

# Negative Evidence: The Substance and Circumstances of COVID-19 Vaccine and Mental Health

Jane M. Orient, M.D.

## Introduction

The COVID-19 global health emergency was a multidimensional worldwide crisis that destroyed lives and disrupted economies on an unprecedented scale.<sup>1-3</sup> The reckless mismanagement of this catastrophe has caused more harm than the COVID-19 virus itself.<sup>4</sup> From the onset of the pandemic, authorities promoted the notion that the development of the COVID-19 vaccine was the only viable solution. All the efforts to mitigate the lethal impact of the novel contagion have been subjugated to serve that dogma. The emphasis was put on the draconian non-pharmacological interventions (NPIs) that destroyed small businesses and restricted personal freedom.<sup>5</sup> The reports about effective early treatments were first ignored and ultimately dismissed as “misinformation.” The weary public was assured that the vaccine was the sole way to move from the authoritarian nightmare of NPIs towards a semblance of normalcy.

Creation of the mRNA COVID-19 vaccine has been heralded as the monumental achievement of contemporary science. Governmental experts asserted that it was absolutely safe and effective in preventing COVID-19 disease and in reducing its severity and mortality.<sup>5-7</sup> However, reality was not consistent with that overly optimistic official narrative.

Previous guest editorials were focused on examining the multitude of somatic (physical) disorders that constituted the dangerous side effects of this arrogantly implemented dubious preventive modality. Those somatic conditions included disorders of hemostasis, autoimmune abnormalities (including VADE), cardiovascular diseases from myocarditis to sudden cardiac deaths, accelerated cancers, infertility, and neurological syndromes.<sup>4,8-17</sup> Such dramatic adverse consequences of the COVID-19 vaccines, which are confirmable by objective tests, have been reported in independent press, on social media, and in the pharmacovigilance databases, including the Vaccine Adverse Event Reporting System (VAERS), National Electronic Injury Surveillance System Cooperative Adverse Drug Event Surveillance Project (NEISSCADES), and the V-Safe Pregnancy Vaccine Registry.<sup>13, 14, 18-20</sup> Predictably, officialdom has been dismissing those reports and attacking the credibility of clinicians and researchers who dared to question the official narrative.

This editorial explores another dark side of mRNA COVID-19 vaccines—the spectrum of mental disorders. Although not as overt as the previously discussed conditions, those side effects are equally devastating and alarming. Both the **substance** (biochemical composition) and the **circumstances** (psychological context) of the administration of the COVID-19 vaccine can be implicated in the induction of serious mental disorders.

This editorial continues the emphasis on “negative evidence,” examining cases in which expected data, conclusions, or facts are notably absent.<sup>21</sup> Negative evidence suggests more than a mere lack of information; it implies that critical details may have been deliberately hidden to obscure wrongdoing. Consequently,

any comprehensive investigation must diligently search for such negative evidence. Unfortunately, this crucial strategy is often overlooked in the research process.

## Challenges of Addressing Psychiatric Side Effects of Vaccines

It has long been recognized that medications prescribed to treat nonpsychiatric diseases can induce psychiatric side effects (PSEs) that mimic diagnoses seen in psychiatry, including depression, anxiety, and psychotic states.<sup>22</sup> However, the discussion of the psychiatric side effects of vaccinations is much more challenging due to the interplay of subjective cultural and political factors and objective issues such as etiological consideration, data quality, generalizability, etc.

## Political Factors

The conversation about the PSEs of vaccines is tainted by the long and acrimonious debate about the relationship between vaccinations and autism. Detailed discussion of this topic is beyond the scope of this editorial, but the following facts have to be highlighted. A large part of the public, many activists, and dissident scholars believe that there is a clear link between vaccines and autism.<sup>23-25</sup> Officialdom keeps asserting that the link between vaccines and autism has been definitively disproven long time ago.<sup>26-29</sup> Yet, it concedes that certain rare psychiatric side effects of vaccines have been observed.<sup>30</sup> For instance, a pilot case-control study by Leslie et al. found a temporal association between certain neuropsychiatric disorders and antecedent vaccinations in children and adolescents.<sup>30</sup> Specifically, this study reported increased incidences of obsessive-compulsive disorder (OCD), anorexia nervosa (AN), and anxiety disorders following influenza vaccinations.<sup>30</sup> Despite this small concession, politicized academia does not encourage the open discussion about potential PSEs of vaccines. Therefore, to protect their careers most mainstream scientists avoid discussing this “politically incorrect” topic.

Another factor interfering with the open discussion of vaccination-related PSEs is the internal division among scientific dissenters regarding the validity of psychiatry as clinical science. There is a vocal group of medical dissidents who embrace the concept of anti-psychiatry. They reject the medical model of psychiatry.<sup>32-35</sup> Therefore, they argue that classic psychiatric diagnoses like “schizophrenia” are invalid since they are mere labels imposed by society to stigmatize and control nonconforming individuals who deviate from social norms. Anti-psychiatrists strongly oppose use of traditional psychiatric terms including “psychosis.” According to them, utilization of the psychiatric nomenclature contributes to stigma and enables manipulation to prop up the oppressive system. Some anti-psychiatry advocates have criticized vaccine skeptics for using classic psychiatric terms.

Moreover, it has been observed that during the COVID-19 pandemic members of both political camps misused the psychiatric phraseology to denigrate the behavior of their

ideological enemies.<sup>36-38</sup> Misuse of psychiatry for political purposes has a long and dark history.<sup>39</sup> The COVID-19 pandemic with its sociopolitical turbulence has added additional entries to this lengthy record. The previously strict scientific terms describing psychiatric diagnoses have been redefined to serve as pejoratives used to demean political opponents. Scientific discourse relies upon the precision of the language used to describe the studied phenomena. Appropriation of psychiatric terminology for the purposes of partisan warfare took that precision away.

