

## The Mind-Body Problem in the Context of Neuropsychiatric Symptoms in Patients with Coronavirus Disease 2019

### ABSTRACT

**Objective:** This study is to determine the possible pathophysiological parameters associated with the development of anxiety and impaired consciousness in patients with acute coronavirus disease (COVID-19).

**Methods:** Descriptive pathophysiological and pathopsychological data was collected from 89 patients hospitalized due to COVID-19 across 7 infectious hospitals, where 14 trainees in psychiatry and neurology collected data from December 2020 to June 2021. Contingency tables and logistic regression analyses were made to reveal associations and to detect predictors of patients' states of anxiety or impaired consciousness.

**Results:** Anxiety and impaired consciousness were observed in 28 patients (31.50%); 22 (25.00%) presented with anxiety symptoms, and 7 (7.90%) had impaired consciousness. The degree of their association was low (Fisher's exact = 0.675 (df = 1),  $P = .495$ ). Different pathophysiological mechanisms were shown to determine the development of anxiety or impaired consciousness within COVID-19. Predictors of anxiety were oxygen saturation (OR = 1.26; 95% CI, 1.04-1.54;  $P = .021$ ), cardiovascular disorders (OR = 0.14; 95% CI, 0.04-0.52;  $P = .003$ ), disorders of the nervous system (OR = 0.05; 95% CI, 0.01-0.84;  $P = .038$ ), and urogenital system (OR = 0.13; 95% CI, 0.02-0.87;  $P = .035$ ). The predictive power of the model was 80.23% ( $P \leq .001$ ). The development of impaired consciousness was associated with age (OR = 1.11; 95% CI, 1.01-1.21;  $P = .025$ ) and C-reactive protein level (OR = 1.02; 95% CI, 0.99-1.04;  $P = .060$ ), and the predictive power of the model was 94.52% ( $P \leq .001$ ).

**Conclusion:** The prevalence of psychopathological disorders associated with acute COVID-19 was high:  $n = 28$  (31.50%) for anxiety and impaired consciousness. Moreover, a 1.00% increase in the saturation index was associated with a 1.3-fold increase in the patient's risk of developing anxiety. Thus, anxiety symptoms may be considered within a personality rather than an infectious-inflammatory response to COVID-19.

**Keywords:** Anxiety disorders, consciousness, C-reactive protein, mind-body relations, oxygen saturation

### Introduction

A historically relevant distinction between the physical and psychic nature of central nervous system performance has its roots in ancient philosophy and was revisited during the Middle Ages. Since then, Cartesian dualism, psychophysical parallelism, or, in other words, the body-mind problem, has not been wholly solved.<sup>1</sup> The extensive development of experimental psychology in the late 19th and early 20th centuries shaped various schools in terms of understanding the solution of Cartesian dualism. For instance, the first scientific laboratory of experimental psychology in Leipzig, founded by W. Wundt, posed the problem of human consciousness within the framework of the fourth Cartesian proposition: physical and nonphysical things cannot interact.<sup>2</sup> Paying attention to its physiological nature, consciousness's psychic phenomenon was evaluated solely as a mental process.<sup>3</sup> Another prominent scientist of that period who founded the world's second experimental



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psychology laboratory in Kazan was V. Bekhterev.<sup>4</sup> Several decades later, he presented an alternative view of mental processes as a complex of fundamentally knowable associative reflexes of the nervous system.<sup>3</sup> Interestingly, 1 of the most important research topics in both laboratories was human consciousness and its empirical assessment through instrumental measurement. However, the nature and evaluation of consciousness within the field of psychiatry continue to be subjects of debate.<sup>5</sup>

In this sense, the factors of external lesion of the central nervous system may still provide sufficient data on psychophysiology or, from the point of view of V. Bekhterev, normal and pathological reflexology. The neurotropism of the SARS-CoV-2 virus in 2022 is beyond doubt.<sup>6</sup> In SARS-CoV-2 infected patients, cognitive impairments, including confusion and agitation, have been shown to affect between 20% to over 50% of individuals in intensive care units.<sup>7</sup> Additionally, delirium is reported to develop in 31% of patients in a coronavirus hospital.<sup>8</sup> Within 6 months after recovery from coronavirus disease 2019 (COVID-19), mental disorders are diagnosed in 34% of convalescents, and for 13%, a first-ever psychiatric diagnosis is made. Among the long-term mental disorders associated with coronavirus, anxiety disorders are detected in 17% of patients who received outpatient care and in 19% of those discharged from hospitals.<sup>9</sup>

Neuroinflammation, microhemorrhages, and brain hypoxia are considered the most likely pathophysiological mechanisms of neuropsychiatric disorders in COVID-19.<sup>10</sup> Nevertheless, the probable commonality of the pathophysiological mechanisms of developing individual components of mental dysfunction in persons infected with SARS-CoV-2 remains poorly understood. Such a common pathophysiological mechanism could make it possible to assess anxiety symptoms and disorders of consciousness as components of the psychopathological syndrome in COVID-19.

