Mohammad Mahdi Aliasin, Niloufar Yazdanpanah and Nima Rezaei*

Neurological and neuropsychological adverse effects of SARS-CoV-2 vaccines – where do we stand?

https://doi.org/10.1515/revneuro-2022-0006
Received January 17, 2022; accepted February 14, 2022; published online March 25, 2022

Abstract: The devastating characteristic of COVID-19 pandemic calls for immediate and effective solutions to tackle it. Vaccines seem to be the only promising and effective way to fight against the novel coronavirus – even against new mutated variants. Because of the rapid development and distribution of numerous COVID-19 vaccines in different platforms, meticulous evaluation of vaccines' safety is more critical than ever – especially given the fact that most of the candidates have not completed the clinical phase. Therefore, to optimize the vaccines' safety and efficacy, it is highly important to carefully report and scientifically discuss the serious adverse effects following vaccination. In this respect, we discuss different neurological and neuropsychological adverse effects of COVID-19 vaccines including demyelinating diseases, Bell's palsy (BP), cerebrovascular complications, seizures, functional neurological disorders (FNDs), and some other rare adverse events, and hypothetical mechanisms which can lead to the reported side effects. Given the fact that the incidence of such events are rare and most of them are treatable, the current review aims to shed light on how much the relationship between COVID-19 vaccines and these complications can be reliable and provide an insight for future studies with much more meticulous methodologies to discuss the possible correlational or causal relationship between these complications and COVID-19 vaccines and elucidate whether or not the neurological side effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines can count as a considerable threat to public health.

Keywords: cerebrovascular complications; COVID-19 vaccines; demyelinating diseases; neurological complications; SARS-CoV-2.

***Corresponding author: Nima Rezaei**, Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Dr. Qarib St, Keshavarz Blvd, 14197 33151 Tehran, Iran; Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), 14197 33151 Tehran, Iran; and Department of Immunology, School of Medicine, Tehran University of Medical Sciences, 14176 13151 Tehran, Iran, E-mail: rezaei_nima@tums.ac.ir. https://orcid.org/0000-0002-3836-1827
Mohammad Mahdi Aliasin, School of Medicine, Tehran University of Medical Sciences, 14176 13151 Tehran, Iran; Students' Scientific Research Center, Tehran University of Medical Sciences, 14177 55331 Tehran, Iran; and Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), 14197 33151 Tehran, Iran. https://orcid.org/0000-0002-9097-7207
Niloufar Yazdanpanah, School of Medicine, Tehran University of Medical Sciences, 14176 13151 Tehran, Iran; Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, 14197 33151 Tehran, Iran; and Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), 14197 33151 Tehran, Iran. https://orcid.org/0000-0003-4333-2163

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel member of Coronaviridae family, which first emerged in Wuhan, China in December 2019. Like the two other human coronaviruses that appeared in 2002 and 2012 respectively, SARS-CoV-2 is an enveloped, single-stranded, and positive-sense RNA virus responsible for a potentially fatal respiratory infection in humans (Hu et al. 2021; Saghazadeh and Rezaei 2020). In January 2020, the World Health Organization (WHO) announced the SARS-CoV-2 outbreak as a public health emergency of international concern (PHEIC). Later on, in February 2020, WHO named the corresponding disease COVID-19 and finally declared it as a pandemic in March 2020 (Hanaei and Rezaei 2020). At the time of writing this manuscript, the cumulative number of confirmed COVID-19 cases has surpassed 328 million people and over 5.5 million individuals have died because of this disease worldwide (Organization 2022).

So far, several strategies have been implemented to overcome the disease at both levels of prevention and treatment including social distancing, wearing masks, pharmacological interventions, oxygen therapy, and invasive methods such as endotracheal intubation and mechanical ventilation. However, among currently available solutions, vaccines seem to be the most promising and effective way to fight against the virus – even against new

mutated variants (Chen and Lu 2021; Cohen and Corey 2020; Parasher 2021; Sanderson 2021).

Although common side effects following vaccination usually reflect its effectiveness and efficient immune response, severe reactions to vaccines may also occur (Andrzejczak-Grządko et al. 2021; Sharifian-Dorche et al. 2021). Similarly, COVID-19 vaccines are not exceptions, and common side effects including pain in the site of injection, fatigue, fever and chills, headache, nausea, myalgia, and swollen lymph nodes have been reported in this regard (Andrzejczak-Grządko et al. 2021). However, there are also dozens of reports concerning severe adverse effects of SARS-CoV-2 vaccines, a well-known example of which is vaccine-induced immune thrombotic thrombocytopenia (VITT) (Sharifian-Dorche et al. 2021). Similar to neurological sequelae of novel coronavirus disease, it is also hypothesized that COVID-19 vaccines may not be without neurological complications (Finsterer and Scorza 2021). The current review aims to provide insight into different kinds of serious neurological and neuropsychological adverse effects reported after COVID-19 vaccination and discuss whether or not clinicians' attention should be drawn in this respect. Since such events are rare and most of them can be treated, further studies with much more meticulous methodologies are needed to discuss the possible correlational or causal relationships between the aforementioned complications and COVID-19 vaccines and shed the light on whether or not the neurological and neuropsychological adverse effects of SARS-CoV-2 vaccines can count as a considerable threat to public health.

Methods

We searched for all types of documents in PubMed, Scopus, and Web of Science, using the keywords including "SARS-CoV-2 vaccines," "COVID-19 vaccines," "COVID-19 vaccination," "neurological," "neuropsychological," "side effects," and "adverse effects." Based on the neurological and neuropsychological adverse effects yielded in the initial search, we completed our search strategy and searched for the documents which discussed the relationship between the aforementioned conditions and COVID-19 vaccines in all platforms undergone clinical studies. Although we aimed to comprehensively review the neurological complications of COVID-19 vaccines, the selection strategy of the studies was not strictly defined since our paper was a narrative – and not a systematic – review.

COVID-19 vaccines

Shortly after the emergence of SARS-CoV-2, different COVID-19 vaccine candidates were introduced and entered the clinical trials to be assessed in cases of efficacy and safety (Tregoning et al. 2020). According to the WHO's latest updates on COVID-19 vaccines on January 14, 2022 (World Health Organization 2021), a total number of 333 vaccine candidates have been developed in different platforms, 139 of which are currently at the clinical phase. The detailed number of vaccine candidates in different platforms and phases is depicted in Figure 1. Although the development of numerous types of vaccines could be a promising tool to put an end to the pandemic, meticulous evaluation of vaccines' safety is more critical than ever – especially given the fact that most of the candidates have not completed the clinical phase (Figure 1). This calls for determination to carefully report and scientifically discuss the serious adverse effects following vaccination. Therefore, vaccine recipients' monitoring and follow up to detect complications is of great importance for further development and optimization of vaccines' efficacy and safety.

Neurological and neuropsychological complications following COVID-19 vaccines

Safety concerns about post-immunization neurological complications have always been a controversial issue and are not merely restricted to COVID-19 vaccines (Miravalle et al. 2010). Based on the chart illustrated in Figure 1, most of the COVID-19 vaccines use the same platforms as other previous vaccines. In other words, it is somehow accepted that the side effects of COVID-19 vaccines resemble previous ones. Table 1 shows different non-COVID-19 viral vaccines that have triggered serious neurological outcomes.

Another reason, which can theoretically justify the possibility of the incidence of neurological adverse effects following SARS-CoV-2 vaccines, is the characteristic of the virus itself. SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE-2) receptor and transmembrane serine protease 2 (TMPRSS2) to enter the target cell with the help of spike protein (S protein). Studies show that high concentrations of both ACE-2 and TMPRSS2 are expressed in the central nervous system (CNS) (Hu et al. 2020; Yachou et al. 2020). Therefore, it is expected that SARS-CoV-2, just like other human coronaviruses, induces different neurological complications in infected individuals. Table 2 reviews the most important neurological complications that occurred as a result of acute infection with different coronaviruses (Algahtani et al. 2016; Almqvist et al. 2020; Anghelina et al. 2009; Arabi et al. 2015; Desforges et al. 2019; Fazzini et al. 1992; Foley et al. 2003; Mora-Díaz et al. 2019; Nagu et al. 2021;

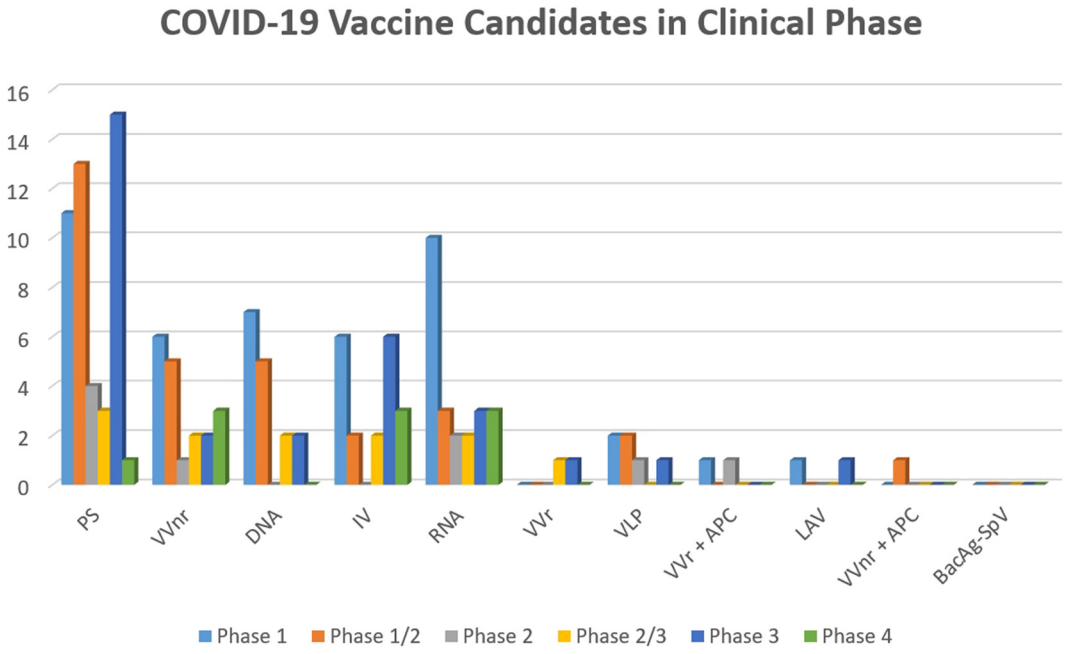

Figure 1: The categorized number of vaccine candidates undergoing clinical phase (declared by WHO).
PS, protein subunit; VVnr, viral vector (non-replicating); IV= inactivated virus; VVr, viral vector (replicating); VLP, virus-like particle; APC, antigen presenting cell; LAV, live attenuated virus; BacAg-SpV, bacterial antigen-spore expression vector.

Table 1: Neurological complications of major non-COVID-19 viral vaccines having similar structures.

Type of vaccine	Type of complications	The vaccine design platform	References
Influenza	Guillain–Barré syndrome, transverse myelitis, neuromyelitis optica, acute disseminated encephalomyelitis, Bell's palsy, abducent nerve palsy, multiple sclerosis, stroke, giant cell arteritis, seizure, brachial plexus neuritis, olfactory dysfunction, functional neurological disorder	Inactivated virus	Miravalle et al. (2010), Principi and Esposito (2019), Agmon-Levin et al. (2009), Cho et al. (2019), Huynh et al. (2008), Stowe et al. (2006), Leiderman et al. (2009), Piyasirisilp and Hemachudha (2002), Famularo et al. (2015), Li et al. (2018), Shaikh et al. (2012), Doty et al. (2014), and Reismann and Singh (1978)
Hepatitis B	Guillain–Barré syndrome, transverse myelitis, neuromyelitis optica, acute disseminated encephalomyelitis, Bell's palsy, abducent nerve palsy, hemorrhagic stroke, brachial plexus neuritis, cerebellar ataxia, multiple sclerosis, encephalitis, myasthenia gravis	Protein subunit	Miravalle et al. (2010), Agmon-Levin et al. (2009), Heekin et al. (2015), Huynh et al. (2008), Alp et al. (2009), Grewal and Zeid (2014), Niu et al. (1999), and Shaw et al. (1988)
Measles-mumps-rubella (MMR)	Guillain–Barré syndrome, transverse myelitis, acute disseminated encephalomyelitis, abducent nerve palsy, seizure, aseptic meningitis, panencephalitis, autism, sensorineural hearing loss, parkinsonism	Live attenuated virus	Principi and Esposito (2019), Agmon-Levin et al. (2009), Huynh et al. (2008), Bourtoulamaiou et al. (2015), Li et al. (2018), and Miravalle et al. (2010)
Japanese encephalitis	Seizure, encephalitis, transverse myelitis, acute disseminated encephalomyelitis, neuromyelitis optica, parkinsonism, multiple sclerosis	Inactivated virus, live attenuated virus	Miravalle et al. (2010), Agmon-Levin et al. (2009), Huynh et al. (2008), Furukawa et al. (2011), and Plesner et al. (1998)
Varicella	Autism, encephalitis, stroke, cerebellar ataxia, stroke, headache, aseptic meningitis, neuropathies, myelitis, ventriculitis, Reye's syndrome, seizure	Live attenuated virus	Miravalle et al. (2010), Piyasirisilp and Hemachudha (2002), MacDonald et al. (2018), and Spencer et al. (2017)
Human papillomavirus	Guillain–Barré syndrome, neuromyelitis optica, Bell's palsy, brachial plexus neuropathy, headache, syncope, complex regional pain syndrome, postural	Protein subunit	Spencer et al. (2017), Menge et al. (2012), Cameron et al. (2016), Debeer et al. (2008), Frisch et al. (2018), Barboi et al. (2020),

