Original research

Somatic symptom disorder in patients with post-COVID-19 neurological symptoms: a preliminary report from the somatic study (Somatic Symptom Disorder Triggered by COVID-19)

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ABSTRACT

Objectives To assess the diagnosis of somatic symptom disorder (SSD) in patients with unexplained neurological symptoms occurring after SARS-CoV-2 infection, also referred to as long COVID.
Design Single-centre observational study.
Participants Adult patients experiencing unexplained long-lasting neurological symptoms after mild COVID. Of the 58 consecutive patients referred in our centre, 50 were included.
Intervention Patients were contacted for a standardised psychometric evaluation by phone, followed by a self-survey.
Main outcome Positive diagnosis of SSD according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5).
Results Although the patients did not meet the DSM-5 criteria for a functional neurological symptom disorder specifically, SSD diagnosis based on DSM-5 criteria was positive in 32 (64%) patients. In the remaining 18 patients, SSD was considered possible given the high score on diagnostic scales. Physical examination were normal for all. Brain MRI showed unspecific minor white matter hyperintensities in 8/46 patients. Neuropsychological assessment showed exclusively mild impairment of attention in 14 out of 15 tested patients, in discrepancy with their major subjective complaint. Forty-five (90%) patients met criteria for Chronic Fatigue Syndrome. Seventeen (32%) patients were screened positive for mood-anxiety disorders, 19 (38%) had a history of prior SSD and 27 (54%) reported past trauma. Additional self-survey highlighted post-traumatic stress disorder in 12/43 (28%), high levels of alexithymia traits and perfectionism. Long-lasting symptoms had a major impact with a high rate of insomnia (29/43, 67%), psychiatric follow-up (28/50, 56%) and work or pay loss (25/50, 50%).
Conclusion A majority of patients with unexplained long-lasting neurological symptoms after mild COVID met diagnostic criteria for SSD and may require specific management.
Trial registration number NCT04889313.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Post-COVID-19 condition, also referred to as long COVID-19, is characterised by frequent neurological symptoms of poor understanding.

WHAT THIS STUDY ADDS

⇒ In this case series of 50 patients with unexplained neurological symptoms persisting more than 1 year after mild COVID-19, a diagnosis of somatic symptom disorder (SSD) can be asserted in 32 (64%) of them according to Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) criteria. Patients who did not strictly meet DSM-5 criteria nevertheless had high scores on SSD scales.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study suggests that a significant number of patients with long-lasting post-COVID-19 symptoms might suffered from SSD, arguing for its screening and specific management in affected patients, and providing new perspectives for research.

INTRODUCTION

While most people with COVID-19 fully recover within weeks of illness, a significant proportion of patients experience a wide range of symptoms that last over several months. This post-COVID-19 condition affects patients regardless of the severity of SARS-CoV-2 infection, and is mostly characterised by fatigue, dyspnoea, anosmia, headaches, joint paint, myalgias, concentration and memory difficulties.[1–4] While neurological and neurocognitive symptoms affect 30%–85% of these patients,[4 5] no study has yet investigated their characteristics, and the underlying mechanisms remain unclear. Unlike inpatients who may have respiratory or neurological sequelae of a severe COVID-19, especially following prolonged intensive care, the so-called 'long COVID-19' remains medically unexplained in patients with mild disease.[2] Data from a prospective cohort of mostly outpatients found 13% of patients had persistent symptoms after the first month, decreasing to 2.3% after 3 months.[3] Other surveys reported a prevalence of 15%–30% after 6 months with a significant impact in the quality of life.[1 2] A

number of symptoms in the first week of illness, age and female sex have been associated with an increased risk of developing long COVID-19.[3 6] Post-COVID-19 condition is now recognised as a major public health problem and physical management guidelines have recently been issued in several countries.[7]

Multiple studies have shown that an acute infectious disease is a common trigger for developing persistent somatic symptoms, especially chronic fatigue syndrome (CFS).[8 9] There is some debate as to the origin of these symptoms, with some considering them to be part of 'functional disorders', a complex nosological framework with multiple overlapping denominations and subtypes (eg, functional somatic syndrome, somatoform disorders, functional neurological disorder, bodily distress syndrome).[10 11] Here, we considered the unifying diagnosis of somatic symptom disorder (SSD) proposed by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).[12] SSD affects approximately 6% of the general population.[13] SSD often results in severe disability, deterioration of quality of life and unemployment, and gives rise to high utilisation of healthcare resources and medical nomadism.[14 15] SSD diagnosis can be made in the context of a concurrently relevant illness, criterion B of DSM-5 diagnosis being the critical issue (excessive thoughts, feelings or behaviours related to the somatic symptoms or associated health concerns).[12]

The aim of the SOMATiC study (SOMAtic symptom disorders Triggered by COVID-19) is to determine whether a positive diagnosis of SSD can be asserted in patients with long-lasting neurological symptoms occurring after mild COVID-19.

