people). In the case of caregivers, the structure was of 3-4 people at home (29.17% with 2, 33.33% with 3). Most answers about the number of rooms during the confinement (Figure 1B) were “more than 3 rooms” in both groups, but the frequency was higher in MS patients (88.64% *vs.* 58.33%, Fisher's test, ***p=0.0062) since few of their homes had only three as compared to caregivers (7% vs. 38%, Fisher's test, p=0.0026). Referring to how both groups have coped with confinement (Figure 1C), 59.09% of MS patients and 66.67% of caregivers rate it as “bearable.” They obtain similar scores in “relatively easy” (MS, 64% *vs.* caregivers, 12.50%) and “difficult” (MS, 18.18% *vs.* caregivers, 6.67%). The 9.09% of the MS patients considered confinement “very difficult” to handle, while only one caregiver (4.17%) referred so.

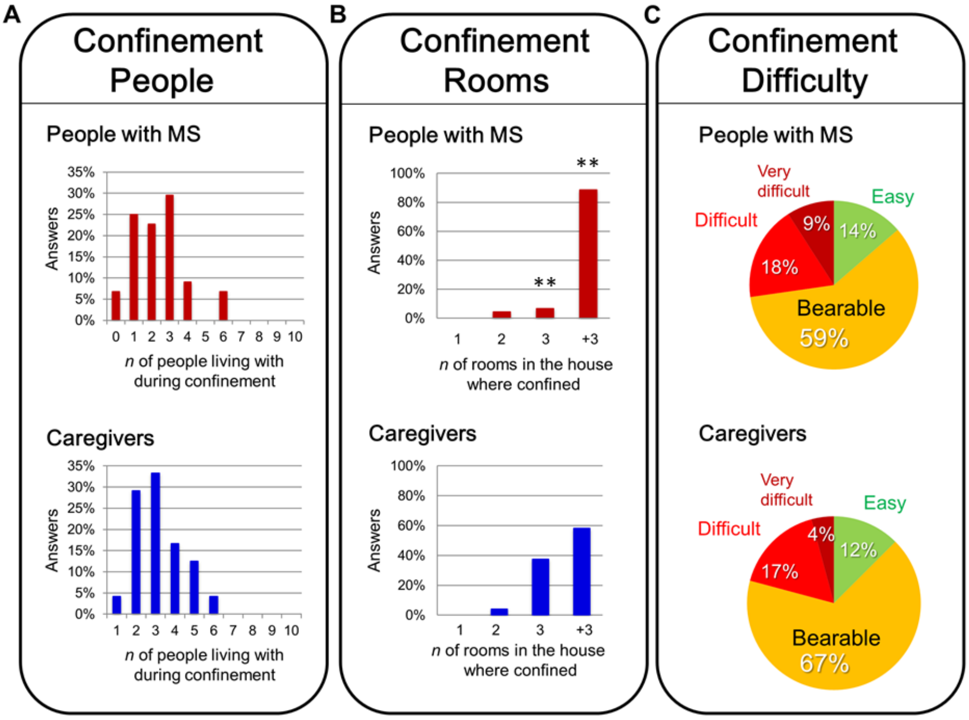

Figure 1. Confinement – People, Rooms, and Difficulty. Sample distribution of the people with MS and caregivers answering to the number of people living with them during the confinement (A), the number of rooms of the house where they were confined (B), and the level of difficulty the found to handle the period of confinement (C). Statistics: Fisher's test, $^{**}p<0.01$ People with MS vs. caregivers.

The open questions on the worst of confinement (Figure 2B) "unable to exit" was the worst for 34.09% of the MS patients, while "not having leisure-walking" was referred in 31.82% of comments. For caregivers, "not having leisure-walking" and "uncertainty-fear" were the most referred concepts (29.17% each) expressed.

On the positive side, the best of confinement (Figure 2C) for the MS patients was “being with the family or having more time with them” with 40.91%, and it was also the most common benefit referred by caregivers (45.83%). On the other hand, one (20.45%) patient and one (12.50%) caregivers regretted and answered with “nothing.”

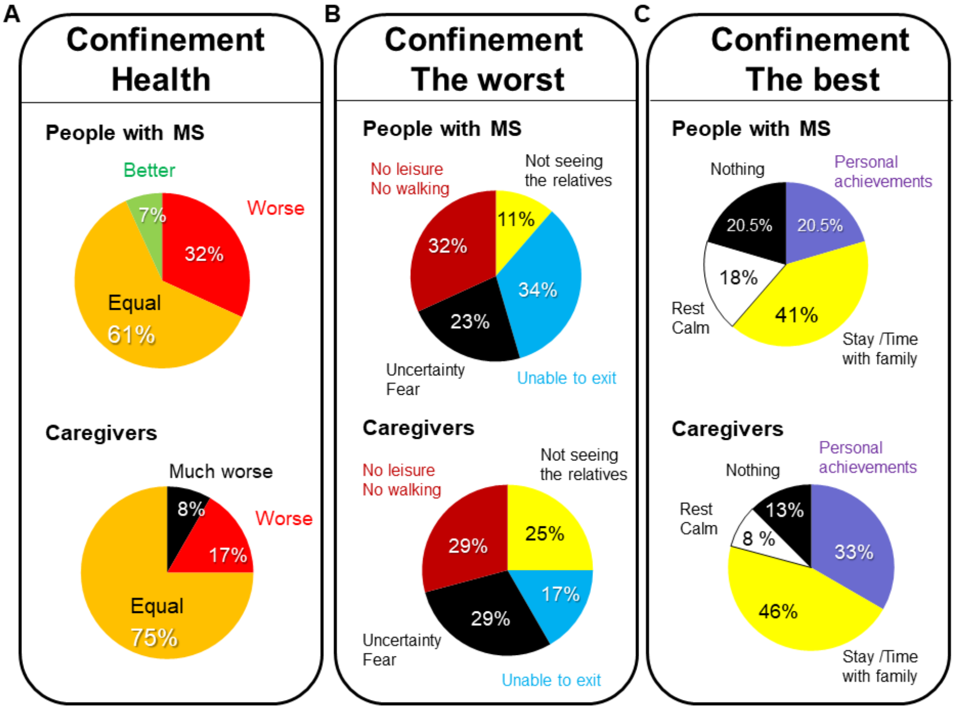

Figure 2. Confinement – Health, The worst, and The best. Sample distribution of the people with MS and caregivers answering to their health status as compared to before the confinement (A), the worse of the confinement (B), and the best of the confinement (C).

