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Review Article

Fragiles but Resilient. The Key Strategies to Cope with Pandemic in Persons with Multiple Sclerosis. A Controlled Web Survey

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Abstract

Background

The SARS-CoV-2 pandemic represented an unexpected psychological stress, being a major threat to health and limiting daily life, especially for the fragile population. How could the people with (pw) Multiple Sclerosis (MS) cope with this emergency?

Objective

To observe the pwMS's psychological reaction in comparison with non affected persons and to evaluate the impact of lifestyle changes on psychological symptoms, due to the pandemic.

Methods

The study was observational, retrospective, controlled, focused on good clinical practice and conducted at Niguarda Hospital. PwMS and controls filled a web survey containing anamnestic data, habits, depression and anxiety self-questionnaires. The primary outcome was the pwMS's psychological anxiety and depression score compared with controls.

Results

On April, 10 2020, 88/165 pwMS and 187 controls joined the study. Unexpectedly, no significant differences between groups were observed for depression mean score: 6.6(5.2) in pwMS and 6.2(4.8) in controls and for anxiety: 5.9(4.8) and 5.0(4.2). PwMS focused on health concern more often than controls, but they respected the restrictions more easily and benefited from practical activities more than controls.

Conclusion

PwMS showed a proper psychological resilience in comparison with controls. These findings might guide the clinical interviews and suggest both the areas to be supported and the strengths to be promoted in pwMS.

Keywords:
Anxiety; depression; Multiple sclerosis; SARS-CoV-2 pandemic; resilience

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Introduction

Multiple Sclerosis (MS) is a chronic, autoimmune, inflammatory and neurodegenerative disease that predominantly affects young individuals, between the ages of 20 and 50, mostly female [1]. People with MS (pwMS) present a high burden of neuropsychiatric comorbidities, such as anxiety and depression (A/D) [2], also associated with fatigue, physical symptoms and cognitive disability, resulting in a lower quality of life and decreased compliance. These conditions are associated with psychological stress and could be responsible for the disease exacerbation [3].

On February 21st, 2020 the first cases of SARS-CoV-2 infection were diagnosed in Italy and on March 11th, eighteen days after, the World Health Organization declared that the infection had become pandemic. A pandemic represents a sudden and major threat to health, that is an unexpected psychological stress, worsened by the general "lockdown" (the necessary severe restrictions on daily life were decided from March 10th, to May 3rd). The phantom of viral infection, the sudden psychosocial changes, the announced economic consequences and the confusing and alarmist information led people to fear and fear can increase anxiety and mental distress, also worsening psychiatric symptoms [4]. People with autoimmune and inflammatory diseases, or treated with immunosuppressive therapy, were immediately considered at a major risk of harmful infection [5]. As a precaution, researchers and clinicians paid great attention to these groups of patients.

Obviously, pwMS are part of the fragile population but, from a psychological point of view, this means that they are paradoxically more used to managing a chronic but unpredictable condition compared to healthy people. Especially in the initial stages of the diagnostic and therapeutic path for MS, and then for relapses, they suffer a forced suspension of their routine habits and professional life (due to the symptoms and the medical visits). Similarly, the SARS-CoV-2 pandemic and the restrictions did the same to the general population. In fact, a great and serious impact on mental human health was described as a result of actual and past pandemics, particularly involving vulnerable groups: older adults, the immunocompromised, subjects with previous clinical and psychiatric conditions, but also relatives of infected patients, residents of high-incidence areas, quarantined people and health professionals, going beyond the division between healthy/diseased people [4,6].

How did this higher risk of infection impact on the psychological status of pwMS during the restrictions? Could the concern for health and for MS, considered as an adjunctive risk factor for SARS-CoV-2 poor prognosis, have stressed the pwMS or have motivated them to better tolerate the lockdown? Moreover, might the pwMS have gained greater resilience to lockdown compared to the general population?

Objectives

We conducted a study to observe the psychological reaction of pwMS during the SARS-CoV-2 emergency. We considered A/D symptoms to find out possible patterns among lifestyle factors and psychological distress. These findings could address the clinical interview and suggest both the critical areas to be supported and the strengths to be promoted. We also collected the same data from volunteers non affected by MS (controls) to compare their answers with those of the fragile MS population.

The primary outcome concerned the rates of anxiety and depression scores in pwMS compared with controls.

The secondary objectives considered the effects of anamnestic and lifestyle factors on A/D. Resilience of pwMS, already studied for adaptation to MS, was also explored in this setting.

Methods

The study design was observational, controlled, based on a web survey, and focused on improvement of quality of the clinical practice. It was approved by the Ethic Committee “Milano Area 3” and conducted at Niguarda Hospital according to the Good Clinical Practice and the Declaration of Helsinki. Personal data have been collected and analyzed in pseudo-anonymous and aggregate form, according to regulation 679/2016 EU.

All subjects were informed on the aim of the study and provided the informed consent. PwMS were enrolled according to the following criteria: adult subjects diagnosed with Multiple Sclerosis [7] who have indicated a valid email address to be contacted by the Niguarda MS Center. Controls were invited to participate using WhatsApp ^{tm} viral message in four different towns besides the city of Milano to involve the northern, central and southern regions of Italy and according to the following eligibility criteria: adult subjects not diagnosed with MS and not working as health professionals.

Statistical Analysis

All data have been validated and then submitted to usual descriptive statistics. Binary and nominal categorical variables have been described with relative and absolute frequency tables, while continuous and ordinal variables have been described as mean and standard deviation or median and range, depending on their distribution, checked by the Shapiro-Francia test. Comparison between nominal and binary variables were carried out by Fisher's exact test, whereas comparisons between continuous variables were done with Student's t test, Welch's test, or with the Mann-Whitney U test with exact algorithm, depending on their distribution and on the homogeneity of variances. Comparisons between ordinal variables were always carried out by the exact Mann-Whitney U test.

Correlations between variables were calculated using Pearson's r, or Spearman's ρ, again, depending on the distribution.

Materials

On April 10th 2020, a total number of 165 pwMS followed up by the MS Center of the Niguarda hospital in Milan received by email an invitation to join the study by filling out a web survey. The survey was built using Google Form, a platform by Google LLC. The study collected the answers about lifestyle, habits and psychological status referred to the two weeks from March 27 to April 10.

