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# Post-stroke depression

## *Depresión despues del infarto cerebral*

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We all know that cerebral vascular disease is one of the leading causes of morbidity and mortality worldwide and that the costs of patient care can destabilize entire families and health systems, so it is important to seek early access to care and prevention. After a cerebral infarction, follow-up by the neurologist is oriented at finding the etiology and initiating timely secondary prevention. However, other comorbidities such as depression can have a major impact on a patient who has had a stroke.

Depression post-stroke is more prevalent in woman and stroke patients had a 55% greater risk for depression than patients with myocardial infarction<sup>1</sup>. At least one third of stroke survivors present mood symptoms post-stroke<sup>2,3</sup> with prevalence ranging from 20% to 60%<sup>4</sup>. In this edition, García-Valadez et al., report the prevalence of post-stroke depression in vascular neurology consultation. They found that although 36.6% of the patients evaluated had criteria for depression, only 1% of them had a previous diagnosis of depression.

Post-stroke depression often has a chronic course and is associated with a variety of adverse health outcomes, including increased disability, morbidity, and mortality. Depression persists after 20 months in 34% of elderly patients with acute stroke and has been associated with worse cognitive and physical outcomes. Post-stroke depression is associated with increased short-term (12 and 24 months) and long-term (10 years) mortality<sup>4</sup>.

Comorbid psychiatric conditions, especially anxiety, are associated with a greater risk of post-stroke depression. Older age, male sex, and non-white race were protective factors<sup>1</sup>. Among the external factor contributing to post-stroke depression is the loss of social support<sup>4,3</sup>.

There are several hypotheses about the genesis of post-stroke depression, such as the disconnection of the brain's prefrontal systems or its modulatory pathways<sup>4</sup>. Decreased serotonin, noradrenaline, and dopamine levels, abnormal neurotrophic response to stroke and dysregulation of the hypothalamic-pituitary-adrenal axis are factors that altered neurogenesis and neuroplasticity<sup>2</sup>. Cerebral infarction lesions in the basal ganglia and left hemisphere have been related to post-stroke depression<sup>3</sup>. Inflammatory and hypoperfusion mechanisms impact brain function influencing depression<sup>4</sup>.

The period of adaptation after stroke can make it complicated to diagnose depression. Some patients may experience "grief", which can be considered a normal emotion in the period of adaptation to the new conditions after stroke, as the patient may be affected by autonomy loss and changes in personal relationships.

Halmiton Depression Rating Scale; 13 and the SF-36 questionnaire are useful to assess the severity of depressive symptoms and response to treatment during follow-up. The assessment can be performed by the neurologist, so the training of neurologists should be enriched with basic neuropsychiatric approaches, to be

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able to initiate treatment in necessary cases and to refer to a psychiatric specialist.

The screening for post-depression stroke could be considered during acute care stay in patient at high risk for depression, during transition points care and considered following discharge to the community<sup>5</sup>. Drug interactions with other drugs and adverse events should be considered in the choice of pharmacological treatment. The cognitive-behavioral therapy is a psychosocial intervention aimed at reducing symptoms of depression.

Remission of depression in the 1<sup>st</sup> month after stroke is associated with better recovery in activities of daily living<sup>4</sup>. In addition, social support is a protective factor against depression through emotional support, motivation for treatment, and support in daily functioning<sup>3</sup>.

In conclusion, we should consider that all patients with stroke have a high risk of developing depression, so we should include in their evaluation screening to search intentionally for depression and initiate timely treatment.

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# Clinical characteristics in a cohort of patients with chronic inflammatory demyelinating polyneuropathy: a retrospective study

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## Abstract

**Objective:** The objective of the study is to evaluate the chronic inflammatory demyelinating polyneuropathy (CIDP) clinical spectrum in a cohort of Mexican patients who benefit from social security. **Methods:** A retrospective study of CIDP patients from 2010 to 2021. We documented neurological deficits, electrophysiological and laboratory parameters, diagnostic characteristics, disease activity, and clinical outcomes. **Results:** 36 cases met the criteria of the EAN/PNS 2021, the mean age was  $58.25 \pm 10.10$  years, 50% were women, and 69.4% used intravenous immunoglobulin (IVIG). Concerning functional status, 63.9% had an independent walk and 86.1% had mild weakness in manual skills. The analysis of functional status showed better results in the IVIG treatment group. **Conclusions:** Similar to previous literature reports, 50% of our patients had stable active disease. Considering the heterogeneity of the disease, more research about treatment initiation and long-term results is warranted.

**Keywords:** Chronic inflammatory demyelinating polyneuropathy. Polyneuropathy. Treatment. Functional status. Outcome characteristics.

## Características clínicas en una cohorte de pacientes con polineuropatía desmielinizante inflamatoria crónica: un estudio retrospectivo

### Resumen

**Objetivo:** Evaluar el espectro clínico de la polineuropatía desmielinizante inflamatoria crónica (PDIC) en una cohorte de pacientes mexicanos beneficiarios de la seguridad social. **Métodos:** Estudio retrospectivo de pacientes con PDIC durante el período 2010-2021. Documentamos déficits neurológicos, parámetros electrofisiológicos y de laboratorio, características de diagnóstico, actividad de la enfermedad y resultados clínicos. **Resultados:** 36 casos cumplieron con los criterios de la EAN/PNS 2021, la edad promedio fue de  $58,25 \pm 10,10$  años, el 50% eran mujeres y el 69,4% utilizaban inmunoglobulina intravenosa. En cuanto al estado funcional, el 63,9% presentaba marcha independiente y el 86,1% presentaba debilidad leve en las habilidades manuales. El análisis del estado funcional mostró mejores resultados en el grupo de tratamiento con inmunoglobulinas intravenosa. **Conclusiones:** Al igual que en informes de la literatura, el 50% de nuestros pacientes tenían enfermedad activa estable. Teniendo en cuenta la heterogeneidad de la enfermedad, se justifica realizar más investigaciones sobre el tratamiento y los resultados a largo plazo.

**Palabras clave:** Polineuropatía desmielinizante inflamatoria crónica. Polineuropatía. Tratamiento. Estado funcional. Características de resultado.

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## Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a disorder of the peripheral nerves and nerve roots causing limb weakness, sensory deficits, hyporeflexia/areflexia with a progressive or relapsing form<sup>1,2</sup>. However, atypical features such as cranial nerve involvement, dysautonomia, and tremor are also reported<sup>3</sup>. CIDP is an immune-mediated disorder with macrophages inducing myelin damage, with consequent activation of complement-dependent antibodies, although its complete pathogenesis and etiology remain uncertain<sup>4</sup>. The USA and Europe report a prevalence of 3-5 cases/100,000 inhabitants/year and an incidence of 0.5-1 cases/100,000 inhabitants/year, being more frequent in men<sup>1,5</sup>. In Latin America, few studies describe the CIDP population; the first epidemiological study in South America and the Caribbean in 2019 reported a prevalence of 2.95 per 100,000 inhabitants<sup>6</sup>. In Mexico, two studies focus on the clinical characteristics and the type of clinical response to treatment<sup>3,7</sup>.

There are two widely accepted guidelines for diagnosis: one proposed by the American Academy of Neurology, described in 2012, and the other from the European Academy of Neurology (EAN) and Peripheral Nerve Society (PNS)<sup>1,2</sup>. At present, the 2021 European criteria are a high-sensitivity diagnostic tool, with definite CIDP and possible CIDP, integrating clinical and neurophysiological findings and supporting criteria<sup>1</sup>. The comparison and validity of functional results in other studies are difficult due to different treatment responses and clinical and electrophysiological characteristics among published studies<sup>8</sup>. A standardized metric for disease severity and assessment of treatment effectiveness has been attempted in a series of grading systems such as inflammatory neuropathy cause and treatment, Inflammatory Rasch-built Overall Disability Scale, and CIDP disease activity status (CDAS)<sup>9,10</sup>. The response to medical treatment is adequate for intravenous immunoglobulin (IVIG) and corticosteroids. CIDP efficacy (study) reported on the long-term efficacy benefits of IVIG treatment. After treatment, 41.5% of patients presented independent walking, and up to 75.6% had manual skills weakness<sup>11,12</sup>.

The study aims to evaluate the CIDP clinical spectrum in a cohort of Mexican patients who benefit from social security and free medical treatment, approaching their clinical and functional status.

## Methods

We performed a retrospective study in a cohort of patients with CIDP diagnosis.

## Patients

We recruited patients with a CIDP diagnosis who regularly attended neurology services at the High Specialty Hospital National Medical Center La Raza in Mexico City from 2010 to 2021. All diagnoses were performed by a neurologist team following the 2021 EAN/PNS criteria for CIDP and possible CIDP<sup>1</sup>. We analyzed clinical records, demographics, clinical presentation, nerve conduction studies (NCS), and laboratory parameters to determine diagnostic characteristics, disease activity, and post-treatment response. We classified patients according to the immunosuppressive treatment received: IVIG, corticosteroid, and other immunomodulatory treatments such as azathioprine and mycophenolate mofetil.

We evaluated disability by applying classical clinical measurement scales and other validated scales in the first visit and during follow-up using CDAS<sup>13</sup>. Then, for analysis, we divided the modified Rankin Scale (mRS) into three categories: 1-2 for mild, 3 for moderate, and 4-5 for severe. We classified manual skills disability using the Medical Research Council scale (MRC) according to hand muscle strength examination, dividing them into three categories: mild for strength 4-5, 3 for moderate, and 2-1 for severe. Finally, for independent walking, we made two groups: one with support walker use and the other without.

For a bivariate analysis and comparison, we classified patients into typical CIDP and its varieties: distal, focal, multifocal, motor, and sensory (previously called atypical). Response to treatment was judged based on the neurologist team's conclusion according to the follow-up data, dividing them into two groups. We considered those with preserved gait, manual skills, and a RANKIN > 3 in the satisfactory response group and another with an unsatisfactory response; we compared our results with previously published series.