Table 1: (continued)

Type of vaccine	Type of complications	The vaccine design platform	References
	tachycardia syndrome, autonomic dysfunction, seizure, narcolepsy, vitiligo, myasthenia gravis, cerebellar ataxia, acute disseminated encephalomyelitis, acute chorea		Hviid et al. (2018), Yonee et al. (2013), Wildemann et al. (2009), and Decio et al. (2014)
Smallpox	Guillain–Barré syndrome, transverse myelitis, acute disseminated encephalomyelitis, Bell's palsy, strokes, multiple sclerosis, poliomyelitis-like syndrome, headaches, encephalitis, aseptic meningitis, Parsonage-Turner syndrome, vertigo	Live attenuated virus	Miravalle et al. (2010), Principi and Esposito (2019), Agmon-Levin et al. (2009), Huynh et al. (2008), and Sejvar et al. (2005)
Poliovirus	Guillain–Barré syndrome, transverse myelitis, acute disseminated encephalomyelitis, Parsonage-Turner syndrome, seizure, vaccine-associated paralytic poliomyelitis, encephalitis	Inactivated virus, live attenuated virus	Miravalle et al. (2010), Principi and Esposito (2019), Agmon-Levin et al. (2009), Huynh et al. (2008), Berglund (1963), and Tian et al. (2020)
Rabies	Neuromyelitis optica, ascending paralysis, headache, vertigo, meningomyeloradiculitis, meningoradiculitis, meningomyelitis, transverse myelitis, acute disseminated encephalomyelitis, seizure, meningoencephalitis, acute inflammatory demyelinating polyradiculoneuropathy, radiculitis, stroke	Inactivated virus	Agarwal et al. (2020), Latimer et al. (1951), Bahri et al. (1996), Agmon-Levin et al. (2009), Huynh et al. (2008), Swaddiwuthipong et al. (1988), Tullu et al. (2003), and Miravalle et al. (2010)
Yellow fever	Neuromyelitis optica, abducent nerve palsy, seizure, acute disseminated encephalomyelitis, transverse myelitis, meningoencephalitis, Guillain–Barré syndrome, Vogt-Koyanagi-Harada, meningomyeloradiculitis, multiple sclerosis, herpes zoster, hemorrhagic fever	Live attenuated virus	Esmanhotto et al. (2021), Goldstein et al. (2019), Bayão et al. (2018), Beirão et al. (2017), Campos et al. (2021), El Nawar et al. (2018), Farez and Correale (2011), Bayas et al. (2007), and Miravalle et al. (2010)

Sharifian-Dorche et al. 2020; Sharma et al. 2019; Tsai et al. 2004; Whittaker et al. 2020; Yeh et al. 2004).

Given the fact that adequate production of S antigen in the body is an important factor for COVID-19 vaccines to trigger an efficient immune response, it is theoretically accepted that these vaccines can lead to certain neurological adverse effects – a common example of which is headache.

On the other hand, it is undeniable that COVID-19 pandemic caused a huge psychological burden and exacerbated mental health issues within societies (Cooke et al. 2020). Considering this amount of anxiety and stress, it can be theoretically accepted that the incidence of psychosomatic disorders may increase. As studies show, the incidence of conversion disorder may increase as a result of global stressors including natural disasters and terrorism. These stressors can also exacerbate the condition in already affected patients (Fasano and Daniele 2021).

Since the development of COVID-19 vaccines, related common side effects have been reported. In this regard, expected minor neurological complications including dizziness, headache, and paresthesia have been widely mentioned (Goss et al. 2021). Nevertheless, scientists' attention was drawn more specifically when two cases of transverse myelitis (TM) were reported in individuals having received ChAdOx1 vaccine. Although one of them had an underlying neurological condition (Goss et al. 2021), further reports of post-vaccination neurological complications raised concerns about whether there could be a causal link between COVID-19 vaccines and the aforementioned adverse effects. Even though no neurological condition counts as a definite contraindication to vaccination against SARS-CoV-2 (Goss et al. 2021), the occurrence of conditions such as Guillain–Barré syndrome (GBS), conversion disorder, and facial palsy may raise the clinical awareness toward neurological side effects of COVID-19 vaccines (Finsterer and Scorza 2021). Due to the diversity of these complications, they are divided into different groups (summarized in Table 3) and elaborated on possible causal or correlational relationships between these rare conditions and COVID-19 vaccines.

Demyelinating diseases

Demyelinating diseases are defined as inflammatory disorders, leading to loss of myelin sheaths, which is usually accompanied by intactness of axons. These types of

Table 2: Neurological complications reported to happen as a result of acute infection with Coronaviridae family in both human and animal studies.

	SARS-CoV-1	MERS-CoV	SARS-CoV-2	Endemic human coronaviruses	Coronaviruses infecting animals
Neurological symptoms and signs	Seizure, headache, neuropathy, olfactory impairment, myalgia, dizziness	Seizure, headache, altered consciousness (coma), ataxia, focal motor deficits, vertigo, and dizziness	Seizure, headache, dizziness and vertigo, ataxia, cerebral edema, anosmia, aguesia, visual agnosia, delirium and hallucination, impaired vision, hyporeflexia, myalgia, neuralgia, leg stiffness, altered consciousness	Headache and dizziness (HCoV-OC43), paresis and paralysis (HCoV-OC43), seizure (HCoV-OC43, HCoV-229-E, HCoV-HKU1 and HCoV-NL63), dysphagia (HCoV-OC43), cerebral edema (HCoV-NL63), speech dysfunction (HCoV-OC43)	Lethargy (FCoV), nystagmus (FCoV), cerebellar ataxia (FCoV), coma (FCoV), paresis and paralysis (FCoV), abnormal behavior (FCoV), seizure (FCoV)
Cerebrovascular conditions	Stroke	Stroke, intracranial hemorrhage	Ischemic and hemorrhagic stroke, cerebral venous sinus thrombosis, CNS vasculitis, transient ischemic attack		Vasculitis (FCoV)
Neuromuscular disorders	Myopathy, critical illness polyneuropathy	Critical illness polyneuropathy	Myasthenia gravis exacerbation, myopathy, critical illness polyneuropathy		
Demyelinating or/and inflammatory conditions	Guillain–Barré syndrome, encephalitis	Guillain–Barré syndrome, Bickerstaff's encephalitis	Acute disseminated encephalomyelitis, Guillain–Barré syndrome, Miller-Fisher syndrome, transverse myelitis, neuromyelitis optica, encephalitis, meningitis, meningoencephalitis, acute hemorrhagic necrotizing encephalopathy, posterior reversible encephalopathy syndrome	Guillain–Barré syndrome (HCoV-OC43), meningitis (HCoV-OC43), acute disseminated encephalomyelitis (HCoV-OC43), multiple sclerosis (HCoV-OC43 and HCoV-229E)	Encephalomyelitis (PHEV, MHV-JHM and MHV-A59, FCoV), meningitis (FCoV) ependymitis (FCoV), animal model multiple sclerosis (MHV-JHM and MHV-A59)
Cranial neuropathies	Olfactory dysfunction		Bell's palsy, abducent nerve palsy, sensorineural hearing loss, olfactory dysfunction, trigeminal neuropathy, glossopharyngeal neuralgia	Facial nerve palsy as a result of GBS (HCoV-OC43)	
Functional disorders			Conversion disorder		

SARS-CoV, severe acute respiratory syndrome coronavirus; MERS-CoV, middle east respiratory syndrome; HCoV, human coronavirus; FCoV, feline coronavirus; PHEV, porcine hemagglutinating encephalomyelitis virus; MHV, mouse hepatitis virus.

disorders can occur due to either direct damage to myelin sheaths or impairment of the myelin-producing cells. Different pathologies can be described as demyelinating disorders. Therefore, diagnosing the exact subtype relies on physical examination, clinical history, neuroimaging, CSF analysis, and neurophysiological studies (Love 2006; Popescu and Lucchinetti 2012). Discussing in the context of SARS-CoV-2 vaccines, various types of demyelinating disorders have been reported so far.

Guillain–Barré syndrome

GBS is an acute autoimmune neuropathy that mostly occurs after infections. It is assumed that adverse autoimmune reactions against the peripheral nervous system (PNS) play a major role in the pathogenesis of this syndrome (Willison et al. 2016; Yazdanpanah and Rezaei 2022). It should be mentioned that although GBS is discussed under the section related to demyelinating

Table 3: An overview of reported neurological adverse events following SARS-CoV-2 vaccines.

Type of complication	Brief overview of the condition	Occurence after COVID-19	Other vaccines following which the condition is reported	Suggested pathophysiology in respect with vaccines	Treatment and prognosis
Demyelinating disorders					
Guillain-Barré syndrome	Immune-mediated neuropathy mostly occurring after infection. Both demyelination and axonal injury may play a role. Clinical manifestations include symmetrical upper and lower limb weakness, hypo/areflexia, paresthesia, cranial neuropathies, autonomic dysfunction and paralysis.	✓	Influenza, oral polio, tetanus, measles-mumps-rubella, human papillomavirus, meningococcal vaccine (Principi and Esposito 2019), smallpox, hepatitis B (Miravalle et al. 2010), yellow fever (Beirão et al. 2017).	Cross-reactivity between S protein and gangliosides or glycoproteins located on myelin sheaths (Karimi et al. 2021; López-Hernández et al. 2022).	IVIg and plasmapheresis. Poor prognosis if left untreated.
Transverse myelitis	Inflammatory conditions in which spinal cord is involved. Sensory, motor and autonomic symptoms may be present. It can occur after both infections and vaccination.	✓	Hepatitis B virus, measles-mumps-rubella, diphtheria-tetanus-pertussis, rabies, typhoid, influenza, oral polio, haemophilus influenzae, Japanese B encephalitis, smallpox, cholera (Agmon-Levin et al. 2009; Miravalle et al. 2010).	Polyclonal or bystander B cell activation leading to cytokine synthesis and subsequent activation of autoreactive T cells. Interaction between SARS-CoV-2 spike protein antibodies and tissue proteins such as myelin basic protein may also play a role (Hirose et al. 2021; Vojdani and Kharrazian 2020).	High-dose IV corticosteroids. Consider plasmapheresis as an alternative therapy. Prognosis may vary based on the patient's underlying conditions and certain predispositions.
Neuromyelits optica	An autoimmune disorder characterized by optic neuritis and transverse myelitis. Mostly triggered by anti-AQP4 autoantibodies. In the minority of cases anti-MOG is involved.	✓	Yellow fever (Esmanhotto et al. 2021), influenza (Cho et al. 2019), Japanese encephalitis (Furukawa et al. 2011), human papillomavirus (Menge et al. 2012), hepatitis B (Heekin et al. 2015), rabies (Agarwal et al. 2020), pneumococcal, tetanus-diphtheria (Fujikawa et al. 2021).	Shedding of AQP4 molecules in response to overactivation of cytotoxic T-cells resulting in occurrence or exacerbation of NMO. Unknown predispositions may exist in individuals developing NMO after vaccination.	Rapid administration of intravenous methylprednisolone after an acute attack can prevent visual damage.
Acute disseminated encephalomyelitis	An autoimmune demyelinating disorder affecting central nervous system mostly happening after infections. Frequently, ADEM is more common in children.	✓	Rabies, diphtheria-tetanus-polio, smallpox, measles, mumps, rubella, Japanese B encephalitis, pertussis, influenza, hepatitis B, pertussis, human papillomavirus (Huynh et al. 2008; Wildemann et al. 2009).	Cell-mediated or humoral response against myelin antigens (e.g., myelin basic protein, myelin oligodendrocyte protein, proteolipid protein) as a result of vaccine-induced inflammation; Increased vascular permeability can also lead to edema and hemorrhage and finally neuronal damage (all triggered by vaccine-induced inflammation).	Timely initiation of immunotherapy (high-dose corticosteroids) can lead to full recovery.