The study aimed to determine the possible pathophysiological parameters associated with the development of the most common mental disorders in patients with COVID-19 in an infectious hospital: anxiety and impairment of consciousness.

Objectives: 1) To describe the main pathophysiological mechanisms of COVID-19 and quantify markers of systemic inflammation as well as respiratory function disorders, 2) to assess the prevalence of impairments of consciousness and anxiety symptoms in patients with acute COVID-19 in an infectious hospital, and 3) to identify the associations between psychopathological and pathophysiological characteristics of patients.

## MAIN POINTS

- *The study demonstrated the disproportionate role of physiological mechanisms concerning the risks of developing certain types of mental disturbances against the background of coronavirus disease 2019 (COVID-19).*
- *The phenomenological and pathophysiological association between the studied anxiety symptoms and consciousness impairments has not been confirmed.*
- *Anxiety symptoms can be considered more of a personal characteristic than a phenomenon caused by an infectious-inflammatory body reaction against the background of COVID-19.*

## Material and Methods

Fourteen residents of the V.M. Bekhterev National Medical Research Center of Psychiatry and Neurology and the S.M. Kirov Military Medical Academy receiving primary specialization in psychiatry (also in subspecialties of psychotherapy and addiction medicine) or neurology assessed the mental status of inpatients with COVID-19 in infectious hospitals during the period of their mandatory practical training from December 2020 to June 2021. A total of 127 patients from 7 infectious hospitals provided voluntary consent to participate in the study. This study was approved by Ethics Committee of V.M. Bekhterev National Medical Research Centre for Psychiatry and Neurology (Approval No: EK I-132-20, Date: November 30, 2000).

### Inclusion Criteria:

- 1) The ability to read, understand, and willingly sign an informed consent form to participate in the study.
- 2) Hospitalization, specifically for a COVID-19 diagnosis.
- 3) The capability to complete all study-related procedures.

### Non-inclusion criteria:

- 1) Extremely severe current medical condition with inadequate respiratory function
- 2) Age under 18 years.

Exclusion criteria: refusal to comply with the study procedures at any stage of the study or absence of sufficient clinical data.

The final analysis included data from 89 participants, for whom comprehensive mental status parameters were gathered.

The following pathophysiological parameters related to disease progression were assessed: C-reactive protein (CRP), body temperature, the extent of lung damage determined by computed tomography (CT), blood oxygen saturation, and respiratory rate. The presence of chronic organ systems, such as cardiovascular, respiratory, nervous, digestive, endocrine, and genitourinary systems, was recorded. The history of mental disorders was also documented.

In the present state examination, both the stage of impaired consciousness and the level of anxiety were assessed. Questions from the semi-standardized interview known as "Present State Examination 10" served as the basis for evaluating these mental states.<sup>11</sup> To achieve standardized descriptions of the mental state and to minimize subjective bias among medical researchers, a preliminary determination of the degree of recorded psychopathological phenomena was made using a dichotomous scale. On this scale, 0 points indicate the absence of abnormalities, while 1 point signifies their presence.

The study design was overseen by an independent ethical committee under internal registry number ЭК-И-132/20. It followed a naturalistic, non-interventional design and involved the collection of anamnestic, sociodemographic data as well as clinical parameters sourced from the original medical records after obtaining informed consent. The study adhered to the Helsinki Declaration and the standard of good clinical practice (GCP).

Statistical data processing was carried out using the Statistical Package for Social Science Statistics software, version 16.0 (SPSS Inc.;

Chicago, IL, USA). The distribution was evaluated by the Kolmogorov–Smirnov method. Since the majority of the data did not follow a normal distribution, we presented descriptive statistics using medians (median) along with the corresponding minimum (min) and maximum (max) values, or the lower (Q25) and upper (Q75) quartiles. The choice was made to enhance the clarity and robustness of data representation. Categorical variables were expressed as n (%). To assess the hypothesis of contingency for the 2 specific psychopathological symptoms under investigation, which were nominal in nature, a Fisher’s exact test was performed. For further analysis, logistic regression was employed, with results presented as odds ratios (OR) with 95% confidence intervals (CI). The significance level was established at  $\alpha = 0.05$ .