## Ethics

We conducted the study following the Declaration of Helsinki, and the local ethics committee approved the investigation protocol.

## Samples

We obtained cerebrospinal fluid (CSF) samples and performed their subsequent analysis with cell and protein quantification to support CIDP criteria, defining albumin-cytological dissociation as a protein level: > 45 mg/dl and a white blood cell count ≤ 50 cells/ $\mu$ L.

The NCS recordings were conducted and reported by a certified neurophysiologist.

### Statistical analysis

For the statistical analysis, we performed descriptive statistics using the SPSS 20 version on Windows. We described cohort characteristics using proportions, mean  $\pm$  SD for continuous data, frequency, and percentage for categorical data. Also, for normality assessment, we used the Shapiro–Wilk test and for bivariate analysis,  $\chi^2$  test, Student t-test, Mann–Whitney U-test, or Kruskal–Wallis test according to its distribution groups. We consider statistically significant differences with  $p < 0.05$ .

### Results

From a sample of 70 patients with suspected CIDP, 36 patients met the criteria for probable and definite CIDP, 50% were female, mean age  $58.25 \pm 10.10$  years (range 35–81), mean disease duration of  $93 \pm 45.11$  months, time to diagnosis  $8.53 \pm 8.1$  months (range 2–48), 25% of patients presented with diabetes mellitus, and 11.1% with another immune-mediated pathology. Lumbar puncture was performed on 35 patients, and 74.2% had albumin-cytological dissociation, with mean proteins in CSF of  $96 \pm 82.26$  mg/dL. Initial symptoms showed weakness as the first symptom in 88.9% of the patients. Paresthesia or dysesthesia in 80.6% was the second most common symptom. The most common initial presentation was four-limb involvement in 72.2% and lower limbs only in 19.4%. We showed the rest of the demographic, clinical, and NCS characteristics in [table 1](#).

Regarding the current functional scales, we found that 41.7% had CDAS 3A (stable active disease > 1 year, on treatment with normal examination), 41.7% CDAS 5C (unstable active disease: abnormal examination with progressive or relapsing course, on treatment), and 8.3% CDAS 3B (stable active disease > 1 year, on treatment with abnormal examination).

Regarding the functionality scales and treatment response, although it did not reach statistical significance, the bivariate analysis showed better functional scores (manual skills, independent walking, mRS) in patients treated with IVIG than other immunosuppressive agents. We represent these results in [Fig 1](#).

We analyzed the treatment response in two separate groups: adequate and unsatisfactory responses. According to functional scales, the results showed statistically significant differences in the mRS scale, independent gait, manual skills, and CIDP variant ([Table 2](#)).

**Table 1.** Clinical, demographic, and functional characteristics of patients with CIDP

Variables	n = 36 (%)
CIDP variant	
Typical	26 (72.2 %)
Multifocal	3 (8.3 %)
Distal	7 (19.4 %)
Current treatment	
IVIG	25 (69.4%)
Prednisone	2 (5.6%)
Nonsteroidal immunosuppressant	8 (22.3%)
Rituximab	1 (2.8%)
Comorbidities	
Diabetes mellitus	10 (27.8%)
Hypothyroidism	6 (16.7%)
Other autoimmune diseases	4 (11.1%)
CSF (proteins mg/dL)	$96 \pm 82.26$ (range 14 - 474)
Prior steroid use	23 (63.9%)
Current functional status	
mRS	
Mild (0-2)	31 (86.1%)
Moderate (3)	5 (13.9%)
Severe (4-5)	0
Independent walk	23 (63.9%)
Manual skills	
Mild (5-4)	31 (86.1%)
Moderate (3)	2 (5.6%)
Severe (2-1)	3 (8.3%)

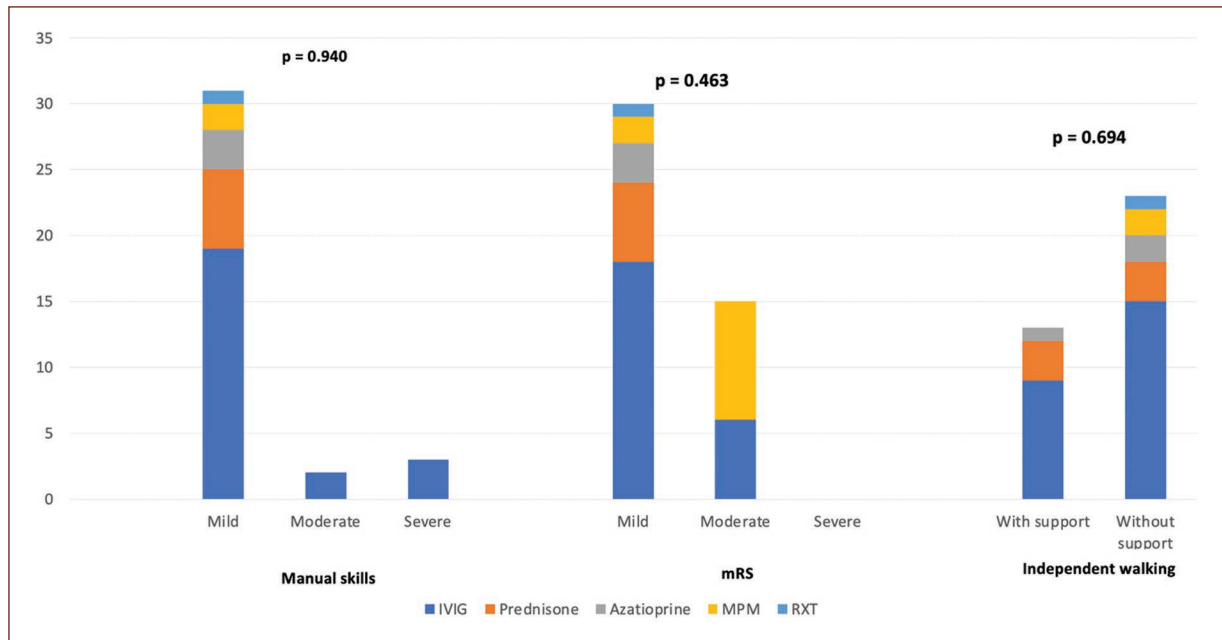
IVIG: intravenous immunoglobulin; CSF: cerebrospinal fluid; mRS: modified Rankin scale; CIDP: chronic inflammatory demyelinating polyneuropathy. Other autoimmune diseases: autoimmune thrombocytopenia (2), ankylosing spondylitis (2).

### Discussion

Few studies report the prevalence of CIDP in the US, Europe, and Latin America, being around 2.81/100,000 inhabitants<sup>1,5,6</sup>.

The heterogeneity in their data may be explained by different diagnostic criteria used. CIDP characteristics are weakness, paresthesia, and dysesthesia in a classically proximal distribution that was present in all our patients. Our CIDP patients share similar characteristics with previous reports: age at presentation, gender, and typical variant predominance<sup>7</sup>. CIDP variants in other series represented 49% and 21.3%, similar to ours with 27.7%<sup>7,8</sup>.

The association between CIDP and diabetes is discussed in two retrospective studies conducted in Europe. It is considered a common and treatable inflammatory neuropathy in these groups of patients<sup>14,15</sup>. Furthermore, a study in Mexico found that diabetes is the main associated comorbidity.<sup>7</sup> In our study, diabetes was present in 27.8% of the patients, similar to other



**Figure 1.** Comparative column chart between functionality scales and actual treatment.

cohorts (20%, 30.4%, and 18%)<sup>14-16</sup>. Other associated factors have been studied: diet, smoking, alcohol consumption, fatigue, toxic exposure, and disability progression and quality of life<sup>17-19</sup>.

The standard recommended treatment by the European and American guidelines is composed of immunomodulatory drugs that have been reported beneficial. IVIG and oral corticosteroids are first-line treatments for CIDP (Class II)<sup>12,20-23</sup>. As part of a public health program, IVIG is more accessible in our hospital than in other centers, where 69.4% of our patients were under this kind of treatment, compared with 21.3 % of another Mexican reference center, 59.3% in the UK, and 42.2% in Serbia<sup>7,14</sup>.

The evaluation of the treatment results for CIDP relies on the neuromuscular expert judgment considering clinical, functional, and electrophysiological evaluation. Patients in other cohorts report different functionality: 23% without symptoms, 50.4% stable active disease with abnormal examination<sup>9</sup>. In our cohort, 50% retain walking and 52.7% manual skills. However, as mentioned in the results, although patients with IVIG and prednisone had improved functional scales, this was not statistically significant. We found no sociodemographic or comorbidity variables significantly associated with disability scales. CDAS is an easy-to-apply tool used to classify long-term outcomes and responses to treatment in patients by a single observer<sup>13</sup>. Albulaihe et al.

reported a prevalence of CDAS-3 (stable active disease with > 1 year on treatment) of 50%, followed by CDAS1-2 of 23%,9 while for other series CDAS-3 ranged from 26% to 53%<sup>10</sup>, similar to our results of 41.7% for CDAS-3 and CDAS-5 (unstable active disease: abnormal examination with progressive or relapsing course) 41.7%. Of the latter, 80% were under immunoglobulin treatment, 6% with corticosteroid, and the rest on other treatments. We made a comparison between adequate and unsatisfactory treatment responses. Although not significant, patients with unsatisfactory responses were younger, with more delay in diagnosis, longer duration of illness, and more protein in their CSF.

## Conclusions

More than 50% of patients have stable active disease with or without abnormalities on examination, but another 40% still have unstable disease despite treatment.

Limitations: first, it is retrospective design. Second, some functional scales already established for CIDP patients were not calculated because of not previously having the appropriate handgrip measuring device. Third, some old files failed to have a complete physical examination or sufficient medical scale information. However, our findings agree with previous scientific descriptions and show the advantages of treatment with IVIG concerning good functional results.