Table 3: (continued)

Type of complication	Brief overview of the condition	Occurence after COVID-19	Other vaccines following which the condition is reported	Suggested pathophysiology in respect with vaccines	Treatment and prognosis
Cranial neuropathies					
Bell's palsy	A peripheral nerve neuropathy caused by facial nerve impairment. Its manifestations include unilateral weakness of facial muscles, dry eye and xerostomia.	✓	Influenza (Stowe et al. 2006), human papillomavirus (Cameron et al. 2016), hepatitis B (Alp et al. 2009), smallpox (Sejvar et al. 2005), meningococcal vaccine (Myers and Mcneil 2018).	Combination of mRNA and lipid nanoparticles may contribute to the production of specific interferons as a result of innate immune response. These interferons along with other cytokines (cytokine storm) can in turn lead to bystander activation of cytotoxic T cells and lead to direct neuronal damage. The cytokine storm itself can also induce an inflammatory state leading to congestion and ischemia of facial nerve at the site of geniculate ganglion (Ozonoff et al. 2021; Warner et al. 2021).	In the majority of cases, full recovery is achieved without any treatment. Corticosteroid therapy is recommended for faster recovery.
Abducent nerve palsy	Sixth cranial nerve neuropathy. Binocular diplopia occurs as a result of this condition.	✓	Yellow fever (Goldstein et al. 2019), measles-mumps-rubella (Bourtoulamaiou et al. 2015), hepatitis B (Grewal and Zeid 2014), influenza (Leiderman et al. 2009), diphtheria-pertussis-tetanus (Reyes-Capo et al. 2021).	Post-immunization inflammation leading to demyelination and restricted vasculitis.	In the majority of cases, full recovery is achieved without any treatment. Corticosteroid therapy is recommended for faster recovery.
Olfactory dysfunction	Altered or decreased sense of smell.	✓	Influenza (Doty et al. 2014), tick-borne encephalitis (Vodicka et al. 2010).	Interaction of ACE-2 receptors in olfactory epithelium and S antigens produced as a result of vaccination (Keir et al. 2021).	In the majority of cases it is resolved by its own. Administration of nasal corticosteroids may lead to faster recovery.
Sensorineural hearing loss	A sudden hearing impairment due to the problem of inner ear.	✓	Tetanus-diphtheria, meningococcal vaccine (De Marco et al. 2018).	Internal auditory artery thrombosis followed by administration of adenoviral vector vaccines can be a hypothetical pathophysiology (Tsetsos et al. 2021). Inflammation, demyelination and fibrosis of acoustic nerve has also been mentioned in this respect (Carol Liu et al. 2020).	In case of VITT suspicion, manage it according to Figure 3. Corticosteroids are not recommended in idiopathic cases (Carol Liu et al. 2020).

Table 3: (continued)

Type of complication	Brief overview of the condition	Occurence after COVID-19	Other vaccines following which the condition is reported	Suggested pathophysiology in respect with vaccines	Treatment and prognosis
Cerbrovascular complications					
Cerebral venous sinus thrombosis	Formation of clot in venous sinuses located in the brain. Mostly affecting youth and presenting with symptoms such as headache (most common), focal neurological deficits and seizure.	✓	No vaccines reported so far.	Vaccine-induced immune thrombotic thrombocytopenia (VITT).	Non-heparin anticoagulants and IVIg (Figure 3).Very poor prognosis if the treatment is not initiated quickly.
Ischemic stroke	A type of brain stroke happening when the blood is not properly supplied to the brain.	✓	Influenza (Famularo et al. 2015), varicella (Macdonald et al. 2018).	Vaccine-induced immune thrombotic thrombocytopenia (VITT).	Non-heparin anticoagulants and IVIg (Figure 3). Very poor prognosis if the treatment is not initiated quickly.
Hemorrhagic stroke	The type of brain stroke happening when blood is leaked out of the brain circulation system as a result of arterial rupture or other causes. It can happen in two forms: intracranial hemorrhage and subarachnoid hemorrhage.	✓	Hepatitis B (NIU et al. 1999)	Vaccine-induced immune thrombotic thrombocytopenia (VITT). Vasculitis has also been introduced as an underlying mechanism for vaccine-induced ICH (Takeyama et al. 2021).	Non-heparin anticoagulants and IVIg (Figure 3).Very poor prognosis if the treatment is not initiated quickly.
Seizures	Seizures happening as a consequence of COVID-19 vaccination mostly occur following other neurological conditions – and not fever. Of these conditions, CVST, hemorrhagic stroke, encephalitis and conversion disorder can be mentioned.	✓	Measles-mumps-rubella, Japanese encephalitis, influenza, pneumococcus, diphtheria-tetanus-pertussis, yellow fever rabies, varicella, polio (Li et al. 2018; Miravalle et al. 2010; Spencer et al. 2017)	Pathophysiology differs based on the underlying condition.	Treatment and prognosis differ based on the underlying condition.
Other rare neurological conditions					
Tolosa-Hunt syndrome	Painful ophthalmoplegia caused by a granulomatous inflammation of the cavernous sinus. Symptoms include headache, diplopia and cranial neuropathy.	×	No vaccines reported so far.	Not fully understood. Although no precise autoimmune mechanism is established for this condition, comorbidity of Tolosa-Hunt syndrome with some autoimmune disorders (e.g. systemic lupus erythromatosis, sarcoidosis and Wegner's granulomatosis) hypothesizes an autoimmune etiology for this condition (Amrutkar and Burton 2021).	Due to lack of evidence, a precise treatment plan has not been established. Administration of corticosteroids may be recommended.Remission varies case by case and may occur within a few days or weeks (Chuang et al. 2021).

Table 3: (continued)

Type of complication	Brief overview of the condition	Occurence after COVID-19	Other vaccines following which the condition is reported	Suggested pathophysiology in respect with vaccines	Treatment and prognosis
Parsonage-Turner syndrome	Brachial plexus neuropathy accompanied by upper limb pain and weakness. It can be triggered by vaccination and cause long-term sequelae.	✓	Typhoid (Kim et al. 2021b), hepatitis B (Shaw et al. 1988), influenza (Shaikh et al. 2012), human papillomavirus (Debeer et al. 2008), polio (Berglund 1963), diphtheria-tetanus-pertussis (Hamati-Haddad and Fenichel 1997), smallpox (Biorklund 1963), shingles and tick-borne encephalitis (Queler et al. 2021).	Not fully understood. Combination of immune system overactivity and certain genetic features may contribute to the development of this condition. Interferon I production in response to mRNA vaccines may also play a role in the pathogenesis of brachial plexus neuritis (Queler et al. 2021).	Administration of pain management medication (e.g. NSAIDs or opioids) plus oral corticosteroids is recommended. Most cases have good prognosis (Feinberg and Radecki 2010).
Small fiber neuropathy	A kind of neuropathy occurring as a result of the impairment in small nerve fibers of the skin (Hovaguimian and Gibbons 2011).	✓	Human papillomavirus (Kafaie et al. 2016), rabies, varicella, Lyme's disease (Souayah et al. 2009).	Autoimmune responses against vaccine adjuvants may account for the underlying mechanism of this condition (Waheed et al. 2021).	Administration of gabapentin might be helpful (Waheed et al. 2021).
Functional neurological disorder	A neuropsychiatric condition usually characterized by impaired neurological function with no accompanied structural pathology. Symptoms may include paralysis, weakness, dysphagia and PNES.	✓	Influenza (Reismann and Singh 1978)	Abnormal beliefs may arouse the attention toward the body and disturb the non-conscious inhibitory role of supplementary motor cortex area on motor activity. As this inhibitory force is disturbed, negative emotional stimuli can lead to abnormal motor symptoms which are interpreted by the patients as involuntary movements due to the disturbance of readiness potentials. (Kim et al. 2021a; Voon et al. 2010).	Physiotherapy, psychotherapy and other experimental treatments including transcutaneous electrical nerve stimulation, transcranial magnetic stimulation, sedative therapies and biofeedback can improve the symptoms. Spontaneous recovery is possible but the prognosis is usually poor (Lehn et al. 2016).

disorders, other presentations of GBS may involve axonal injury – as is the case with acute motor axonal neuropathy (AMAN) (Malek and Salameh 2019). The clinical presentations of GBS may include bilateral limb weakness, cranial neuropathies, hypo/areflexia, autonomic dysfunction, paresthesia, and paralysis (Malek and Salameh 2019; Willison et al. 2016). The progressive and life-threatening characteristic of GBS necessitates an immediate clinical care and attention. Intravenous immunoglobulin (IVIg) and plasma exchange have been proven to be effective strategies in most cases of GBS (van den Berg et al. 2014).

GBS can also occur after COVID-19 infection, mostly in its classic form, which is acute inflammatory demyelinating polyneuropathy (AIDP) (Abu-Rumeileh et al. 2021). However, the link between GBS and novel coronavirus vaccines is controversial and remains to be established (Lunn et al. 2021). So far there have been several reports of GBS following vaccination against SARS-CoV-2 (Oo et al. 2021; Woo et al. 2021). It is not well understood how COVID-19 vaccines can induce GBS. One theory highlights the key role of autoimmune reactions caused by the cross-reactivity between vaccine epitopes and antigens located on myelin sheaths. In a detailed manner, it is hypothesized that S protein, which is produced as a result of immunization against SARS-CoV-2, can bind to the sialic acid located on the gangliosides and glycoproteins of the neurons' cell membrane. Therefore, antibodies attacking to S proteins might also respond against the antigens on the myelin sheaths (Karimi et al. 2021; López-Hernández et al. 2022).

Although rare, the occurrence of GBS cases after administration of COVID-19 vaccines, especially in individuals with no history of prior infection (Matarneh et al. 2021; McKean and Chircop 2021; Rao et al. 2021; Razok et al. 2021; Trimboli et al. 2021), may hypothesize a possible causal association between GBS and COVID-19 vaccines. In addition, there is also an observational study demonstrating an increase in the number of GBS cases to a significant extent, which strengthens vaccine safety concerns (Woo et al. 2021). Furthermore, increase in the number of post-vaccination GBS cases with age (Li et al. 2021) may suggest certain predispositions to such side effects. On the other hand, the association between GBS and other vaccines, such as swine flu vaccine (Oo et al. 2021), may also strengthen COVID-19 vaccine apprehension. Although the benefits of global vaccination dramatically outweigh the risk of contracting GBS (Lunn et al. 2021), further studies with larger populations should be conducted to reach the most conclusive results.

Transverse myelitis

TM is a term referring to a group of conditions with an inflammatory character, leading to spinal cord impairment. Since the spinal cord is affected in TM, sensory, motor, and autonomic symptoms occur. Similar to GBS, TM can develop after infections and vaccination. However, other etiologies including paraneoplastic syndromes, systemic autoimmune disorders, drug toxicity, and demyelinating conditions such as multiple sclerosis (MS) and neuromyelitis optica (NMO) may also play a role (Beh et al. 2013; Frohman and Wingerchuk 2010). Because misdiagnosis of TM and administration of wrong treatments may worsen the condition and have serious consequences (Beh et al. 2013), accurate diagnosis and proper management of TM is of great importance.

TM counts as one of the neurological sequelae of the novel coronavirus disease (Ismail and Salama 2021). In addition, TM has rarely happened following COVID-19 vaccination (Goss et al. 2021). Although the possibility of coincidence cannot be ruled out considering the rareness of such event, there are a few points to be considered.

First, previous findings bring up the fact that association between TM and vaccination may not be a mere coincidence (Shah et al. 2018). Second, the acute onset of symptoms after receiving COVID-19 vaccines (Fitzsimmons and Nance 2021; Gao et al. 2021; Khan et al. 2021) suggests a temporal association between TM and the vaccines. Third, there are also several theories that can justify the occurrence of TM following COVID-19 vaccination. According to Agmon-Levin et al. immunization can lead to TM with the help of the following mechanisms: 1) cross-reaction between foreign antigens and self-antigens, 2) overactivation of antigen presenting cells and the subsequent autoimmune response, and 3) polyclonal or bystander B cell activation which can lead to cytokine synthesis and activation of autoreactive T cells (Agmon-Levin et al. 2009).

With respect to the report of Hirose et al. from a patient who developed TM following COVID-19 vaccination and had positive oligoclonal bands only in his CSF and an intact blood-brain barrier, it is assumed that intrathecal production of IgG antibodies had initiated the autoimmune response. Therefore, the third mechanism mentioned above can explain the occurrence of post-COVID-19 vaccination TM (Hirose et al. 2021).

Moreover, interaction between antibodies against SARS-CoV-2 spike proteins and tissue proteins, namely myelin basic protein (MBP), contributes to the initiation of SARS-CoV-2 autoimmune complications (Vojdani and Kharrazian 2020). Since these antibodies are also produced

in response to vaccination, the incidence of such events following COVID-19 vaccines may not be unlikely.

Nueromyelitis optica

NMO is an autoimmune disorder in connection with optic neuritis and TM. NMO is mostly triggered by IgG autoantibodies against aquaporin 4 water channels (anti-AQP4). However, in the minority of cases, IgG autoantibodies attacking myelin oligodendrocyte glycoproteins are involved (anti-MOG). The latter autoantibodies are also found in some patients with acute disseminated encephalomyelitis (ADEM). In both subtypes, demyelination occurs as a result (Jarius et al. 2020).