Concerning fear that MS will worsen during the pandemic (Figure 3A), 47.73% of the people with MS answered with a "No" as compared to 52.27% who affirmed that "yes", they were afraid (18.18%) or “sometimes” (34.09%). For their counterparts, the caregivers, half of them answered "Yes" (50%) and 29.17% “sometimes”, as compared to 21.1% who said "no". Thus, statistically significant differences were found with regards to this fear, with people not afraid of worsening of MS being higher among the patients than in the caregivers' group (Fisher's test, *p=0.0379), and a significantly lower number of people with MS affirming to be worried about it than their caregivers (Chi-square, 6.118, 1df, *p=0.0134).

When individuals were asked if they were afraid of getting infected and sick with COVID-19, 34.09% MS patients answered both “Yes” and 34.09% “No”. In contrast, caregivers were more afraid, as only 2 of them (8.33%) answered negatively, and the other 22 (91.7%) were afraid, with 48.83% affirmative "yes" or 43.5% “sometimes”.

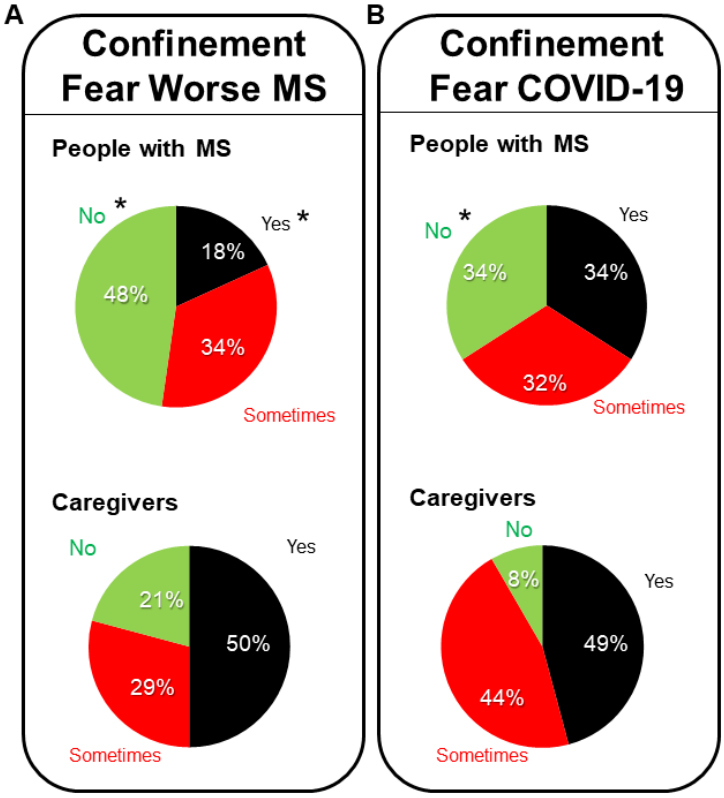

Figure 3. Confinement – Fears of worsening of MS and COVID-19 related fears. Sample distribution of the people with MS and caregivers answering their fears of MS being worsened during the confinement (A), and fears about getting infected and ill with COVID-19 (B). Statistics: Fisher's test or Chi-square, *p<0.05 People with MS vs. caregivers.

3.3. Fatigue, Self-compassion, and Compassion in people with MS and Caregivers

Table 2 and Table 3 depict the analysis of the dimensions of the perception of quality of life-related to the physical and emotional health of MS patients in the last 4 weeks of June and early July 2020 post confinement. On average, values of moderate health were found in the state of general health, physical function and role, body pain, vitality, social function, emotional role, and perceived mental health. The data also indicated that the physical health of these patients has not interfered with their daily activities and their perception of health. This also included their prospects and resistance to getting ill in these times of the COVID-19 pandemic that presented moderate average levels.

The results obtained on the assessment of mental health related to anxiety, depression, and self-control remained within normal values of mental well-being. However, the self-compassion scores of MS patients presented a medium-high level. Based on the cut-off points, it was found (Table 2) that there were high fatigue levels, mainly physical and cognitive fatigue. However, psychosocial fatigue remained at a medium level. The great dispersion obtained in the fatigue results (DT 8.99 and DT 9.6, respectively, in the group of people with MS) should be noted.

The caregivers of people with MS obtained high scores in compassion, as well as in their health levels and quality of life-related to a good perception of health-related to their physical function, vitality, mental and emotional health. On the other hand, the scores related to fatigue were lower than the cut-off point, which indicated the absence of physical, cognitive, or psychosocial fatigue. However, a great dispersion in the results should also be noted (DT 8.6; DT 8.7) in this group.

Table 2. Descriptive statistics of Self-compassion, Health and Fatigue variables in people with MS.

People with MS (N=44)	Mean	Median	SD	Range	Min	Max	95% (IC)
Self-compassion	3.22	3.16	0.565	2.08	2.25	4.33	3.05- 3.39
Physical function	20.90	22	5.838	20	10	30	19.13- 22.68
Physical role	5.79	5.50	1.636	4	4	8	5.29- 6.29
Emotional role	5.36	6	1.122	3	3	6	5.02- 5.70
Social function	7.97	8	2,085	8	2	10	7.34- 8.61
Body pain	7.72	8	2.433	8	3	11	6.98- 8.46
Vitality	13.90	15	4.917	17	5	22	12.41- 15.40
General health (PCS)	17.18	17	3,642	14	10	24	16.07- 18.28
Mental health (MCS)	23.20	23	3.825	15	15	30	22.04- 24.36
Global health (HRQoL)	102.06	103	17.775	63	68	131	96.66- 107.47
Physical fatigue	20.18	23	8,994	34	0	34	17.44- 22.91
Cognitive fatigue	15.06	18.50	9.604	33	0	33	12.14- 17.98
Psychosocial fatigue	3.56	4	1.921	8	0	8	2.98- 4.15
Global fatigue	38.81	43.50	17.838	61	0	61	33.39- 44.24

Confidence interval= 95% (IC); Min= mínimum; Max=maximun; SD= Standard desviation.

Table 3. Descriptive statistics of Compassion, Health and Fatigue variables in MS caregivers.