**Table 2.** Comparison between adequate and unsatisfactory treatment response according to its functional scales, clinical evolution

Variables	Adequate response (n = 20)	Unsatisfactory response (n = 16)	p
Age (years)	60.45 ± 8.2	55.5 ± 11.7	0.147
Time to diagnosis (months)	6.5 ± 3.5	7.06 ± 4.05	0.662
Disease duration (months)	90 ± 43.09	96.75 ± 48.6	0.662
CSF (proteins mg/dL)	82.58 ± 46.17	113.91 ± 113.3	0.270
mRS			
Mild	20	10	0.003
Moderate	0	6	
Severe	0	0	
Independent walking			0.000
With support	0	3	
Without support	20		
Manual skills			0.027
Mild	20	11	
Moderate	0	2	
Severe	0	3	
Actual treatment			0.570
IVIg	12	12	
Prednisone	3	3	
AZT	2	1	
MPM	2	0	
RTX	1	0	
CIDP variant			0.022
Typical	16	10	
Multifocal	3	0	
Distal	1	6	

IVIg: intravenous immunoglobulin; MPM: mycophenolate mofetil; RTX: rituximab; mRS: modified Rankin Scale; AZT: azathioprine; CIDP: chronic inflammatory demyelinating polyneuropathy.

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**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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# Cognitive impairment in older adults with DM and HBP in a primary care setting

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## Abstract

**Objective:** We conducted a cross-sectional study to identify, characterize, and compare the presence of cognitive impairment in patients with diabetes mellitus (DM) and patients with high blood pressure (HBP) who were seen in primary care. **Methods:** Consecutive patients over the age of 65 with DM or HBP who attended outpatient consultation at the Family Medicine Unit No. 51 of the Mexican Institute of Social Security in Guadalajara were included in the study. The Montreal Cognitive Assessment (MoCA) test was applied to detect the presence of cognitive impairment. **Results:** A total of 177 patients (59.9% men) with DM (59.9%) or HBP (40.1%) were included in the study. It was found that 44.1% of the participants had cognitive impairment. **Conclusions:** The prevalence of cognitive impairment in older adults with DM or HBP is higher than in older adults without these comorbidities. The use of a quick and easy screening test such as the MoCA test in this group of patients could allow for early detection and impact on timely referral, approach, and management.

**Keywords:** Cognitive impairment. Arterial hypertension. Diabetes mellitus.

## Deterioro cognitivo en adultos mayores con DM y HAS en un primer nivel de atención

### Resumen

**Objetivo:** Realizamos un estudio transversal para identificar, caracterizar y comparar la presencia de deterioro cognitivo en pacientes con DM y pacientes con HAS atendidos en el primer nivel de atención. **Métodos:** Se incluyeron pacientes consecutivos mayores de 65 años con DM o HAS que acudieron a consulta externa a la Unidad de Medicina Familiar N° 51 del Instituto Mexicano del Seguro Social de Guadalajara. Se aplicó el MoCA test para detectar la presencia de deterioro cognitivo. **Resultados:** Se incluyeron un total de 177 pacientes (59.9% hombres) con DM (59.9%) o HAS (40.1%). Se encontró que el 44.1% de los participantes presentaba deterioro cognitivo. **Conclusiones:** La prevalencia de deterioro cognitivo en adultos mayores con DM o HAS es mayor que en los adultos mayores sin estos comórbidos. El utilizar una prueba de tamizaje rápida y sencilla como la prueba MoCA en este grupo de pacientes podría permitir una detección temprana y e impactar en una referencia, abordaje y manejo oportunos.

**Palabras claves:** Deterioro cognitivo. Hipertensión arterial. Diabetes mellitus.

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## Introduction

### *Clinical context*

Cognitive impairment is a clinical syndrome characterized by the loss or decrease of mental functions in different domains such as memory, orientation, calculation, comprehension, judgment, language, visual recognition, behavior, and personality. This concept differs from dementia because it does not affect the functionality of the individuals who experience it<sup>1,2</sup>. Cognitive impairment increases with age, and it constitutes an important condition, particularly in the population over 65 years of age, with an estimated prevalence of 8%<sup>3</sup>. As a consequence of the demographic transition we are facing, our country has presented an increase in the frequency of cognitive impairment, becoming a public health problem.

Cognitive impairment is a consequence of neurodegeneration. Neurodegeneration is a multicausal process, and multiple comorbidities have been implicated in its progression<sup>4-7</sup>. Cognitive impairment in the Mexican population is closely related to highly prevalent chronic degenerative diseases, including diabetes mellitus (DM) and high blood pressure (HBP), which together add up in our country to a prevalence of up to 60.2%<sup>8,9</sup>.

On the other hand, DM has been associated with an increased risk of cognitive impairment and dementia from 1.5 to almost 3 times when compared with non-diabetic subjects<sup>10</sup>, while in patients with HBP, a prevalence of cognitive impairment of 30% has been found, 3 times higher than in the general population<sup>11</sup>.

Despite these alarming figures, there are few studies that describe the presence of cognitive impairment in patients with diabetes or hypertension in our population<sup>1,12-15</sup>, so the objective of this study was to identify, characterize, and compare the presence of cognitive impairment in patients with DM and patients with HBP attended at the first level of care.

### *Methods for detecting cognitive impairment*

There are different screening tests to detect cognitive impairment, among the most frequently used are the mini-mental state examination (MMSE) and the Montreal Cognitive Assessment (MoCA).

For this study, we chose the MoCA test because it has a higher sensitivity (82-90%), and specificity (75-89%), and it has been validated in Mexico; as well as because it

has a time of application just a few minutes longer than the MMSE (which has a sensitivity of 80% and specificity of 77.5%)<sup>16</sup>.

The MoCA test has the following sections: visuospatial (0-5 points), naming (0-3 points), memory (not scored), attention (0-6 points), language (0-3 points), abstraction (0-2 points), delayed recall (0-5 points), and orientation (0-6 points). The maximum score is 30 points, with a cutoff point for cognitive impairment of < 26<sup>17,18</sup>.

Additionally, because depression can contribute to or alter cognitive performance, it was decided to screen for this condition in this study. For this, the abbreviated Yesavage geriatric depression scale (GDS) was used, which has a sensitivity of 84% and specificity of 95% for detecting depression. In this scale, scores of 0-4 are considered normal, according to age, education, and complaints; 5-8 indicates mild depression; 9-11 indicates moderate depression; and 12-15 indicates severe depression<sup>19,20</sup>.

## Methods

This was an observational, cross-sectional, and descriptive study, approved by a local Research Ethics Committee with project registration R-2020-1305-083. The sample consisted of 189 consecutive patients who attended the outpatient consultation at the Family Medicine Unit No. 51 of the Mexican Institute of Social Security in Guadalajara. Patients with the following inclusion criteria were selected non-randomly (non-probabilistic convenience sampling): over 65 years of age of both sexes with DM or HBP who agreed to participate in the study, signing the informed consent. As exclusion criteria, the diagnosis of psychiatric diseases (including depression) or behavioral disorders, illiteracy, and presence of comorbidities, as well as patients who had any impairment to communicate, were considered. Patients who did not adequately complete all their assessments were excluded from the study.

Data collection was carried out over a period of 6 months. First, a questionnaire was administered to collect sociodemographic variables of interest: age, gender, education level, marital status, number of prescribed drugs, and other associated comorbidities. The weight and height of the patients were requested to calculate their body mass index (BMI), which for the purposes of this study was considered: underweight < 18.5, normal weight 18.5-24.99, overweight > 25, and obesity > 30. The presence of depression was ruled out with the GDS scale, considering it positive when the patient had a score of 5-15. Subsequently, to assess

the presence of cognitive impairment, the MoCA test was applied, taking 26 as the cutoff point, and defining as a patient with cognitive impairment those who had a score of 0-25 points.

Statistical analysis of the data was performed using the statistical software SPSS, version 20.0 for Windows. Descriptive statistics were used for the variables collected, both central tendency measures and dispersion measures. Due to the non-parametric distribution of the sample, the Chi-square test was used to establish if there was a significant difference in the cognitive impairment profile of patients with DM versus patients with HBP in each of the sections evaluated by the MoCA test, considering a significance level of  $p < 0.05$ .

## Results

Of 189 patients included in the study, 12 were excluded from the study: 11 for having a score greater than 4 on the GDS and 1 for not completing the necessary assessments. Therefore, 177 cases were included in the analysis. The mean age was 74.02 years (range 60-93), and the sociodemographic characteristics are shown in [table 1](#). About 59.9% of the patients had DM while the other 40.1% was given by patients with HBP. About 61.1% did not have other associated comorbidities.

When evaluating the presence or absence of cognitive impairment using the MoCA test, it was found that 44.1% of participants had cognitive impairment, obtaining an average of 22.36 points and a mode of 29 points. About 43% of patients with DM had cognitive impairment, while 44% of patients with HBP had it. Regarding the comparison of the results obtained in the sections of the MoCA test of the group of patients with DM versus patients with HBP, each section was analyzed ([Table 2](#)).

In terms of visuospatial skills, patients with diabetes show worse results, with a score of 0, with a higher frequency of 8.5%; compared to 3.4% with the same rating of patients with hypertension. In the naming section, patients with diabetes have twice as many cases, in terms of the lower score.

In the attention section, patients with diabetes have a mostly negative distribution of cases, the accumulated lower cases (from 0 to 5) to the highest score, which is 6, represent 58.1%. For patients with hypertension, this situation only occurs with 45.1%.