MATERIALS AND METHODS

Study design and participants

We conducted an observational single centre study in the Neurology Unit of Delafontaine Hospital (Saint-Denis, France). We reviewed all consecutive patients referred in this centre for specialised post-COVID-19 consultation to a referent neurologist (TdB) from May 2020 to April 2021. Most of the patients were included in the PERSICOR cohort whose first results were previously published.[4] Patients were contacted by phone to invite them to participate in the SOMATiC study. Participants gave oral consent before taking part of the study. The study is reported on ClinicalTrials.gov (ID NCT04889313).

Inclusion criteria were the following: adults (18 years-old or older); mild acute COVID-19 managed on an outpatient basis; post-COVID-19 symptoms including neurosensorial or neurocognitive disturbances; general and infectious workup excluding another disease. We excluded the patients who were hospitalised during the acute phase of illness, those with suspected de novo neurological pathology unrelated to COVID-19, and those who refused to participate in the study.

Data collection

The results of physical examination carried out by the referring neurologist (TdB), the brain MRI findings and the cognitive evaluation performed by the neuropsychologist (JD) were extracted from the patient records. Data from phone interviews and psychometric tests were collected by a trained internist (AK).

Phone interview

A semistructured questionnaire was used to specify acute illness characteristics (screening of 13 symptoms of COVID-19, results of SARS-CoV-2 nasopharyngeal rt-PCR and/or serology), postacute clinical course (screening of 25 symptoms of long COVID-19), consumption of care, history of pre-existing

functional disorders and of physical or psychological traumas. History of trauma was considered if the patient answered positively to the question 'Have you had a physical or psychological trauma in your life?', accepting some degree of subjectivity in their response. A psychometric evaluation was carried out based on validated scales including PHQ15 (Patient Health Questionnaire-15),[16] SSD12–B criteria scale,[16] SOFA (Schedule Of Fatigue and Anergia),[17] Hospital Anxiety and Depression Scale.[18]

Self-administered survey

After the phone interview, a self-administered survey was sent by e-mail, including the following scales: Insomnia Severity Index,[19] TAS20 (Toronto Alexithymia Scale),[20 21] IES-R (The Impact of Event Scale – Revised) with COVID-19 as the index event,[22] WHO-Quality Of Life-BREF,[23] modified HF-MPS (Hewit & Flett - Multidimensional Perfectionism Scale).[24]

SSD diagnosis assessment and evaluation of risk factors for SSD

The main objective of the study was to determine the prevalence of SSD among the study population. SSD is defined in the DSM-5 by one or more symptoms having a significant functional impact (criterion A), with behaviours, thoughts or feelings that appear disproportionate to the symptoms (criterion B) and a chronic evolution (criterion C). A positive SSD diagnosis was established according to this definition using validated scores,[16] with all the following criteria: a PHQ15 score ≥12 (criterion A); an SSD12 score≥23 (criterion B); an evolution of symptoms ≥4 weeks for criterion C.[25]

Alexithymia, perfectionism and history of trauma were measured as potential risk factors for SSD.[10 26–32]

Statistical method

The results are expressed as numbers and percentages for categorical variables and as median and IQR for quantitative variables. Association between the scores of scales used for the diagnosis of SSD (ie, the PHQ15 and the SSD12) and of pre-existing psychological risk factors of SSD (ie, alexithymia, perfectionism and history of trauma) was analysed using a linear regression model adjusted for gender and age. SSD diagnosis criteria were compared between patients with laboratory confirmed COVID-19 and those without microbiological documentation, using T test for quantitative variables and χ^2 test for binary variables. All statistical analyses were performed using the statistical R software. A p<0.05 was considered significant.