MS caregivers (N=24)	**Mean**	**Median**	**SD**	**Range**	**Min**	**Max**	**95% (IC)**
Compassion	3.84	3.9	0.442	1.5	2.96	4.54	3.65 – 4.03
Physical function	26.13	28	4.902	16	14	30	24.01 – 28.25
Physical role	6.78	8	1.565	4	4	8	6.10 – 7.45
Emotional role	4.83	5	1.267	3	3	6	4.27 – 5.37
Social function	7.13	7	2.262	8	2	10	6.15 – 8.10
Body pain	8.48	9	2.644	9	2	11	7.33 – 9.62
Vitality	14.65	15	3.961	14	7	21	12.93 – 16.36
General health (PCS)	20.35	21	4.323	17	10	27	18.47 -22.21
Mental health (MCS)	20.52	22	5.265	22	7	29	18.24 – 22.79
Global health (HRQoL)	108.87	117	21.808	86	52	138	99.43 – 118.29
Physical fatigue	11.82	9	8.680	32	1	33	8.06 – 15.58
Cognitive fatigue	11.91	10	8.789	30	0	30	8.11 – 15.71
Psychosocial fatigue	2.86	2	2.399	7	0	7	1.83 – 3.90
Global fatigue	26.60	23	18.376	64	5	69	18.66 – 34.55

Confidence interval= 95% (IC); Min= mínimum; Max=maximun; SD= Standard desviation.

3.4. Correlations between Self-compassion in People with MS and Compassion in Caregivers with Physical and Mental Health, including Fatigue.

The analysis between the psychological variables of self-compassion and compassion and the different physical and mental health variables, including fatigue, a bilateral correlation with Spearman's coefficient is depicted in Table 4.

The correlations between self-compassion in the people with MS and the scales of physical role, social function, vitality, and global health were positive and statistically significant (**p <0.01, *p <0.05). Negative correlation was found between global fatigue and cognitive fatigue. The impact of fatigue (cognitive and global) in people with MS showed significant correlations with the psychological variables of self-compassion.

The compassion scale completed by caregivers did not show a significant correlation or Association with the variables related to the mental, physical or global health, nor fatigue.

Table 4. Correlations between psychological variables of compassion and self-compassion and variables of health and fatigue in a sample of people with MS and their caregivers (Rho Spearman method).

	***rho* Self-Compassion**	***rho* Compassion**
Physical function	0.155	0.247
Physical role	**0.330***	-0,011
Emotional role	0.191	-0.054
Social function	**0.387****	-0.052
Body pain	0.269	-0.089
Vitality	**0.456****	0.084
General health (PCS)	0.296	0.328
Mental health (MCS)	0.278	0.134
Global health (HRQoL)	**0.436****	0.170
Physical fatigue	-0.285	0.023
Cognitive fatigue	**-0.380***	0.132
Psychosocial fatigue	-0.262	-0.036
Global fatigue	**-0.455****	0.040

PCS, physical component summary; MCS, mental component summary; HRQoL Health-related Quality of Life; rho= rho Spearman; * $p < 0.05$; ** $p < 0.01$.

3.5. Regression analysis of Self-compassion in MS patients and Compassion in Caregivers

Two regression analyses were carried out, considering the criteria variables, the global fatigue and the perception of global health, and as explanatory variables, the psychological variables of self-compassion mentioned (Table 5). In the final model, self-compassion was maintained as an explanatory factor in 19% of the global health variance in people with MS (Table 5). The regression analysis was also performed in the sample of caregivers, considering global health and fatigue as the dependent variables and compassion as the independent and explanatory variable. However, the study results did not reveal that compassion was a predictive / explanatory factor for overall health and fatigue in the sample of caregivers.

Table 5. Regression analysis of Self-Compassion on the Global Health, Health-related Quality of Life. Stepwise method.

Model	R	R^2	R^2 adjusted	ESE	Chance R^2	F-chance	gl1	gl2	*p-value*
1	0.441a	0.194	0.175	16.144	0.194	10.129	1	42	0.003**

Dependent variable: Global health (HRQoL). Predictors in the model: Constant and Self-Compassion ESE: estimated standard error, **$p<0.01$

4. Discussion and implications

4.1. Sociodemography, COVID-19 confinement and fears

The COVID-19 pandemic lockdown, with the paralysis of economic activity, the closure of educational centers, and the confinement of the entire population for weeks were extraordinary situations and multiple stress-generating stimuli at the societal and individual level that persists today. Home confinement is an unprecedented situation that is not exempt from implications in people's physical and psychological well-being [37]. The sociodemographic status and cultural background can make a difference in the impact of these stressors associated with the COVID-19 pandemic, mainly in those who already have a disease condition, their caregivers, and their families. In the present work, the status of the people with MS was good enough to provide a 'sociodemographic' resistance to the individuals, helpful to hamper the effects of lockdown. Family structure at home was of 2 or 3 people, in houses with high vital space (more than three rooms). From a gender perspective, ratios in the sample of participants with MS showed an overrepresentation of females, in agreement with the general prevalence of the disease with a 65:35 female: male ratio, which is on the increase [16,38,39]. In a recent online survey by Zhang et al. [40] to people with MS from Sevilla, a southern Spanish area, and several provinces of China, including a high proportion of young patients, no differences in self-reports on social-laboral effects of confinement were identified regarding sex. In their work, despite Spanish people with MS had greater economic stability and social support, similar perceptions of the pandemic's social and laboral consequences were reported, with the use of social networks and family support being also similar in both groups.

To our knowledge, the present work is the first to analyze the effect of confinement in both people with MS and their caregivers, providing a bio-psycho-social approach. In agreement with the traditional gender population dedicated to caring for the older people or sick, mainly in familialist countries like Spain and Italy, caregivers were also predominantly female [41,42].

According to the mean age of the sample and their marital status, and considering that MS mainly affects young subjects, we can infer that MS was experienced from its chronic nature in most of the participants. This is also important to consider regarding the open questions about the best/worse of the confinement since the patients' physical limitations and fatigue impede their quality of life.

Despite more patients considered confinement more difficult than caregivers, they were less afraid of worsening MS or COVID-19 but recognized the worsening of their heath during the strict lockdown. The reference to the inability to exit and not to do their regular walks and rehabilitation programs as the worst of the confinement, aware about the impact that the restrictive conditions had in their lives. Despite this can be easily predicted for physical health, it is noteworthy that lack or substantial reduction of physical activity also may have prevented MS patients and caregivers from its beneficial effects on mood. The impact of the constraints on the mental health of patients and caregivers should not be underestimated. Conversely, a recent report showed that moderate-intensity physical activity was an effective strategy to modulate emotional distress during the COVID-19 pandemic in a population of working mothers experiencing heightened levels of parenting stress [43].