Besides NMO cases following COVID-19 infection (Batum et al. 2020; Rafique et al. 2021; Shaw et al. 2020), only four cases of NMO following COVID-19 vaccination have been reported so far (Badrawi et al. 2021; Chen et al. 2021; Fujikawa et al. 2021; Khayat-Khoei et al. 2021); neither causal nor correlational association can be established in this regard. Moreover, there is a lack of evidence concerning the pathophysiology of COVID-19 vaccine-induced NMO, which challenges presuming a link between COVID-19 vaccines and NMO. As mentioned earlier, SARS-CoV-2 uses ACE-2 receptors to enter the target cells. One of the tissues in which ACE-2 receptor is highly expressed is the nasal epithelium (Hamming et al. 2004). Moreover, animal studies also confirm the presence of AQP4 water channels in the olfactory epithelium and their role in the olfaction mechanism (Lu et al. 2008; Sørbø et al. 2007). It could be hypothesized that invasion of SARS-CoV-2 to nasal epithelium and the subsequent cytokine storm, which is responsible for recruiting cytotoxic T cells, leads to cell lysis and release of AQP4 molecules. These released molecules might trigger humoral response in individuals with the history of previous NMO attacks or genetic susceptibility to autoimmune diseases. Hence, the occurrence or exacerbation of NMO following COVID-19 infection could be rationalized. Similar mechanism might also apply to COVID-19 vaccines as the inflammatory response is also triggered by immunization.

On the other hand, according to a systematic review assessing the relationship between NMO and vaccination, the possibility of such event after vaccination cannot be totally rejected (Vanood and Wingerchuk 2019). It is also believed that administration of intravenous methylprednisolone (IVMP) shortly after the onset of an acute attack can most likely prevent permanent visual sequel (Jarius et al. 2020). Thus, due to the crucial need for urgent management, clinicians are advised to bear in mind the possibility of NMO following vaccination.

Acute disseminated encephalomyelitis

ADEM is another type of demyelinating disorders. Similar to other demyelinating conditions, immune reactions are involved in the pathogenesis of ADEM. Immunotherapy counts as the standard of care in ADEM and could accelerate the recovery. ADEM typically affects children (Pohl et al. 2016).

The association between ADEM and SARS-CoV-2 infection has already been established (Zamani et al. 2021). There are also some case reports presenting ADEM occurring after COVID-19 vaccination (Cao and Ren 2021; Kania et al. 2021; Rinaldi et al. 2021). Of note, one ADEM-like presentation has also been reported following coronavirus inactivated vaccine (Ozgen Kenangil et al. 2021). Most of the aforementioned cases were successfully recovered. Therefore, considering the proper response of ADEM to immunotherapy and its association with other vaccines, ADEM may be included in the differential diagnosis list when approaching to a patient with neurological signs and symptoms following receipt of SARS-CoV-2 vaccines.

It remained to be elucidated why ADEM occurs after vaccination – particularly after COVID-19 vaccines. Inflammatory responses are usually involved in the immunization process. It is thought that post-immunization inflammation can lead to cellular or humoral responses against myelin antigens, including myelin oligodendrocyte protein, MBP, and proteolipid protein. Moreover, increased vascular permeability as a result of inflammation can lead to hemorrhage and perivascular edema, finally leading to neuronal damage. Rinaldi et al. also reported a case of ADEM following immunization against SARS-CoV-2 whose autoantibodies and anti-SARS-CoV-2 IgM titers were undetectable, which highlights the role of cell-mediated autoimmunity rather than humoral response (Anilkumar et al. 2021; Rinaldi et al. 2021).

Cranial neuropathies

Different types of cranial neuropathies are thought to be related to COVID-19 vaccines – the most well-known of which is Bell's palsy (BP) (also known as facial palsy).

BP was one of the first adverse events reported in the initial phases of the clinical trials of COVID-19 vaccines (Burrows et al. 2021). Although facial nerve inflammation may result in demyelination, we deliberate on the possible link between facial palsy and COVID-19 vaccines under a separate section due to the abundance of its cases related to SARS-CoV-2 vaccines. While BP has occurred following

different types of COVID-19 vaccines, the significant increase in BP incidence after administration of mRNA-based vaccines put forward a possible causal association between BP and mRNA vaccines (Sato et al. 2021).

BP is a peripheral nerve neuropathy, in which the seventh cranial nerve (CN VII) is affected. In this condition, unilateral weakness or paralysis of the facial muscles occurs as a result of lower motor neuron involvement. Since the facial nerve also carries parasympathetic fibers to salivary and lacrimal glands, a patient with facial nerve palsy may also experience xerophthalmia and xerostomia. Without any treatments, about 70% of BP patients will be completely recovered. While different triggers, including reactivation of herpes simplex virus and GBS, are assumed to contribute to the development of BP, its precise etiology remains to be recognized (Eviston et al. 2015).

Recent incidence of BP following influenza vaccines has brought to scientists' attention the possibility of developing BP after vaccination. On the other hand, a noticeable number of BP cases having received mRNA-based COVID-19 vaccines reinforces the link between vaccination and BP. According to an analysis of self-reporting cases based on Vaccine Adverse Event Reporting System (VAERS), a statistically significant relationship between BP and mRNA-based SARS-CoV-2 vaccines can be established. However, due to the biases inherent in self-reporting system, any conclusion should be drawn cautiously in this respect (Sato et al. 2021). Moreover, given the harmless and manageable nature of this condition, public stress concerning this complication should not lead to vaccine hesitancy within societies.

Suggested mechanisms of the association between mRNA vaccines and BP assumes that the combination of mRNA and lipid nanoparticles in these kinds of vaccines may contribute to the production of specific interferons as a result of innate immune response. These interferons along with other cytokines (cytokine storm) can in turn lead to bystander activation of cytotoxic T cells and lead to direct neuronal damage. Moreover, the cytokine storm itself can induce an inflammatory state, leading to congestion and ischemia of the facial nerve at the site of geniculate ganglion (Ozonoff et al. 2021; Warner et al. 2021). Putting together, these mechanisms are thought to lead to vaccine-induced BP.

BP is not the only cranial neuropathy occurring following COVID-19 vaccination. In this regard, there have been cases of abducent nerve palsy (Reyes-Capo et al. 2021), olfactory dysfunction (Keir et al. 2021; Konstantinidis et al. 2021), sensorineural hearing loss (Jeong and Choi 2021; Tsetsos et al. 2021), and NMO (Badrawi et al. 2021; Chen et al. 2021; Fujikawa et al. 2021; Khayat-Khoei et al. 2021). Detailed information about these conditions and their relation to COVID-19 vaccines are provided in Table 3.

Cerebrovascular complications

Since the emergence of SARS-CoV-2, a number of infected patients have experienced cerebrovascular complications (Mishra et al. 2020). It is known that SARS-CoV-2, similar to other coronaviruses, enters the target cells via ACE-2 receptor. Given the expression of ACE-2 receptor in different parts of the human body including endothelia (Mishra et al. 2020), vascular injury as a consequence of COVID-19 infection may lead to a hypercoagulable state (Kichloo et al. 2020), causing life-threatening complications in different organs.

However, the presence of such complications in the context of COVID-19 vaccination raised questions about the possible underlying mechanism and safety concerns (Sharifian-Dorche et al. 2021). It is known that VITT can contribute to the clot formation after administration of SARS-CoV-2 vaccines (Sharifian-Dorche et al. 2021). Although VITT has also occurred following mRNA vaccines, it is mostly connected with the vaccines containing adenoviral vectors (Sharifian-Dorche et al. 2021). The mechanism of VITT is somehow similar to heparin-induced thrombocytopenia. In other words, VITT is a variant of autoimmune heparin-induced thrombocytopenia (aHIT) (Arepally and Ortel 2021), in which IgG autoantibodies binds to the complex of heparin and platelet factor 4 (PF4). Then the newformed complex binds to FcRγIIA receptors located on platelets. As a result, platelets are activated and a coagulation cascade is initiated, leading to thrombocytopenia (Arepally and Ortel 2021; Sharifian-Dorche et al. 2021).

VITT is thought to happen in a similar way (Figure 2). It is postulated that the DNA particle assembled in the adenovirus-based vaccines makes a complex with PF4 and anti-PF4. Then, the aforementioned complex binds to platelets FcRγIIA receptors. Consequently, platelet microparticles are released and the coagulation process is initiated (Sharifian-Dorche et al. 2021). Although any organ can be involved in VITT theoretically, it typically affects cerebral and splanchnic veins in cases related to SARS-CoV-2 vaccines (Arepally and Ortel 2021; Sharifian-Dorche et al. 2021). In the following sections, three cerebrovascular conditions that occur as a result of VITT are covered.

Cerebral venous sinus thrombosis

Cerebral venous sinus thrombosis (CVST) is a type of cerebrovascular disorder which, contrary to arterial strokes,

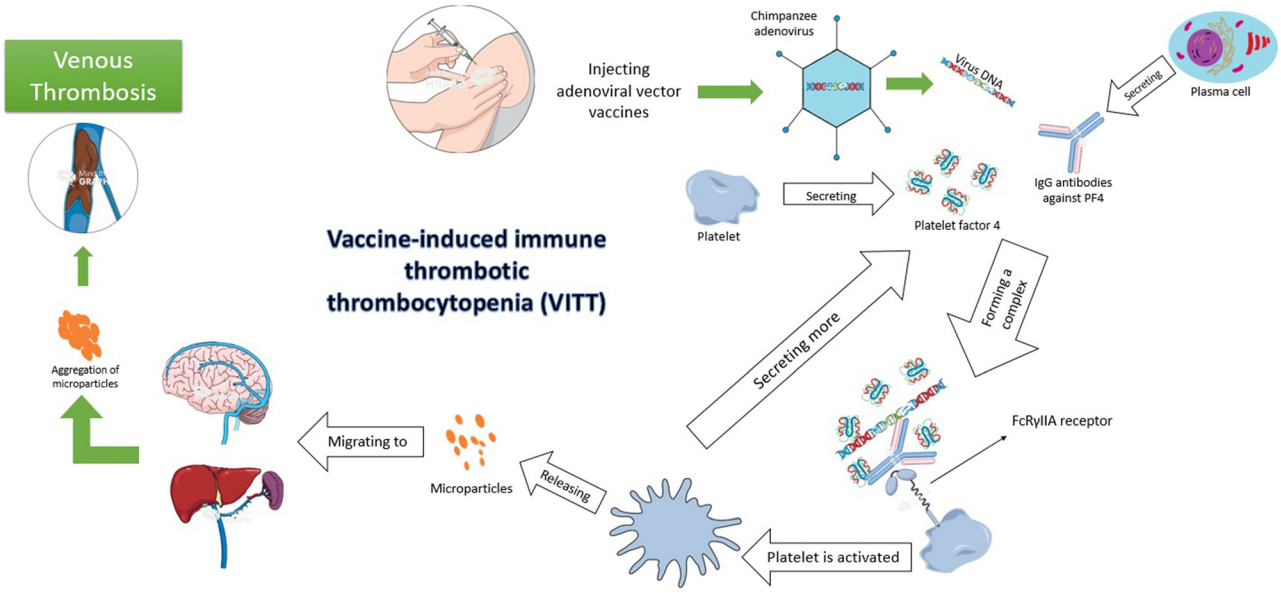

Figure 2: Vaccine-induced thrombotic thrombocytopenia pathophysiology (created by mindthegraph.com).

mostly affects the youth (Stam 2005). Symptoms may differ based on the site of the affected vein. Nevertheless, headache is the most common symptom associated with CVST. As the condition progressed, focal neurological signs may also occur as a result of seizure and cerebral venous infarction. Early diagnosis and timely management of CVTS may increase the chance of complete recovery (Sharifian-Dorche et al. 2021).

CVST has been reported following administration of COVID-19 vaccines. As mentioned earlier, VITT triggered by COVID-19 vaccines has a propensity to cause thrombosis in splanchnic and cerebral veins. In this regard, a recognizable number of individuals have presented with CVST after receiving SARS-CoV-2 vaccines – especially adenovirus-based ones. According to a recent systematic review, out of the total number of 49 patients presented with CVST after administration of ChAdOx1 nCoV-19 and Ad26.COV2 vaccines, 19 of them died, highlighting the life-threatening characteristic of CVST (Sharifian-Dorche et al. 2021). Although headache is a common side effect of COVID-19 vaccines, prolonged headaches accompanied by symptoms such as blurred vision may be an alarm symptom of CVST in individuals vaccinated with adenoviral vector vaccines. If the aforementioned symptoms coexist with VITT manifestations, including petechiae, easy bleeding and bruising, the clinical suspicion toward post-vaccination CVST is strengthened (Sharifian-Dorche et al. 2021).

Due to the potential fatal nature of VITT, any related symptoms presenting up to four weeks after administration of adenoviral vector vaccines should be clinically investigated (Arepally and Ortel 2021). Once diagnosed, VITT should be carefully managed (Figure 3).

Administration of non-heparin anticoagulants along with high-dose IVIg (1 g/kg daily for at least two days) is the first-line therapy for VITT. IVIg inhibits platelet activation by hindering anti-PF4 antibodies from binding to FcRγIIA receptors. As a result, platelet count comes back to normal. Expert opinions indicate that high-dose glucocorticoids may increase the platelet count as well. Plasmapheresis is another option, which can decrease the levels of autoantibodies contributing to the hypercoagulable state. Of note, platelet transfusion and administration of heparin must be avoided in VITT patients because of the risk of further platelet activation and coagulation. It is shown that platelet transfusion significantly increases the mortality rate and the risk of arterial thrombosis in HIT patients and it may be considered only in case of severe bleeding. Aspirin and P2Y12 inhibitors are not recommended due to the lack of evidence. Invasive interventions, including thrombectomy, are recommended in patients whose condition worsens despite receiving routine treatments (Arepally and Ortel 2021; Ferro and Canhao 2014; Pai et al. 2021; Rizk et al. 2021; Sharifian-Dorche et al. 2021).