RESULTS

From 1 May 2020 to 30 April 2021, 58 patients were seen in consultation for neurological post-COVID-19 symptoms assessment (figure 1). Eight patients were excluded: one had a diagnosis of primitive lateral sclerosis, one had severe COVID-19 requiring hospitalisation, two refused to participate and four were unreachable (figure 1). We included 50 patients who participated in the phone interview. Among them, 43 completed the additional self-survey.

General characteristics of the study population

Forty-one (82%) patients were women with a median (IQR) age of 46 (39–51) years and graduate level education for 39 (78%) (table 1). Forty (80%) patients had the first symptoms of COVID-19 during the first wave of the epidemic in France, between February and April 2020. Twenty-one (42%) patients were caregivers and/or worked in healthcare facilities, among
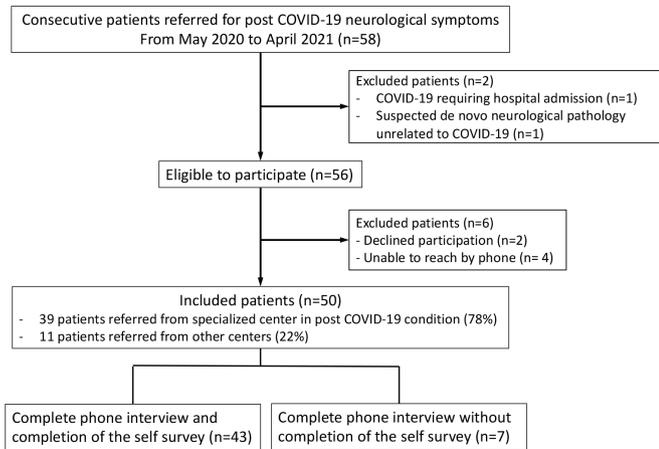
Figure 1 Population study of patients with post-COVID-19 neurological symptoms.

whom 16 out of 21 (76%) felt that they had been contaminated at their workplace. SARS-CoV-2 infection was microbiologically documented (positive nasopharyngeal RT-PCR and/or positive serology) in 32 (64%) patients. Most frequent symptoms of COVID-19 were fatigue (39/50, 78%), fever (35/50, 70%) and cough (34/50, 68%). The median (IQR) number of symptoms during COVID-19 per patient was 6.[5–8]

Post-COVID-19 condition

The phone interview took place after a median (IQR) of 425 (403–429) days after the first COVID-19 symptoms (table 1). At this time, all patients still had symptoms, with a median (IQR) of 13[12–16] symptoms per patients. None of the patients presented with an isolated complaint regarding altered voluntary motor or sensory function specifically. Therefore, none the patients met the DSM-5 criteria for a functional neurological symptom disorder per se. Fatigue and pain were both reported by 49 (98%) patients, with pain referring mostly to headaches (n=41, 82%). Cognitive complaints were notified by 48 (96%) patients, including 45 (90%) reporting impaired attention, 41 (82%) poor memory and 39 (78%) missing words. Among the 47 (94 %) patients suffering from neurosensory symptoms, 38 (76%) described dysesthesia. Other frequent symptoms were sleep disorders (n=40, 80%), dizziness (n=24, 48%) or gait impairment (n=13, 26%), and non-neurological symptoms (figure 2). Forty-four (88%) patients described their symptoms as fluctuant or intermittent, with a periodicity that could range from a few hours to several months. Some triggers for the symptoms could be identified, such as psychological stress or negative emotions in 23 (46%) patients or physical exertion in 26 (52%). In contrast, 20 (40%) patients considered rest to be a calming factor. A general trend towards improvement was reported by 36 (72%) patients.

Neurological workup

All patients had a normal neurological physical examination (table 2), that is, showing no focal neurological deficit, no gait or movement disorder, no clinical signs in favour of a nervous system lesion. There was no systematic screening for specific signs suggestive of functional neurological disorder. MRI was performed for 49 (98%) patients and reported no significant abnormalities. The results of 46/49 MRI were reviewed, showing that 8/46 (17%) patients had minor supratentorial FLAIR white matter hyperintensities (WMH) of the deep and/

Table 1 Sociodemographic and clinical characteristics of the study sample (N=50)