As resistance/resilient aspects, both patients and caregivers agreed that "staying or time with the family" was among the best of the confinement. Although these spontaneous answers were also expected, these statements are supported by cultural and traditional roots since long-term care models in Spain and Italy are usually labeled as familialist or family-based [41,42]. Although the worst of lockdown was reclusion and lack of walks, the caregivers also referred to lack of leisure and uncertainty-fear, which would agree with caregivers' compassion role. This also agreed with their fears about the worsening of the MS, or themselves getting infected and ill of COVID-19 and the associated risk of death. Pessimistic answers in some patients and caregivers were also noted when they answered with a simple 'nothing' to what was 'the best'. Depressive symptoms, loneliness, insomnia, daily life fatigue have been reported as common disruptions of mental well-being during COVID-19 confinement [6-10]. A prospective cohort study by Andreu-Caravaca et al. [44] conducted in Murcia, middle-eastern Spanish area, investigated the effects of home-confinement on the low sleep quality, cardiac autonomic dysfunction, and poor quality of life, as some of the most prevalent symptoms in people with MS which worse with the progress of MS and also with physical inactivity. Their results showed that the strict confinement worsened the sleep quality, but not their cardiac autonomic control as measured by heart rate variability, nor their health-related quality of life. The worsening of these three variables is among the major-stress related symptoms reported during lockdown with sleep disorders (the socalled coronasomnia) as one of the most prevalent in this COVID-19 scenario [6-9]. In these and other respects, during the period of confinement, Reguera-García et al. [45] conducted a study on 84 people with MS belonging to MS Associations in Castilla and Leon, a northwest area of Spanish. Their work reports average levels of 'sense of coherence' (SOC-13), high levels of 'resilience '(ER-14), and also of 'coping' (COPE-28), primarily through active confrontation and religion. These psychological variables were correlated among them but were not related to the moderate to high score levels of physical activity (IPAQ-SF) recorded in this sample population.

4.2. Fatigue, self-compassion, and compassion in people with MS and caregivers

In this study, the impact of fatigue on the physical, cognitive, emotional, and psychosocial dimensions was analyzed. The fatigue evaluated in people with MS and caregivers showed similar results to those reported in a cohort of 227 patients with MS where fatigue was a persistent symptom during the 18 months of duration of the study in 86.8% of participants [46]. In another longitudinal study on a population of 267 patients with MS, where fatigue severity was assessed three times/year, 38% had persistent fatigue (FSS > 5 on all 3 occasions), 37% had sporadic fatigue (FSS > 5 in 1 or 2 occasions), and 25% did not have fatigue [47].

Self-compassion was evaluated in people with MS in times of the COVID-19 pandemic in Teruel during the months following the confinement in June July 2020, and the results showed a high score for self-compassion. From Buddhist philosophy, self-compassion postulates that suffering is a connatural and inevitable condition in human beings. Therefore, it is necessary to tune in to it and have the predisposition to alleviate it [48]. Furthermore, scientific evidence about the psychological aspects, both functional and dysfunctional, is associated with the construct of self-compassion [49]. In the healthcare setting, compassion would allow emotional commitment to patients and their needs [50]. Some studies show that the experience of “self-compassion” protects against stress and anxiety, eliminating thoughts that decrease self-confidence [51]. Self-compassion also helps to connect with negative emotions and develop strategies to address difficulties, take responsibility for negative events, and foster an internal dialogue with kindness and understanding with the personal deficiencies that cause suffering [52].

The present results in people with MS highlight the relevance of self-compassion in their lives in relation to social variables and quality of life variables related to their health in terms of fatigue, physical role, energy, or vitality. This ability to be self-compassionate can be an important source of resistance and resilience since it implies accepting that suffering, failure, and one's own defects as part of the human condition, evaluating openness towards one's own suffering, experiencing feelings of kindness towards oneself, with a posture free of negative judgments in the face of suffering, as described by Neff [28]. The present results showed that a higher score in self-compassion correlated positively with the variables of depression and anxiety or mental health. This construct has explanatory and had predictive validity concerning the global health state (health-related quality of life) in the sample of people with MS the Teruel Study. Therefore, according to Yarnell et al. [53], if it is an ability to open up to the experience of pain without reacting to it, we will have to delve into the study of this construct and see the influence and impact of the social environment to which the individual belongs.

Consistent with the results of our study, there is scientific evidence on the benefits of self-compassion. Self-compassion has been associated with physical and emotional well-being, emotional intelligence, social function, satisfaction with life, feelings of competence, happiness, optimism, and knowledge. Self-compassionate people adhere better to diet treatments, exercise, and anti-tobacco addiction programs and reduce procrastination. Self-compassion has also been associated with a decrease in anxiety and depression. It should be noted that self-compassionate people improve their self-esteem, but it does not depend on comparing themselves with others. People who score high on self-compassion find a way to comfort themselves when they fail by learning and growing from their mistakes in a resilient way. They are able to motivate themselves instead of criticizing themselves [54].

According to Gilbert et al. [55], with reference to self-compassion, he discovered that different subsystems of the nervous system are activated when we are compassionate and when we feel threatened. When the threat system is activated in a particular way by challenging situations, where sadness, anger, or fear appear, we likely attack ourselves, abandon ourselves, or block ourselves in anxious worry. However, when the compassion system is activated, the body interprets it as a security signal; we console ourselves, encourage ourselves, and relate kindly to ourselves. This research showed that different brain areas are activated when self-critical and self-compassionate [56]. Therefore, the interpretive process, partly at the unconscious level of the patient with MS, could explain the ability to protect and give security to their immune system already damaged by MS and not harm it to a greater extent due to their negative emotions.

Rogers [57] also referred to the relevance of the paradox of life: when a person accepts him/herself as he/she is, he/she can change. Research has shown that the more we push ourselves, beat ourselves up trying to improve, the harder it is to make a change. Self-compassion is one of the foundations of change. In the present work, the sample of people with MS had moderate scores on self-compassion and was more likely to learn from their mistakes and to re-commit to their goals. Gilbert et al. [58] also showed that people who suffer from depression and anxiety realize that their thoughts are irrational, but they cannot stop thinking about them. MS patients did not score high levels in distress, anxiety, and depression; therefore, it is expected that they have changed the tone of their conversations when talking about their disease and established cordial relationships. They have their emotional pain but share it with others from a more caring and healing position, as well as comforting for the collective of the association to which ATUEM belongs. The critical role belonging to associative MS networks had during the strict confinement was also referred to in the Castilla-León study [44], and it is always implicit in the existence of these associations where social understanding and support are so needed.