### Cultural factors

Terms “mental” disorders and “physical” disorders are used frequently by the general public. For most laymen, the difference between those two categories is intuitively obvious: the former describes the ailments of the “mind” and the latter the diseases of the “body,” a classification rooted in the old Cartesian philosophical concept of mental-somatic duality,<sup>40</sup> a persuasive axiom that dominated Western culture for so long that it is now taken for granted. However, there is an ongoing polemic regarding the precise definition, classification, etiology, and even the existence of mental disorders.<sup>32-34,41-46</sup> That still unresolved debate reflects the various viewpoints on what constitutes a “healthy mind” among clinicians, researchers, patients, and activists.<sup>47-49</sup> Unfortunately, some of those perspectives are being skewed by the recent barrage of ideology-driven cultural confounders. The culture war resulting from the rampant politicization of all aspects of life has not spared psychiatry.<sup>50-52</sup> The definitions of mental health and pathology have been adjusted to fit politically correct agendas.<sup>53-55</sup> These ideological manipulations increased tensions among different psychiatric schools and eroded the credibility of psychiatric experts among the public.

### Objective Challenges

Political and cultural biases aside, there are numerous objective factors that contribute to the difficulty in proving a causal relationship between COVID-19 vaccine and mental disorders as side effects. Those include:

- **Mixed etiology:** the distinction between mental and somatic disorders is not always as clear-cut as expected, because many mental disorders have biological underpinnings, and somatic disorders can have psychological components.<sup>55, 56-58</sup>
- **Temporal relationship and specificity:** Establishing a clear temporal relationship between vaccine exposure and the onset of mental symptoms is crucial but often challenging. Additionally, as mentioned above mental disorders can have multifactorial etiologies, making it hard to attribute symptoms specifically to the one factor such as mRNA vaccine.<sup>59</sup>
- **Uncertain pathomechanisms:** Our understanding of the etiology and pathogenesis of mental diseases has improved significantly over the past few decades. However, the precise pathomechanisms of many mental disorders remain unknown or are subject to dispute. For instance, it has been established that the pathophysiology of psychotic disorders such as schizophrenia involves multiple neurotransmitter systems, including dopamine, glutamate, and GABA, but the exact mechanisms involved are not well understood.<sup>60</sup> This uncertainty can lead to both excessive speculation about the existence of the links between immunizations and mental disorders and to arbitrary dismissals of the legitimate concerns about PSEs of COVID-19 vaccines.
- **Subjective diagnostic criteria:** Unlike many somatic illnesses, mental disorders cannot be diagnosed through objective

ancillary tests such as blood work or imaging. Instead, diagnoses rely on clinical observations and assessments of a person’s symptoms, which can be subjective and influenced by cultural and societal norms.<sup>61</sup>

- **Diagnostic heterogeneity:** Patients with the same diagnosis can present with a wide range of symptoms and severity levels, making it difficult to define clear boundaries between disorders.<sup>62</sup> For example, borderline personality disorder (BPD) has nine diagnostic criteria, and a person needs to meet only five of them for diagnosis, resulting in 256 distinct presentations of BPD.<sup>63</sup>
- **Confounding variables:** Many mentally ill patients often already have multiple overt or latent physical and/or mental co-morbidities. For instance, older patients can suffer from type 2 diabetes, hypertension, COPD, and other age-related disorders and therefore are treated with various medications, making it difficult to isolate the effect of a single new substance such as COVID-19 vaccine. Younger patients may suffer from not-yet-diagnosed early schizophrenia.<sup>60</sup> Some patients may choose to not disclose significant risk factors for developing mental illness. For instance, they might surreptitiously abuse drugs or alcohol, engage secretly in a promiscuous lifestyle, or hide experiencing various psychological traumas. All such confounding factors can either obscure or falsely suggest a link between COVID-19 vaccination and mental disorders.<sup>64</sup>
- **Variability in individual responses:** Genetic, biographical, and environmental factors can influence how individuals respond to medications and vaccines, leading to variability in adverse effects.<sup>30,65-67</sup> This makes it difficult to generalize findings from clinical trials to the broader population.
- **Quality of data:** Large reporting systems and case reports, which are commonly used in pharmacovigilance, often lack the methodological rigor needed to establish causality in terms of mental illness. These reports can be biased and incomplete, limiting their reliability.<sup>59,68</sup>
- **Ethical constraints:** Randomized controlled trials (RCTs) are the gold standard for establishing causality. However, performing RCTs is typically not feasible for studying adverse mental health effects due to ethical concerns and the need for long-term follow-up. Observational studies, while useful, can only establish associations, not causation.<sup>64,69</sup>
- **Generalizability issues:** Even if an RCT of mental disorders as a side effect of the COVID-19 vaccination could somehow be performed, the strict inclusion and exclusion criteria in a properly designed RCT could limit the generalizability of the findings to the real-world population, where patients may have different characteristics and risk factors.<sup>70</sup>

### **The Importance of Mental Health Considerations**

Despite these challenges and the complex and controversial nature of the concept of “mental disorders” as adverse effects of the COVID-19 vaccine, considerations of patient safety require setting aside partisan and sectarian quarrels.

The mandated mass injection of a potentially psychogenic **substance** (mRNA COVID-19 vaccine) under the highly psychotraumatic **circumstances** of pandemic are per se conducive to the development of certain peculiar ailments. These conditions do not meet the criteria for typical “somatic diseases” since they cannot be diagnosed by objective ancillary tests. However, they fit well into the category of “mental disorders” as defined in the mainstream medicine based upon standards contained in

Statistical Manual of Mental Disorders (DSM-5).<sup>43-45,61</sup>

Unlike their somatic counterparts, the mental side effects of COVID-19 vaccinations are hard to diagnose and can be missed initially, but they are seriously harmful. They have long-lasting negative impact on affected individuals, their families, friends, co-workers, and ultimately on the whole society.