Age, years, median (IQR)	46 (39–51)
Women n, (%)	41 (82)
Healthcare worker, n, (%)	21 (42)
Comorbidities, n, (%)	39 (78)
Hypertension	5 (10)
Diabetes	1 (2)
Hypothyroidism	8 (16)
Anxiety or depressive disorders	5 (10)
Endometriosis	4 (8)
Migraine	4 (8)
Current cigarette smoking, n, (%)	7 (14)
Alcohol consumption >3 times/week, n, (%)	3 (6)
Educational level, n, (%)	
Below end of high school	1 (2)
End of high school	10 (20)
Tertiary education	39 (78)
Having children, n, (%)	35 (70)
Date range of first COVID-19 symptoms, n, (%)	
From mid-February 2020 to end of April 2020	40 (80)
From May 2020 to November 2020	10 (20)
Family or friends affected by severe COVID-19	13 (26)
No of symptoms per patient during acute COVID-19, median (IQR)	6 (5–8)
Type of symptoms during acute COVID-19, n, (%)	
Asthenia	39 (78)
Fever	35 (70)
Cough	34 (68)
Headaches	32 (64)
Diffuse pain	30 (60)
Anosmia	29 (58)
Dyspnoea	25 (50)
ENT symptoms	24 (48)
Digestive symptoms	18 (36)
Chest pain	14 (28)
Palpitations	8 (16)
Dizziness	7 (14)
Dysesthesia	1 (2)
Microbiological documentation*, n, (%)	32 (64)
Time from first COVID-19 symptoms to phone interview, days, median (IQR)	425 (403–429)
No of symptoms per patient at phone interview, median (IQR)	13 (12–16)
Fluctuation of post-COVID-19 symptoms, n (%)	44 (88)
Presence of worsening factors, n (%)	37 (74)
Stress or negative emotions, n (%)	23 (46)
Physical effort, n, (%)	26 (52)
Both, n (%)	13 (26)
Presence of soothing factors, n (%)	41 (82)
Rest, n (%)	20 (40)
Other (medication, physical activities, complementary medicine)	32 (64)
None	9 (18)
General trend of improvement, n (%)	36 (72)

*Positive RT-PCR on nasopharyngeal swab and/or positive COVID-19 serology. ENT, ears, nose and throat.

or periventricular white matter corresponding to Fazekas grade 1. Patients with WMH were non significantly older that those without WMH (median age 50 years IQR (49–56) vs 46 IQR (40–51) p=0.28). Fifteen (30%) patients underwent a neuropsychological assessment, highlighting an impairment of attention
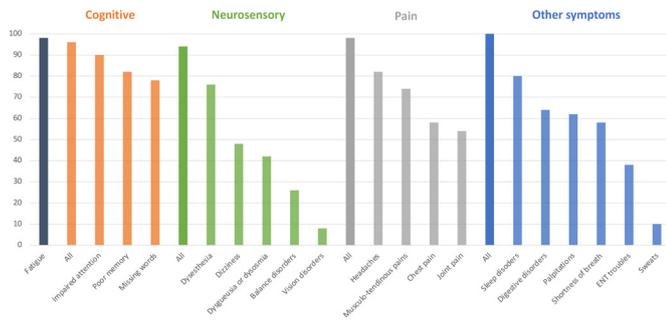
Figure 2 Type and percentage of post-COVID-19 symptoms of the population study (n=50).

for almost all of them (n=14, 93%). The degree of impaired attention was variable with some patients having mild deficit resulting in isolated difficulties in divided, sustained or selective attention (n=8, 53%). Others had additional difficulties in some attentional-related executive functions such as working memory, verbal fluency or information processing speed (n=6, 40%). All patients had normal performances in language, episodic memory and visuospatial tests.

SSD assessment
Regarding SSD assessment, criterion A (PHQ 15≥12) was met by 47 (94%) patients, criterion B (SSD12≥23) by 33 (66%) patients and criterion C (evolution≥4 weeks) by all (table 2). According to DSM-5 criteria, a positive diagnosis of SSD was definite for 32 (64%) patients with the association of criteria A, B and C. Seventeen (34%) patients did not meet criterion B, three quarters of whom had a SSD12 score just below the threshold, between 16 and 23, with a particularly low score for some proposals such as 'I think that doctors do not take my symptoms seriously' (online supplemental table 1). Whether the diagnosis of COVID-19 was documented or not did not significantly change the results of the SSD12 and PHQ15 (online supplemental table 2).