The web survey provided five sections totally reported in the Supplementary Table 4A: the first included the study and the privacy disclosures with the consent. The second section contained multiple choice questions about socio-demographics, MS anamnestic data and ongoing treatment, previous history of anxiety and depression with related treatment, satisfaction with the information received by the MS Center, changes in MS treatment. The third section referred to the health perception, the need for economic or logistic support and the lifestyle habits during the SARS-CoV-2 restrictions. These last were: the everyday life coping strategies, the home and the family relationships, the physical activities, the job changes, the impact of media news. The fourth section investigated the feared or objective SARS-CoV-2 symptoms, the mourning of relatives, friends or neighbors caused by the virus. The final section consisted of two structured self administered questionnaires: "The 7-items Generalized Anxiety Disorder Scale" (GAD-7) [8] for anxiety and "The Patient Health Questionnaire" (PHQ-9) [9] for depression. Both of these brief screenings were based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition, Text Revision) (DSM-IV-TR) [10], respectively for the General Anxiety Disease and for the Major Depressive Episode. The items had response options ranging from 0 to 3 (0=Not at all; 1=Several days; 2=More than half the days; 3=Nearly every day) with higher scores indicating more severe symptoms.

The GAD-7 has a sum score ranging from 0 to 21. This measure was validated in the general population [9] and in other specific populations, including in MS for clinical and research purposes [12]. A cut point of 10 or greater provided sensitivity and specificity higher than 0.80 [8] .

The PHQ-9 includes nine items with a sum score ranging from 0 to 27; it's commonly used for screening and diagnosis of depression also in pwMS [13]. A cut-off score greater than or equal to 10 has been suggested as indicative of significant depressive symptoms [14] and it has also been considered a suitable screening tool to measure depression in pwMS.

Results

Demographics

A total number of 88 web surveys were correctly returned from MS outpatients and 187 from controls. Please refer to (Table 1) for sample characteristics and to (Table 2) for MS treatment details and changes due to the pandemic.

PwMS reported satisfaction regarding the communication with the MS Center in 81% of cases. 8/88 pwMS asked for logistic support for food or other activities and in one case no help was given.

The controls answered for the most part from the North of Italy (87.5% of cases). 95% of subjects report a discrete-good healthy state, while a chronic condition was reported in 20% of cases. 3/177 controls asked for logistic support for food or other activities and 4/177 asked for economic aid, but in 2/177 the financial help was not given.

Primary Outcome

Considering the mild cut-off suggested for PHQ-9≥10, the depressive symptoms occurred in 24.5% of pwMS and in 17.6% of controls, with a comparable mean score.

According to the cut-off GAD-7≥10, deriving from the ROC analysis, 16.4% of the sample presented moderately anxious symptoms; the mean score was overlapping in the two groups and means "mild symptoms". No significant difference between groups was detected for A/D scores.

Anamnestic Data

Psychological data and treatments were collected in Table 3. As expected, A/D symptoms were more frequent in MS group compared to controls. PwMS reporting to suffer from depression were confirmed

Table 1. Socio-demographic and clinical characteristics of participants

Characteristics	pwMS (n.88)	controls (n.177)	p=
Female sex, No. (%)	64 (73%)	122 (69%)	p=0.773 *
Age, mean (SD), y	44.5 (9.8)	43.9 (11.3)	p=0.641 **
Self employed, No. (%)	7 (8)	16 (9)	p=0.812 *
Employed, No. (%)	58 (65.9)	124 (70.1)	
Other job condition:			
Fired/suspended for the pandemic	4 (4.5)	5 (2.8)	
Unemployed, No. (%)	9 (10.2)	8 (4.5)	
Retired, housewife, student, No. (%)	10 (11.4)	24 (13.6)	
Smart working, No. (%)	32 (36.4)	60 (34.7)	p=0.786 *
Satisfying house living space	70 (80.5)	144 (84.7)	p=0.384 *
Sport, No. (%)	32 (36.4)	85 (48)	**p=0.046** ***
Sport suspended, No. (%)	19 (21.6)	44 (24.9)	
No physical activity, No. (%)	37 (42)	48 (27.1)	
SARS-COV2 symptoms (subjective), No. (%)	13 (14.8)	46 (26)	**p=0.042** *
Mourning for SARS-COV2 of known people, No. (%)	24 (27.3)	43 (24.3)	p=0.652 *

(*) Fisher's exact Test; (**) Welch's Test; (***) Chi2(2) Test; (°) Mann Whitney test.

to have a more severe PHQ-9 score ($p<0.0001$) and those still receiving support with alternative strategies (telemedicine) resulted more depressed compared to the others ($p=0.014$). Differently, we noted that all the subjects referring to be anxious presented more severe GAD-7 score ($p<0.0001$) but the anxiety status of supported persons didn't differ from that of non supported, maybe because in

Table 2. Clinical MS characteristics and treatment.

MS treatment details	pwMS(n.88)
Median EDSS (range)	2 (1-7)
MS duration, mean (SD), y	13 (11.5)
No MS treatment No. (%)	10 (11.3)
MS treatment to be started, No. (%)	3 (3.4)
MS treatment:	
first line - injective, No. (%)	32 (36.4)
first line - oral, No. (%)	24 (27.3)
second line - oral, No. (%)	10 (11.4)
second line - infusion, No. (%)	9 (10.2)
MS treatment delayed	2 (2.3)
MS treatment delivered in the MS center closer to the patient's home	3 (3.4)

Table 3. Psychological symptoms and treatment

A/D symptoms and treatment	pwMS (n.88)	controls (n.177)	p=
A/D symptoms reported, No. (%)	23 (26.1)	21 (11.9)	**p=0.005 ***
No A/D treatment, No. (%)	65 (73.8)	148 (83.6)	**p=0.001 ***
A/D treatment reported:			
complementary, No. (%)	2 (2.3)	7 (4)	
psychotherapy, No. (%)	5 (5.7)	14 (7.9)	
ansioliticos and/or antidepressant, No. (%)	11 (12.5)	5 (2.8)	
drugs and psychotherapy, No. (%)	5 (5.7)	3 (1.7)	
Psychological treatment by telemedicine	13 (14.8)	12 (6.8)	
Psychological treatment suspended	10 (11.3)	2 (1.1)	
Psychological treatment in the past	19 (21.6)	55 (31.1)	
None (psychological treatment)	44 (50)	98 (55.4)	
GAD-7 score, mean, (SD)	5.9 (4.8)	5 (4.2)	p=0.167 °
0–4: minimal anxiety	40 (46.5)	92 (54.1)	
5–9: mild anxiety	30 (34.9)	52 (30.6)	
10–14: moderate anxiety	8 (9.3)	19 (11.2)	
15–21: severe anxiety	8 (9.3)	7 (4.1)	
GAD-7 greater than or equal to 10 No. (%)	16 (18.60)	26 (15.3)	
PHQ-9 score, mean, (SD)	6.6 (5.2)	6.2 (4.8)	p=0.752 °
0-4: No symptoms	36 (43.4)	74 (44.3)	
5-9: Few symptoms	25 (30.1)	61 (36.5)	
10-14: Moderate symptoms	15 (18.1)	21 (12.6)	
15-19: Moderately/severe symptoms	4 (4.8)	7 (4.2)	
>20: Severe Depression	3 (3.6)	4 (2.4)	

the latter the concern about the pandemic might have worsened the anxiety status. About MS history, the Spearman Correlation between actual psychological symptoms and time from diagnosis was not significant (GAD-7: n. 87, rho -0.1486, p=0.17; PHQ-9: n. 83, rho -0.1040, p=0.35).