Authorities have consistently recognized the heightened risks of developing mental disorders associated with COVID-19 disease and circumstances of the pandemic among patients and even in clinicians caring for them.<sup>71-75</sup> However, the same authorities have recklessly ignored the obvious risks of mental disorders linked to the mRNA COVID-19 vaccine's biochemical properties and circumstances of its administration. Use of such a double standard in the risk assessment was likely motivated by an undisclosed agenda.

This dark episode of the agenda-driven selective blindness of authorities should serve as an argument against any future vaccine mandates.

### The Pragmatic Definition of the Mental Side Effects of the Vaccine

The controversies regarding mental illness are acknowledged, but clinical medicine is not a strict dogmatic science. Its practice frequently requires pragmatic flexibility to serve the best interest of the patients. Here, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) is used as the basis for the identification of mental side effects of COVID-19 vaccinations. The DSM-5 standards are imperfect, but they are close to the best diagnostic tools currently available. Since they are obviously tainted by political bias they should be treated as guidelines not as a rigid diagnostic instrument. Most of the DSM-5 parts that are ideologically skewed can be easily identified and ignored.<sup>76,77</sup>

Mental disorder as defined by DSM-5 is "a syndrome characterized by clinically significant disturbance in an individual's cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental processes underlying mental functioning."<sup>61</sup> This definition highlights that mental disorder involves a dysfunction (a failure of a mental mechanism to perform its natural function) that is considered harmful based on social norms.<sup>44</sup> Such framing is helpful in putting the emphasis on the fact that mental side effects of COVID-19 vaccination ultimately result in a harmful dysfunctionality that affects not only the patient but also his social network.

**Mental Disorders are classified** in the DSM-5 into categories based on shared features and symptoms.<sup>61,78</sup> The DSM-5 employs a combination of categorical and dimensional approaches to improve diagnostic precision in view of the complexity of mental disorders. Therefore, DSM-5 categorizes mental disorders into distinct groups, such as mood disorders, anxiety disorders, psychotic disorders, and personality disorders, among others. Most pertinent categories are listed in Table 1. Each category encompasses specific disorders that share common features and symptoms. For example, psychotic disorders are defined by the presence of symptoms such as delusions, hallucinations, and disorganized thinking, with distinctions made based on symptom duration and severity.<sup>61,78</sup> The DSM-5 also emphasizes the importance of symptom duration, intensity, and context to ensure that diagnoses reflect significant dysfunction and distress, distinguishing pathological conditions from normal variations in behavior.<sup>79</sup>

**Table 1.** Selected major categories of mental disorders according to DSM-5<sup>61</sup>

Category	Description	Examples
Neurodevelopmental disorders	Disorders that typically emerge in childhood and affect cognitive, social, and emotional development.	Autism spectrum disorder Attention-deficit hyperactivity disorder (ADHD)
Schizophrenia spectrum and other psychotic disorders	Disorders involving disturbances in thinking, perception, and behavior, often including delusions and hallucinations	Schizophrenia Schizophreniform disorder Schizoaffective disorder
Bipolar and related disorders	Disorders involving fluctuations between periods of elevated mood (mania) and periods of low mood (depression)	Bipolar I and II disorder Cyclothymic disorder
Depressive disorders	Disorders involving persistent sadness, loss of interest, and other symptoms that affect mood and functioning	Major depressive disorder (MDD) Persistent depressive disorder Disruptive mood dysregulation disorder (DMDD)
Anxiety disorders	Disorders involving excessive fear, worry, and anxiety that interfere with daily life	Generalized anxiety disorder Social anxiety disorder Panic disorder
Obsessive-compulsive and related disorders	Disorders involving recurrent, intrusive thoughts (obsessions) and repetitive behaviors (compulsions)	Obsessions Compulsions
Trauma- and stressor-related disorders	Disorders that develop in response to traumatic or stressful events	Post-traumatic stress disorder (PTSD) Acute stress disorder
Dissociative disorders	Disorders involving disruptions in consciousness, memory, identity, or perception.	Dissociative identity disorder (DID) Dissociative amnesia Depersonalization/derealization
Somatic disorders	Disorders involving physical symptoms that cannot be fully explained by a medical condition	Conversion disorder Factitious disorder Pseudocyesis
Feeding and eating disorders	Disorders involving disturbances in eating behavior and body image	Anorexia and bulimia nervosa Binge-eating disorder
Personality disorders	Disorders involving enduring patterns of thinking, feeling, and behaving that deviate from cultural expectations and cause significant impairment in functioning	Borderline personality disorder Antisocial personality disorder Narcissistic personality disorder

### Potential Causes of COVID-19 Vaccine-related PSEs

The notion that the novel mRNA COVID-19 vaccine can be associated with induction of psychiatric side effects is perfectly sensible for any unbiased person familiar with the current etiological models of mental disorders, the properties of COVID-19 vaccines, and circumstances of their administration.