Additional psychometric evaluation
Forty-five (90%) patients fulfilled the criteria for CFS according to the SOFA scale. The quantification of care consumption showed a median number of eight different physicians, seven laboratory workup and six radiological examinations per patient. Twenty-three (46%) patients were treated in a rehabilitation programme with a perceived benefit for most of them (16/23, 70%).

When asked about their feeling during the acute infection, 38 (76%) patients described significant anxiety (≥5/10 on a Likert scale), 30 (60%) patients a marked social isolation, 29 (58%) patients a fear of infecting their relatives and 30 (60%) patients expressed a significant fear of dying. Twenty-eight per cent of patients (12/43) met the criteria for a COVID-19 related post-traumatic stress disorder (IES-R≥39). Nineteen (38%) patients declared at least one functional disorder prior to COVID-19, such as digestive disorders, diffuse pain or abnormal fatigue. A history of physical or psychological trauma was declared by 27 (54%) interviewed patients and 7 (14%) had previous psychiatric care. Thirteen (26%) patients had a relative who had a severe form of COVID-19. Twenty-eight (56%) patients reported current psychiatric follow-up. The screening by the HAD scale was positive (ie, a subscore ≥11) for depression in 8 (16%) patients and for anxiety in 13 (26%). Two-thirds (29/43, 67%) had insomnia. Quality of life was altered in at least one area for 57% (24/42)

Table 2 Diagnostic workup of post-COVID-19 neurological symptoms and psychometric evaluation at follow-up (N=50)

Neurological clinical examination, n (%)	50 (100)
Presence of abnormalities, n (%)	0
Brain MRI examination, n (%)	49 (98)
Minor white matter hyperintensities, n/N (%)	8/46 (17)
Neurocognitive testing, n (%)	15 (30)
Mild impairment of attention* n/N, (%)	8/15 (53)
Impairment of attention and related dysexecutive dysfunction† n/N, (%)	6/15 (40)
Normal neurocognitive testing n/N, (%)	1/15 (7)
Positive diagnosis of somatic symptom disorder	
Positive criterium A (PHQ15 ≥12), n/N, (%)	47/50 (94)
Positive criterium B (SSD12 ≥23), n/N, (%)	33/50 (66)
Positive criterium C (evolution 4 weeks), n/N, (%)	50/50 (100)
Three positive criteria (A+B+C), n/N, (%)	32/50 (64)
Positive diagnosis of chronic fatigue syndrome (SOFA ≥3), n/N, (%)	45/50 (90)
Consumption of care during the follow-up period	
No of physicians consulted per patient, median (IQR)	8 (5–9)
No of blood testing per patient, median (IQR)	7 (4–10)
No of radiological examinations per patient, median (IQR)	6 (3–7)
Patients included in a rehabilitation programme, n, (%)	23 (46)
Reported feelings during acute COVID-19 (Likert scale 5/10) n/N, (%)	
Feeling distressed	38/50 (76)
Feeling isolated	30/50 (60)
Fear of infecting loved ones	29/50 (58)
Fear of dying	30/50 (60)
Psychiatric comorbidities	
COVID-19-related post-traumatic stress (IES-R ≥39), n/N, (%)	12/43 (28)
Positive anxiety screening (HAD anxiety score ≥11), n/N, (%)	13/50 (26)
Positive depression screening (HAD depression score ≥11), n/N, (%)	8/50 (16)
Insomnia (ISI ≥8), n/N, (%)	29/43 (67)
On-going psychiatric follow-up, n/N, (%)	28/50 (56)
History of trauma, n/N, (%)	27/50 (54)
History of Somatic Symptom Disorder, n/N (%)	19/50 (38)
Personality testing	
High level of alexithymia traits (TAS20 ≥61), n/N, (%)	18/43 (42)
High level of self-oriented perfectionism (HF-MPS ≥20/35), n/N, (%)	33/42 (79)
Personal and social impact of post-COVID symptoms	
Significant work and/or pay loss	25/50 (50)
Social isolation	27/50 (54)
Affected quality of life in at least one area, n/N, (%)	24/42 (57)

*Sustained, divide and/or selective attention, with no other cognitive dysfunction.
†Attention deficit associated with working memory dysfunction, verbal fluency deficit and/or slow information processing. No abnormalities in other executive functions, language, episodic memory nor visuospatial tests.
HAD, Hospital Anxiety and Depression Scale; HF-MPS, Hewit & Flett-Multidimensional Perfectionism Scale; IES-R, The Impact of Event Scale-Revised; ISI, Insomnia Severity Index; SOFA, Schedule Of Fatigue and Anergia; TAS, Toronto Alexithymia Scale.

of patients. Twenty-five (50%) patients reported a work loss or a significant pay cut and 27 (54%) experienced social isolation.