Compassion has been approached from different areas such as philosophy, positive psychology, social, neuropsychology, pedagogy, and spirituality, both in the East and in the West [59]. Lazarus and Lazarus [60] stated that compassion involved understanding the emotional state of others and that it was associated with a desire to alleviate or reduce the suffering of another person [61]. Compassion is considered an affective experience related to emotions, moral values, judgments about oneself and towards others and is also associated with personal and social well-being and depends on the culture, social context evaluated [62,63]. However, in the present study, the results of the caregivers of people with MS did not reveal information and did not show an association of the compassion construct with their quality of life related to their physical and emotional health. Our study hypothesized an association between the compassion and self-compassion constructs and the predictive and explanatory capacity of health outcomes, but the results address different outcomes from those contemplated by the current literature.

Within the adversities, unfavorable conditions, and multiple mourning processes with sudden and massive loss of human lives of the current COVID-19 pandemic, psychotherapeutic interventions based on self-compassion and compassion would be indicated in these particular psychological and medical conditions of people with neurodegenerative diseases, as are patients with MS. In addition, these interventions can be developed, operationalized, and improved through practice. According to Kirby [64], there are programs based on compassion with empirical evidence, such as Compassion Focused Therapy [65], Mindful Self-Compassion Training [66]. Following the proposal of Strauss et al. [67] and after the results of the present study, one of the lines of psychological approach would be to conceptualize compassion as a cognitive, affective, and behavioral process that would enhance five elements referred to both self-compassion and others: a) being aware of suffering, b) assuming it as a universal phenomenon in the human condition, c) showing empathy for those who suffer and connect with their emotions, d) being tolerant of the annoying feelings that are aroused by the response (anguish, anger, fear) by remaining open and accepting the sufferer and e) being motivated to act and alleviate suffering.

Developing compassion and self-compassion entails enhancing other psychological variables and favors interpersonal relationships and their social function, such as empathy, sympathy, love, altruism, prosocial behaviors, and feelings of pity [57]. Also, sensitivity appears as the ability to respond to the emotions of others and to be able to perceive the need for care from others, the motivation to act or respond to the suffering of others, tolerance to anxiety, and the ability not to judge, since they are relevant, as the authors emphasized that compassion consists of helping others without overidentifying with their suffering and without judging them. In this way, we can feel compassion for someone we do not like or have no affinity with us [44].

5. Limitations

The study's limitations refer to to the inherent cultural and social factors and the size of the sample population. Due to the difficulties of recruiting people with MS but primarily caregivers in the chronological scenario, the study does not allow us to generalize the results of the general population with MS. Since the impact of confinement would strongly depend on the living conditions and the demographic structure of the cities, we decided to choose the people with MS of ATUEM that gathers together patients from a high-altitude and small 14,809 km2 area in a mountainous region of eastern Spain, with a humid subtropical bordering on a cold semi-arid climate. From its 134,572 (2018) population, about a quarter live in Teruel, the capital, with a low population density, making it the least populated provincial capital in the country and providing a more homogeneous sample at the demographic, cultural, and environmental level. However, as discussed, similarities have been found in the decene of works carried by MS Associations. Through the different approaches and topics addressed, together, a complete picture of the effects of strict confinement in people with MS can be offered to gain knowledge in this respect that will be helpful for better preventive/therapeutical interventions and decision making on public health.

6. Conclusions

The results of MS patients and caregivers concerning COVID-19 confinement and their fears indicated that despite living in better housing conditions, more patients considered confinement more difficult than caregivers. Surprisingly, they were less afraid of worsening MS during the pandemic COVID-19, probably due to acceptance and self-compassion. Still, the patients recognized worsening of their health status as compared to before the pandemic. The worst of lockdown was reclusion and lack of walks. For the first time, in this scenario, caregivers' report is recorded on parallel to the people they care. They also referred to lack of leisure and uncertainty-fear. Both groups agreed that the best was ‘Staying with the family or having more time with it,’ but some complained, reporting a simple ‘nothing’.

In the second part of the study, the answers of patients and caregivers to the battery of psychological tests, indicated that:

1) Self-compassion evaluated after the post-confinement in the months of June-July 2020 of the MS patients remained at a moderate-high level.

2) MS patients perceived their physical and emotional health during June-July 2020 at medium and moderate levels.

3) The fatigue of MS patients during June July 2020 presented high scores, mainly in physical and cognitive fatigue.

4) The self-compassion of the group of MS patients significantly correlated with fatigue and global health (physical and emotional) and presented explanatory validity with a 19% variance of global health.

5) The high compassion of the caregivers of MS patients did not show relationships with any physical or emotional health variable, nor with fatigue scales.

Overall, this study reveals the importance of the self-perception of these patients towards their neurodegenerative disease that inherently implies severe physical, psychological, and social stress. It also analyses the explanatory capacity of the factors that promote self-compassion, the patient's own commitment response to alleviate suffering. It has also revealed psychological variables and coping styles that can limit or hinder the expression of the human capacity from dealing with the disease in all its physical and psychological aspects.

The temporal moment to raise the above questions, depending on their personal, family, social and professional situations in the middle of the COVID-19 pandemic and after the most extraordinary period of strict confinement that never experienced before, allow the results of this study to be useful and clinically relevant to envision the impact of the pandemic and the design of the post-COVID era for these patients and their caregivers.

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Institutional Review Board Statement: The study was carried out following the deontological standards recognized by the Declaration of Helsinki (52nd General Assembly Edinburgh, Scotland, October 2000), the Standards of Good Clinical Practice, and complying with current legislation and current Spanish legal regulations that regulate research, clinical practice in humans (Royal Decree 1720/2007 that develops the organic law 15/99 and Law 14/2007 of Biomedical Research. ATUEM was one of the institutions in which the application was carried out and it had the approval and review of the Spanish Multiple Sclerosis Association (EME). The objective of the research was explained to the participants and the people who voluntarily expressed interest in participating were given their informed consent and the protocol with the objective tests. Therefore, the information generated in this study has been considered strictly confidential between the participating parties. The data will be protected from uses not allowed by people outside the research and the confidentiality of the same will be respected in accordance to Organic Law 15/1999, of December 13, on the Protection of Personal Data and Law 41/2002, of November 14, basic law regulating patient autonomy and rights and obligations regarding information and clinical documentation.