### Etiology and Pathogenesis of Mental Disorders

The understanding of the etiology of mental diseases has evolved significantly over the past few decades. Historically, the causes of psychiatric disorders were unknown, and early etiological theories relied on speculation. During the early 19th century, the prevailing view among psychiatrists (then known as *alienists*) was that mental illness did not have any organic basis.<sup>80,81</sup> Therefore, mental disorders were defined as the presence of abnormal behavior without any identifiable physical causes.<sup>82</sup> This approach persisted until the mid-19th century

when the discovery of monocausal agents for infectious diseases influenced psychiatry, leading to the search for *single* causes of mental illnesses, such as neurochemical imbalances or specific genetic mutations.<sup>83</sup>

Contemporary research caused the shift from monocausal theories to recognition of the multifactorial nature of psychiatric disorders. Advances in genomic technologies have identified numerous genetic variants associated with mental illnesses, highlighting their polygenic nature. Genome-wide association studies (GWAS) have revealed that psychiatric disorders are influenced by many common genetic variants with small effect sizes, and these variants often overlap across different disorders.<sup>84,85</sup> In addition to genetic factors, environmental influences are now acknowledged as critical components in the etiology of mental disease. Studies have shown that environmental exposures such as stress (psychological trauma), infections, and toxins interact with genetic predispositions to influence the risk of developing psychiatric conditions.<sup>86</sup> This gene-environment interaction underscores the complexity of mental illness etiology.<sup>87</sup>

**Epigenetic** mechanisms, including DNA methylation and histone modifications, have also been implicated in the pathogenesis of mental disorders.<sup>88</sup> These epigenetic changes can result from various environmental influences, such as stress, diet, medications, toxins, etc., and may lead to lasting alterations in neural circuit function contributing to the development and progression of psychiatric conditions.<sup>88,89</sup>

The role of **immune dysregulation** in psychiatric disorders such as schizophrenia and major depressive disorder has increasingly been recognized. Altered cytokine profiles and immune system abnormalities have been observed in a subset of patients, suggesting that immune mechanisms may contribute to the pathophysiology of these conditions.<sup>90</sup>

Previously underappreciated **metabolic factors** appear to play a significant role in the pathogenesis of mental disorders. Specifically, mitochondrial dysfunction and impaired brain energy metabolism have been recently proposed as mechanisms underlying psychiatric disorders.<sup>91</sup> Evidence suggests that mitochondrial abnormalities and oxidative stress play a role in the etiology and progression of mental conditions including bipolar disorder, major depressive disorder, schizophrenia, and autism.<sup>92-94</sup> Chronic psychological stress can induce mitochondrial allostatic load, characterized by structural and functional changes in mitochondria, leading to oxidative stress, inflammation, and apoptosis. This process is thought to predispose individuals to psychiatric disorders by disrupting cellular homeostasis.<sup>93</sup> Additionally, alterations in mitochondrial dynamics, such as fission, fusion, biogenesis, and mitophagy have been observed in psychiatric conditions, further supporting the role of mitochondrial dysfunction in these disorders.<sup>94</sup>

**Neurobiological (neurological) factors** play a significant role in the etiology and pathophysiology of various mental disorders. These factors include alterations in neurotransmitter systems, neuroinflammation, and neurotrophic factors.

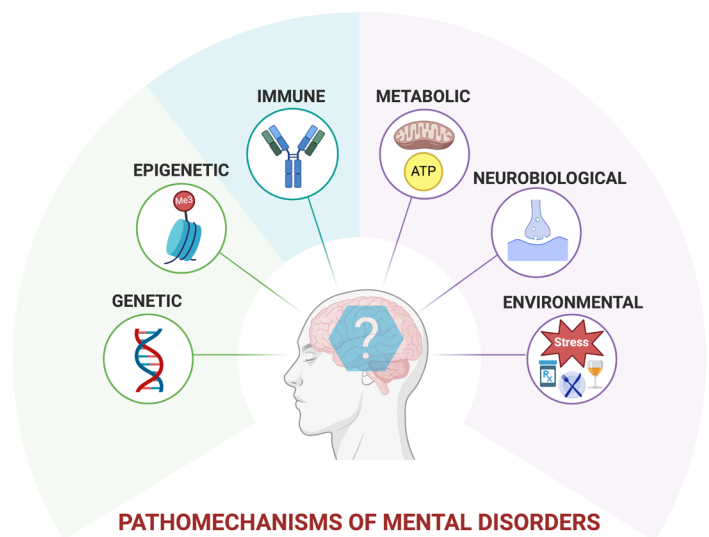
**Alterations in neurotransmitter systems**, particularly dopamine and glutamate, are central to the pathophysiology of psychotic disorders such as schizophrenia. Excess synaptic levels of dopamine and glutamate lead to increased postsynaptic stimulation, contributing to psychotic symptoms. Deficiencies in  $\gamma$ -aminobutyric acid (GABA) inhibitory interneurons and hypofunctioning N-methyl-D-aspartate (NMDA) glutamate receptors disrupt the inhibitory-excitatory balance, further exacerbating these symptoms.<sup>59</sup>

**Neuroinflammation** and microglial activation are implicated in the pathophysiology of psychiatric disorders such as major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia. Increased inflammatory responses and oxidative stress can stimulate microglia, leading to the release of pro-inflammatory cytokines like interleukin-1 $\beta$  (IL-1 $\beta$ ) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), which contribute to brain pathology leading to mental disorders.<sup>95</sup>

**Neurotrophic factors** such as brain-derived neurotrophic factor (BDNF) and its interactions with immune-inflammatory pathways are key components in the pathophysiology of mood disorders and schizophrenia. Lowered BDNF levels are associated with disruptions in neurotrophic signaling and activated immune-inflammatory pathways, leading to neurotoxicity and synaptic dysfunction.<sup>95,96</sup>

The causative relationship between **environmental factors** and mental disorders has been recognized for a long time. These factors include psychological and physical stress and exposure to pollutants, toxins, medications, etc.<sup>86,97</sup> Psychological stress appears to be especially impactful since even the stress of living in an urban environment and being exposed to the extreme weather can produce a variety of serious mental disorders through mechanisms including increased oxidative stress, systemic inflammation, disruption of the blood-brain barrier, over-stimulation of brain regions involved in stress regulation such as the amygdala and the perigenual anterior cingulate cortex,<sup>98</sup> as well as epigenetic dysregulation as mentioned above.<sup>88</sup>

In summary, as shown in Figure 1, it has been well established that mental disorders result from the complex interplay of genetic, epigenetic, immune, metabolic, neurobiological and environmental factors.<sup>60,88,99,92</sup> While the specific details of these interactions remain unknown, the current knowledge is sufficient to implicate COVID-19 vaccine as a potential culprit in triggering a variety of mental disorders.