When patients were asked how much they thought their symptoms were related to COVID-19, 48 (96%) had a high conviction for the statement (score ≥5/10 on a Likert scale).

Forty-two per cent of patients (18/43) had high levels of alexithymia traits (TAS20 score ≥61), with a significant statistical correlation of the TAS20 score with the SSD12 score (r=0.45

(95% CI 0.24 to 0.66) ; p<0.001) and the PHQ15 score (r=0.11 (95% CI 0.01 to 0.22), p=0.03) (online supplemental table 3). History of trauma was not associated with the PHQ15 score (r=0.83 (95% CI −1.58 to 3.24), p=0.49) or the SSD12 score (r=3.82 (95% CI −1.45 to 9.08), p=0.15). Self-oriented perfectionism scale was≥20/35 for 79% of patients (33/42) and was correlated with the SSD12 score (r=0.67 (95% CI 0.20 to 1.13), p<0.01) but not with the PHQ15 score (r=0.05 (95% CI −0.17 to 0.27), p=0.66).

DISCUSSION

To our knowledge, this is the first study to assess SSD diagnosis among patients with long-lasting unexplained post-COVID-19 neurological symptoms. As in other 'long COVID-19' reports, the population study is characterised by a strong predominance of middle-aged women[3 6] and a wide range of neurological and extraneurological symptoms with a fluctuating course.[26] Three-quarters of patients experienced more than five symptoms during acute illness, which have been associated with long COVID-19.[3 6 33] Neurological symptoms were neither related to physical examination abnormalities nor to brain MRI lesions. The rate of minor WMH in this study (17%) is in accordance with previous reports in the general population in this range of age,[34] arguing for non-specific findings. Cognitive tests mostly showed mild attentional difficulties, in discrepancy with the level of their subjective complaint. This profile of neuropsychological assessment is non-specific. Similar cognitive abnormalities have been described in patients with dysimmune systemic diseases such as lupus erythematosus[35 36] but is also in patients with functional disorders, such as in 50%–90% of patients with fibromyalgia, CFS or functional neurological disorder.[37] Impairment of attention may also be the consequence of fatigue, insomnia and/or of anxiety and depressive disorders. Quantification of effort and detection of negative response bias requiring performance validity tests (PVTs) were not performed. However, PVT failure rate does not appear to be higher among patients with functional disorders compared with other clinical conditions.[38] Nearly two-thirds of patients formally met the criteria for SSD according to DSM-5, the remaining third not fulfilling the criterion B despite a high SSD12 scale. The mean score of SSD12 was 27, whereas other studies reported a mean score of 6 in healthy subjects, 12 in patients with chronic disease, and 20 in patients with SSD.[39 40] In addition, some proposals of SSD12 scale such as 'I think that doctors do not take my symptoms seriously' might be less suitable in the context of a new disease pandemic with a particular interest of the medical community, especially in long COVID-19 specialised centre. The study also highlighted that 90% of patients with Long COVID-19 met the criteria for CFS, which is well described in other postinfectious context,[8 9] hence these long-lasting symptoms may not be specific to SARS-Cov2 infection itself. CFS is a heterogeneous condition thought to be of multifactorial aetiology, although it is in some quarters framed as a functional disorder.[27 41]

Several risk factors for SSD could been identified among the patients. More than half reported a fear of dying during first days of COVID-19, and a quarter had characteristics of post-traumatic stress disorder, which has been associated with a significant excess risk of developing SSD.[42] The fact that most patients were infected during the first wave of epidemic also argues for a potential traumatic experience, especially in a population with many caregivers, particularly exposed to anxiety at that time. Alexithymia and perfectionism, which are broad personality styles but also known risk factors for SSD,[10 26 27] were detected in respectively 42% and 79% of the patients. Such level of alexithymia traits is present in only 10% of general population.[21 43] The score achieved by the patients on the TAS20 scale was 59 in median, close to the median score of 58 found in a population of patients with fibromyalgia, vs 39 for healthy individuals.[44] Half the patients reported a history of past trauma, which is also a predisposing factor for SSD.[28] Almost 40% of the patients had a history of functional disorder prior to COVID-19. Such an association of different functional disorders is commonly described and has contributed to the proposal of unifying diagnosis categories such as the SSD.[11] Another study have demonstrated a positive diagnosis of fibromyalgia—a subtype of functional disorder with predominance of diffuse pain—in 57% of 30 patients with unexplained long-lasting post-COVID-19 symptoms.[33]