Ischemic stroke and hemorrhagic stroke

According to the Centers for Disease Control and Prevention (CDC), the two major types of strokes are ischemic stroke and hemorrhagic stroke. Ischemic stroke happens when the blood is not properly supplied to the brain while the other type of stroke (hemorrhagic stroke) occurs when

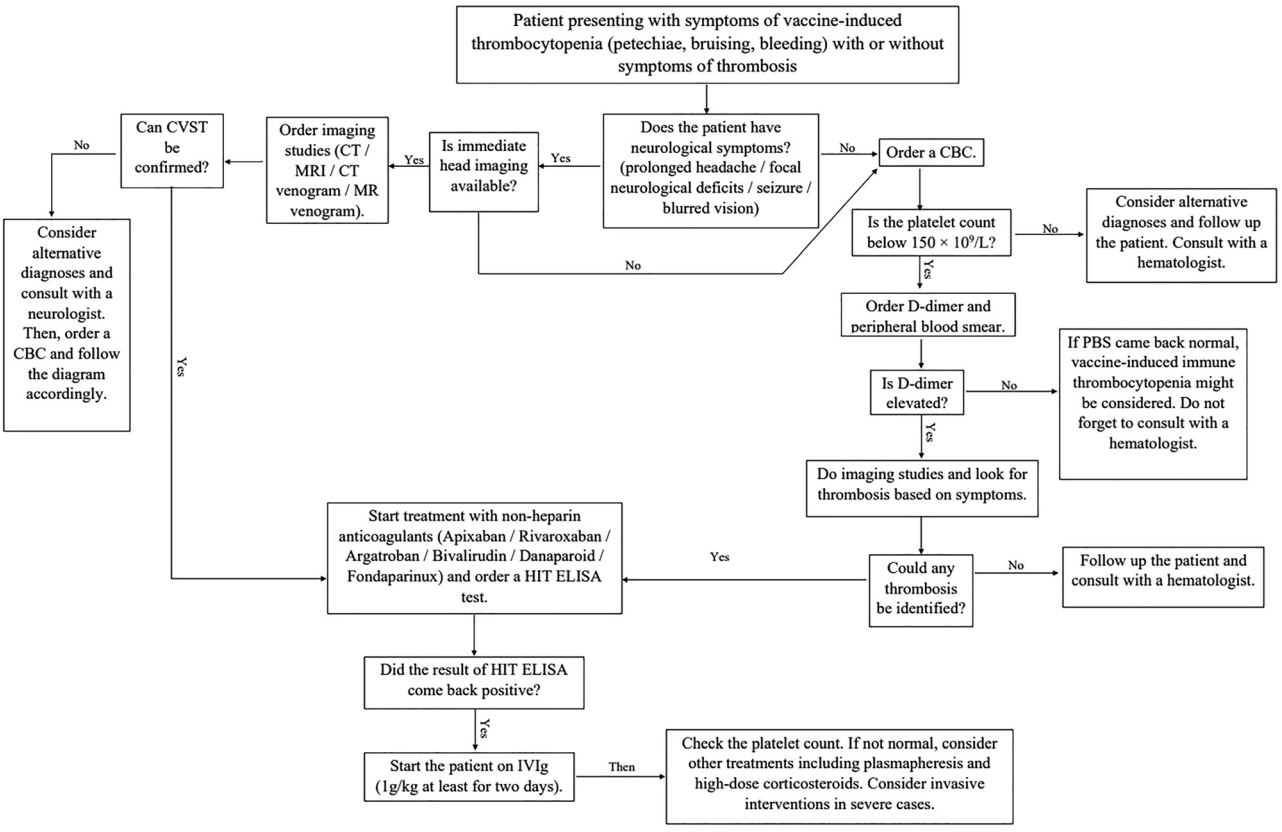

Figure 3: Management of vaccine-induced thrombotic thrombocytopenia.

blood leaks in the brain following arterial rupture or other causes. The latter is also divided to two subtypes, namely intracranial hemorrhage (ICH) and subarachnoid hemorrhage (SAH). While ischemic stroke is mostly caused by thromboembolic events, conditions such as hypertension and aneurysm may lead to hemorrhagic stroke (Centers for Disease Control and Prevention 2021).

Although the incidence rate of ischemic stroke is generally more than CVST, in case of VITT triggered by COVID-19 vaccination quite the opposite is true. In other words, because VITT mostly occurs in veins, the incidence of ischemic stroke following COVID-19 vaccines are relatively unlikely. Nevertheless, there are a few reports of ischemic strokes due to arterial thrombosis following VITT – particularly affecting middle cerebral arteries (Sharifian-Dorche et al. 2021).

In case of hemorrhagic stroke, the situation is different given the possibility of its occurrence following CVST. Increased intracranial pressure as a consequence of CVST may lead to cerebral edema and the leakage of blood into the brain. CVST can be complicated by both ICH and SAH. Therefore, timely and proper management of CVST may also prevent from such complications. Although using anticoagulants in case of CVST can increase the chance of brain hemorrhage, its risk no way outweighs the risk of life-threatening problems occurring as a result of thrombus progression. Therefore, ICH and SAH in CVST patients are not considered as contraindications for anticoagulant therapy. In fact, appropriate management of CVST can significantly reduce the risk of other serious neurological sequelae.

Seizure

The association between vaccination and seizure is not a newly emerging issue. Although vaccine-induced seizure is not considered as a distinct neurological disease and it occurs as an indirect consequence of other neurological conditions related to vaccines, we discuss it in a separate section due to its important link with vaccination, as an indirect effect induced by other adverse effects of COVID-19 vaccination. Vaccination is the second leading cause of febrile seizures (FS) (also known as fever-induced seizures) which are defined as the seizures happening up to 72 h following a vaccine shot (Li et al. 2018). Prolonged FS is considered as a risk factor for temporal epilepsy. Although the exact physiopathology of FS is not fully understood,

animal studies suggest that alterations in specific ion channels along with increased neuronal firing triggered by certain cytokines may account for the development of FS. Moreover, genetic factors including mutations in γ_2 subunits of $GABA_A$ receptor and sodium channels, and decreasing seizure threshold by some types of cytokines (especially IL-1) can also account for the development of fever-induced seizures (Dube et al. 2009; Li et al. 2018).

While there are several reports of FS cases due to pediatric COVID-19 infection (Smarrazzo et al. 2021), there is a lack of evidence whether or not SARS-CoV-2 vaccines can trigger FS (Lu et al. 2021). However, the possible incidence of FS following COVID-19 vaccination can be attributed to certain conditions – a well-known example of which is Dravet syndrome (DS) (Clayton et al. 2021). DS is an epileptic encephalopathy presented with early-onset FS followed by subsequent afebrile seizures later in life. According to a national survey conducted by Clayton et al. a small number of DS patients complained of an increase in the frequency of seizures after the first dose of COVID-19 vaccines. However, this number was not worrisome and DS is not counted as a contraindication for SARS-CoV-2 vaccines (Clayton et al. 2021).

Seizures happening as a consequence of COVID-19 vaccination mostly occur following other neurological conditions – and not fever. There are several conditions which can present with seizure following COVID-19 vaccination. CVST can lead to the blockage of venous circulation and subsequent cerebral edema, which, in turn, may cause venous rupture and hemorrhagic stroke. This cascade of events can lead to acute symptomatic seizures (Mehvari Habibabadi et al. 2018; Schaller and Graf 2004). Conditions causing encephalopathy can also predispose individuals to seizures. For example, Liu et al. reported two cases of COVID-19 vaccine-induced encephalopathy who developed seizure in the absence of fever (Liu et al. 2021). It is postulated that mRNA-based and DNA-based vaccines induce the production of SARS-CoV-2 S proteins. Interaction between these proteins and ACE-2 receptors reduces the level of brain-derived neurotrophic factor (BDNF). As a result, inflammatory responses may increase and induce seizure (Liu et al. 2021). As another example, Kwon and Kim reported a case of post-vaccination autoimmune encephalitis after AstraZeneca vaccine in which the patient had experienced an episode of seizure for the first time in her life. Seizures recurred after a few weeks as her condition was exacerbated (Kwon and Kim 2021). Although no causality can be established in this regard, the relevance of autoimmune encephalitis to COVID-19 vaccines cannot be theoretically rejected due to the neurotropism of the SARS-CoV-2 antigen (Yachou et al. 2020). On the other hand, given the fact that encephalitis has occurred following non-COVID-19 vaccines (Huynh et al. 2008), the possibility of its occurrence after COVID-19 vaccines might not be totally rejected.

Surprisingly, vaccine-induced seizures can also be triggered by psychological stressors. As discussed in the section of functional disorders in this article, psychogenic non-epileptic seizure (PNES) is considered as a typical symptom of conversion disorder (Tsui et al. 2017). PNES can also happen as a consequence of the fear of vaccination – whose scientific term is immunization stress-related response (ISRR) (Gold et al. 2020; Lu et al. 2021).

Although seizure should not be considered as a direct side effect of COVID-19 vaccines, further studies are needed to shed light on different predispositions, which might count for the risk factors of vaccine-induced conditions that might be complicated by seizures in COVID-19 vaccine recipients.

Other rare neurological complications

Besides the disorders discussed so far, some patients have presented with a number of uncommon neurological manifestations, which are thought to have a possible relation to SARS-CoV-2 vaccines.

Some cases of infrequent and unusual neurological presentations have been reported in patients vaccinated against COVID-19. In this regard, there have been cases of aphasia following administration of both adenoviral vector-based and mRNA vaccines (Finsterer and Korn 2021; Sharifian-Dorche et al. 2021), small fiber neuropathy (Waheed et al. 2021), and other complications including Tolosa-Hunt syndrome (Chuang et al. 2021) and Parsonage-Turner syndrome (Queler et al. 2021). Detailed information about these conditions and their relation to COVID-19 vaccines are provided in Table 3.

Take the note that the rareness of the above-mentioned complications and other similar conditions in no way denies the possibility of their occurrence post-COVID-19 vaccination. This statement is further emphasized given the fact that most of them can be properly managed and leave no significant sequelae if treated opportunely.

Functional neurological disorder

Functional neurological disorder (FND, also called conversion disorder) is usually assumed a non-structural neuropsychiatric condition typically characterized by impaired

neurological function with no accompanied structural pathology (Lehn et al. 2016). According to Diagnostic and Statistical Manual of Mental Disorders (DSM-5), patients with FND commonly present with sensory or motor neurological dysfunction, which is incompatible with the estimated condition at the time of diagnosis. However, the overlap between FNDs and neurostructural disorders should not be neglected given the fact that this boundary has become more obscure these days (Tinazzi et al. 2021a). In addition, there might also be an overlay between different phenotypes of FND and therefore patients with FND might present with incongruent and varied symptoms such as paralysis, weakness, dysphagia, and PNES (Tinazzi et al. 2021b; Tsui et al. 2017). FND patients usually suffer significantly from functional impairments, which makes harder for them to act normally in different social and occupational states.

Several risk factors are assumed to have a link with FNDs. Other than psychological stressors and predispositions, conditions triggered by physical traumas and preexisting pain can contribute to the development of FNDs (Stone et al. 2009). In other words, FNDs can also happen regardless of the presence of psychological stressors as main triggers. However, the role of such stressors and mental conditions should never be underestimated in this context.

It is undeniable that the current pandemic has left a huge psychological burden on the world and a large number of people has gone through stressful and traumatic events. According to a meta-analysis conducted by Cooke et al. (2020), about one fourth of adults are in need of mental health services during the current pandemic. On the other hand, misinformation and spread of false beliefs and exaggeration about potential side effects of vaccines in the ongoing infodemic has put a large psychological pressure on societies and exacerbated vaccine hesitancy.

Considering the above-mentioned psychological burden, the incidence of FNDs in the current era may not be unlikely. Spread of health anxiety and public fear related to COVID-19 along with worldwide quarantine and lockdown on one hand (Fasano and Daniele 2021), and the widespread misinformation and pseudoscientific statements released by antivaxxers on the other hand, are attributed to the emergence of psychological stressors within different populations. As mentioned earlier, there is also strong evidence on the fact that natural disasters and terrorism can increase the incidence rate of FNDs (Fasano and Daniele 2021).

Not surprisingly, different cases of FND have been reported after administration of SARS-CoV-2 vaccines (Ercoli et al. 2021; Fasano and Daniele 2021). Although a part of this information is obtained from questionable videos uploaded on social media (Kim et al. 2021a), there are a few points which should be taken into consideration.