Table 4A. English translation of the web survey of the study from the original Italian language

Section	Content
Title	"DIMMI COME STAI" "How are you" survey
I	Includes the study and the privacy disclosures with the informed consent.
II	Contains multiple choice questions about socio-demographics, MS anamnestic data and current treatment, previous history of anxiety and depression with related treatment.
	a. Socio-demographics

Table 4A (continued)

Section	Content
	1. Phantasy code: xxx
	2. Gender: male/female
	3. Age: aa
	4. Province of residence (or actual domicile if different): xxx
	b. Multiple sclerosis/chronic disease anamnestic data and current treatment
	5. The onset date of multiple sclerosis/chronic disease was: dd/mm/yyyy
	*5bis. My health status is: low/enough/discrete/good
	6. I am being treated for multiple sclerosis/chronic disease: Yes/no/Not yet (I'm completing the clinical investigations)
	*6bis. If you want, indicate the name of the disease you are being treated for: xxxxxx
	7. I am being treated for multiple sclerosis/chronic disease with the following drug: xxxx
	8. During this SARS-CoV-2 emergency period, I am continuing the therapy: as scheduled/it is suspended/it has been postponed/it is given to me in a hospital closer to my residence
	c. Previous history of anxiety and depression with related treatment
	9. I suffer from anxious depressive symptoms: no/no, I have suffered from this in the past/yes, I'm currently suffering
	10. I am being treated with: anxiolytics-antidepressants/anxiolytics-antidepressants and psychotherapy/psychotherapy/natural therapies/I don’t follow (or have not followed) any treatment
	11. I am continuing the psychological treatment: I've ended the psychological treatment in the past/I suspended the psychological treatment/I’m continuing the psychological treatment by phone
	d. Satisfaction with the information received by the MS Center
	12. I succeeded successfully to communicate with my referral medical centre/specialist for information and practical guidance: I got no answer-I got effective answers (1-10)
III	Refers to the health perception, the need for economic or logistic support and the lifestyle habits during the SARS-CoV-2 restrictions
	a. health concern
	13. How did you react at the beginning of the SARS-CoV-2 emergency?
	13a. I worried about myself: not at all/quite/much/very very much (0-3)
	13b. I worried about my family: not at all/quite/much/very very much (0-3)
	13c. I felt more at risk than other people: not at all/quite/much/very very much (0-3)
	13d. I worried about my illness: not at all/quite/much/very very much (0-3)
	b. need for economic or logistic support
	14. Have you asked for support from the associations or the public institutions?: I didn't ask for support/I have not received support despite the request/I received support for food or other types of activities
	c. everyday life coping strategies

Table 4A (continued)

Section	Content
	15. How are you acting with respect to the SARS-CoV-2 emergency ? (Please ask for each sentence: never/some days/for more than half of the days/almost every day) (1-4)
	15a. I respect the restrictions, they make me feel safe
	15b. Restrictions make me nervous
	15c. I just listen to the information
	15d. I feel stuck and can't do anything
	15e. I'm hyperactive
	15f. I keep busy: practical actions gratify me
	15g. I use the time to do things I usually wouldn't do and I can stay focused
	15h. My head's always elsewhere, I can't concentrate
	15i. I always think about health issues
	15l. I pray and trust in God
	15m. I try to anticipate what will happen
	15n. I'm always on the phone to make sure friends and family are okay
	15o. I arranged to continue my activities by video call
	15p. I refuse to use video calls or distract myself, it is not a time to think about futile things
	15q. They are exaggerating the problem
	15r. I try not to think about it by eating
	15s. I'm distressed for those who are sick and I can't help
	15t. I try to defuse the situation with my loved ones
	d. home and the family relationship
	16. How many people live with you, in the same house? (indicates the number of adults and minors): nn
	17. Is there enough space for everyone?: not at all-a lot (1-4)
	18. Right now, how often the friends and relatives you interact with more frequently, appear:
	18a. missing: never/some days/for more than half of the days/almost every day
	18b. irritant: never/some days/for more than half of the days/almost every day
	18c. enjoy the company: never/some days/for more than half of the days/almost every day
	18d. suffocating: never/some days/for more than half of the days/almost every day
	18e. stimulating: never/some days/for more than half of the days/almost every day
	18f. unbearable: never/some days/for more than half of the days/almost every day
	19. Can you stay indoors: easily-it causes me enormous discomfort (1-4)
	20. When you go out, you feel: terrified-happy (1-4)

Table 4A (continued)

Section	Content
	e. physical activities
	21. Please select all applicable items about physical exercise and/or physiotherapy:
	21a. I can't do it for physical reasons: true/false
	21b. I wouldn't do it anyway, I don't like it: true/false
	21c. I am not in treatment: true/false
	21d. It is usually tiring, so I'm taking the opportunity to rest: true/false
	21e. I feel the need but it has been interrupted: true/false
	21f. I feel the need and continue it at home, as I can: true/false
	f. job changes
	22. What is your current employment status? (please select all applicable items)
	22a. I am working as usual: true/false
	22b. I work according to different schedules and methods as per company indications: true/false
	22c. I'm working from home: true/false
	22d. I'm on vacation / layoffs: true/false
	22e. I am self-employed and cannot work due to restrictions: true/false
	22f. I don't have a job: true/false
	22g. I am a homemaker: true/false
	23. Since the beginning of the SARS-CoV-2 restrictions, which of the following work-related statements do you agree with? (please select all the applicable items)
	23a. I am working too much: true/false
	23b. I am a housewife and housekeeping is more demanding: true/false
	23c. Luckily I am working, so I keep busy: true/false
	23d. I am missing work: true/false
	23e. I am missing the work environment: true/false
	23f. I am relieved not to have to leave for work: true/false
	23g. I don't work and I feel better because I am less fatigued: true/false
	23h. I am a housewife and now my relatives are helping me: true/false
	23i. I am worried about losing my job: true/false
	23l. I am worried about the economic aspect: true/false
	g. impact of media news
	24. Are you listening to the radio and television information on the SARS-CoV-2 emergency?: I follow the news and updates as much as possible/many times a day/daily/I try to avoid them