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References

1. UNICEF. Monitoring and mitigating the secondary impacts of the coronavirus disease (COVID-19) pandemic on WASH services availability and access. UNICEF technical note https://www.unicef.org/documents/monitoring-and-mitigating-secondary-impacts-coronavirus-disease-covid-19-pandemic-wash. Accessed May 24, 2021.
2. World Health Organization. Mental health & COVID-19. https://www.who.int/teams/mental-health-and-substance-use/covid-19 Accessed May 24, 2021
3. Giménez-Llort L. The key role of chronosystem in the socio-ecological analysis of COVID. In: *Actas del VII Congreso Internacional de Investigación en Salud. Volumen I*. Madrid (2020).
4. Pan, K. Y.; Kok, A.; Eikelenboom, M.; Horsfall, M.; Jörg, F.; Luteijn, R. A.; Rhebergen, D.; Oppen, P. V.; Giltay, E. J.; Penninx, B. The mental health impact of the COVID-19 pandemic on people with and without depressive, anxiety, or obsessive-compulsive disorders: a longitudinal study of three Dutch case-control cohorts. The lancet. Psychiatry, 2021, *8*(2), 121–129. doi.org/10.1016/S2215-0366(20)30491-0

5. Varga, T. V.; Bu, F.; Dissing, A. S.; Elsenburg, L. K.; Bustamante, J.; Matta, J.; van Zon, S.; Brouwer, S.; Bültmann, U.; Fancourt, D., Hoeyer, K., Goldberg, M., Melchior, M., Strandberg-Larsen, K., Zins, M., Clotworthy, A., & Rod, N. H. Loneliness, worries, anxiety, and precautionary behaviours in response to the COVID-19 pandemic: A longitudinal analysis of 200,000 Western and Northern Europeans. The Lancet regional health. Europe, 2021, *2*, 100020. doi.org/10.1016/j.lanepe.2020.100020
6. Invitto, S., Romano, D., Garbarini, F., Bruno, V., Urgesi, C., Curcio, G., Grasso, A., Pellicciari, M. C., Kock, G., Betti, V., Fiorio, M., Ricciardi, E., de Tommaso, M., Valeriani, M. Major Stress-Related Symptoms During the Lockdown: A Study by the Italian Society of Psychophysiology and Cognitive Neuroscience. *Front. Public Health*. 2021, *9*, 636089. doi.org/10.3389/fpubh.2021.636089
7. Bartoszek A, Walkowiak D, Bartoszek A, Kardas G. Mental well-being (depression, loneliness, insomnia, daily life fatigue) during covid-19 related home-confinement - a study from poland. *Int J Environ Res Public Health.*, 2020, 17:7417. doi: 10.3390/ijerph17207417
8. Ferrer-Torres A and Giménez-Llort L Confinement and the Hatred of Sound in Times of COVID-19: A Molotov Cocktail for People With Misophonia. *Front. Psychiatry*, 2021, *12*:627044. doi: 10.3389/fpsyt.2021.627044
9. Ferrer-Torres A and Giménez-Llort L. Sound of silence in times of COVID-19: Distress and loss of cardiac coherence in people with Misophonia by real, imagined or evoked trigger sounds. *Front. Psychiatry*, 2021, in press doi: 10.3389/fpsyt.2021.638949
10. Brooks, S. K., Webster, R. K., Smith, L. E., Woodland, L., Wessely, S., Greenberg, N., & Rubin, G. J. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet*, 2020, *395*, 912–920. https://doi.org/10.1016/S0140-6736(20)30460-8
11. Gustin, L., and Wagner, L. The butterfly effect of caring – clinical nursing teachers understanding of self-compassion as a source to compassionate care. *Scand J Caring Sci*. 2013, 27(1), 175–183. doi: 10.1111/j.1471-6712.2012.01033.x
12. Barnard, L., and Curry, J. Self-Compassion: Conceptualizations, correlates, & interventions. *Rev. Gen. Psychol.* 2011, *15*, 289-303. doi: 10.1037/a0025754
13. Neff, K. The science of self-compassion. En C. Germer & R. Siegel (Eds.). *Compassion and wisdom in psychotherapy.* **2011**, New York: Guilford Press.
14. Bluth, K., Roberson, P., and Gaylord, S. A Pilot Study of a Mindfulness Intervention for Adolescents and the Potential Role of Self-Compassion in Reducing Stress. *Explore*, **2015**, 11(4), 292– 295. doi: 10.1016/j.explore.2015.04.005.
15. Reich, D.S., Lucchinetti, C.F., and Calabresi, P.A. Multiple Sclerosis. *N Engl J Med.* **2018**, *378*, 169-180. doi: 10.1056/NEJMra1401483. doi: 10.1056/NEJMra1401483
16. Thompson, A.J., Baranzini, S.E., Geurts, J., Hemmer, B., and Ciccarelli, O. Multiple sclerosis. *Lancet.* **2018**, 391, 1622-1636. doi: 10.1016/S0140-6736(18)30481-1.
17. Ferreira, M.L. Cognitive deficits in multiple sclerosis: a systematic review. *Arq Neuropsiquiatr.* **2010**, 68, 632-641. doi: 10.1590/s0004-282x2010000400029
18. González-Siles, P. Bases cerebrales de la fatiga en pacientes de esclerosis múltiple. Una revisión bibliográfica. **2018**, Universitat Jaume I.TFM. doi: 10.1590/s0004-282x2010000400029.
19. Costa-Frossard L, Moreno-Torres I, Meca-Lallana V, García-Domínguez JM. Documento EMCAM (Esclerosis Múltiple Comunidad Autónoma de Madrid) para el manejo de pacientes con esclerosis múltiple durante la pandemia de SARS-CoV-2 *Rev Neurol.* **2020**,70, 329-340. Spanish. doi: 10.33588/rn.7009.2020155.
20. Sadeghmousavi, S., Rezaei, N. COVID-19 and Multiple Sclerosis: Predisposition and Precautions in Treatment. *SN comprehensive clinical medicine.***2020**, 1–6. Advance online publication. https://doi.org/10.1007/s42399-020-00504-9
21. Pérez C. A. Looking ahead: The risk of neurologic complications due to COVID-19. *Neurology. Clinical practice*, **2020**, *10*, 371–374. https://doi.org/10.1212/CPJ.0000000000000836
22. Louapre C., Collongues N., Stankoff B., Giannesini C., Papeix C., Bensa C., Deschamps R., Créange A., Wahab A., Pelletier J., et al. Clinical Characteristics and Outcomes in Patients with Coronavirus Disease 2019 and Multiple Sclerosis. *JAMA Neurol.* **2020,** 77, 1079–1088. doi: 10.1001/jamaneurol.2020.2581
23. Seyed M., Sahraian M.A., Rezaeimanesh N., Naser A. Psychiatric Advice During COVID-19 Pandemic for Patients with Multiple Sclerosis. Iran. J. Psychiatry Behav. Sci. **2020**,*14*:e103243. doi: 10.5812/ijpbs.103243.
24. Moss B.P., Mahajan K.R., Bermel R.A., Hellisz K., Hua L.H., Hudec T., Husak S., McGinley M.P., Ontaneda D., Wang Z., et al. Multiple sclerosis management during the COVID-19 pandemic. Mult. Scler. J. **2020**,*26*,1163–1171. doi: 10.1177/1352458520948231.
25. McDonald, W.I., Compston, A., Edan, G., Goodkin, D., Hartung, H.P., Lublin, F., McFarland, H., Paty, D., Polman, C., Reingold, S., Sandberg-Wollheim, M., Sibley, W., Thompson, A., van der Noort, S., Weinshenker, B., and Wolinsky, J. Recommended diagnostic criteria for multiple Sclerosis: guidelines from the international panel on the diagnosis of multiple Sclerosis. *Ann Neurol* **2001,** *50*, 121-127. doi: 10.1191/1352458505ms1135oa
26. Polman, C., Reingold, S., Edan, G., Filippi, M., Hartung, H.P., Kappos, L., Lublin, F., Metz, L., McFarland, H., O'Connor, P., Sandberg-Wollheim, M., Thompson, A., Weinshenker, B., and Wolinsky, J. Diagnostic Criteria for Multiple Sclerosis: 2005 Revisions to the "McDonald Criteria*"*. *Ann Neurol*, **2005,** *58*, 840–846. doi: 10.1002/ana.20703
27. Alonso, J., Prieto, L., and Anto, J.M. La versión española del SF-36 Health Survey (Cuestionario de Salud SF-36): in instrumento para la medida de los resultados clínicos. *Med Clin* (Barc),**1995**, 104, 771-776. doi: 10.1157/13074369
28. Neff, K. The Development and Validation of a Scale to Measure Self-Compassion. *Self and Identity*, **2003**, *3*, 223-250. doi: 10.1080/15298860390209035