First, unlike what most clinicians might think, FND is a common complaint among outpatient visits in neurology settings and should not be considered as a diagnosis of exclusion – especially considering the possibility of the overlap between FND and different neurological conditions. According to experts, many of the videos uploaded on media as medical mysteries are FNDs – even those that are not related to vaccination. Therefore, more awareness toward FND is necessary in clinical setting (Kim et al. 2021a; Tinazzi et al. 2021a).

Second, the incidence of FND following COVID-19 vaccination should not be interpreted as toxicity of vaccines themselves and can even happen after normal saline injection. In fact, FND is a multi-dimensional disorder and many known and unknown interconnected biological and socio-psychological factors can account for this disorder. Therefore, mental processing of beliefs, emotions and threats, and aroused attention toward the body may play a major role in the pathogenesis of FND accordingly. In other words, abnormal beliefs, such as pseudoscientific beliefs about devastating side effects of COVID-19 vaccines, may arouse the attention toward the body and lead to abnormal motor symptoms. Moreover, given the disturbance of readiness potentials in FND patients, they might think that the symptoms are involuntary (Edwards et al. 2012; Kim et al. 2021a; Voon et al. 2010).

Finally, dissemination of correct information and proper public education are the key factors to overcome this issue. Nocebo responses, which are defined as adverse effects occurring in the placebo arm of randomized controlled trials, are known to be attributed to the anxiety and false beliefs people have about vaccines' adverse effects. Studies show that providing patients with correct information regarding nocebo responses may lead to a reduction in the incidence rate of these responses. Therefore, while public fear about FND and other nocebo effects can worsen the vaccine hesitancy, informing people of the exact nature of FND and safety of the vaccines can build trust between the healthcare system and the populace. For example, if people know that FND occurs psychosomatically, and not as a result of vaccination, much of the health anxiety on this issue will be settled (Haas et al. 2022; Kim et al. 2021a).

Existing challenges

Undeniably, vaccines are the most effective and practical way to tackle the current pandemic. However, since they

are being rapidly distributed and widely used, their safety is an important matter of issue than ever. Meanwhile, several challenges have been existed from the early days of the COVID-19 pandemic in societies' strategies to combat the disease and in establishing a firm link between the associated complications of COVID-19 infection with the virus, in which the remarkable effect of the infodemic and numerous invalid report sources could not be neglected (Mohamed et al. 2021; Yazdanpanah et al. 2020). The same story has been initiated about COVID-19 vaccination and its adverse effects.

Although different studies emphasize the fact that neurological side effects of COVID-19 vaccines are rare (Lu et al. 2021; Patone et al. 2021), the probability of incidence of such complications should not be underestimated. In other words, it should be accepted that COVID-19 vaccines might not be without neurological complications. Studies support the fact that individuals receiving SARS-CoV-2 vaccines are statistically more prone to develop neurological complications (Patone et al. 2021). However, here are some important points that should be considered.

There are lessons we can learn from previous experiences. As mentioned earlier, concerns about neurological side effects of vaccines is an old discussion. In 1998, Wakefield et al. raised the hypothesis that MMR vaccination might cause autism in children. Since they were working on the association between measles vaccine and inflammatory bowel disease (IBD), the link between autism and IBD found in their study reinforced their hypothesis. Surprisingly, eight out of 12 children enrolled in their study (who had the history of IBD and developmental disorders including autism) experienced exacerbation of their behavioral problems after receiving MMR vaccine according to their physicians or parents. These findings and the way media interpreted them resulted in a huge public fear of MMR vaccination. The outcome of such fear was not favorable. Many parents refused to vaccinate their child and measles outbreak occurred consequently in the United Kingdom. Although a large number of large-scale studies statistically rejected the causal link between MMR vaccine and autism, MMR vaccine coverage was still less than before even after 10 years. However, because of the retraction of Wakefield's article and abundant evidence approving the safety of MMR vaccines, vaccine acceptance rate gradually increased and measles was finally eliminated in 2016 (DeStefano and Shimabukuro 2019).

Another helpful experience is about influenza vaccine and GBS. Safety concerns about the swine flu vaccine were raised in 1976 when studies showed vaccine recipients were eight times more likely to develop GBS. These findings prompted the United States government to suspend swine flu vaccination program. Later studies found inconsistent results and the issue still remained controversial. Finally, after the emergence of H1N1 virus and the following pandemic in 2009, cumulative analysis of available data showed that unvaccinated people were at a much higher risk for GBS compared to vaccinated individuals. This was because of the fact that influenza infection itself could result in more harm than influenza vaccine. In other words, refusing vaccines because of the risk of GBS could predispose individuals much more to developing this condition (Vellozzi et al. 2014).

Given the two above-mentioned experiences, similar course might be ongoing for COVID-19 vaccines. Currently, much of the literature regarding neurological complications of COVID-19 vaccines consists of small population researches. It could be hypothesized that if studies with very large amount of population (as studies on influenza and MMR vaccines) are conducted, the risk of such complications might be obtained very low. Alternatively, looking for certain modifiable or non-modifiable risk factors that predisposes the patients to overreact to COVID-19 vaccines and develop serious adverse outcomes is highly recommended. For example, it is shown that post-COVID-19 vaccination GBS rate increases by age and females who are between 30 and 49 years old are at the highest risk of CVST triggered by VITT (Ashrani et al. 2021; Li et al. 2021). This approach helps experts to determine exact contraindications or cautions that should be taken into consideration when encountering COVID-19 vaccines.

Another approach should focus on the comparison between COVID-19 vaccines and COVID-19 infection itself. In other words, pros and cons of vaccination over the disease itself must be precisely determined. As preliminary studies show, as in the history of influenza vaccine, the risk of developing neurological complications following SARS-CoV-2 vaccines is far less than the same risk after COVID-19 infection itself (Patone et al. 2021). Further studies with large populations are recommended to achieve more precise information in this regard.

Studies should also focus on the different features of various vaccine platforms. It is shown that some adverse outcomes are more likely to happen after certain vaccine platforms. For example, CVST is much more related to adenoviral vector vaccines (Sharifian-Dorche et al. 2021). Doing so, information gathered by vaccine surveillance reports can help healthcare systems to compare different platforms and determine which ones fit better in different populations. Further studies investigating the possibility of neurological complications triggered by different types of vaccines are strongly recommended. This can also guide the policymakers to decide and act properly.

Conclusions

COVID-19 vaccines, with all their effectiveness, are not without neurological side effects. In this review, different neurological complications of COVID-19 vaccines are discussed. Obviously, cerebrovascular complications are the most life-threatening side effects of COVID-19 vaccines and adequate attention should be drawn toward them in the clinical setting. Among other conditions discussed in this paper, demyelinating disorders can also lead to significant morbidity if left untreated. Immunotherapy could be considered in these conditions.

BP is reported as a frequent side effect of COVID-19 vaccines – especially mRNA vaccines. More researches with more meticulous methodologies are needed to investigate the relationship between BP and mRNA vaccines. Moreover, further studies also recommended to discover the propensity of BP for mRNA vaccines and shed the light on precise mechanisms. Importantly, given the harmless and manageable nature of this condition, public stress concerning this complication should not lead to vaccine hesitancy within societies.

Vaccination is one of the main known etiologies for FS. Although no cases of FS have been reported as a result of immunization against SARS-CoV-2, its possibility should never be neglected, as it has happened following other previous vaccines. Seizure can also complicate other neurological conditions, which are thought to have a link with vaccination – a well-known example of which is CVST.

Some rare conditions that have occurred after COVID-19 vaccination were also discussed, including unusual cranial nerve dysfunctions and brachial plexus neuropathy; whether these conditions have a causal or coincidental relationship with COVID-19 vaccines remains unknown given the lack of evidence in the current literature.

Lastly, FNDs that are attributed related to the psychological burden of the current pandemic were comprehensively discussed. Although psychological stressors may count as a risk factor for different psychosomatic disorders, FND is relatively more important to discuss – since it can be mistaken for other devastating neurological diseases and impose anxiety on societies. In this regard, it is necessary to be cautious of the socio-psychological atmosphere regarding COVID-19 vaccination. As discussed earlier, lessons we learned from MMR vaccine hesitancy and the increase in number of FND cases in the current pandemic put an emphasis on the fact that psychological stressors and vaccine hesitancy fueled by social media misinterpretations might have a larger burden than ever expected. Therefore, dissemination of correct information and proper public education are the key factors to overcome the above-said issue and can build trust between healthcare system and the populace. Of note, the current review was also intended to be in line with the aforementioned goal.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.
Research funding: None declared.
Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

References

Abu-Rumeileh, S., Abdelhak, A., Foschi, M., Tumani, H., and Otto, M. (2021). Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. J. Neurol. 268: 1133–1170.

Andrzejczak-Grządko, S., Czudy, Z., and Donderska, M. (2021). Side effects after COVID-19 vaccinations among residents of Poland. Eur. Rev. Med. Pharmacol. Sci. 25: 4418–4421.

Agarwal, A., Garg, D., Goyal, V., Pandit, A.K., Srivastava, A.K., and Srivastava, M.P. (2020). Optic neuritis following anti-rabies vaccine. Trop. Doct. 50: 85–86.

Agmon-Levin, N., Kivity, S., Szyper-Kravitz, M., and Shoenfeld, Y. (2009). Transverse myelitis and vaccines: a multi-analysis. Lupus 18: 1198–1204.

Algahtani, H., Subahi, A., and Shirah, B. (2016). Neurological complications of Middle East respiratory syndrome coronavirus: a report of two cases and review of the literature. Case Rep. Neurol. Med. 2016: 3502683.

Almqvist, J., Granberg, T., Tzortzakakis, A., Klironomos, S., Kollia, E., Öhberg, C., Martin, R., Piehl, F., Ouellette, R., and Ineichen, B.V. (2020). Neurological manifestations of coronavirus infections - a systematic review. Ann. Clin. Transl. Neurol. 7: 2057–2071.

Alp, H., Tan, H., and Orbak, Z. (2009). Bell's palsy as a possible complication of hepatitis B vaccination in a child. J. Health Popul. Nutr. 27: 707–708.

Amrutkar, C. and Burton, E.V. (2021). *Tolosa-hunt syndrome*. StatPearls. StatPearls Publishing LLC, Treasure Island (FL, USA).

Anghelina, D., Zhao, J., Trandem, K., and Perlman, S. (2009). Role of regulatory T cells in coronavirus-induced acute encephalitis. Virology 385: 358–367.

Anilkumar, A.C., Foris, L.A., and Tadi, P. (2021). *Acute disseminated encephalomyelitis*. StatPearls. StatPearls Publishing LLC, Treasure Island (FL, USA).

Arabi, Y.M., Harthi, A., Hussein, J., Bouchama, A., Johani, S., Hajeer, A.H., Saeed, B.T., Wahbi, A., Saedy, A., Aldabbagh, T., et al. (2015). Severe neurologic syndrome associated with Middle East respiratory syndrome corona virus (MERS-CoV). Infection 43: 495–501.

Arepally, G.M. and Ortel, T.L. (2021). Vaccine-induced immune thrombotic thrombocytopenia (VITT): what we know and don't know. Blood 138: 293–298.

Ashrani, A.A., Crusan, D.J., Petterson, T., Bailey, K., and Heit, J.A. (2021). Age- and sex-specific incidence of cerebral venous sinus

thrombosis associated with Ad26.COV2.S COVID-19 vaccination. JAMA Intern. Med 182: 80–83.

Badrawi, N., Kumar, N., and Albastaki, U. (2021). Post COVID-19 vaccination neuromyelitis optica spectrum disorder: case report and MRI findings. Radiol. Case Rep. 16: 3864–3867.

Bahri, F., Letaief, A., Ernez, M., Elouni, J., Chekir, T., Ben Ammou, S., and Jemni, L. (1996). [Neurological complications in adults following rabies vaccine prepared from animal brains]. Presse Med. 25: 491–493.

Barboi, A., Gibbons, C.H., Axelrod, F., Benarroch, E.E., Biaggioni, I., Chapleau, M.W., Chelimsky, G., Chelimsky, T., Cheshire, W.P., Claydon, V.E., et al. (2020). Human papillomavirus (HPV) vaccine and autonomic disorders: a position statement from the American Autonomic Society. Clin. Auton. Res. 30: 13–18.

Batum, M., Kisabay Ak, A., and Mavioğlu, H. (2020). Covid-19 infection-induced neuromyelitis optica: a case report. Int. J. Neurosci.: 1–7, https://doi.org/10.1080/00207454.2020.1860036.

Bayão, T.S., Cupertino, M.D.C., Gomes, A.P., and Siqueira-Batista, R. (2018). Yellow fever vaccination and neurological complications. Rev. Soc. Bras. Med. Trop. 51: 723–724.

Bayas, J.M., González-Alvarez, R., and Guinovart, C. (2007). Herpes zoster after yellow fever vaccination. J. Trav. Med. 14: 65–66.

Beh, S.C., Greenberg, B.M., Frohman, T., and Frohman, E.M. (2013). Transverse myelitis. Neurol. Clin. 31: 79–138.

Beirão, P., Pereira, P., Nunes, A., and Antunes, P. (2017). Yellow fever vaccine-associated neurological disease, a suspicious case. BMJ Case Rep. 2017: 1–3.