Table 4A (continued)

Section	Content
	25. How do you consider the media news?
	25a. News is useful: not at all/quite/much/very very much
	25b. After news I feel a weight on my stomach: not at all/quite/much/very very much
	25c. If I listen to news in the evening I happen to sleep badly: not at all/quite/much/very very much
	25d. News is not always reliable: not at all/quite/much/very very much
	25e. News makes me pained: not at all/quite/much/very very much
	25f. After news, I don't think that the emergency: not at all/quite/much/very very much
	25g. News makes me lose hope: not at all/quite/much/very very much
	25h. News agitates me: not at all/quite/much/very very much
	25i. News motivates me to follow the restrictions: not at all/quite/much/very very much
	25l. News makes me think: not at all/quite/much/very very much
IV	Contain the feared or objective SARS-CoV-2 symptoms, the mourning of relatives, friends or neighbors caused by the virus.
	a. feared or objective SARS-CoV-2 symptoms
	26. Are you in quarantine due to the SARS-CoV-2 virus?: yes/noyes, together with other family members
	27. Have you had symptoms caused by the SARS-CoV-2 virus?
	yes/no/I'm/was afraid of having any/I had the suspicion but it was not confirmed by the doctors
	b. mourning of relatives, friends or neighbors caused by the virus.
	28. Are you in mourning for the death of persons close to you due to SARS-CoV-2 virus? (please select all applicable items): yes, family members/yes, friends/yes, acquaintances/yes, people who live near me/no, none
V	Consist of the two following brief self administered questionnaires about the psychological status and of the final considerations and tips
	29. The Patient Health Questionnaire (PHQ-9)
	30. The 7-items Generalized Anxiety Disorder Scale (GAD-7)
	31. Final considerations (if you wish, write here in detail): xxx
	32. Tips (if you wish, write here what you would add or change in the questionnaire): xxx

* Questions for controls only.

Health Perception

The pwMS expressed concern for their MS course, considering themselves at higher risk and, in general, they were more worried about their health compared to controls (Figure 1) with a significative correlation with anxiety but not with depression. The concern for MS course and the perception to be at higher risk of infection were associated with A/D. Please refer to the Table 5A that reports this and all the correlations mentioned in the following paragraphs between A/D and the studied variables. On the other hand, controls didn't consider themselves at higher risk but the concern for their health was

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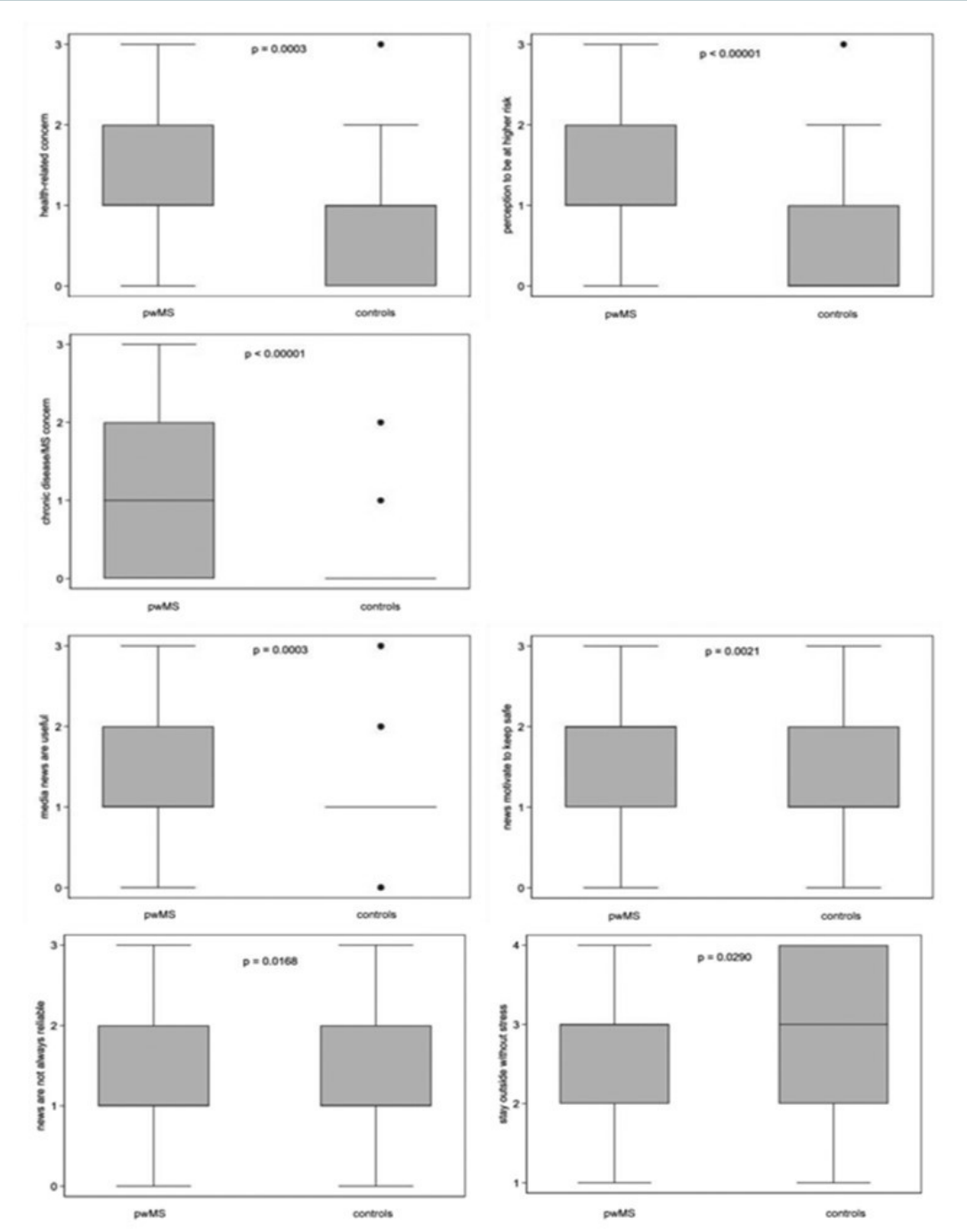

Figure 1. Significant differences between pwMS and controls in perception about "health" (box plot n. 1-3), in "media news" (box plot n. 4-6) and in "stay outside" (box plot n. 7) (p-values are according to exact Mann-Whitney U test).

also associated with A/D, with a closer correlation between their psychological status and the concern for their other chronic condition when present.