**Figure 1.** Putative pathomechanisms of mental disorders

### Circumstances of COVID-19 Vaccine Administration as a Cause of PSEs

The historical drama of the COVID-19 pandemic took place in a complex sociopolitical milieu characterized by the pervasive politicization of medicine, extreme political polarization, and

partisan power asymmetry favoring the left wing.<sup>50,99</sup> Those emotionally charged circumstances led to creation of the two contradictory partisan narratives regarding the COVID-19 vaccine. According to the prevailing right-wing opinion, the novel mRNA COVID-19 vaccine mandated by the left-wing-aligned health authorities was neither safe nor effective. This view was driven by the reasonable distrust of the left-wing-affiliated experts and officials. It was augmented by the social media reports of the serious side effects of the vaccine. And it was solidified by the statements of the right-wing-associated scientific dissidents, influencers, and politicians. However, despite their strong opposition to being vaccinated, due to the power asymmetry many vaccine skeptics had no choice but to submit to the mandate or suffer the devastating consequences of refusal. As a result, a large part of the American public has been subjected to numerous types of psychological trauma, such as stress caused by: fear of being forced to receive vaccine and suffering serious adverse effects, fear of death and disability when actually experiencing vaccine's side effects, concerns of loved ones being injured by the vaccine, distress about possibility of losing a job and economic hardship due to non-compliance with vaccine mandate, actual loss of job and economic hardship due to non-compliance with vaccine mandate, a feeling of being deprived of personal freedom,<sup>100</sup> distress about being pushed to commit the crime of falsifying vaccination records,<sup>101</sup> horror caused by suspicions that their own government may run a program that injures citizens, and many other similar concerns.

**Psychological stress** has been proven to be one of the strongest factors causing a variety of mental disorders via well-described pathomechanisms. Thus, it seems apparent that the sole circumstance of mandated administration of COVID-19 vaccine constitutes a strong risk factor for development of mental disorders. The biggest paradox here is that even those vaccine skeptics who did not receive the COVID-19 vaccination could still experience some form of stressful reaction to the vaccination mandates and hence have been put at the increased risk of developing mental illness. The lucky ones could be protected by their genetic makeup.

Only a few studies have examined the stress level associated with the administration of the COVID-19 vaccine according to partisan affiliation.<sup>102-105</sup> Though the number of those studies is low, their results indicate that partisan affiliation influences stress levels associated with the COVID-19 vaccine in the ways discussed above. For example, the study by Konstantopoulos et al. examined the relationship between known vaccine hesitancy factors and vaccine uptake within two major political parties. This study primarily focused on vaccine uptake, but it highlighted the high level of stress related to vaccine administration that was influenced by political beliefs.<sup>104</sup>

### **The Substance of COVID-19 Vaccines as a Cause of PSEs**

The negative impact on mental health of the circumstances surrounding COVID-19 vaccine administration is easy to explain. However, physicians are increasingly being asked whether the components or mechanism of action of this novel mRNA vaccine could cause psychiatric diseases. These inquiries reflect patients' concerns about mental issues following vaccine administration affecting themselves or their loved ones.

Unfortunately, understanding the role that the "**substance**" of the vaccine can play in etiology of mental disorders is very challenging. We use term "**substance**" of the COVID-19 vaccine to denote its **components** (mRNA, lipid nanoparticles,

excipients), its **product** (spike protein), and its **mechanism of action** (induction of immunity by using genetically modified mRNA). All those aspects are enormously complex, confusing, and virtually impervious to those who do not intensely study such esoteric subjects as molecular biology, immunology, biochemistry, pharmacogenetics, virology, biophysics, etc.

In less politicized times, the public would primarily rely on academic experts for guidance. Unfortunately, we live in the era of the subjugation of academia to ideology and the pharmaceutical industry. Hence, the official scholars, although extremely knowledgeable and scientifically accomplished, cannot be trusted. They are no longer credible to a large part of the public. Scientific dissidents cannot be entirely relied upon either. They are a very heterogeneous group. Many are brave, competent, and honest. However, others overstate their qualifications and are motivated more by profit than by benevolence. Such deception is difficult to conceal in the long run. Hence, some members of the public still trust dissidents more than official experts but have doubts about them. Therefore, they frequently turn to their personal doctors for the ultimate opinion about potential psychiatric side effects of COVID-19 vaccine, even if those physicians are not psychiatrists. Such requests may be very challenging for many physicians.