Berglund, A. (1963). Paralytic brachial neuritis after poliomyelitis vaccination. Sven. Lakartidn. 60: 37–39.

Biorklund, H. (1963). Acute shoulder neuritis after smallpox vaccination. Sven. Lakartidn. 60: 1772–1774.

Bourtoulamaiou, A., Yadav, S., and Nayak, H. (2015). Benign recurrent sixth (abducens) nerve palsy following measles-mumps-rubella vaccination. Case Rep. Pediatr. 2015: 734516.

Burrows, A., Bartholomew, T., Rudd, J., and Walker, D. (2021). Sequential contralateral facial nerve palsies following COVID-19 vaccination first and second doses. BMJ Case Rep. 14: 1–3.

Cameron, R.L., Ahmed, S., and Pollock, K.G. (2016). Adverse event monitoring of the human papillomavirus vaccines in Scotland. Intern. Med. J. 46: 452–457.

Campos, W.R., Cenachi, S.P.F., Soares, M.S., Gonçalves, P.F., and Vasconcelos-Santos, D.V. (2021). Vogt-Koyanagi-Harada-like disease following yellow fever vaccination. Ocul. Immunol. Inflamm. 29: 124–127.

Cao, L. and Ren, L. (2021). Acute disseminated encephalomyelitis after severe acute respiratory syndrome coronavirus 2 vaccination: a case report. Acta. Neurol. Belg 1–3, https://doi.org/10.1007/%2Fs13760-021-01608-2.

Carol Liu, Y.C., Ibekwe, T., Kelso, J.M., Klein, N.P., Shehu, N., Steuerwald, W., Aneja, S., Dudley, M.Z., Garry, R., and Munoz, F.M. (2020). Sensorineural hearing loss (SNHL) as an adverse event following immunization (AEFI): case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine 38: 4717–4731.

Chen, j. and Lu, H. (2021). New challenges to fighting COVID-19: virus variants, potential vaccines, and development of antivirals. Biosci. Trends 15: 126–128.

Centers for Disease Control and Prevention (2021). Types of stroke. Available at: <https://www.cdc.gov/stroke/types_of_stroke.htm>.

Chen, S., Fan, X.R., He, S., Zhang, J.W., and Li, S.J. (2021). Watch out for neuromyelitis optica spectrum disorder after inactivated virus vaccination for COVID-19. Neurol. Sci. 42: 3537–3539.

Cho, J.H., Park, Y., and Woo, N. (2019). A case of neuromyelitis optica spectrum disorder following seasonal influenza vaccination. Mult. Scler. Relat. Disord. 30: 110–113.

Chuang, T.Y., Burda, K., Teklemariam, E., and Athar, K. (2021). Tolosa-hunt syndrome presenting after COVID-19 vaccination. Cureus 13: e16791.

Clayton, L.M., Balestrini, S., Cross, J.H., Wilson, G., Eldred, C., Evans, H., Koepp, M.J., and Sisodiya, S.M. (2021). The impact of SARS-CoV-2 vaccination in Dravet syndrome: a UK survey. Epilepsy Behav. 124: 108258.

Cohen, M.S. and Corey, L. (2020). *Combination prevention for COVID-19*. American Association for the Advancement of Science.

Cooke, J.E., Eirich, R., Racine, N., and Madigan, S. (2020). Prevalence of posttraumatic and general psychological stress during COVID-19: a rapid review and meta-analysis. Psychiatr. Res. 292: 113347.

De Marco, F., De Cesare, D.P., Di Folco, F., Massoni, F., Tomei, G., Di Luca, N.M., Sacco, C., Tomei, F., and Serafino, R. (2018). Post vaccinal temporary sensorineural hearing loss. Int. J. Environ. Res. Publ. Health 15, https://doi.org/10.3390/ijerph15081780.

Debeer, P., De Munter, P., Bruyninckx, F., and Devlieger, R. (2008). Brachial plexus neuritis following HPV vaccination. Vaccine 26: 4417–4419.

Decio, A., Balottin, U., De Giorgis, V., and Veggiotti, P. (2014). Acute chorea in a child receiving second dose of human papilloma virus vaccine. Pediatr. Allergy Immunol. 25: 295–296.

Desforges, M., Le Coupanec, A., Dubeau, P., Bourgouin, A., Lajoie, L., Dubé, M., and Talbot, P.J. (2019). Human coronaviruses and other respiratory viruses: underestimated opportunistic pathogens of the central nervous system? Viruses 12: 1–28.

Destefano, F. and Shimabukuro, T.T. (2019). The MMR vaccine and autism. Annu. Rev. Virol. 6: 585–600.

Doty, R.L., Berman, A.H., Izhar, M., Hamilton, H.B., Villano, D., Vazquez, B.E., Warrum, M.N., and Mahbob, M. (2014). Influenza vaccinations and chemosensory function. Am. J. Rhinol. Allergy 28: 50–53.

Dube, C.M., Brewster, A.L., and Baram, T.Z. (2009). Febrile seizures: mechanisms and relationship to epilepsy. Brain Dev. 31: 366–371.

Edwards, M.J., Adams, R.A., Brown, H., Pareés, I., and Friston, K.J. (2012). A Bayesian account of 'hysteria. Brain 135: 3495–3512.

El Nawar, R., Bayle, P., Girbovan, A., Marque, S.J., Servan, J., and Pico, F. (2018). Meningomyeloradiculitis following yellow fever 17D vaccination: a case report. J. Neurovirol. 24: 642–646.

Ercoli, T., Lutzoni, L., Orofino, G., Muroni, A., and Defazio, G. (2021). Functional neurological disorder after COVID-19 vaccination. Neurol. Sci. 42: 3989–3990.

Esmanhotto, B.B., Rocha, I.M., Vilar, C.R.L., Haluch, R.F., and Valença, T.P. (2021). Neuromyelitis optica associated with yellow fever vaccination. Acta Neurol. Belg. 121: 567–569.

Eviston, T.J., Croxson, G.R., Kennedy, P.G., Hadlock, T., and Krishnan, A.V. (2015). Bell's palsy: aetiology, clinical features and multidisciplinary care. J. Neurol. Neurosurg. Psychiatry 86: 1356–1361.

Famularo, G., Minisola, G., and Gasbarrone, L. (2015). Ischemic stroke after influenza vaccination. Ann. Pharmacother. 49: 747.

Farez, M.F. and Correale, J. (2011). Yellow fever vaccination and increased relapse rate in travelers with multiple sclerosis. Arch. Neurol. 68: 1267–1271.

Fasano, A. and Daniele, A. (2021). Functional disorders after COVID-19 vaccine fuel vaccination hesitancy. J. Neurol. Neurosurg. Psychiatry 93: 339–340.

Fazzini, E., Fleming, J., and Fahn, S. (1992). Cerebrospinal fluid antibodies to coronavirus in patients with Parkinson's disease. Mov. Disord. 7: 153–158.

Feinberg, J.H. and Radecki, J. (2010). Parsonage-turner syndrome. HSS J. 6: 199–205.

Ferro, J.M. and Canhao, P. (2014). Cerebral venous sinus thrombosis: update on diagnosis and management. Curr. Cardiol. Rep. 16: 523.

Finsterer, J. and Korn, M. (2021). Aphasia seven days after second dose of an mRNA-based SARS-CoV-2 vaccine. Brain Hemorrhages 2: 165–167.

Finsterer, J. and Scorza, F.A. (2021). SARS-CoV-2 vaccines are not free of neurological side effects. Acta Neurol. Scand. 144: 109–110.

Fitzsimmons, W. and Nance, C.S. (2021). Sudden onset of myelitis after COVID-19 vaccination: an under-recognized severe rare adverse event, Available at: SSRN 3841558.

Foley, J.E., Rand, C., and Leutenegger, C. (2003). Inflammation and changes in cytokine levels in neurological feline infectious peritonitis. J. Feline Med. Surg. 5: 313–322.

Frisch, M., Besson, A., Clemmensen, K.K.B., Valentiner-Branth, P., Mølbak, K., and Hviid, A. (2018). Quadrivalent human papillomavirus vaccination in boys and risk of autoimmune diseases, neurological diseases and venous thromboembolism. Int. J. Epidemiol. 47: 634–641.

Frohman, E.M. and Wingerchuk, D.M. (2010). Transverse myelitis. N. Engl. J. Med. 363: 564–572.

Fujikawa, P., Shah, F.A., Braford, M., Patel, K., and Madey, J. (2021). Neuromyelitis optica in a healthy female after severe acute respiratory syndrome coronavirus 2 mRNA-1273 vaccine. Cureus 13: e17961.

Furukawa, Y., Komai, K., and Yamada, M. (2011). Neuromyelitis optica after Japanese encephalitis vaccination. Eur. J. Neurol. 18: e26–e27.

Gao, J.J., Tseng, H.P., Lin, C.L., Shiu, J.S., Lee, M.H., and Liu, C.H. (2021). Acute transverse myelitis following COVID-19 vaccination. Vaccines 9: 1–7.

Gold, M.S., Macdonald, N.E., Mcmurtry, C.M., Balakrishnan, M.R., Heininger, U., Menning, L., Benes, O., Pless, R., and Zuber, P.L.F. (2020). Immunization stress-related response - redefining immunization anxiety-related reaction as an adverse event following immunization. Vaccine 38: 3015–3020.

Goldstein, E.J., Bell, D.J., and Gunson, R.N. (2019). Yellow fever vaccine-associated neurological disease: it is not just the silver generation at risk. BMJ Case Rep. 12: 1–4.

Goss, A.L., Samudralwar, R.D., Das, R.R., and Nath, A. (2021). ANA investigates: neurological complications of COVID-19 vaccines. Ann. Neurol. 89: 856.

Grewal, D.S. and Zeid, J.L. (2014). Isolated abducens nerve palsy following neonatal hepatitis B vaccination. J. Am. Assoc. Pediatr. Ophthalmol. Strabismus 18: 75–76.

Haas, J.W., Bender, F.L., Ballou, S., Kelley, J.M., Wilhelm, M., Miller, F.G., Rief, W., and Kaptchuk, T.J. (2022). Frequency of adverse events in the placebo arms of COVID-19 vaccine trials: a systematic review and meta-analysis. JAMA Netw. Open 5: e2143955.

Hamati-Haddad, A. and Fenichel, G.M. (1997). Brachial neuritis following routine childhood immunization for diphtheria, tetanus, and pertussis (DTP): report of two cases and review of the literature. Pediatrics 99: 602–603.

Hamming, I., Timens, W., Bulthuis, M.L., Lely, A.T., Navis, G., and Van Goor, H. (2004). Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J. Pathol. 203: 631–637.

Hanaei, S. and Rezaei, N. (2020). COVID-19: developing from an outbreak to A pandemic. Arch. Med. Res. 51: 582–584.

Heekin, R., Gandhy, C., and Robertson, D. (2015). Seronegative neuromyelitis optica spectrum disorder following exposure to hepatitis B vaccination. Case Rep. Neurol. 7: 78–83.

Hirose, S., Hara, M., Koda, K., Natori, N., Yokota, Y., Ninomiya, S., and Nakajima, H. (2021). Acute autoimmune transverse myelitis following COVID-19 vaccination: a case report. Medicine 100: e28423.

Hovaguimian, A. and Gibbons, C.H. (2011). Diagnosis and treatment of pain in small-fiber neuropathy. Curr. Pain Headache Rep. 15: 193–200.

Hu, B., Guo, H., Zhou, P., and Shi, Z.-L. (2021). Characteristics of SARS-CoV-2 and COVID-19. Nat. Rev. Microbiol. 19: 141–154.

Hu, J., Jolkkonen, J., and Zhao, C. (2020). Neurotropism of SARS-CoV-2 and its neuropathological alterations: similarities with other coronaviruses. Neurosci. Biobehav. Rev. 119: 184–193.

Huynh, W., Cordato, D.J., Kehdi, E., Masters, L.T., and Dedousis, C. (2008). Post-vaccination encephalomyelitis: literature review and illustrative case. J. Clin. Neurosci. 15: 1315–1322.

Hviid, A., Svanström, H., Scheller, N.M., Grönlund, O., Pasternak, B., and Arnheim-Dahlström, L. (2018). Human papillomavirus vaccination of adult women and risk of autoimmune and neurological diseases. J. Intern. Med. 283: 154–165.

Ismail, I.I. and Salama, S. (2021). Association of CNS demyelination and COVID-19 infection: an updated systematic review. J. Neurol. 269: 1–36.

Jarius, S., Paul, F., Weinshenker, B.G., Levy, M., Kim, H.J., and Wildemann, B. (2020). Neuromyelitis optica. Nat. Rev. Dis. Prim. 6: 85.

Jeong, J. and Choi, H.S. (2021). Sudden sensorineural hearing loss after COVID-19 vaccination. Int. J. Infect. Dis. 113: 341–343.

Kafaie, J., Kim, M., and Krause, E. (2016). Small fiber neuropathy following vaccination. J. Clin. Neuromuscul. Dis. 18: 37–40.

Kania, K., Ambrosius, W., Tokarz Kupczyk, E., and Kozubski, W. (2021). Acute disseminated encephalomyelitis in a patient vaccinated against SARS-CoV-2. Ann. Clin. Transl. Neurol 8: 2000–2003.