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Table 5A. Comparisons of lifestyle, habits and contextual variables between groups by the exact Mann-Whitney U test and correlations with PHQ-9 and GAD-7 psychological score using the Spearman's ρ

	PHQ-9						GAD-7								
	pwMS			controls			pwMS			controls					
	Spearman's correlation test												Mann Whitney test		
Contextual variables	**n. obs**	**rho**	**p**	**n. obs**	**rho**	**p**	**n. obs**	**rho**	**p**	**n. obs**	**rho**	**p**	**N. MS**	**controls**	**P**
Concern for health	79	0.126	0.268	155	0.223	0.005	79	0.246	0.029	155	0.184	0.022	84	171	**0.0003**
of relatives	79	0.173	0.128	155	0.257	0.001	79	0.283	0.011	155	0.208	0.009	85	173	0.687
to be at higher risk	79	0.236	0.037	155	0.048	0.549	79	0.228	0.044	155	0.119	0.166	85	168	**0.00001**
for chronic condition/MS	79	0.341	0.002	155	0.306	0.0001	79	0.350	0.002	155	0.339	0.00001	84	160	**0.00001**
Coping															
I keep busy	71	-0.581	0.00001	161	-0.236	0.003	72	-0.440	0.0001	160	-0.139	0.079	87	173	**0.005**
I concentrate on unusual things	71	-0.331	0.005	161	-0.263	0.001	72	-0.292	0.0129	160	-0.231	0.0033	85	174	0.466
I try to defuse the situation with my loved ones	71	-0.142	0.239	161	-0.058	0.466	72	-0.181	0.128	160	-0.007	0.927	86	168	0.134
They are exaggerating the problem	71	-0.003	0.982	161	-0.015	0.850	72	-0.066	0.581	160	-0.099	0.212	83	168	0.417
Restrictions make me nervous	71	0.420	0.0003	161	0.263	0.001	72	0.524	0.00001	160	0.257	0.001	85	172	0.424
I feel stuck and can't do anything	71	0.492	0.00001	161	0.493	0.00001	72	0.498	0.00001	160	0.454	0.00001	83	171	0.176
I can’t concentrate	71	0.621	0.00001	161	0.676	0.00001	72	0.656	0.00001	160	0.656	0.00001	85	172	0.751
I refuse to use video calls or distract myself, it is not this the time	71	0.141	0.239	161	0.067	0.399	72	0.214	0.071	160	0.055	0.492	81	169	0.067
I pray and trust in God	71	0.163	0.174	161	0.122	0.124	72	0.123	0.302	160	0.153	0.053	84	171	0.289
I'm hyperactive	71	0.186	0.119	161	0.322	0.00001	72	0.338	0.004	160	0.423	0.00001	84	173	0.378
I don’t think by eating	71	0.457	0.0001	161	0.402	0.00001	72	0.348	0.003	160	0.352	0.00001	82	168	0.247
I try to anticipate what will happen	71	0.213	0.075	161	0.150	0.057	72	0.292	0.013	160	0.186	0.0187	84	170	0.403

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Table 5A (continued)

	PHQ-9						GAD-7								
	pwMS			controls			pwMS			controls					
	Spearman's correlation test												Mann Whitney test		
I'm worried because of people being ill	71	-0.011	0.925	161	0.360	0.00001	72	0.173	0.147	160	0.412	0.00001	85	169	0.642
I arranged to continue my activities by video call	71	-0.084	0.484	161	-0.043	0.587	72	-0.087	0.469	160	0.022	0.783	84	173	**0.01**
I respect the restrictions, they make me feel safe	71	-0.037	0.756	161	-0.051	0.522	72	-0.032	0.791	160	-0.046	0.567	86	175	**0.009**
I always think about health issues	71	0.296	0.012	161	0.352	0.00001	72	0.457	0.0001	160	0.360	0.00001	85	170	**0.0002**
I just listen to the information	71	0.291	0.014	161	0.254	0.001	72	0.281	0.017	160	0.162	0.041	85	172	**0.0002**
I'm always on the phone to make sure my beloved are okay	71	0.139	0.247	161	0.297	0.0001	72	0.292	0.013	160	0.334	0.00001	85	171	**0.027**
Beloved perception															
irritant	78	0.390	0.0004	156	0.403	0.00001	82	0.375	0.0005	156	0.435	0.00001	85	165	0.838
missing	78	0.023	0.844	156	0.360	0.00001	82	0.077	0.494	156	0.293	0.0002	86	173	0.253
suffocating	78	0.451	0.00001	156	0.350	0.00001	82	0.420	0.0001	156	0.377	0.00001	86	164	0.802
stimulating	78	-0.029	0.802	156	-0.098	0.221	82	-0.030	0.786	156	-0.117	0.147	85	165	0.203
unbearable	78	0.288	0.011	156	0.350	0.00001	82	0.360	0.001	156	0.356	0.00001	85	163	0.673
enjoy the company	78	0.159	0.165	156	0.014	0.858	82	0.184	0.097	156	-0.054	0.501	85	163	0.694
living space	->	->	->	->	->	->	->	->	->	->	->	->	87	170	0.121
happy to go out	80	-0.265	0.018	167	-0.263	0.001	84	-0.245	0.025	167	-0.329	0.00001	85	177	**0.029**
discomfort to stay at home	80	0.256	0.022	167	0.227	0.003	84	0.356	0.001	167	0.156	0.043	88	176	0.700
Media news reaction															
The frequency of listening to news	->	->	->	->	->	->	87	0.047	0.664	166	0.039	0.614	88	176	0.058
News is useful	82	-0.184	0.098				86	-0.152	0.163	165	0.177	0.023	87	172	**0.0003**
I feel a weight on my stomach	79	0.452	0.00001				83	0.494	0.00001	162	0.590	0.00001	83	164	0.962

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Table 5A (continued)

	PHQ-9						GAD-7								
	pwMS			controls			pwMS			controls					
	Spearman's correlation test												Mann Whitney test		
I sleep badly	81	0.513	0.00001				84	0.490	0.00001	162	0.469	0.00001	84	165	0.655
Are not always reliable	82	0.096	0.389				85	0.033	0.765	163	0.052	0.511	85	167	0.017
Make me pained	82	0.183	0.100				86	0.156	0.150	161	0.390	0.00001	86	166	0.866
I always think about the emergency	82	0.3749	0.0005				85	0.548	0.00001	160	0.395	0.00001	85	163	0.398
Make me hopeless	82	0.5598	0.00001				85	0.607	0.00001	161	0.435	0.00001	85	164	0.892
I fell agitate	82	0.5619	0.00001				86	0.611	0.00001	163	0.541	0,00001	86	166	0,513
Motivate me to respect the restrictions	83	-0.1201	0,276				86	0,002	0,987	162	0.061	0,439	66	166	**0,002**
Make me thoughtful	82	-0.0762	0,496				86	-0,023	0,831	167	0.178	0,022	86	173	0,751
PHQ_tot	79	1	-	155	1	-	79	0,781	0.00001	155	0.792	0,00001	83	167	0,752
GAD_tot	79	0.7809	0,00001	155	0,792	0,00001	79	1	-	155	1	-	87	167	0,167
EDSS	83	0,1284	0,247	->	->	->	83	-0,672	0,546	->	->	->	->	->	->

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All subjects were worried about their families, with a closer and significative correlation for controls compared to pwMS.