The language dimension behaved as follows, 58.4% of patients with diabetes obtained a maximum rating, while 64.7% of patients with hypertension obtained this score. In the abstraction section, 81.1% of patients with

**Table 1.** Sociodemographic characteristics of the sample

Variable	Total % (n = 177)
Age (mean $\pm$ standard deviation)	74.02 (7.34)
Gender % (n)	
Female	40.1 (71)
Male	59.9 (106)
Educational level % (n)	
Elementary school	73.4 (130)
Secondary	21.5 (38)
High school	4 (7)
Degree	1.1 (2)
Civil status % (n)	
Widowed	52 (92)
Married	26.6 (47)
Divorced	16.4 (29)
Common-law	4.5 (8)
Single	0.005 (1)
BMI % (n)	
Normal	20.9 (37)
Overweight	66.1 (117)
Obesity	13 (23)
Associated comorbidities % (n)	
0	61.6 (109)
1	33.3 (59)
2	5.1 (9)
Number of drugs used % (n)	
0	7.9 (14)
1	12.4 (22)
2	45.8 (81)
3	28.2 (50)
4	7.9 (14)

BMI: body mass index

diabetes obtained a maximum rating, while 84.5% of patients with hypertension also obtained this score. With regard to the distribution of delayed recall, 59.4% of patients with diabetes obtained the maximum approval rating, while this occurred in 66.19% of hypertensive patients.

Finally, in the last section corresponding to orientation, it was found that 7.5% of patients with diabetes obtained a score of 0, a situation that only occurred in 2.8% of patients with hypertension.

## Discussion

With the aging population, it is expected that the prevalence of DM, HBP, and cognitive impairment will increase progressively<sup>21</sup>. In Mexico, census data from 1990 and 2020 indicates that the population aged 60 and over has increased from 5 million to 15.1 million, respectively, corresponding to a 6-12% increase in the population. The

**Table 2.** Comparison of the score obtained in the MoCA in both groups

Domain evaluated (points)	Diabetics (n = 106)	Hypertensive (n = 71)	p
Executive function			
0	15	6	0.772
1	16	11	
2	19	9	
3	15	13	
4	29	23	
5	12	9	
Denomination			
0	3	1	0.734
1	4	1	
2	6	5	
3	93	64	
Attention			
0	16	4	0.105
1	8	2	
2	2	5	
3	8	4	
4	9	10	
5	8	7	
6	55	39	
Language			
0	62	46	0.751
1	7	4	
2	7	5	
3	30	16	
Abstraction			
0	86	60	0.329
1	5	1	
2	15	10	
Deferred recall			
0	63	47	0.733
1	1	0	
2	8	6	
3	11	7	
4	4	2	
5	19	9	
Orientation			
0	8	2	0.588
1	3	4	
2	6	4	
3	1	4	
4	1	1	
5	1	0	
6	86	56	

MoCA: Montreal Cognitive Assessment

doubling or even tripling of the number of cases anticipates that it will also occur in the three pathologies<sup>21-23</sup>. Therefore, studying the interrelationship between these three variables is becoming increasingly important.

The working universe in this study had a male predominance and an average age of 74 years. When analyzing the population, it is found that some of the main characteristics are representative of the Mexican

population in this age group, such as: the predominant marital status is widowhood, a high frequency of overweight and obesity, and low education level<sup>24</sup>.

The presence of cognitive impairment was also found in 44% of the participants, which constitutes 5.5 times more than what was found in the general Mexican population (ENASEM study). These data coincide with multiple studies that have found an increase in the prevalence of cognitive impairment in patients with DM and HBP compared to the general population<sup>25-27</sup>.

Several hypotheses have been proposed about how both DM and HBP participate in cognitive impairment in patients. Due to the complex nature of DM, numerous explanations have been proposed for how it could cause cognitive impairment. These include the fact that it is an important cardiovascular risk factor, increasing the incidence of strokes. In the non-vascular pathogenesis, we find the effects of dysglycemia in which both hyperglycemia and hypoglycemia are common in diabetic patients; these have deleterious effects on cognition due to the increase in oxidative stress and consequent damage to brain tissue. On the other hand, certain mechanisms have been found in how hyperinsulinemia negatively affects neuronal functioning related to the pathophysiological cascade of beta-amyloid: an increase in tau protein phosphorylation and a decrease in the ability of the insulin-degrading enzyme to eliminate beta-amyloid as the concentration of insulin in the central nervous system increases. Structural correlates of these facts have been described, with cortical and subcortical atrophy, especially affecting the hippocampus and the prefrontal cortex<sup>21,28-32</sup>.

On the other hand, the pathophysiology of hypertension is related to cognitive impairment in a multivariate way. Emerging evidence suggests that HBP causes remodeling of cerebral blood vessels, causing dysfunction in cerebral perfusion. With the dysfunction of flow autoregulation, it is postulated that the elimination of potentially harmful proteins such as beta-amyloid is limited, which it is worth mentioning has been found in higher concentrations in these patients. In addition, evidence of structural changes in neuroimaging associated with the increase in systolic blood pressure has been found, with a lower cerebral volume in these patients<sup>11,33</sup>.

Several studies have been conducted to characterize cognitive impairment in patients with DM and HBP. In patients with DM, alterations in all cognitive domains have been found, with the most affected being attention and processing speed<sup>29,34,35</sup>. On the other hand, in patients with HBP, greater impairment of executive function, processing speed, and semantic memory has been found<sup>11</sup>.

Despite this, no significant differences were found when comparing the results of the MoCA test sections of diabetic versus hypertensive patients in this study.

The relationship between cognitive impairment, diabetes, and hypertension is not completely understood, but it is becoming clear that cognitive impairment, which was traditionally seen as a primary neurodegenerative disorder, is not dissociated from other chronic degenerative diseases that tend to coexist in the same individual.

A cognitive study, including a neuropsychological test in the first level of care, should be considered in patients with a history of diabetes and hypertension. On the other hand, it is essential to take the above aspects into consideration, as they could affect the patient's ability to adhere to their treatment. Early identification of these patients provides an opportunity to delay or even prevent the progression of cognitive impairment, so the timing of treatment is a major factor in prognosis<sup>36,37</sup>.

In patients with mild-to-moderate dementia without treatment, there is a 2-point decline per year in the MMSE test, which is reduced to 0.5 points/year when treatment with acetylcholinesterase inhibitors is started. This has a positive long-term impact as it reduces mortality and preserves the ability of patients to perform a greater number of instrumental activities of daily living<sup>37</sup>.

The importance of early diagnosis will become more important with the use of monoclonal antibodies against amyloid beta, which has only shown effectiveness in the early stages of Alzheimer's disease<sup>38,39</sup>.

Finally, it is necessary to point out that the following limitations were found in the present study: a more extensive neuropsychological evaluation was not performed, a non-randomized and small convenience sample was used, and the sample was from a single primary care center. In addition, there were confounding factors, such as the use of multiple medications, cardiovascular risk factor and the relative control of the principal pathologies (hypertension and diabetes mellitus).

Future research is needed to assess the impact of cognitive impairment on metabolic control in patients and to develop therapeutic strategies that are tailored to their individual abilities. In addition, the neuropsychological profile of cognitive impairment in patients with hypertension and diabetes should be characterized using larger studies in our population.

## Conclusion

The findings of this study reveal that older adults with diabetes or hypertension have a 5.5-fold higher prevalence of cognitive impairment compared to the

population over 65 years of age without these comorbidities. This suggests that it is important to include a cognitive assessment such as the MoCA test as part of the primary care approach for these patients, as cognitive impairment can affect their ability to adhere to treatment and achieve therapeutic goals. Thus cognitive screening should be performed in all people with DM or HBP in order to guide reference to neurology services and to guide adaptations in their activities of daily living management of comorbidities.

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The authors declare that this work was carried out with the authors' own resources.

## Conflicts of interest

The authors declare that they have no conflicts of interest.

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# High prevalence of depression found in post-ischemic stroke patients assessed in routine vascular clinic in a University Hospital from Mexico

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## Abstract

**Objective:** The objective of this study was to determine the prevalence of depression in ischemic post-stroke patients in a routine vascular clinic evaluation in Mexico. **Methods:** Consecutive patients with ischemic stroke between January 2017 and July 2018 were enrolled. National Institute of Health Stroke Scale and Hamilton scales were used to assess neurological deficit and depression, respectively. The mRs was used to evaluate the degree of dependence in daily activities and the Barthel Index was used to measure functional independence. Quality of life was assessed using the SF-36 questionnaire. Follow-up appointment was performed between 3 months and 2 years post-stroke. **Results:** Of the 162 patients who met study inclusion criteria, 93 were contacted at 2 years of follow-up. Fifty-six were men (60.2%) and 37 were women (29.8%), with an average age of 63.5. About 36.6% of participants met the criteria for depressive disorder. **Conclusions:** There is a high prevalence of depression among patients who have suffered ischemic stroke as assessed in a routine vascular clinic evaluation.

**Keywords:** Ischemic stroke. Depression. Neurovascular clinic. Post-stroke care.

## Alta prevalencia de depresión en pacientes después de un ictus isquémico evaluados de rutina en la clínica neurovascular de un Hospital Universitario de México

### Resumen

**Objetivo:** Determinar la prevalencia de depresión después de un ictus isquémico en la evaluación de rutina de una clínica vascular en México. **Métodos:** Se incluyeron pacientes consecutivos con ictus isquémico de enero 2017 a julio 2018. Se realizaron las escalas clínicas del NIH para ictus y la escala de Hamilton para evaluar su estado funcional y la depresión, respectivamente. La escala modificada de Rankin se utilizó para evaluar el grado de dependencia en las actividades de la vida diaria y el índice de Barthel para medir el grado de la independencia funcional. La calidad de vida se evaluó con el cuestionario SF-36. Se dio seguimiento entre los 3 meses y 2 años posteriores al ictus. **Resultados:** De los 162 pacientes que cumplieron los criterios de inclusión, se logró contactar a 93 pacientes en el seguimiento a 2 años. 56 hombres (60.2%) y 37 mujeres (29.8%), con un promedio de edad de 63.5 años. El 36.6% de los participantes cumplieron los criterios de depresión. **Conclusión:** Hay una alta prevalencia de depresión entre los pacientes que han sufrido un ictus isquémico al ser evaluados de rutina en una clínica neurovascular.