**Results**

The dataset included 40 men and 49 women, with a median age of 49 years (ranging from a minimum of 19 to a maximum of 95 years). A confirmed diagnosis of COVID-19 was established through PCR testing in 70 cases (78.70%), through CT scans in 10 cases (11.20%), and based on characteristic clinical symptoms in 9 patients (10.10%).

Eleven (12.90%) patients had a history of chronic disorders of the endocrine system, 13 (14.60%) had respiratory system disorders, 29 (32.60%) patients had cardiovascular system disorders, 19 (21.30%) had gastrointestinal system disorders, 5 (5.70%) had disorders of the nervous system, and 6 (6.70%) had disorders of the genitourinary system. Furthermore, 6 (6.70%) patients had been diagnosed with a mental disorder in the past. The median number of concomitant diseases was 1 (min 0; max 4).

The degree of lung lesions corresponding to level CT 0 was detected in 9 (12.00%) participants, CT 1 in 30 (40.00%) participants, CT 2 in 23 (30.70%) participants, and CT 3 in 13 (17.30%) participants. The median body temperature of the patients was 37.5 °C (Q25 = 37.0; Q75 = 38.5), the median level of CRP was 10.0 mg/L (Q25 = 5.4; Q75 = 36.5), the saturation median was 96% (Q25 = 92.3; Q75 = 98), and the respiratory rate median was 18 (Q25 = 16; Q75 = 21).

The psychopathological manifestations the study focused on, namely anxiety and impaired consciousness, were present in 28 patients (31.50%); specifically, 22 (25.00%) experienced anxiety symptoms, and 7 (7.90%) presented with impaired consciousness. The only significant predictor of the presence of either type of psychopathological disorders as identified through binary logistic regression, was the age of the patients (OR = 1.07; 95% CI, 1.04-1.11;  $P \leq .001$ ). At the same time, the degree of association between impaired consciousness and anxiety symptoms in patients was low. Only 1 person experienced both conditions concurrently (Table 1).

Table 2 outlines the significant predictors of anxiety development in patients hospitalized due to COVID-19. The predictive ability of the

**Table 1.** Association Between Impaired Consciousness and Anxiety Symptoms in COVID-19 Patients

Presence of Psychopathological Symptoms		Impaired Consciousness n (%)		Fisher’s Exact test (df), P
		No	Yes	
Anxiety symptoms n (%)	No	60 (68.2%)	6 (6.8%)	0.675 (1) P = .495
	Yes	21 (23.9%)	1 (1.1%)	

**Table 2.** Clinical and Anamnestic Predictors Associated with the Risk of Anxiety in COVID-19 Patients According to the Resulting Model of Logistic Regression Analysis

Anamnestic and Clinical Parameters of Patients	P	Odds Ratio (OR)	95% CI
Saturation	.021	1.26	1.04-1.54
Absence of cardiovascular diseases	.003	0.14	0.04-0.52
Absence of neurological diseases	.038	0.05	0.01-0.84
Absence of diseases of the genitourinary system	.035	0.13	0.02-0.87
Constant	.050	2.44e <sup>-11</sup>	1.03e <sup>-19</sup> -0.00573

**Table 3.** Demographic and Clinical Predictors Associated with Impaired Consciousness in COVID-19 Patients According to the Resulting Model of Logistic Regression Analysis

Demographic and Clinical Parameters of Patients	P	Odds ratio (OR)	95% CI
Age	.025	1.11	1.01-1.21
C-reactive protein	.060	1.02	0.99-1.04
Constant	.004	3.83e <sup>-5</sup>	4.03e <sup>-8</sup> -0.04

constructed model was 80.23% ( $P < .001$ ), with a sensitivity of 0.938 and a specificity of 0.591. The Hosmer–Lemeshow goodness-of-fit statistics yielded a value of 10.4 (df = 6), with a  $P$  value of .110.

Table 3 presents significant and trending predictors of developing impairments of consciousness in hospitalized patients with COVID-19. The predictive ability of this model was 94.52% ( $P < .001$ ) with a sensitivity of 0.985 and a specificity of 0.571. The Hosmer–Lemeshow goodness-of-fit statistics showed a value of 1.4 (df = 8), with a  $P = .995$ .