Long-lasting post-COVID-19 symptoms had a major impact on patients' lives with a high prevalence of insomnia, a frequent work or pay loss, a high level of care consumption and a frequent need of psychiatric care. While most patients showed a trend towards improvement, none of them described complete clinical remission. A significant worsening of life have been demonstrated in outpatients with long-lasting post-COVID-19 symptoms.[1] Considering long COVID-19 as at least partly explained by a functional disorder is of major interest, given that its early and appropriate medical management is a key point to improve this condition and limit long-term disability. The mainstay of care is to avoid medical nomadism and multiple paraclinical tests, to manage psychiatric comorbidities, and to promote progressive and regular physical activity, cognitive–behavioural therapy and formalised therapeutic education supports.[11]

SSD diagnosis, however, does not exclude other concomitant mechanism such as viral persistence or inflammation or other pathogenic pathways being explored in long COVID.[45] The pathophysiology of functional disorders itself is increasingly although incompletely understood, integrating psychological and neurobiological perspectives.[46 47] Some environmental factors, such as infectious-induced inflammation, may be a trigger of long-lasting behavioural alterations.[47] Some studies have shown a cerebral hypometabolism in 18F-Fluoro-Desoxy-Glucose (FDG) brain Position Emission Tomography (PET) imaging in patients with Long COVID, while other did not.[48] More recently, some studies demonstrated an increased risk of cardiovascular diseases[49] and of cerebral microstructural changes involving limbic and olfactory cortical system[50] after SARS-CoV-2 infection. So far, there is no compelling evidence that such features are correlated with persistent neurological symptoms.[48 51 52]

The study has a number of limitations. It is a single-centre study with a small sample size and no control group. A majority of the patients came from a long COVID specialised centre, which may introduce selection biases, such as an over-representation of healthcare workers and of particularly severe condition. Further studies with a larger sample size are needed to confirm the results. The analysis of risk factors was exploratory and did not include multiple testing correction. Additionally, not all patients had laboratory confirmation of SARS-CoV-2 infection, as during the first wave of the French pandemic very few microbiological tests were available for mild illness. Nevertheless, there was no difference between patients with laboratory confirmed infection and those without, regarding SSD scales scores. As this study focused on neurological symptoms, we did not collect the details of the exhaustive work-up carried out in a specialised centre for post-COVID condition, which did not reveal any organic abnormality explaining the extraneurological symptoms. It would be interesting in futures studies, to compare these data with those

of patients with neurological symptoms related to other conditions, such as traumatic brain injury, systemic lupus or functional neurological disorder, implementing extensive biological investigations such as cerebrospinal fluid neurofilament light chain.

CONCLUSION

While awaiting scientific advances on the mechanisms underlying both SSD and long-lasting post-COVID-19 symptoms, there is an urgent need to raise awareness regarding the potential intricate connection of these two conditions. Identifying the post-COVID-19 conditions that correspond to SSD would allow early appropriate clinical management for many patients, therefore, limiting the major public-health impact of this disabling condition.

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Supplementary Table 1. Details and scores of SSD DSM-5 diagnostic criteria