Job

PwMS with an employment contract appeared more anxious (p=0.0207) and depressed (p=0.0407) compared to controls and only the latter felt themselves protected from smart working (p=0.0120), that otherwise determined overwork (p=0.002).

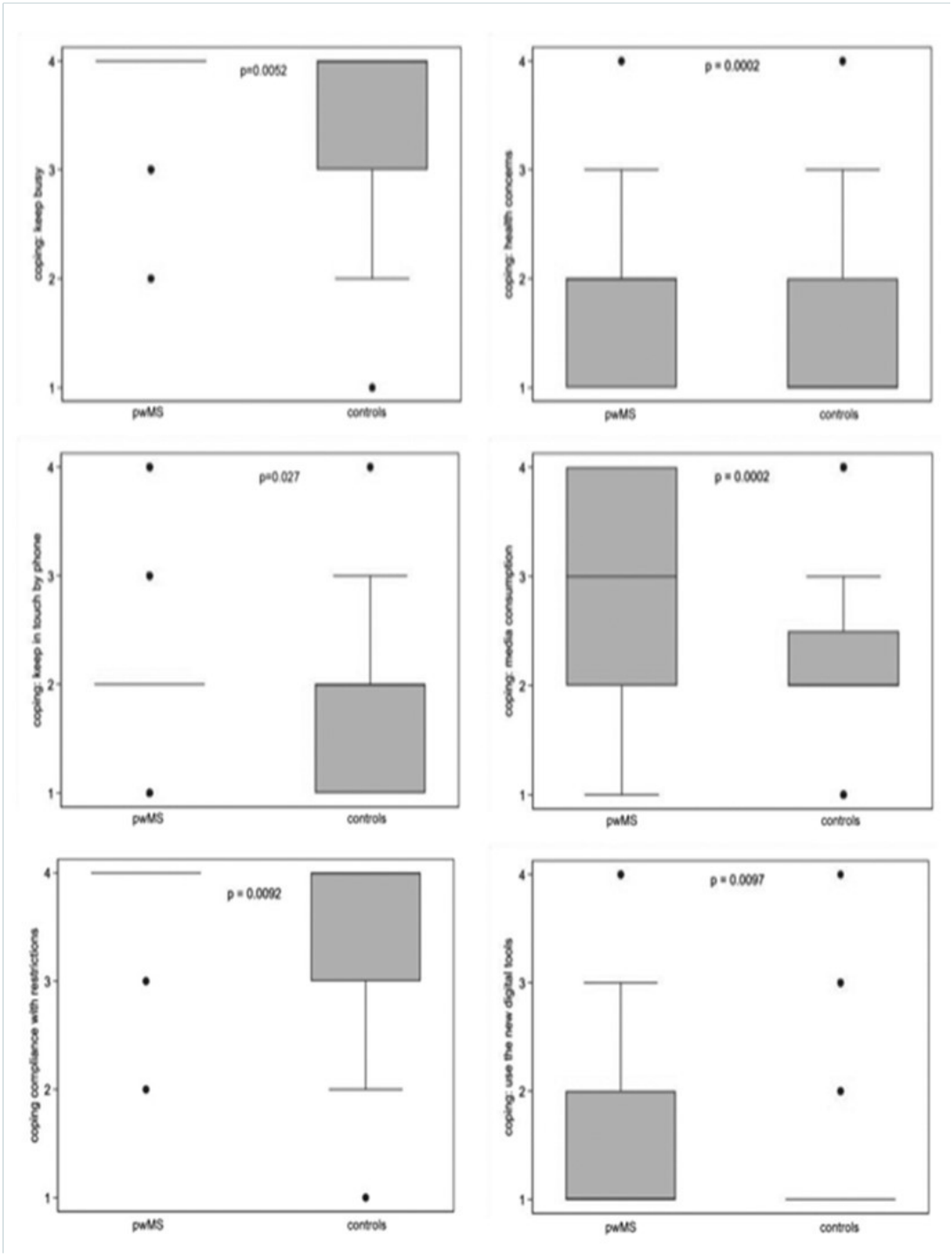

Figure 2. Significant differences between pwMS and controls in daily coping strategies (p-values are according to exact Mann-Whitney U test).

Daily Coping Strategies

We observed in all subjects two adaptive strategies that improved the A/D psychological status: to stay focused on unusual activities and to keep busy on self-rewarding practical actions. Both should be remarked during psychological consultations, especially the latter which is more used (p=0.005) and more effective for pwMS (Figure 2).

On the other hand, the strategies that positively correlated with anxiety and depression in all the sample were: feeling stuck and doing anything; feeling the head elsewhere; feeling nervous; feeling hyperactive; eating to avoid thinking.

Moreover pwMS tended to adopt more than controls the following coping strategies, associated with psychological burden: thinking always about health issues, just listening to the news (Figure 2).

These themes should be investigated during the clinical interviews to provide psycho-educational support.

Empathy seemed to show a greater and significant emotional impact only in controls, as shown by these sentences: “I’m distressed for those who are sick and I can’t help”, “I'm always on the phone to make sure friends and family are safe”.

News

In general, the emotional reaction to media news was strictly associated with the psychological burden in all the subjects, and is expressed especially in these terms: feeling a weight on the stomach; sleeping badly; reflecting on the emergency; feeling hopeless, restless, pained. Compared to controls, pwMS reported more frequently to follow the news all day long, considering this more useful and reliable, in order to respect the restrictions and to feel protected (Figure 1). Psychological status didn’t correlate with these considerations in pwMS except for frequency of news listened; on the contrary, controls felt more anxious when they affirmed to doubt about the utility of the news and to reflect on that.