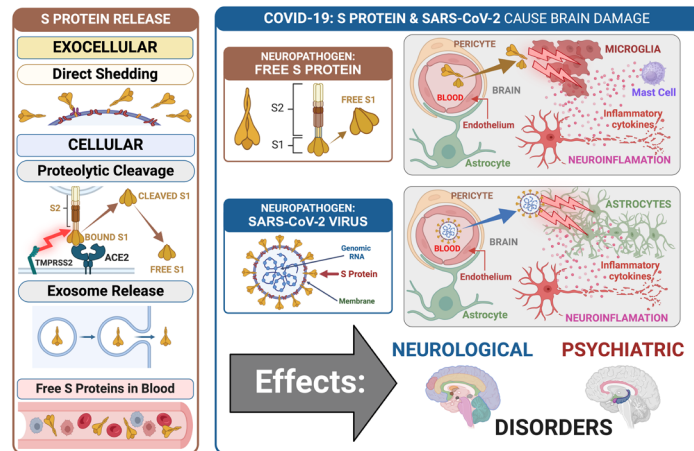
Commenting about potential links between the substance of mRNA vaccines and mental disorders requires much more cutting-edge scientific knowledge than discussing virtually any other type of side effects of this vaccine. Most clinicians are not advanced scientists. They know more about fundamental sciences than the general public does. However, they cannot keep up with non-clinically relevant scientific progress, due to heavy patient loads, extensive documentation requirements, and compulsory recertification programs. Yet, many practitioners are being asked now by their patients to be the arbiters deciding which one of the two conflicting narratives about psychiatric adverse effects of COVID-19 vaccine is correct. And under current circumstances, many physicians would like to be able to provide objective and fact-based opinions on this subject. The discussion below is intended to assist those clinicians in this difficult task. This short text cannot replace the extensive study of all complex topics related to the question at hand. However, it introduces the essential scientific concepts needed to understand the possible psychopathogenic effects of novel mRNA vaccine.

Theoretically all the vaccine's components, its product, and its mechanism of action can be implicated as factors capable of causing mental disorders. However, to date only spike protein has been unequivocally proven to cause various mental disorders. The role of other elements remains speculative.

### **Spike Protein: a Proven Psychopathogenic Factor**

Extensive research has demonstrated that during COVID-19 disease both SARS-CoV-2 virus and especially its spike protein (S protein) can affect the brain by disrupting the blood-brain barrier and subsequently inducing neuroinflammation and causing neuronal cell death.<sup>106-110</sup> As shown in Figure 2, during COVID-19 disease the release of the S Protein can occur via variety of mechanisms including exocellular direct shedding or cellular processes like protein cleavage and exosome release. As a result, S protein can circulate in the blood. The circulating S protein can include both the S1 and S2 subunits. The S protein is initially synthesized as a single polypeptide and then cleaved into the S1 and S2 subunits by host cell proteases. The S1 subunit

is responsible for binding to the angiotensin-converting enzyme 2 (ACE2) receptor on host cells, while the S2 subunit mediates the fusion of the viral and host cell membranes. Both whole S protein and its S1 subunit can cross the blood-brain barrier and cause neuroinflammation through interaction with microglia and mast cells. Whole SARS-CoV-2 virus can also penetrate the blood-brain barrier, but it causes neuroinflammation through stimulation of astrocytes not microglia. Depending upon the site, intensity, and character of the neuroinflammation, this process can produce either classic neurological diseases or cause the conditions currently classified as “mental disorders” including the cognitive deficit of so-called “long COVID.”



**Figure 2.** Role of S protein in the etiology of neurological and psychiatric disorders during COVID-19 disease

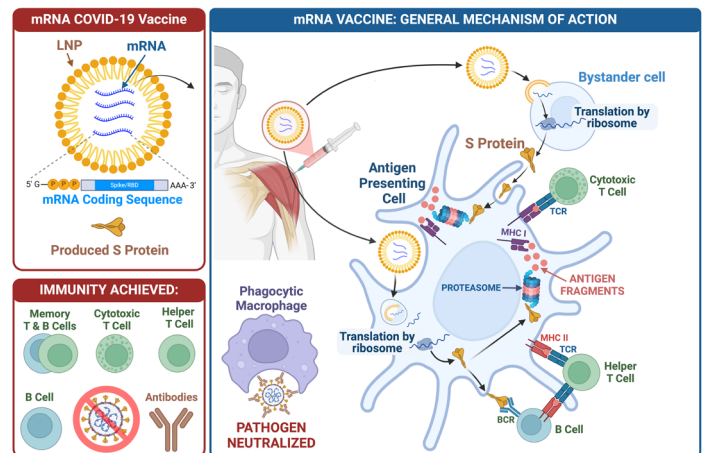
Recent studies have shown that the S1 subunit can induce cognitive deficits and anxiety-like behavior in mice by causing neuronal cell death in the hippocampus and by activating glial cells, which release pro-inflammatory cytokines such as interleukin-1 $\beta$ .<sup>106</sup> This suggests a non-cell autonomous mechanism whereby the spike protein indirectly causes neuronal damage via glial activation. Additionally, the spike protein can act as a pathogen-associated molecular pattern (PAMP), engaging Toll-like receptors (TLR2 and TLR4) on microglia, leading to neuroinflammatory responses. This includes the release of cytokines like IL-1 $\beta$ , IL-6, and TNF, which contribute to neuroinflammation and behavioral changes.<sup>107,108</sup> Moreover, the spike protein’s disruption of the blood-brain barrier allows it to enter the central nervous system and directly affect brain cells. The perivascular inflammation and neuronal damage further contribute to the cognitive and psychiatric symptoms observed in COVID-19 patients.<sup>109,111</sup>

### Dispute over the Distribution of Vaccine-Generated S Protein

Astonishingly, officialdom has held that the same spike protein that was shown to cause serious mental disorders in patients with COVID-19 was supposed to be harmless when produced by the mRNA vaccine. This bold claim was based upon the initial assumption that spike protein produced by vaccine stays in the tissue at the injection site and therefore does not circulate in the body. This idea was zealously propagated by various “science communicators”<sup>112</sup> rather than actual scientists, who were more reserved about it. For example, Derek Lowe writes: “The Spike protein produced by vaccination is not released in a way that it gets to encounter the ACE2 proteins on

the surface of other human cells at all: it’s sitting on the surface of muscle and lymphatic cells up in your shoulder, not wandering through your lungs causing trouble.” He concedes that “some” of the vaccine makes it into the bloodstream, but he dismisses that as a potential problem.<sup>112</sup>