29. García-Campayo, J., Navarro-Gill, M., Andrés, E., Montero-Marin, J., López-Artal, L., and Demarzo, M. Validation of the Spanish versions of the long (26 items) and short (12 items) forms of the Self-Compassion Scale (SCS). *Health and quality of life outcomes.* **2014,** 12(1), 1-9. doi:10.1186/1477-7525-12-4.
30. Raes, F., Pommier, E., Neff, K. D., and Van Gucht, D. Construction and factorial validation of a short form of the selfcompassion scale. *Clin Psychol Psychothe.* **2011,** *18*(3), 250-255. doi: 10.1002/cpp.702
31. Pommier, E. A. The compassion scale (Doctoral Dissertation). University of Texas at Austin. **2010**. doi: 10.1177/1073191119874108
32. Brito, G. Cultivating healthy minds and open hearts: A mixed-method controlled study on the psychological and relational effects of compassion cultivation training in Chile (Doctoral Dissertation). **2014** Institute of Transpersonal Psychology.
33. Kos, D., Kerckhofs, E., Carrea, I., Verza, R., Ramos, M., and Jansa, J. Evaluation of the Modified Fatigue Impact Scale in four different European countries. *Mult Scler.* **2005**, *11*, 76-80. doi: 10.1191/1352458505ms1117oa
34. Larson, R.D. Psychometric properties of the modified fatigue impact scale. *Int J MS Care. Spring*, **2013**, *15*, 15-20. doi: 10.7224/1537-2073.2012-019
35. Fisk, J.D. and Doble, S.E. Construction and validation of fatigue impact scale for daily administration (D-FIS). *Qual Life Res*, **2002,** *11*, 263-272. DOI: 10.1023/a:1015295106602
36. Pavan, K., Schmidt, K., Marangoni, B., Mendes, M.F., Tilbery, C.P., and Lianza, S. Multiple sclerosis: cross-cultural adaptation and validation of the modified fatigue impact scale. *Arq Neuropsiquiatr*. **2007**, *65*, 669-673. doi.org/10.590/1809-2950/12654921042014
37. Wang,C.,Pan, R.,Wan, X., Tan, Y., Xu,L., Ho,C.S. et al. Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in China. *Int J Environ Res Public Health*, **2020**, 17, 1729, doi: 10.3390/ijerph17051729
38. Goldenberg, M. Multiple Sclerosis Review. *P T*. **2012,** *37*, 175–184.
39. Borghi, M., Cavallo, M., Carletto, S., Ostacoli, L., Zuffranieri, M., Picci, R.L., et al. Presence and Significant Determinants of Cognitive Impairment in a Large Sample of Patients with Multiple Sclerosis. *PLoS ONE*. **2013**, 8: e69820. https://doi.org/10.1371/journal.pone.0069820.
40. Zhang, G. X., Sanabria, C., Martínez, D., Zhang, W. T., Gao, S. S., Alemán, A., Granja, A., Páramo, C., Borges, M., & Izquierdo, G. Social and professional consequences of COVID-19 lockdown in patients with multiple sclerosis from two very different populations. Consecuencias sociolaborales del confinamiento por la COVID-19 en pacientes con esclerosis múltiple en dos poblaciones muy diferentes. *Neurologia (Barcelona, Spain)*, **2021**, *36*, 16–23. https://doi.org/10.1016/j.nrl.2020.08.002lllllllllllllllñf
41. Casanova, G., Lamura, G., & Principi, A. Valuing and Integrating Informal Care as a Core Component of Long-Term Care for Older People: A Comparison of Recent Developments in Italy and Spain. *J Aging Soc Policy.* **2017**. *29*(3), 201–217. https://doi.org/10.1080/08959420.2016.1236640
42. Giménez-Llort, L, Parente, A.F. Subjectivity Around Grandparents and Other Elderly People Determines Divergence of Opinion as to the Importance of Older People Living in Family or in Nursing Homes. *EC Neurology*, **2019**, 11.10, 968-976.
43. Limbers, C. A., McCollum, C., & Greenwood, E. Physical activity moderates the Association between parenting stress and quality of life in working mothers during the COVID-19 pandemic. *Ment Health Phys Act*, **2020**,*19*, 100358. https://doi.org/10.1016/j.mhpa.2020.100358
44. Reguera-García, M. M., Liébana-Presa, C., Álvarez-Barrio, L., Alves Gomes, L., & Fernández-Martínez, E. Physical Activity, Resilience, Sense of Coherence and Coping in People with Multiple Sclerosis in the Situation Derived from COVID-19. *International journal of environmental research and public health.***2020,** *17*(21), 8202. https://doi.org/10.3390/ijerph17218202
45. Téllez, N., Río, J., Tintoré, M., Nos, C., Galán, I., and Montalban, X. Fatigue in multiple sclerosis persists overtime: a longitudinal study. *J Neurol*, **2006,** 253, 1466-1470. doi: 10.1007/s00415-006-0247-3
46. Lerdal, A., Gullowsen, E., Krupp, L., and Dahl, A.A. A prospective study of patterns of fatigue in multiple Sclerosis. *Eur J Neurol.* **2007**; 14 (12): 1338-1343. doi: 10.1111/j.1468-1331.2007.01974.x.
47. Andreu-Caravaca, L., Ramos-Campo, D., Manonelles, P., Abellán-Aynés, O., Chung, L. H., & Rubio-Arias, J. Á. Effect of COVID-19 home confinement on sleep monitorization and cardiac autonomic function in people with multiple Sclerosis: A prospective cohort study. *Physiol & beh*, **2021**, *237*, 113392. Advance online publication. https://doi.org/10.1016/j.physbeh.2021.113392
48. Musa, G. Mindfulness y Auto-Compasión: Un estudio correlacional en estudiantes universitarios. (Tesis de Licenciatura). Universidad de Chile, Santiago de Chile-Chile. **2013**. https://doi.org/10.30849/rip/ijp.v52i2.504
49. López, A., Sanderman, R., Smink, A., Zhang, Y., Van Sonderen, E., Ranchor, A., and Schoevers, M. A Reconsideration of the Self-Compassion Scale's Total Score: SelfCompassion versus Self-Criticism. *PLoS ONE*. **2015.** 10(7), 1-12. doi: 10.1371/journal.pone.0132940.
50. Reyes, M. Self-compassion: A concept analysis. *J Holist Nurs,* **2012,** 30, 81-90. doi: 10.1177/0898010111423421. doi: 10.1177/0898010111423421
51. Woo, L.,and Kyeong, L. Self-compassion as a moderator of the relationship between academic burn-out and psychological health in Korean cyber university students. Personality and Individual Differences, **2013,** *54*, 899-902. doi: 10.1016/j.paid.2013.01.001.
52. Albertson, E., Neff, K., and Dill-Shackleford, K. Self-Compassion and Body Dissatisfaction in Women: A Randomized Controlled Trial of a Brief Meditation Intervention. Mindfulness, **2014,** 6(3), 444-454. doi: 10.1007/s12671-014-0277-3.
53. Yarnell, L., Stafford, R., Neff, K., Reilly, E., Knox, M., and Mullarkey, M. Metaanalysis of gender differences in self-compassion. Self and Identity, **2015,** 14, 499-520. doi: 10.1080/15298868.2015.1029966
54. Neff, K. The science of self-compassion. En C. Germer & R. Siegel (Eds.). Compassion and wisdom in psychotherapy. New York: Guilford Press. **2011a**.