Family

In all subjects, psychological status was strongly associated with negative family relations. The burden increased the more the relatives were considered irritant, suffocating, unbearable.

Home

For pwMS the difficulty to stay at home was associated with living space (p=0.012) and not related to family as conversely happened in controls, who were only conditioned by stressful domestic relations.

Stay Outside

The discomfort of staying at home was similar in all subjects but pwMS reported more frequently the fear to go outside (Figure 1). Both factors correlated with anxiety and depression, even if the association was closer in controls, who seemed to tolerate worse the restrictions, possibly because they didn’t feel at higher risk to be infected.

Sport

PwMS practiced less physical activity compared to controls. Nearly 20% of subjects in both groups stopped the physical activity, but no difference in terms of A/D was detected compared to persons who continued sport. (PHQ-9: p=0.0984; GAD-7: p=0.1992).

SARS-CoV-2

We considered all the controls because no differences were observed in SARS-CoV-2 related variables selecting only the northern population. Among the subjects who reported the suspect to be infected by the virus, only the controls showed a significant psychological reaction. Participants reported a similar rate of persons deceased for SARS-CoV-2 among family, friends or neighbors and reacted with a comparable emotional response but in cases of mourning, controls were more frequently worried to be infected (p=0.026).

Discussion

The study received a good feedback by pwMS and the web survey represented a very useful tool, as other examples of telemedicine, in an outstanding period of restrictions [16]. Despite the possible selection bias due to the voluntary enrollment, socio-demographic characteristics didn't differ between groups and this was a favorable element which encouraged us to proceed with the comparison. Moreover, the geographical distribution of the sample didn't determine a significant difference in the perception of SARS-CoV-2 related variables, as reported in other studies [17,18], allowing us to consider the sample as a whole.

A/D rate in pwMS proved comparable with the results of other Italian surveys conducted during the SARS-CoV-2 lockdown even if collected with different questionnaires. Considering the clinical cut-off, Capuano [19] reported a similar rate of 16.4% for anxiety, evaluated with the State section of the State-Trait Anxiety Inventory, and a lower rate of 11.9% for depression, evaluated with the Beck Depression Inventory II (BDII>18).

Regarding the severity class of A/D symptoms, Zanghì [18] according to the Depression, Anxiety and Stress Scale, reported comparable data with a rate of 42.1% for mild/moderate anxiety class and a rate of 44.4% for mild/moderate depression class (Table 3).

Moreover we must consider that the results of psychological assessment might be influenced by the specific questionnaire administered and that we collected an emotional snapshot of the acute phase of the pandemic, without a follow up to check the evolution of the psychological reaction over time. For these reasons we decided to consider the PHQ-9 and GAD-7 normative data referred to pwMS and to the general population as additional control for each group.

Regarding the PHQ-9 tool, our findings (Table 3) are consistent with pwMS literature data collected before the pandemic; in fact Terrill [21] reported a mean score of 7.5 (5.5) points in 513 pwMS, and Amtmann [14] detected a mean score of 6.6 points in 455 pwMS with the following rate of depression for each frequency class: minimal = 42.4%; mild=33.2%; moderate=16.3%; severe=8.1%.

The PHQ-9 normative data in the general population shows a prevalence rate of moderate to high severity of depressive symptoms of 5.6% with a mean range of 2.9 (3.5) [22] while in our data controls reported three times higher scores.

Literature data concerning GAD-7 indicate a rate of 6.2% in the general population [23] with a mean score of 2.95 (3.3) [22] that are twice as much compared to our data in controls. Korostil [25] reported the rate of 19% in pwMS which is similar to our results.

In summary, A/D findings were similar to the published pre-pandemic data for pwMS and higher for the controls, considering pwMS and the normative data. These findings support the hypothesis that the psychological reaction of pwMS in the first period of lockdown was limited. In fact the A/D scores were not higher compared to the expected in pwMS. On the contrary the controls showed higher values than the normative ones, suggesting an acute psychological reaction. Maybe PwMS mainly concentrated on the psychological reactions to the SARS-CoV-2 pandemic, dissociating the MS, also because the questions were not referred, as usual, only and specifically to the MS perception. Despite this possible limitation, the central role of MS in thoughts and emotions of pwMS is underlined by the answers about the health concern, by the coping strategies and by the importance of the correlation with A/D as described below and overall reported in Supplementary Table 2A. Furthermore we placed the A/D brief screening questionnaire at the end of the survey with the indication to consider the psychological state in general.

Looking at the variables studied, first of all health perception, pwMS considered themselves at higher risk for the infection, upon advice from experts and new regulatory norms, showing more caution and fear to go outside. So they might have been more resilient to tolerate the restrictions and the cohabiting relatives. When a suspect of infection occurred, PwMS tended to show lower A/D symptoms than controls.

The correlation between health themes and the psychological reaction resulted closer in controls, suggesting that the pandemic was the main trigger for them, while in pwMS other factors might be involved, first of all MS. Nevertheless pwMS with recent MS diagnosis, supposedly being more used

to tolerate the change of daily habits, didn't show more resilience in terms of lower A/D score. In a larger study [26] that share with us the relevant role of the personal coping to bear the lockdown, the time since diagnosis with other factors as gender, antidepressant, living arrangements or employment status didn't predict an impact of the pandemic on the personal life.

About daily life, most of the coping strategies were common in both groups. Staying active and focused on practical tasks resulted in the best adaptive strategy, being more effective in this fragile population, as reported in a similar Italian study and in the previously cited international survey [18,26].

Despite this, pwMS selected more frequently some maladaptive strategies: they were more used to think about health, to continue by video calls the usual activities and to keep in contact by phone with relatives and friends, even if this increased anxiety (Figure 2). These daily habits should be inquired and supported during the clinical visits.

Media news showed an important and negative impact on A/D. PwMS reported to listen to the news more frequently compared to the controls but, even if they considered the news reliable and useful to keep on respecting the lockdown, these considerations didn't affect their psychological status while the doubts on reliability of news increased anxiety in controls (Figure 1).

According to other studies the physical activity [27], the MS duration and employment status [26] were not associated with the psychological reaction during the lockdown. Job by itself is a vexed theme for pwMS [28] and represents a primary source of stress. Maybe for this reason the A/D scores were not associated with the actual changes in working habits, as happened for controls.

Conclusions

Despite the small sample and the possible selection bias due to the voluntary enrollment, these results might suggest that pwMS showed a proper psychological resilience during the first acute phase of the SARS-CoV-2 pandemic. They respected the restrictions more easily, being more aware of the priority of health. However, they tended more often to use phone and video calls and to focus on the media news and on health concerns, fueling A/D. Clinicians should pay attention to enquire about these specific maladaptive strategies considering the chance of a specific psychological intervention to support them in the different phases of the pandemic.