The official narrative on the mechanism of action of the messenger RNA (mRNA) COVID-19 vaccines, such as BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna), is illustrated in Figure 3. This novel class of vaccines utilizes synthetic mRNA to instruct cells to produce the SARS-CoV-2 S Protein, which is the target antigen for these vaccines.<sup>113,114</sup> The mRNA in these vaccines is nucleoside-modified to enhance stability and translation efficiency. The term “nucleoside-modified” refers to the incorporation of chemically modified nucleosides into the mRNA sequence. Specifically, modifications such as pseudouridine and N1-methylpseudouridine are commonly used. This mRNA is encapsulated in lipid nanoparticles (LNPs) to protect it from degradation and facilitate its delivery into host cells.<sup>115-117</sup> Naked mRNA is inherently unstable and prone to rapid degradation by extracellular ribonucleases (RNases) and self-hydrolysis. Encapsulation within LNPs protects the mRNA from these degradative processes, ensuring its stability until it reaches the target cells.



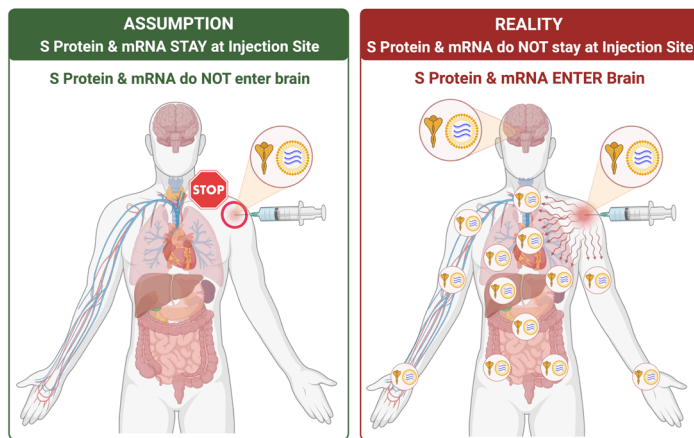
**Figure 3.** The design and general mechanism of action of mRNA COVID-19 vaccine. Abbreviations: BCR: B cell receptor; TCR: T cell receptor. MCH I and MCH II: major histocompatibility complex class I and II respectively.

Upon administration, the LNPs deliver the mRNA into the cytoplasm of host cells: either any bystander cells (like myocytes) or antigen presenting cells. The host cell’s ribosomes then translate the mRNA into the SARS-CoV-2 S protein. This protein is expressed on the surface of the host cells, where it is recognized by the immune system as a foreign antigen. This recognition triggers both humoral and cellular immune responses, including the production of neutralizing antibodies and the activation of T cells, which together confer protection against COVID-19.<sup>118</sup> Specifically, the S protein made on the ribosomes can stimulate the immune system in many ways. Intracellular antigen is first broken down into smaller fragments by the proteasome complex. Subsequently those fragments are presented on the cell surface to cytotoxic T cells by major histocompatibility complex (MHC) class I proteins. Activated cytotoxic T cells kill infected cells by secreting cytolytic molecules, such as perforin and granzyme. Moreover, secreted antigens can be taken up

by cells, degraded inside endosomes, and presented on the cell surface to helper T cells by MHC class II proteins. Helper T cells accelerate the clearance of circulating pathogens by stimulating B cells to produce neutralizing antibodies, as well as by activating phagocytes such as macrophages via inflammatory cytokines. The lipid nanoparticles not only protect the mRNA but also act as adjuvants, enhancing the immune response.<sup>118</sup> The mRNA is eventually degraded by normal cellular processes, ensuring that it does not integrate into the host genome.<sup>117</sup>

In summary, according to this narrative the mRNA COVID-19 vaccines safely leverage the body's "cellular machinery" to produce **locally** the viral antigen, thereby eliciting a robust immune response that provides protection against SARS-CoV-2 infection, without the risk of exposing the patients to circulating pathogenic S protein.

If all the above statements were true, then this novel vaccine would be indeed extremely safe in terms of not being able to induce any of the psycho-pathogenetic processes discussed above. Unfortunately, as visualized in Figure 4, this officially promoted initial assumption was too good to be true. Despite mainstream efforts to censor any dissent, several authors dared to question the reassuring dogma.



**Figure 4.** Initial assumption and the reality of the distribution of the S protein produced by the mRNA COVID-19 vaccine

For example, Oldfield et al. discuss the theoretical possibility of spike protein crossing the blood-brain barrier and causing inflammation.<sup>119</sup> Those authors point out that available data indicates that the spike protein from SARS-CoV-2 and even those generated by current mRNA vaccines can cross the blood-brain barrier and may cause inflammation or blood clots in the brain.<sup>119,120</sup> Therefore, if vaccine-induced expression of spike proteins is not confined to the injection site, COVID-19 vaccines may be implicated in the induction of mental disorders similar to those seen in patients with COVID-19. The authors call for more research to formulate definitive conclusions.

Similarly, Khayat-Khoei et al. reported several cases of CNS inflammation following mRNA vaccination.<sup>121</sup> Specifically, they described clinical and MRI features of neuroinflammation and demyelination in seven individuals who received mRNA COVID-19 vaccines. Within 21 days of the vaccine administration these patients developed neurologic symptoms and MRI findings consistent with active CNS demyelination involving brain, optic nerve, and/or spinal cord. The authors point out that their findings are consistent with previous anecdotal reports suggesting that the vaccines may be associated with neuroinflammatory processes

involving brain, spinal cord, and peripheral nervous system. Therefore, they posit that large prospective studies are required to further investigate any possible relationship between COVID-19 vaccines and acute CNS neuroinflammation and demyelination, both of which may be involved in the pathogenesis of mental disorders. It is very telling that four years later, no such studies have been performed, at least not in the U.S.