**Palabras clave:** Ictus isquémico. Depresión. Consulta neurovascular. Cuidados post-ictus.

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## Introduction

According to the World Health Organization, since the year 2000, stroke has been the second largest cause of mortality worldwide<sup>1</sup>. Stroke is a disease classified by the presence of radiological, clinical, or pathological evidence of brain damage, which can be due to ischemia or hemorrhage in a defined cerebral vascular territory<sup>2</sup>. Around 87% of strokes are ischemic in which blood flow is impaired due to a blood clot, and 10% are hemorrhagic<sup>3</sup>. Although most research surrounding prevention and intervention occurs in first world countries, more than 85% of strokes occur in low- and middle-income countries<sup>4</sup>. On the other hand, mental health disorders are becoming more common and are expected to increase by 2030<sup>5</sup>.

Mental health is still severely underfunded in many third world countries. In Mexico, only 2% of the total funding in health services is dedicated to mental health<sup>6</sup>, and of that 2%, more than three quarters of the money is dedicated to the maintenance of mental health hospitals<sup>7</sup>. This means services aimed at treating mental health difficulties are typically underfunded which is evidenced by the fact that < 40% of primary care centers have protocols to address mental health disorders<sup>6</sup>. Meanwhile, the prevalence of depression in the Mexican population ranges from 4 to 7.9%<sup>8</sup>. The ability for people to seek mental health assistance is further exacerbated by the stigma that prevails in society toward those seeking mental health care which is often fueled by the media<sup>7,9</sup>. However, according to one study, patients can also feel stigma from mental workers themselves<sup>8</sup>.

Depression in post-stroke patients occurs in almost a third of all patients and is considered the most common and important neuropsychiatric complication affecting the quality of life and prognosis of patients<sup>10</sup>. Depression has been shown to increase mortality rates by up to 10 times, therefore highlighting the importance of this condition in detrimentally affecting the recovery of patients<sup>11</sup>.

Despite the plethora of studies highlighting the prevalence and impact of depression in those who have suffered strokes, there is limited research which studies this in developing countries. This is important because there is a lack of information regarding the prognosis of these patients, as mental health services might not be available to most of them. This study aimed to bridge current gaps in knowledge by determining the prevalence and implications of depression for those

who have suffered ischemic stroke in a routine vascular clinic evaluation in Mexico.

## Material and methods

A prospective cohort with a transversal evaluation was done. Patients with ischemic stroke who arrived to the Neurology Service from the Hospital Universitario "Dr. Jose Eleuterio Gonzalez" in Monterrey, Nuevo Leon, Mexico, from January of 2017 to July 2018 were recruited. The following clinical scales were performed to evaluate severity of stroke and functionality while the patients were at the hospital: the National Institute of Health Stroke Scale (NIHSS)<sup>12</sup>, mRs<sup>13</sup>, Barthel<sup>14</sup>, and the Trial of Org 10172 in Acute Stroke Treatment (TOAST)<sup>15</sup>. The NIHSS scale measures the neurological deficit of the patient. The Rankin scale measures the degree of disability or dependence in daily activities, the Barthel index assesses functional independence, and TOAST is used to classify the etiology of the stroke. The exclusion criteria were patients under 18 years old, history of depression or mental disorders, and aphasia.

The follow-up was completed by present evaluation and by phone. In the follow-up, the aforementioned clinical scales were used, and two new scales were added: the Hamilton Depression Rating Scale (HDRS; 13) and the SF-36 questionnaire<sup>16</sup>. The HDRS is a questionnaire used to assess the severity of depressive symptoms and to evaluate the response to treatment. Patients were categorized as depressed if they scored higher than 8. Patients completed the SF-36 questionnaire in person, and this was used to evaluate their quality of life. Patients with depression were sent to the neuropsychological clinic.

A descriptive analysis of the demographic and clinical variables was conducted. For the categorical variables, a univariate analysis with the exact "X" test was performed. For the categorical and variance variables, a Fisher's test was conducted. For the continuous nonparametric variables, Mann-Whitney's test was performed. Finally, a logistic multivariate regression analysis was done to identify independent risk factors. Results are expressed in percentages and medians with standard deviations ( $\pm$ ). Statistically significant values are considered to be  $p < 0.05$ . SPSS version 20.0 was used to perform all the statistical analyses.

## Results

In total, 93 out of 162 eligible patients were evaluated in routine neurovascular clinic and contacted by phone between 3 months and 2 years post-stroke event. The remaining 69 eligible patients could not be contacted or did not come to the presential evaluation. Fifty-six (60.2%) of the patients were male and 27 (29.8%) were female. The average age was  $63.5 \pm 14.08$  ranging from 34 to 91 years. The mean time since the stroke and the clinical or telephonic evaluation was 93 weeks. The most common risk factors for ischemic stroke were high blood pressure, diabetes mellitus, and cardiopathy (Table 1).

More than half of the patients enrolled in this study had minor or moderate impairment defined by a value less than 11 as measured by the NIHSS scale (Table 1) during their hospitalization. Less than 25% of the patients were categorized with a moderate to severe or severe impairment (Table 1).

In the follow-up performed between 3 months and 2 years after the stroke event, more than 85% of patients showed minor or no impairments as measured by the NIHSS scale (Table 1).

The follow-up also showed that 34 patients (36.6%) (Table 2) presented as having a depressive disorder as classified by the HDRS: 28% had mild depression, 3.2% moderate depression, 4.3% severe depression, and 1.1% very severe depression. About 8.6% reported having had suicidal ideation, and 3 patients (3.2%) had thought about how to carry it out (planning). No suicides were carried out. In addition, depressed patients tended to have higher scores in all the HDRS points except for hypochondriasis and insight when compared to non-depressed patients (Table 2).

Meanwhile, the SF-36 scale found that non-depressed patients had higher scores for quality of life than depressed patients. Only 1% of the patients who met the criteria for having depression were receiving treatment at the time of the study. The complete details of the differences between depressed and non-depressed patients are described in table 2.

All the patients that were diagnosed with depression were sent to be evaluated and treated by psychiatrists.

## Discussion

This study found a high prevalence of depressive disorders among ischemic stroke patients in a routine vascular clinic evaluation (36.6%). These findings are in line with results from other studies regarding the

prevalence of depression in post-stroke patients<sup>17,18</sup>. It is important to mention that only 1% of the patients that met the criteria for depression in this study were already in treatment, suggesting that many people who suffer stroke do not receive a diagnosis of depression or receive mental health treatment.

One study in Colombia found that post-stroke patients had overall more depression and stress when compared to age-matched controls<sup>19</sup>. Indeed, another study involving ischemic stroke, intracerebral hemorrhage, or cerebral venous thrombosis showed that depression and vascular cognitive impairment were common findings appearing in almost half of the patients<sup>20</sup>.

Depression is a frequent disorder in the Mexican population and stigma toward mental health disorders is prevalent in society<sup>21,22</sup>. This may explain why many participants did not have any previous diagnosis of depression despite scoring highly for symptoms of depression.

This is the first study conducted in Mexico which evaluates depression in post-stroke patients in a routine vascular clinical evaluation which evaluates ischemic stroke only. There is other research that shows a higher amount of depression in patients who have suffered a stroke or vascular disorder (near 50%) compared to this study (36.6%). This difference might be related to the inclusion of different pathologies, and by the different age gap, with a mean age of 56 compared to 63.5<sup>20</sup>.

Remission of post-stroke depression in the first few months after the stroke event is associated with greater recovery in activities of daily life<sup>23</sup>. Therefore, conducting a longer follow-up might have provided a more detailed assessment of the quality of life of our patients.

There are plenty of different treatments for depression, the most used worldwide being pharmacological with SSRIS and TCA<sup>24</sup>. Other therapies, such as CBT or acupuncture, should also be used as an adjuvant to improve the outcome<sup>24,25</sup>. Research is now focusing on the role that gut microbiota plays in depression, showing a different path that could also benefit the outcomes of the actual therapy<sup>26</sup>.

The result from this study highlights the importance of screening for depression in post-stroke patients in the rutinary vascular clinic evaluation even if they do not have clear symptoms of depression, as prevalence is high among these patients.