**Discussion**

The most common neuropsychiatric symptoms in patients with COVID-19, which the study focused on, demonstrated varying patterns of association with the pathophysiological mechanisms of SARS-CoV-2 infection. Although the overall incidence of anxiety symptoms or impaired consciousness was high (31.50% of the sample), there were no common clinical predictors for the presence of any of these neuropsychiatric symptoms other than patients’ age. The association between the occurrence of neuropsychiatric conditions and patients’ age does not bear significant novelty.<sup>7,9</sup> However, these findings do not corroborate the notion that there are no viable tools for evaluating the pathophysiological predictors of neuropsychiatric symptoms in SARS-CoV-2 infection. Conversely, each mental disturbance, when assessed on its own, had specific associations with sociodemographic and clinical parameters.

The more frequently observed symptom (n = 22 (25.00%) of the sample), anxiety, was unexpectedly predicted by higher oxygen saturation in patients. It was also more common in cases with previous cardiovascular, urogenital, or neurological disorders. Continuing the discourse of psychophysical parallelism raised in the introduction to the article, this psychopathological phenomenon against the background of COVID-19 appears to be a mental disturbance caused by the “self-determination of the organisms with their appropriate reactions to the surrounding world” (Bekhterev, V. (1908). Psyche

und Leben. [Mind and Life]. 2nd ed. Wiesbaden: Bergmann). It is well known from the theory and praxis of cognitive behavioral therapy that the belief in one's vulnerability can provoke emotional dysregulation.<sup>12</sup> Empirical evidence also suggests that medical comorbidity is associated with higher levels of psychological stress in people during the pandemic, even in its initial stages, when the population incidence of COVID-19 was still extremely low.<sup>13</sup> Thus, in the present study, patients with a history of cardiovascular, urogenital, or neurological disorders and those with a more favorable current physical condition and unimpaired respiratory function showed a tendency to develop anxiety.

According to the study, consciousness as one of the main mental processes is less frequently impaired in acute infection with SARS-CoV-2 (n = 7 (7.90%) of the sample) and is less associated with the subjective characteristics of inpatients. On the one hand, the marginal significance of its relation to the C-reactive protein level was affected by the low prevalence of this type of severe neuropsychiatric disorder in the sample. On the other hand, an increase in CRP per 1 mg was associated with patients in the coronavirus-infection ward with a 2.00% higher risk of impaired consciousness. The identified composition of predictors of impaired consciousness characterizes the significance of physiological mechanisms in developing neuropsychic symptoms in patients with the acute course of COVID-19.

The key strength of the study lies in its naturalistic design, which collects data on the relationship between simultaneously presented neuropsychiatric disturbances and pathophysiological characteristics of patients in coronavirus-infection wards. This design yielded significant clinical predictors. However, the study's limited sample size restricts the generalizability of its findings. Another limitation was the absence of a psychometric scale, which would have allowed for a quantitative rather than qualitative evaluation of the severity levels of anxiety and impaired consciousness in patients.

The study demonstrated the disproportionate role of physiological mechanisms concerning the risks of developing certain types of mental disturbances against the background of COVID-19. At the same time, the phenomenological and pathophysiological association between the studied anxiety symptoms and consciousness impairments has not been confirmed. Moreover, regression analysis data indicate that a 1.00% increase in the saturation index was associated with a 1.3-fold increase in patients' anxiety risk. Thus, in the results obtained, anxiety symptoms can be considered more a personal characteristic than a phenomenon caused by an infectious and inflammatory body reaction.

The most prevalent psychopathological traits among patients hospitalized due to COVID-19, as highlighted in this current naturalistic study, do not entirely align with the assumption of mind-body parallelism. Notably, anxiety and impairments in consciousness exhibit distinct characteristics: anxiety appears rooted in personal reactivity within a subset of subjectively vulnerable patients, whereas consciousness impairments seem to possess a more physiological basis. This suggests the potential consideration of consciousness impairments as indicators of an adverse progression of infection in COVID-19 ward patients. Simultaneously, anxiety responses in patients experiencing a more favorable course of coronavirus infection could potentially benefit from a psychotherapeutic approach.

**Data availability statement:** The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Ethics Committee Approval:** This study was approved by Ethics Committee of V.M. Bekhterev National Medical Research Centre for Psychiatry and Neurology (Approval No: EK I-132-20, Date: November 30, 2020).

**Informed Consent:** Written informed consent was obtained from the patients who agreed to take part in the study.

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