In 2023, Russian scientists published a meticulous review of experimental studies on humans and rodents regarding the biodistribution of mRNA vaccines, their constituents (mRNA and lipid nanoparticles), and their encoded antigens (S proteins).<sup>122</sup> Those authors expressed surprise that although the mRNA vaccines have been used on a massive scale for more than three years the complete picture of the biodistribution of its components and products is still not well established. It took the scholars who are outside of the area of American academic influence to note the negative evidence related to the subject of biodistribution of the spike proteins generated by the novel vaccine.

Similarly, South Korean researchers were daring enough to perform a large population-based cohort study of psychiatric adverse effects of COVID-19.<sup>123</sup> The cumulative incidences per 10,000 of PSEs were assessed in one week, two weeks, one month, and three months after COVID-19 vaccination in the large cohort containing 2,027,353 patients. Authors concluded that COVID-19 vaccination increased the risks of depression; anxiety, dissociative, stress-related, and somatoform disorders; and sleep disorders. However, it reduced the risk of schizophrenia and bipolar disorder. They recommended that special cautions are necessary for administering additional COVID-19 vaccinations to populations vulnerable to PSEs.

### Real World Data on PSEs of COVID-19 Vaccines

In addition to the few aforementioned formal scientific articles exploring the possibility of the COVID-19 vaccination-associated PSEs, the medical literature contains only a modest number of simple case reports of such adverse reactions in adults and adolescents.<sup>124-128</sup>

In contrast, social media, blogs, and informal internet news sites contain a plethora of witness reports, ad hoc VAERS summaries, and commentaries about patients who developed conditions that meet the DSM-5 criteria for mental disorders after receiving the COVID-19 vaccination.<sup>129-131</sup> Such informal reports do not carry the weight of formally conducted scientific studies performed in the academic centers by qualified researchers. However, in the view of mainstream academia's censorious attitude towards any claim that COVID-19 vaccination can cause PSEs, those tacit data are the best evidence of the existence of COVID-19 vaccine-related adverse effects. It is noteworthy that despite this presence in the right-wing information exchange ecosystem the concerns about the psychiatric side effects of COVID-19 vaccination have only recently entered the broader public discourse. In the past they were overshadowed by the much more easily discerned and faster developing somatic complications of the vaccines.

### The Official Response to Concerns about PSEs of COVID-19 Vaccination

Officialdom ignored the public concerns about PSEs of COVID-19 vaccine for a long time, but in view of the increasing

pressure eventually took a position on that issue. According to the majority of academic experts, the concerns that COVID-19 vaccines could cause mental disorders are not supported by current evidence. On the contrary, there are published data indicating that COVID-19 vaccines have beneficial effects on mental health by alleviating pandemic-related stress and anxiety.

A meta-analysis by Lee et al. found no significant association between COVID-19 vaccination and psychiatric adverse events, such as depression and anxiety, suggesting that vaccination does not exacerbate these conditions.<sup>132</sup> Similarly, a study by Chen et al. reported that vaccinated individuals had lower odds of experiencing anxiety and depression compared to those who were not vaccinated, indicating a potential protective effect of vaccination on mental health.<sup>133</sup> Furthermore, research by Coley et al. demonstrated that COVID-19 vaccinations were associated with improved mental health outcomes, including reduced odds of depression among vaccinated individuals, and highlighted potential spillover effects such that higher state vaccination rates correlated with lower anxiety and depression rates.<sup>134</sup> This suggests that vaccination may in fact contribute to mental well-being by reducing the perceived risk of COVID-19 infection and its associated stressors.

Additionally, a study by Perez-Arce et al. found that receiving the first dose of a COVID-19 vaccine was associated with significant improvements in mental health, as measured by reductions in mental distress scores.<sup>135</sup> This aligns with findings from Koltai et al., who observed declines in psychological distress following vaccination, potentially mediated by reduced perceived risks of infection, hospitalization, and death.<sup>136</sup>

The results of those well-designed and well-powered studies by mainstream scientists are shocking and unbelievable for any right-wing-affiliated vaccine skeptic. Those findings directly contradict his tacit real-world observations and expectations. They negate the abundant information he sees on his favored social media platforms and news outlets. Those unexpected conclusions seem to refute the case reports and theoretical basis of the pathogenesis of COVID-19 vaccine-related PSEs discussed above. How is such discrepancy even possible?

There may be a simple explanation for this shocking incongruence. It is possible that the studies demonstrating the positive impact of COVID-19 vaccines on mental health have mainly captured the reaction of the left-wing-aligned vaccine-accepting members of the American public. As demonstrated by the study by Zhou et al., the attitudes of left-wing-aligned persons towards various aspects of the COVID-19 pandemic are perfectly opposite to those of right-wing affiliated individuals.<sup>137</sup> While right-leaning persons dreaded the side effects of the vaccine, left-leaning persons saw the COVID-19 vaccine as true protection from the dreaded COVID-19 infection. Those drastically opposite perceptions demonstrate the immense scale of political polarization and the depth of the partisan divide over COVID-19.

## Conclusions

The concern that both the substance and circumstances of COVID-19 vaccine administration may cause psychiatric side effects (PSEs) is well-founded and deserves to receive much more attention. The limited research, focused primarily on scores of mental distress, is negative evidence of a serious impact that would, if acknowledged, force discontinuation of the mass-vaccination campaign and rethinking the expanded use of mRNA technology.

This dark episode of administrative overreach shows the need to purge leftist ideologues from positions of power and restore the old credibility and impartiality of academic experts, with the goal of serving patients' safety rather than partisan or sectarian agendas.

**Jane M. Orient, M.D.**, is a practicing general internist and serves as executive director of AAPS and managing editor of the Journal. Contact: jane@aapsonline.org.

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