Nevertheless, this study also has weaknesses. One of them is that the follow-up was not divided by time periods, which might have shown that depression might become common as the patients have to struggle or adapt to their disabilities. In addition, there is no information about the outcomes of the depressed

**Table 1.** Population characteristics, neurological deficits, and differences between depressed and non-depressed patients

Patients with ischemic stroke (n = 93)			
Demographic and clinical variables of the population	Non-depressed patients (n = 59)	Depressed patients (n = 34)	p-value
Male, n (%)	37 (62.7%)	19 (55.9%)	NS
Age, media $\pm$ SD	62 $\pm$ 3	66 $\pm$ 4	NS
Cardiovascular risk factors			
Hypertension	42 (71.2%)	28 (82.4%)	NS
Diabetes	26 (44.1%)	13 (38.2%)	NS
Smoking	22 (37.3%)	9 (26.5%)	NS
Sedentarism	31 (52.5%)	23 (67.6%)	NS
Dyslipidemia	14 (23.7%)	11 (32.4%)	NS
Alcohol consumption	19 (32.2%)	11 (32.4%)	NS
Heart disease	13 (22%)	11 (32.4%)	NS
Previous stroke	9 (15.2%)	6 (17.6%)	NS
Drug abuse*	3 (5.1%)	1 (2.9%)	NS
Ischemic Stroke Etiology, n (%) TOAST			
Atherosclerosis	23 (39.0%)	12 (41.2%)	NS
Small vessels disease	9 (15.3%)	4 (11.8%)	NS
Cardioembolism	8 (13.6%)	8 (23.5%)	NS
Indeterminate	19 (32.2%)	8 (23.5%)	NS
Vascular territory **			
Carotid (ICA, MCA, ACA)	41 (69.5%)	21 (61.8%)	NS
Vertebrobasilar (PCA, SCA, PICA, BA)	12 (20.3%)	7 (20.6%)	
Neurological functional scales:			
NIHSS at hospital admission			
NIHSS 1-5	27 (45.8%)	9 (26.5%)	0.049
NIHSS 6-12	25 (42.4%)	9 (26.5%)	
NIHSS 13-18	6 (10.2%)	12 (35.3%)	
NIHSS >18	1 (1.7%)	4 (11.8%)	
NIHSS at hospital discharge			
Without deficit	14 (23.7%)	6 (17.6%)	0.038
NIHSS 1-5	31 (52.5%)	6 (17.6%)	
NIHSS 6-12	13 (22.0%)	12 (35.3%)	
NIHSS 13-18	1 (1.7%)	9 (26.5%)	
NIHSS >18	0	1 (2.9%)	
Modified Rankin scale (mRS) and Barthel Index for Activities of Daily Living.			
mRS at discharge	2 (1-5)	3 (2-5)	< 0.01
Barthel index; media $\pm$ SD	76.2 $\pm$ 9	49.4 $\pm$ 7	< 0.001
Days of hospitalization, n (range)	6.4 (2-14)	6.71 (2-19)	NS
NIHSS at the interview moment (between 3 months and 2 years after stroke).			
Without deficit	35 (59.3%)	7 (20.6%)	< 0.030
NIHSS 1-5	22 (37.3%)	16 (47.1%)	
NIHSS 6-12	2 (3.4%)	8 (23.5%)	
NIHSS 13-18	0	3 (8.8%)	
NIHSS >18	-	-	
mRS at follow-up	1 (0-4)	3 (1-4)	< 0.01
Barthel at follow-up	96.9 $\pm$ 5	76.5 $\pm$ 7	< 0.001
Time of follow-up, days	663.4	633.5	NS

\*Marihuana, cocaine or toluene.

\*\*Vascular territory information available for only 81/93 patients.

NIHSS: National Institutes of Health Stroke Scale; mRS: modified Rankin scale.

**Table 2.** Differences between depressed and non-depressed patients as assessed using the Hamilton depression scale and the SF-36 questionnaire

Hamilton scale at the follow-up interview			
Items of Hamilton scale and SF-36	Non-depressed patients n = 59 (%)	Depressed patients n = 34 (%)	p-value
Depressive mood	16 (27.1)	29 (85)	< 0.001
Psychiatric anxiety	1 (1.7)	14 (41.2)	< 0.001
Somatic anxiety	11 (18.6)	17 (50.0)	0.002
Gastrointestinal somatic symptoms	15 (25.4)	16 (47.1)	0.029
General somatic symptoms	8 (12.6)	23 (67.6)	< 0.001
Genital symptoms	10 (16.9)	18 (52.9)	< 0.001
Hypochondriasis	4 (6.8)	5 (14.7)	NS
Weight loss	3 (5.1)	21 (61.8)	< 0.001
Insight	1 (1.7)	2 (5.9)	NS
Feelings of guilt	9 (15.3)	24 (70.6)	< 0.001
Suicidal thoughts	1 (1.7)	16 (47.71)	< 0.001
Initial insomnia	12 (20.3)	26 (76.5)	< 0.001
Insomnia during the night	6 (10.2)	16 (47.71)	< 0.001
Delayed insomnia	9 (15.3)	13 (38.2)	< 0.001
Effect in work and interests	24 (40.7)	33 (97.1)	< 0.001
Retardation (apathy)	5 (8.5)	15 (44.1)	< 0.001
Agitation	4 (6.8)	19 (55.9)	< 0.001
SF-36 questionnaire			
Limitations in physical activities (health problems)	70.91	51.32	0.001
Limitations in usual activities (physical)	76.69	27.94	< 0.001
Limitations in usual activities (emotional)	89.83	83.33	NS
Vitality	73.38	56.76	< 0.001
General mental health	88.13	72.11	< 0.001
Limitations in social activities	93	69.85	< 0.001
Body pain	88.98	59.26	< 0.001
General health perceptions	69.76	51.02	< 0.001

patients that were referred to receive pharmacological therapy.

## Conclusions

Depression in post-stroke patients is common in a routine vascular clinic evaluation, and more efforts should be made to diagnose and treat this condition in those suffering stroke.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

**Use of artificial intelligence for generating text.** The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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# Effects of the COVID-19 pandemic on mental health and cognition after isolation and reassessment of remote care. A review article

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## Abstract

*This article comprehensively reviews existing literature about the consequences of social isolation after the COVID-19 pandemic on mental health and cognition. The objective is to provide useful information that will help to identify the lack of data on some side effects post-pandemic. In addition, the aim is to advocate for research, which leads to evidence of these abnormalities. A search was performed in the databases Pubmed/Medline, Scopus, Science Direct, and Web of Science, from the beginning of the COVID-19 pandemic to the present. The terms used were COVID-19, isolation, cognition, remote care, mental health, age, and technology. Finally, 51 articles were selected that coincided with the terms, objectives that were relevant to the work. In addition, the articles met the methodological and validity criteria provided by the databases. Some studies were found that report various degrees of affectation in brain functions in subjects who remained isolated during the severe acute respiratory syndrome coronavirus type 2 pandemic, whether they have been infected or not. From the analysis of the distinct studies, notable differences between countries according to their economic resources, housing conditions, age, the existence of comorbidities, and emerging intervention tools such as remote care, were some of the main factors that influenced the coping strategies of individuals who were confined. Furthermore, it is evident that there remains a critical need for research employing standardized and specialized neuropsychological tests to measure cognition accurately. In the same way, investigating the effectiveness of current intervention strategies and designing those that are appropriate for each population, given the specific characteristics of the comorbidity caused by the extraordinary situation experienced by the COVID-19 pandemic.*

**Keywords:** COVID-19. Isolation. Cognition. Remote care. Mental health.

## Efectos de la pandemia de COVID-19 en la salud mental y la cognición después del aislamiento y la reevaluación de la atención remota. Un artículo de revisión

### Resumen

*El presente artículo revisa lo descrito hasta la fecha acerca de las consecuencias del aislamiento social tras la pandemia por COVID-19 en la salud mental y la cognición, con la finalidad de proporcionar un bagaje de información útil en el encauce de acciones para la identificación de los posibles huecos en la información y la elaboración de investigaciones que ayuden*

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a esclarecer las interrogantes aún existentes. Se realizó una búsqueda en las bases de datos Pubmed/Medline, Scopus, ScienceDirect, Web of Science, del inicio de la pandemia por COVID-19 a la actualidad, utilizando los términos COVID-19, aislamiento, cognición, atención remota, salud mental, edad y tecnología. Finalmente se seleccionaron 51 artículos que coincidían con los términos, objetivo y resultaban relevantes para nuestra revisión. Los hallazgos demuestran que el daño cerebral posterior a síndrome respiratorio agudo por coronavirus tipo 2, las implicaciones en la anatomía del SN por el aislamiento, la edad, diferencias entre países, los recursos económicos, las condiciones en la vivienda y las herramientas emergentes de intervención como la atención remota, son algunos de los factores que se destacaron en los estudios. Todavía falta la implementación de investigaciones que midan la cognición con pruebas neuropsicológicas estandarizadas y especializadas. Así mismo, falta por analizar exhaustivamente la aplicabilidad de estrategias de intervención ya existentes y diseñar intervenciones adecuadas a cada población dadas las características específicas de los daños causados por la situación extraordinaria vivida por la pandemia por COVID-19.

**Palabras clave:** COVID-19. Aislamiento. Cognición. Atención remota. Salud mental.

## Effects of social isolation due to the COVID-19 pandemic on mental health and cognition

Humans present a social nature that, through evolution, increases the probability of survival. In contemporary group dynamics, interpersonal relationships are predominantly established through oral and written communication especially when the individual is unable to relate and suffers from social isolation. Several studies show that social deprivation produces mental and emotional dysfunction, without achieving conclusive results. It has been described that loneliness in humans negatively affects their mental health, with the consequent discerning decline<sup>1</sup>.

The COVID-19 disease is caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) and induces different clinical manifestations, although the respiratory system is the main damage, affectations have been shown in other systems. The mental effects of social segregation depend on several factors such as age, gender, educational level, extension, and especially if this was forced or by own determination, as were the preventive measures imposed in the recent COVID-19 pandemic<sup>2</sup>.

Although a wide variety of symptoms have been described and numerous sequelae continue to be identified to date, those that predominate during the acute phase are headache, fever, cough, shortness of breath, muscle pain, fatigue, anosmia, and ageusia. These symptoms can be of a different magnitude (mild or severe,) when these get worse, the blood oxygenation is reduced and the patient may require hospitalization and even intubation, in these conditions; abnormalities of the nervous system (NS) are also frequently presented<sup>3</sup>.

Because of the neurotropism of the virus, which reaches the brain most likely through the olfactory epithelium,

associated neurological signs have been reported in a great number of patients such as neuroinflammation, polyneuritis, autoimmune response, or cerebral affection behind systemic alterations<sup>4</sup>.

Many patients who suffer mild or severe COVID-19 do not fully recover from its sequelae for weeks or even months; most of their symptoms are related to the respiratory system, NS, and cognitive and psychiatric disorders<sup>5</sup>. However, several studies show the consequences of social seclusion after the COVID-19 pandemic and its relationship with alterations in mental and cognitive health. Therefore, the aim of this review was to systematically analyze information related to post-COVID mental and cognitive impairments.