55. Gilbert, P., McEwan, K., Irons, C., Bhundia, R., Christie, R., Broomhead, C., and Rockliff, H. Self-harm in a mixed clinical population: The roles of self-criticism, shame, and social rank. *Br J Clin Psychol*. **2010**, *49*, 563-576 doi: 10.1348/014466509X479771
56. Longe, O., Maratos, F., Gilbert, P., Eans, G., Volker, F., Rockliff, H., and Rippon, G. Having a word with yourself: Neural correlates of selfcriticism and self-reassurance. *Neuroimage*, **2010,** *49*(2). 1849-1856. doi:10.1016/j.neuroimage.2009.09.019
57. Rogers, C. On becoming a person: A therapist's view of psychotherapy. **1961**, Boston: Houghton Mifflin.
58. Gilbert, P., McEwan, K., Gibbons, L., Chotai, S., Duarte, J., and Matos, M. Fears of compassion and happiness in relation to alexithymia, mindfulness, and self-criticism. *Psychol Psychother.* **2012,** *85*(4), 374-390. doi: 10.1111/j.2044-8341.2011.02046.x
59. Poch, C., and Vicente, A. (). La acogida y la compasión: Acompañar al otro. En J. C. Mèlich & A. Boixader (coords.), *Los márgenes de la moral: Una mirada ética a la educación* **2010**, 86-100. Barcelona: GRAÓ.
60. Lazarus, R. S., and Lazarus, B. N. *Passion and reason: Making sense of our emotions.* **1996** New York, NY: Oxford University.
61. Regner, E. Compasión y gratitud, emociones empáticas que elicitan las conductas prosociales. En M. C. Richaud & J. E. Moreno (Comp.), *Investigación en Ciencias del Comportamiento. Avances Iberoamericanos* **2009** (pp. 281-298). Buenos Aires: CIIPME - CONICET. DOI: https://doi.org/10.35670/1667-4545.v18.n2.20801
62. Mercadillo, R. E., Díaz, J. L., and Barrios, F. A. Neurobiología de las emociones morales. *Salud Mental,* **2007**, *30*(3), 1-11. Recuperado de http://www.revistasaludmental.mx
63. Ostrosky-Solís, F., and Vélez-García, A. E. Neurobiología de la sensibilidad moral. *Revista Neuropsicología, Neuropsiquiatría y Neurociencias,* **2008,** *8*, 115-126. Recuperado de https://dialnet.unirioja.es
64. Kirby, J. N. Compassion interventions: The programmes, the evidence and implications for research and practice. *Psychol Psychother.* ***2017.*** doi: 10.1111/papt.12104
65. Gilbert, P., and Procter, S. Compassionate mind training for people with high shame and self-criticism: Overview and pilot study of a group therapy approach. *Clin. Psychol. Psychother.* **2006,** *13*(6) 353. doi: 10.1002/cpp.507.
66. Germer, C. K., and Neff, K. D. Self-compassion in clinical practice. *J Clin Psychol.* **2013,** *69*, 856-867. doi: 10.1002/jclp.22021
67. Strauss, C., Taylor, B. L., Gu, J., Kuyken, W., Baer, R., Jones, F., and Cavanagh, K. What is compassion and how can we measure it? A review of definitions and measures. *Clin Psychol Rev.* **2016,** *47*, 15-27. doi: 10.1016/j.cpr.2016.05.004