Ethical Compliance Section

Funding

The authors have no funding to disclose.

Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Milano Area 3 Ethic Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Digital Informed consent was obtained from all individual adult participants included in the study.

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Appendix

Competing Interests

The authors declare no conflict of interest.

References

1. Howard J., Trevick S., Younger D.S. (1996). Epidemiology of Multiple Sclerosis. *Neurol Clin*, 34(4): 919-939.
2. R A Marrie, Reingold S., Cohen J. The incidence and prevalence of psychiatric disorders in multiple sclerosis: a systematic review. 2015. *Mult Scler*, 21(3): 305-17. https://doi.org/10.1177/1352458514564487
3. Mohr D.C. and Cox D. (2001). Multiple Sclerosis: Empirical Literature for the Clinical Health Psychologist. *Journal of Clinical Psychology*, 57(4): 479–499. https://doi.org/10.1002/jclp.1042
4. Ornell F., Schuch J.B., Sordi A.O. (2020). ‘‘Pandemic fear’’ and COVID-19: mental health burden and strategies. *Braz J Psychiatry*, 42(3):232-235. https://doi.org/10.1590/1516-4446-2020-0008
5. Wu C., Chen X., Cai Y., et al. (2020). Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med*, 180(7): 934–943. https://doi.org/10.1001/jamainternmed.2020.0994
6. Pfefferbaum B., North C.S. (2020) Mental Health and the Covid-19 Pandemic. *N Engl J Med*, 383:510-512. https://doi.org/10.1056/nejmp2008017
7. Thompson A.J., Banwell B.L., Barkhof F. et al. (2018). Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*, 17: 162–173.
8. Spitzer R.L., Kroenke K., Williams J.B.W. et al. (2006). A Brief Measure for Assessing Generalized Anxiety Disorder. The GAD-7. *Arch Intern Med*, 166 :1092–1097. https://doi.org/10.1001/archinte.166.10.1092
9. Kroenke K., Spitzer R.L., Williams J.B. (2001). The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*, 16(9): 606–13.
10. American Psychiatric Association (2000): *Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR (Text Revision)*, 4th ed, Washington, DC: American Psychiatric Association.
11. Lowe B., Decker O., Muller S., et al. (2008) Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Med Care*, 46: 266–274.
12. Honarmand K., Feinstein A. Validation of the Hospital Anxiety and Depression Scale for use with multiple sclerosis patients. 2009. *Mult Scler*, 15: 1518–1524. https://doi.org/10.1177/1352458509347150
13. Patrick S., Connick P. (2019). Psychometric properties of the PHQ-9 depression scale in people with multiple sclerosis: A systematic review. *PLoS One* Epub 19 Feb 2019;14(2): e0197943. https://doi.org/10.1371/journal.pone.0197943
14. Amtmann D. 2014. Comparing CESD-10, PHQ-9, and PROMIS Depression Instruments in Individuals with Multiple Sclerosis. Rehabil Psychol,59(2): 220–229. https://doi.org/10.1037/a0035919
15. Kurtzke J.F. (1983) Rating neurological impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*, 33: 1444–1452. https://doi.org/10.1037/t28980-000
16. Capra R., Mattioni F. (2020). Tele-health in neurology: an indispensable tool in the management of the SARS-CoV-2 epidemic. *Journal of Neurology*, 267: 1885–1886. https://doi.org/10.1007/s00415-020-09898-x
17. Forte G., Favieri F., Tambelli R., Casagrande M. The enemy which sealed the world: effects of COVID-19 diffusion on the psychological state of the Italian population. 2020. *J Clin Med*, 9 (6):1802. https://doi.org/10.3390/jcm9061802
18. Donisi V., Gajofatto A., Mazzi M.A., Gobbin F., Busch I.M., Ghellere A. and Rimondini M. (2021) Insights for Fostering Resilience in Young Adults With Multiple Sclerosis in the Aftermath of the COVID-19 Emergency: An Italian Survey. *Front. Psychiatry*, 11:588275. https://doi.org/10.3389/fpsyt.2020.588275
19. Capuano R., Altieri M., Bisecco A. et al. (2021) Psychological consequences of COVID-19 pandemic in Italian MS patients: signs of resilience? *J Neurol*, 268: 743–750
20. Zanghì A. et al. (2020). Mental health status of relapsing-remitting multiple sclerosis Italian patients returning to work soon after the easing of lockdown during COVID-19 pandemic: A monocentric experience. *Mult Scler Relat Disord*, 46:102561. https://doi.org/10.1016/j.msard.2020.102561

21. Terrill A.L., Hartoonian N., Beier M. et al. (2015) The 7-item Generalized Anxiety Disorder Scale as a tool for measuring generalized anxiety in multiple sclerosis. *Int J MS Care*, 17(2): 49–56. https://doi.org/10.7224/1537-2073.2014-008
22. Kocalevent R.D., Hinz A., Brähler E. (2013) Standardization of the depression screener patient health questionnaire (PHQ-9) in the general population. *Gen Hosp Psychiatry*, 35(5): 551–5. https://doi.org/10.1016/j.genhosppsych.2013.04.006
23. Kroenke K, R L Spitzer, J B Williams. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. 2007. *Ann Intern Med*, 146: 317–325. https://doi.org/10.7326/0003-4819-146-5-200703060-00004
24. Löwe B., Decker O., Müller S. et al. (2008). Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Med Care*, 46(3): 266–74. https://doi.org/10.1097/mlr.0b013e318160d093
25. Korostil M., Feinstein A. (2007) Anxiety disorders and their clinical correlates in multiple sclerosis patients. *Mult Scler* 2007; 13: 67–72. https://doi.org/10.1177/1352458506071161
26. Morris-Bankole H., Ho A.K. (2021) The COVID-19 Pandemic Experience in Multiple Sclerosis: The Good, the Bad and the Neutral. *Neurol Ther*, 10:279–291. https://doi.org/10.1007/s40120-021-00241-8
27. Reguera-García M.M., Liébana-Presa C., Álvarez-Barrio L. et al. (2020) Physical Activity, Resilience, Sense of Coherence and Coping in People with Multiple Sclerosis in the Situation Derived from COVID-19. *Int. J. Environ. Res. Public Health*, 17:8202. https://doi.org/10.3390/ijerph17218202
28. Raggi A., Covelli V., Schiavolin S. et al. (2016) Work-related problems in multiple sclerosis: a literature review on its associates and determinants. *Disabil Rehabil*, 38(10): 936–44.

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