## Effects of isolation by COVID-19 pandemic on mental health

According to the World Health Organization, mental health is defined as “a state of well-being in which a person is aware of their own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to contribute to their community.” Considering this conceptualization, it is evident that COVID-19 has profoundly altered the healthy lifestyle that has been maintained for more than 70 years, impacting the physical, social, and mental health of patients<sup>6</sup>.

According to reports from the Pan American Health Organization in 2021, the pandemic generated a considerable increase in risk factors associated with suicide such as abuse, difficulties in accessing health services, and unemployment, among others. A year after the pandemic began, 50% of the people who responded to the World Economic Forum survey reported a worsening of their mental health. Furthermore, suicide is positioned as the third cause of death among young people aged 20-24 in America<sup>7</sup>.

In 2018 the suicide rate was 5.4/100 000 inhabitants meanwhile in 2021 was 10.9 men and 2.4 women/100 000 inhabitants, positioned as the year with the highest suicide rate during the pandemic<sup>8</sup>.

In a study carried out where events were analyzed before and after the pandemic, they found that emergency care due to the action of self-harm without necessarily aiming at death increased by 38.4% after the pandemic. The most common mechanism of damage was the ingestion of drugs and of these, benzodiazepines were the most used, finally, when they were not drugs, alcohol was the most used substance that caused toxic effects in individuals and the mixture with benzodiazepines was common. Moreover, it was men who most frequently resorted to toxic mechanisms<sup>9</sup>.

Young people were especially affected with very similar effects across various countries<sup>10</sup> and among the most prevalent disorders were stress, anxiety, depression, and suicidal tendencies, especially within vulnerable population<sup>11</sup>.

Since the onset of the pandemic, confinement and restricted social contact were implemented as preventive measures. This implied avoiding crowded places, discontinuing various leisure and work activities that involved contact with others, and maintaining physical distance between individuals. In response to these directives, people found themselves confined to their homes, which then transformed into multifunctional spaces for both recreation and work and this social behavior soon became a challenge<sup>12</sup>.

The structural characteristics and spatial layout of residences wield a significant influence on the psychological well-being of their occupants. Inadequate housing characterized by small dimensions, availability of their services, or materials can negatively impact the emotional state of its residents. Moreover, factors such as overcrowding, or a prolonged period spent within confined spaces can exacerbate mental health issues. The confinement in unsuitable living conditions during the COVID-19 emergency has been associated with anxiety and depression<sup>13,14</sup>.

Furthermore, overcrowding is strongly associated with psychiatric symptoms and interpersonal conflicts in children, youths, and adults, or between them. In addition to the heightened risk of infectious-contagious disease transmission, the confinement imposed by COVID-19 has increased intra-family conflicts, and at work, it has been related to less commitment and worse performance<sup>15</sup>. The situation in New York serves as a notable example of overcrowding since there is a disproportion

between the number of square meters available and the city's population<sup>16</sup>.

Social segregation prevention measures during the COVID-19 pandemic inadvertently extended the duration that people spent together in confined spaces, thereby unexpectedly increasing the likelihood of contagion within households. Moreover, there was the coexistence of several generations in the same home, many older adults were infected by the younger ones, and this senile population was highly vulnerable; they had the strongest death rate due to the severity of the infection. Social distance could not be established in reduced housing for economic reasons; an analysis which took as reference the zip code of different areas of New York revealed that overcrowding was related to the increased rate of infections and its consequences<sup>17</sup>.

An example of populated homes is precisely the city of New York, its overcrowding rate, that is, the housing units occupied by equal or < 1 person per room in 2013 alone, was 2 times higher than the average rate in the US<sup>18</sup>.

Overcrowding is a condition that increases the complexity of the challenge in mental health care, in penitentiary centers where prison inmates are more susceptible to viral contagion. A study was conducted in France, and the following measures were implemented: personnel restructuring, cancellation of voluntary psychiatric hospitalizations, prioritization of the most serious cases, and emphasis on hygiene procedures. A significant impact of confinement on this population was found; they showed symptoms of forced withdrawal from substances, anxiety, and decompensation of those patients whose follow-up was temporarily suspended<sup>19</sup>.

In a published cross-sectional study, they found that the probability of infection was highly variable depending on the building and the neighborhood, with the highest rates of infection being in those people who lived in houses with a greater number of people and, in contrast, the lowest possibility of infection was in buildings with high values where there was also more space for living<sup>20</sup>.

An investigation in Italy through online surveys of more than 1000 subjects analyzed the relationship between the duration of forced isolation and the adequacy of the living space on mental health during the COVID-19 pandemic, considering the days of confinement, the regional level of infections and the quantity and quality of social contacts. The longer the isolation was the greater the mental-health problems, and the more affected person-to-person relationships<sup>21</sup>.



## **Influence of age during isolation due to COVID-19 on mental health**

A total of 103 patients from various reference centers were analyzed after 7 days of confinement, 97 of them completed the self-applied Zung anxiety scale. Subsequently, the participants were divided into groups according to age, those patients under 35 years of age were more likely to present anxiety<sup>22</sup>.

In a retrospective study, conducted in Ireland, young people aged 18 and over who were in isolation or quarantine were analyzed. Questionnaires were applied to measure post-traumatic stress, perceived stigma, and depression. The control group was those in isolation and the case group were those in isolation or quarantine for COVID-19. The total sample consisted of 502 selected subjects, contacted telephonically for questionnaire responses, with age and duration of separation identified as primary factors. The depression questionnaire was significantly correlated with isolation time, the more time isolated, the greater the symptoms of depression. It was also found that women had higher scores in depression and post-traumatic stress.

Other factors such as pre-existing mental conditions, smoking, and the place where individuals remained during isolation or quarantine were significantly correlated with depression scores, although, symptoms of depression and anguish were present in the total sample, possibly due to the confinement there were higher anxiety and depression. Moreover, these two disorders were increased in the younger participants, alongside a concurrent presence of perceived discrimination<sup>23</sup>.

In the initial months of the pandemic were established actions to contain its spread through social distancing, the effects of this quarantine were studied in adults aged 18 and older, employing an online questionnaire. Parameters such as time in isolation, level of compliance with established norms, whether isolation was mandatory or voluntary, presence of stressors, and coping strategies were assessed. A majority of the participants were confined following local regulations contacts, with approximately 35% voluntarily isolating themselves at the time of data collection. The minimum isolation time was just over 2 weeks, and the maximum was 1 month.

The results showed a significant relationship between age and the perception of isolation. This produced worse effects in the youngest, such as poor coping strategies and work-related stressors; those who lost their jobs or consumed psychoactive substances reported elevated levels of loneliness. In addition, when analyzing

physical exercise, this was not related to the degree of isolation; the level of satisfaction with life was significantly lower in those individuals who reported greater social detachment<sup>24</sup>.

Throughout history, the study of behavior in other pandemics has found in several studies that children and adolescents are more susceptible to developing mental health problems such as depression, this is due to various factors, among which, are the central NS biological immaturity, a smaller repertoire of coping strategies and specifically during the pandemic, the lack of access to resources that they normally have in the school environment such as activities and mental health services. Furthermore, adolescents at the high school level are those who presented greater depressive symptoms<sup>25</sup>. According to the 2022 Mental Worldwide State Report, it is young people between 18 and 24 years of age and adults over 65 years who have considerably lower mental well-being. Age was the factor founded with the most influence, surpassing others such as gender.

## **Effect of isolation due to COVID-19 pandemic and his illness on cognition**

In a multinational study of 57 countries across Europe, America, Oceania, Africa, and, predominantly Asia, post-traumatic stress disorder (PTSD) after COVID-19 was assessed online using the Revised Impact of Events Scale. A group with PTSD symptoms was compared with another asymptomatic group and more than 900 valid answers were obtained, approximately 70% reported being in voluntary confinement, those who did not have a partner showed a higher incidence of PTSD symptoms, and also those older than low economic income. On the African, American, Oceanian, and European continents, a larger number of people with PTSD symptoms were found and the opposite was found in Asia. Those subjects to forced containment had a greater tendency to develop these symptoms, additionally, individuals with a higher educational level exhibited a lower risk<sup>26</sup>.

In 2021, another global online study was conducted during the COVID-19 confinement, a questionnaire divided into two sections was applied, the first included sociodemographic data and questions about coping mechanisms and stressors, meanwhile the second included the 21-item depression, anxiety, and stress scale, also known as DASS-21. Almost 700 evaluations were collected, and more than half of the evaluated subjects showed signs of anxiety, stress, and depression.

It was also found that the duration of confinement and lack of exercise were associated with increased stress, anxiety, and depression, whereas the presence of the family reduced stress levels. On the other hand, in Canada (America), Pakistan (Asia), and the United Kingdom (Europe) higher levels of stress, anxiety, and depression were found<sup>27</sup>.

Alzueta and Cols (2020), analyzed the impact of the COVID-19 pandemic and its social restrictions or quarantines on mental health in a global population of adults between April and May 2020. The DASS-21 questionnaires for depression were administered and tested for generalized anxiety disorder-7. In addition, participants were queried on sociodemographic data and other circumstances related to the conditions in which the pandemic was happening, such as infection with COVID-19 and severity of confinement. A four-level classification was established to understand the preventive measures implemented in each country, ranging from not following specific restrictions to severe limitations, such as complete house confinement. Participants were asked to report which of these levels they had been following up to the immediate week before the study.

The survey was disseminated on social networks and a digital platform was used to answer the questionnaires, from a total sample size of 9,083 individuals across 59 countries, 6,882 subjects were selected for analysis. The results demonstrated that engagement in activities was associated with a reduction in symptoms of depression but concurrently correlated with an increase in symptoms of anxiety. Depressive symptoms were associated with separation from family or close friends and difficulties adjusting to the home office<sup>28</sup>.