	All patients (N=50)	Patients with positive A and B criteria (N=32)	Patients with negative A and/or B criteria (N=18)
PHQ15 (criterion A) median score (IQR) *	16 (14-21)	20 (15-22)	15 (12-17)
Median score per proposal† (IQR)			
'Stomach pain'	1 (0-2)	1 (1-2)	0.5 (0-1)
'Back pain'	1 (0.3-2)	2 (1-2)	0.5 (0-1)
'Pain in your arms, legs, or joints (knees, hips, etc.)'	2 (1-2)	2 (1.75-2)	2 (1-2)
'Menstrual cramps'	0 (0-1)	0 (0-1)	0 (0-0)
'Headaches'	2 (1-2)	2 (1-2)	2 (1-2)
'Chest pain'	1 (0.3-2)	2 (1-2)	1 (0-1.8)
'Dizziness'	1 (0-1)	1 (0-2)	1 (0-1)
'Fainting spells'	0 (0-1)	0 (0-1)	0 (0-1)
'Feeling heart pound or race'	1 (0-2)	1.5 (1-2)	1 (0-1)
'Shortness of breath'	2 (1-2)	2 (1-2)	2 (1-2)
'Pain or problems during sexual intercourse'	0 (0-0)	0 (0-1)	0 (0-0)
'Constipation, loose bowels, or diarrhea'	1 (0-2)	1 (0-2)	1 (0-2)
'Nausea, gas, or indigestion'	1 (0-2)	1 (1-2)	0 (0-1)
'Feeling tired or having low energy'	2 (2-2)	2 (2-2)	2 (2-2)
'Trouble sleeping'	2 (1-2)	2 (1-2)	1 (1-2)
SSD12 (criterion B) median score (IQR) **	27 (20-33)	32 (28-36)	17 (16-21)
Median score per proposal‡ (IQR)			
'I think that my symptoms are signs of a serious illness'	2 (1-3)	2.5 (1-4)	1 (0-2)
'I am very worried about my health'	3 (2-3)	3 (2-3)	2 (2-3)
'My health concerns hinder me in everyday life'	2 (1-3)	3 (2-3)	1 (0-2)
'I am convinced that my symptoms are serious'	2 (1-3)	3 (2-3)	1 (0-2)
'My symptoms scare me'	2 (1-3)	3 (2-4)	1 (1-2)
'My physical complaints occupy me for most of the day'	2 (1-3)	3 (2-4)	2 (0-2)
'Others tell me that my physical problems are not serious'	1 (0-2)	2 (0-3)	0 (0-1)
'I am worried that my physical symptoms will never stop'	3 (2-3)	3 (3-4)	2 (2-2)
'My worries about my health take my energy'	2 (1-3)	3 (2-3)	1.5 (0-2)
'I think that doctors do not take my physical complaints seriously'	1 (1-3)	2 (1-3)	1 (0-1)
'I am worried that my physical symptoms will continue into the future'	3 (2.25-4)	4 (3-4)	2 (2-3)
'Due to my physical symptoms, I have a poor concentration on other things'	3 (2-4)	3 (2-4)	2.5 (1-3)

* PHQ15: Patient Health Questionnaire 15, positive A criterion if ≥ 12

†Each proposal is scored from 0 to 2

** SSD12: Somatic Symptom Disorder – B criteria, positive B criterion if ≥ 23

‡ Each proposal is scored from 0 to 4

Supplementary Table 2: DSM-5 Diagnosis Criteria (SSD12 and PHQ15 scores) in patients with documented COVID-19 (n=32) and non-documented COVID-19 (n=18)

	Documented COVID-19 N = 32	Non documented COVID-19 N=18	*p*
PHQ15 score, median (IQR)	16 (14 – 20)	17.5 (14.25 – 21.75)	0.33
SSD12 score, median (IQR)	25 (25- 35.2)	28 (24 – 33)	0.37
Positive diagnosis of SSD*, n (%)	18 (56%)	14 (77%)	0.13

* Positive diagnosis of SSD : PHQ15 ≥ 12 + SSD12 ≥ 23 + evolution ≥ 4 weeks
PHQ15 : Patient Health Questionnaire 15 ; SSD12 : Somatic Symptom Disorder – B criteria scale ; SSD : Somatic Symptom Disorder

Supplementary Table 3: Correlation between alexithymia, perfectionism, history of trauma and DSM-5 Diagnosis Criteria, adjusted on age and sex (N=50)

	Correlation coefficient (95% CI)	p
Correlation between PHQ15 (criterion A) score and		
- Alexithymia (TAS20) score	0.11 (0.01; 0.22)	0.03
- Self-orientated perfectionism scale score	0.05 (-0.17; 0.27)	0.66
- History of trauma	0.83 (-1.58; 3.24)	0.49
Correlation between SSD12 (criterion B) score and		
- Alexithymia (TAS20) score	0.45 (0.24; 0.66)	< 0.001
- Self-orientated perfectionism scale score	0.67 (0.20; 1.13)	< 0.01
- History of trauma	3.82 (-1.45; 9.08)	0.15

PHQ15 : Patient Health Questionnaire 15 ; SSD12 : Somatic Symptom Disorder – B criteria scale ; TAS: Toronto Alexithymia Scale