Cognition allows the integration of information derived from both external and internal stimuli. Studies examining community segregation and its impact on cognitive and mental health levels have approached the subject from diverse perspectives including objective and subjective or perceived social isolation<sup>29</sup>. Other studies have been based on various life stages childhood, adolescence, youth, adults, and finally, senescence. Many authors agree that the immature brain during childhood and adolescence is particularly vulnerable and might be a failure in personal relationships in adult life<sup>30</sup>.

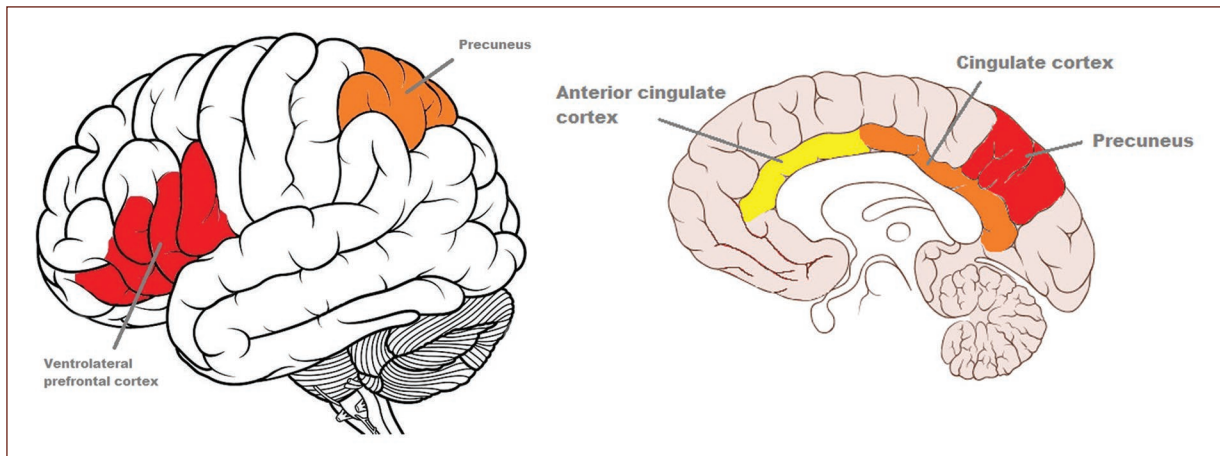
Electroencephalography has revealed elevation in theta waves in reactions against social rejection<sup>31</sup>, meanwhile functional magnetic resonance imaging (MRI) studies identified the areas related to these negative emotions: bilateral medial pre-frontal and posterior cingulate cortex, right pre-cuneus and ventrolateral pre-frontal cortex (Fig. 1)<sup>32</sup>.

Using functional MRI has revealed which social rejection shares somatosensory representations with physical pain and identified the following areas related to a variety of negative emotions such as hurt feelings, loneliness, jealousy, guilt, shame, and anxiety; these areas were bilateral medial pre-frontal and posterior cingulate cortex, the right pre-cuneus, and the ventrolateral pre-frontal cortex<sup>32</sup>.

Research focusing on the mental health effects of social restraint during adulthood and senescence allowed us to establish a correlation between age and the decrease in executive functioning. In addition, this population has a low frequency of visits, and their friendly relationships are reduced by physical deterioration and the loss of dead partners in old age<sup>33</sup>. Gender is a variable that is considered to determine the degree of cognitive impairment, a study published in 2020 analyzed the relationship between social confinement on memory and these subjects showed that the greater the isolation, the greater was also the affectation of memory to age<sup>34</sup>. Thus, it has been demonstrated that in old age, the risk of cognitive impairment is heightened and this deterioration occurs more rapidly when individuals are in a social isolated state<sup>35</sup>. In a 4-year investigation, intellectual functions related to verbal fluency and memory processes were measured at the beginning of the study and 4 years later. The analysis aimed to discern relationships between segregation, the number of personal interactions, the perception of loneliness, educational level, and cognitive function, thus, the researchers concluded that feelings of loneliness and detachment were significantly associated with poorer cognitive functioning<sup>36</sup>.

Actually, there are few studies on the awareness status after COVID-19; however, notable findings have been obtained. In the USA, they were examined hospitalized patients, revealing that a quarter of them presented problems with short-term memory<sup>37</sup>. On the other hand, a study in the UK showed the neurological sequelae of COVID-19 with 26% of the sample manifesting dementia-like discerning symptoms<sup>38</sup>. An investigation conducted in Italy showed a strong correlation between mental health stage with fatigue and executive function impairment. Individuals who had suffered SARS-CoV-2 infection exhibited poorer performance in cognition and more symptoms such as fatigue, mood, and cognition compared to uninfected individuals<sup>39</sup>.

Although the findings are limited due to the ongoing nature of the pandemic, there is preceding information about the presence of cognitive alterations after acute infections of the respiratory system such as pneumonia



**Figure 1.** This figure shows the brain areas activated in fMRI studies of COVID-19 patients under isolation: the ventrolateral pre-frontal cortex, pre-cuneus, anterior cingulate cortex, and cingulate cortex in a left lateral view of the complete brain and a middle sagittal slice.

and acute respiratory distress syndrome, in COVID-19 the prolonged hypoxia accompanied by systemic damage and the viral neuroinflammation may explain these deficits<sup>40</sup>. Therefore, there is a high risk that patients recovered from COVID-19 may experience neuropsychological alterations in executive functions and emotional state, with a strong negative impact on the quality of life and daily activities, therefore, it is crucial to provide treatment strategies to minimize these effects.

The effects on executive functions of the quarantined people positive for COVID-19 are poorly understood, however, Santangelo et al. showed that psychological symptoms and the appearance of cerebral alterations using a virtual platform that evaluated perceived failures in memory and attention, as well as resilience, styles of coping, depression, anger, and anxiety. The tests were diffused through social networks for 22 days, involving over 4,000 participants. Approximately 30% reported having perceived mental disorders at least once. Unemployed people reported a higher frequency of these alterations and resilience was identified as a crucial factor mediating symptoms of anger, depression, and cognitive alterations<sup>41</sup>.

Other studies have aimed to measure the impact of social restriction for COVID-19 on emotions and higher executive functions, even in uninfected individuals' whose significant deficits were identified<sup>42</sup>. Subjects with moderate cognitive impairment (MCI), confinement caused a deterioration in their daily instrumental activities<sup>43</sup>. Meanwhile, in patients with diagnosed minor dementia, the pandemic prevented in-person cerebral stimulation therapies. Instead, new tools such as telecare were used, demonstrating the clinical value of technologies in such cases<sup>44</sup>.

### Impact of technology during isolation due to the COVID-19 pandemic: new lines of treatment

Generational gaps became more evident during the pandemic, the virtual environment was friendlier to young people and there were changes in the use of technological tools. A study with young people from different countries revealed an increase in the use of cell phones and social networks, as well as a decrease in sociability, which was replaced by an increase in communication through social networks. Sleeping hours increased and changed the resting schedule and heart rate, the younger spent more time in confinement, resulting in reduced physical activity<sup>45,46</sup>.

Remote care was an emerging tool in the face of the health contingency, this allowed to alleviate some of the most urgent needs of the patients. Although the critical stage of COVID-19 has passed, the usefulness of this resource has been demonstrated, nevertheless; the online contact requires previous preparation. The need to avoid physical contact also made it possible to redefine therapeutic protocols, even in intensive care units, where personal interaction is very limited, moreover; remote care reduced the number of health workers for consultations<sup>47</sup>.

During this pandemic, the concept of "Tele-health" emerged, and there was a need to use unconventional sites to provide care both virtually and by telephone, this extended beyond initial consultations to encompass follow-up appointments and even post-treatment releases. Consequently, the value of the telephone consultation to solve urgent situations was reevaluated,

and likewise, the importance of the virtual consultation. It was also shown that remote evaluation of psychiatric and cognitive alterations was possible, as well as data collection by questionnaires and interviews<sup>48</sup>.

In the case of psychiatric patients and those with some cognitive alteration, one of the main challenges was to preserve the continuity of treatment, apart from maintaining favorable conditions in their accommodation. In the case of the pandemic, cerebral alterations have been identified both in those who were infected, as in their auxiliary, positive outcomes have been achieved for them with cognitive-behavioral therapy, this includes organization of the living space, home visits, and regular visits to COVID mental health units, which have specialized personal. In cases of hospitalized patients, family interaction must be online<sup>49</sup>.

Although remote psychological intervention has already been successfully experimented with this new modality makes it necessary to legislate on the terms of confidentiality and privacy in a bidirectional manner<sup>50</sup>. Much remains to be understood about the brain alterations induced by the COVID-19 virus and their long-term effects. Consequently, there is a need to propose the most suitable neuropsychological intervention based on comprehensive research.

## Conclusion

After this review, factors were evidenced that enabled the identification of the most vulnerable population in the face of the secondary effects of the pandemic. They were young people, with a low level of education, who had to remain in overcrowded conditions due to the limited size of their homes and the necessity to adapt. Those who did not have the necessary resilience suffered affectation of their emotional state and their social and work performance.

Actually, in studies conducted in several countries aimed at identifying the sequelae caused by confinement post-pandemic, there was a consensus in which the greatest affectation occurred in the vulnerable population, either due to old age or the presence of comorbidities. In the same way, various studies demonstrated the persistence of lasting mental disorders, however; it is necessary to use more specific tools that allow defining the type of cognitive impairment, its severity, and particularly, its persistence and reversibility.

To better understand the long-term effects of COVID-19 on brain function, it will be necessary to conduct longitudinal studies tracking the cognitive evolution of patients who have experienced cognitive impairment. This

should involve using blood biomarkers to reveal any alterations of molecular mechanisms in living subjects and pathological analysis of homogenized brain tissue or immunocytochemical analysis of brain tissue sections in patients who have passed away.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

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