Karimi, N., Boostani, R., Fatehi, F., Panahi, A., Okhovat, A.A., Ziaadini, B., Basiri, K., Abdi, S., Sinaei, F., Rezaei, M., et al. (2021). Guillain-Barre syndrome and COVID-19 vaccine: a report of nine patients. Basic Clin. Neurosci. J 12: 703–710.

Keir, G., Maria, N.I., and Kirsch, C.F.E. (2021). Unique imaging findings of neurologic phantosmia following Pfizer-BioNtech COVID-19 vaccination: a case report. Top. Magn. Reson. Imag. 30: 133–137.

Khan, E., Shrestha, A.K., Colantonio, M.A., Liberio, R.N., and Sriwastava, S. (2021). Acute transverse myelitis following SARS-CoV-2 vaccination: a case report and review of literature. J. Neurol. 269: 1–12.

Khayat-Khoei, M., Bhattacharyya, S., Katz, J., Harrison, D., Tauhid, S., Bruso, P., Houtchens, M.K., Edwards, K.R., and Bakshi, R. (2021).

COVID-19 mRNA vaccination leading to CNS inflammation: a case series. J. Neurol. 269: 1–14.
Kichloo, A., Dettloff, K., Aljadah, M., Albosta, M., Jamal, S., Singh, J., Wani, F., Kumar, A., Vallabhaneni, S., and Khan, M.Z. (2020). COVID-19 and hypercoagulability: a review. Clin. Appl. Thromb. Hemost. 26, 1076029620962853.
Kim, D.D., Kung, C.S., and Perez, D.L. (2021a). Helping the public understand adverse events associated with COVID-19 vaccinations: lessons learned from functional neurological disorder. JAMA Neurol. 78: 789–790.
Kim, J.G., Kim, S.Y., Oh, H.S., and Jo, D.H. (2021b). Parsonage-Turner syndrome following typhoid vaccination. Yonsei Med. J. 62: 868–871.
Konstantinidis, I., Tsakiropoulou, E., Hähner, A., De With, K., Poulas, K., and Hummel, T. (2021). Olfactory dysfunction after coronavirus disease 2019 (COVID-19) vaccination. Int. Forum Allergy Rhinol. 11: 1399–1401.
Kwon, H. and Kim, T. (2021). Autoimmune encephalitis following ChAdOx1-S SARS-CoV-2 vaccination. Neurol. Sci. 43: 1487–1489.
Latimer, F.R., Webster, J.E., and Guardjian, E.S. (1951). Neurological complications of rabies vaccine; report of two cases. AMA Arch. Neurol. Psychiatr. 65: 16–28.
Lehn, A., Gelauff, J., Hoeritzauer, I., Ludwig, L., Mcwhirter, L., Williams, S., Gardiner, P., Carson, A., and Stone, J. (2016). Functional neurological disorders: mechanisms and treatment. J. Neurol. 263: 611–620.
Leiderman, Y.I., Lessell, S., and Cestari, D.M. (2009). Recurrent isolated sixth nerve palsy after consecutive annual influenza vaccinations in a child. J. Am. Assoc. Pediatr. Ophthalmol. Strabismus 13: 317–318.
Li, X., Lin, Y., Yao, G., and Wang, Y. (2018). The influence of vaccine on febrile seizure. Curr. Neuropharmacol. 16: 59–65.
Li, X., Ostropolets, A., Makadia, R., Shaoibi, A., Rao, G., Sena, A.G., Martinez-Hernandez, E., Delmestri, A., Verhamme, K., Rijnbeek, P.R., et al. (2021). Characterizing the incidence of adverse events of special interest for COVID-19 vaccines across eight countries: a multinational network cohort study. medRxiv.
Liu, B.D., Ugolini, C., and Jha, P. (2021). Two cases of post-moderna COVID-19 vaccine encephalopathy associated with nonconvulsive status epilepticus. Cureus 13: e16172.
López-Hernández, J.C., Lisette, B.-R., Adib, J.D.S., Eunice, M.-J., Elizabeth, L.-M., Erika, G.-L., and Steven, V.-C. (2022). Guillain-Barré syndrome following SARS-CoV-2 vaccination: is there a real association? Neuroimmunol. Rep. 2: 100050.
Love, S. (2006). Demyelinating diseases. J. Clin. Pathol. 59: 1151–1159.
Lu, D.C., Zhang, H., Zador, Z., and Verkman, A.S. (2008). Impaired olfaction in mice lacking aquaporin-4 water channels. Faseb. J. 22: 3216–3223.
Lu, L., Xiong, W., Mu, J., Zhang, Q., Zhang, H., Zou, L., Li, W., He, L., Sander, J.W., and Zhou, D. (2021). The potential neurological effect of the COVID-19 vaccines: a review. Acta Neurol. Scand. 144: 3–12.
Lunn, M.P., Cornblath, D.R., Jacobs, B.C., Querol, L., Van Doorn, P.A., Hughes, R.A., and WillisoN, H.J. (2021). COVID-19 vaccine and Guillain-Barré syndrome: let's not leap to associations. Brain 144: 357–360.
Macdonald, S.E., Dover, D.C., Hill, M.D., Kirton, A., Simmonds, K.A., and Svenson, L.W. (2018). Is varicella vaccination associated with pediatric arterial ischemic stroke? A population-based cohort study. Vaccine 36: 2764–2767.
Malek, E. and Salameh, J. (2019). Guillain-barre syndrome. Semin. Neurol. 39: 589–595.
Matarneh, A.S., Al-Battah, A.H., Farooqui, K., Ghamoodi, M., and Alhatou, M. (2021). COVID-19 vaccine causing Guillain-Barre syndrome, a rare potential side effect. Clin. Case Rep. 9: e04756.
Mckean, N. and Chircop, C. (2021). Guillain-Barré syndrome after COVID-19 vaccination. BMJ Case Rep. 14, https://doi.org/10.1136/bcr-2021-244125.
Mehvari Habibabadi, J., Saadatnia, M., and Tabrizi, N. (2018). Seizure in cerebral venous and sinus thrombosis. Epilepsia Open 3: 316–322.
Menge, T., Cree, B., Saleh, A., Waterboer, T., Berthele, A., Kalluri, S.R., Hemmer, B., Aktas, O., Hartung, H.P., Methner, A., et al. (2012). Neuromyelitis optica following human papillomavirus vaccination. Neurology 79: 285–287.
Miravalle, A., Biller, J., Schnitzler, E., and Bonwit, A. (2010). Neurological complications following vaccinations. Neurol. Res. 32: 285–292.
Mishra, A.K., Sahu, K.K., George, A.A., Sargent, J., and Lal, A. (2020). Cerebrovascular events in COVID-19 patients. Monaldi Arch. Chest Dis. 90: 333–336.
Mohamed, K., Yazdanpanah, N., Saghazadeh, A., and Rezaei, N. (2021). Cognitive biases affecting the maintenance of COVID-19 pandemic. Acta Biomed. 92: e2021102.
Mora-Díaz, J.C., Piñeyro, P.E., Houston, E., Zimmerman, J., and Giménez-Lirola, L.G. (2019). Porcine hemagglutinating encephalomyelitis virus: a review. Front. Vet. Sci. 6: 53.
Myers, T.R. and Mcneil, M.M. (2018). Current safety issues with quadrivalent meningococcal conjugate vaccines. Hum. Vaccines Immunother. 14: 1175–1178.
Nagu, P., Parashar, A., Behl, T., and Mehta, V. (2021). CNS implications of COVID-19: a comprehensive review. Rev. Neurosci. 32: 219–234.
Niu, M.T., Salive, M.E., and Ellenberg, S.S. (1999). Neonatal deaths after hepatitis B vaccine: the vaccine adverse event reporting system, 1991-1998. Arch. Pediatr. Adolesc. Med. 153: 1279–1282.
Oo, W.M., Giri, P., and De Souza, A. (2021). AstraZeneca COVID-19 vaccine and Guillain- Barré syndrome in Tasmania: a causal link? J. Neuroimmunol. 360: 577719.
Organization, W.H. (2022). Global situation of COVID-19, Available at: <https://covid19.who.int/> (Accessed 17 January 2022).
Ozgen Kenangil, G., Ari, B.C., Guler, C., and Demir, M.K. (2021). Acute disseminated encephalomyelitis-like presentation after an inactivated coronavirus vaccine. Acta Neurol. Belg. 121: 1089–1091.
Ozonoff, A., Nanishi, E., and Levy, O. (2021). Bell's palsy and SARS-CoV-2 vaccines. Lancet Infect. Dis. 21: 450–452.
Pai, M., Chan, B., Stall, N.M., Grill, A., Ivers, N., Maltsev, A., Miller, K.J., Odutayo, A., Razak, F., Schull, M., et al. (2021). Vaccine-induced immune thrombotic thrombocytopenia (VITT) following adenovirus vector COVID-19 vaccination, Available at: <https://covid19-sciencetable.ca/sciencebrief/vaccine-induced-immune-thrombotic-thrombocytopenia-vitt-following-adenovirus-vector-covid-19-vaccination/>.
Parasher, A. (2021). COVID-19: current understanding of its pathophysiology, clinical presentation and treatment. Postgrad. Med. 97: 312–320.
Patone, M., Handunnetthi, L., Saatci, D., Pan, J., Katikireddi, S.V., Razvi, S., Hunt, D., Mei, X.W., Dixon, S., Zaccardi, F., et al. (2021). Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection. Nat. Med. 27: 2144–2153.

Piyasirisilp, S. and Hemachudha, T. (2002). Neurological adverse events associated with vaccination. Curr. Opin. Neurol. 15: 333–338.

Plesner, A.M., Arlien-Soborg, P., and Herning, M. (1998). Neurological complications to vaccination against Japanese encephalitis. Eur. J. Neurol. 5: 479–485.

Pohl, D., Alper, G., Van Haren, K., Kornberg, A.J., Lucchinetti, C.F., Tenembaum, S., and Belman, A.L. (2016). Acute disseminated encephalomyelitis: updates on an inflammatory CNS syndrome. Neurology 87: S38–S45.

Popescu, B.F. and Lucchinetti, C.F. (2012). Pathology of demyelinating diseases. Annu. Rev. Pathol. 7: 185–217.

Principi, N. and Esposito, S. (2019). Vaccine-preventable diseases, vaccines and Guillain-Barre' syndrome. Vaccine 37: 5544–5550.

Queler, S.C., Towbin, A.J., Milani, C., Whang, J., and Sneag, D.B. (2021). Parsonage-turner syndrome following COVID-19 vaccination: MR neurography. Radiology 302: 84–87, 211374.

Rafique, S., Wasim, A., Sultan, T., and Ahmad, A. (2021). Post-COVID neuromyelitis optica spectrum disorder. J. Coll. Phys. Surg. Pakistan 31: 138–140.

Rao, S.J., Khurana, S., Murthy, G., Dawson, E.T., Jazebi, N., and Haas, C.J. (2021). A case of Guillain-Barre syndrome following Pfizer COVID-19 vaccine. J. Community Hosp. Intern. Med. Perspect. 11: 597–600.

Razok, A., Shams, A., Almeer, A., and Zahid, M. (2021). Post-COVID-19 vaccine Guillain-Barré syndrome; first reported case from Qatar. Ann. Med. Surg. 67: 102540.

Reismann, J.L. and Singh, B. (1978). Conversion reactions simulating Guillain-Barré paralysis following suspension of the swine flu vaccination program in the USA. Aust. N. Z. J. Psychiatr. 12: 127–132.

Reyes-Capo, D.P., Stevens, S.M., and Cavuoto, K.M. (2021). Acute abducens nerve palsy following COVID-19 vaccination. J. Am. Assoc. Pediatr. Ophthalmol. Strabismus 25: 302–303.

Rinaldi, V., Bellucci, G., Romano, A., Bozzao, A., and Salvetti, M. (2021). ADEM after ChAdOx1 nCoV-19 vaccine: a case report. Mult. Scler.: 13524585211040222, https://doi.org/10.1177/13524585211040222.

Rizk, J.G., Gupta, A., Sardar, P., Henry, B.M., Lewin, J.C., Lippi, G., and Lavie, C.J. (2021). Clinical characteristics and pharmacological management of COVID-19 vaccine-induced immune thrombotic thrombocytopenia with cerebral venous sinus thrombosis: a review. JAMA Cardiol 6: 1451–1460.

Saghazadeh, A. and Rezaei, N.J.E.R.O.C.I. (2020). Immune-epidemiological parameters of the novel coronavirus–a perspective. Expert. Rev. Clin. Immunol. 16: 465–470.

Sanderson, K. (2021). COVID vaccines protect against Delta, but their effectiveness wanes. Nature, https://doi.org/10.1038/d41586-021-02261-8.

Sato, K., Mano, T., Niimi, Y., Toda, T., Iwata, A., and Iwatsubo, T. (2021). Facial nerve palsy following the administration of COVID-19 mRNA vaccines: analysis of a self-reporting database. Int. J. Infect. Dis. 111: 310–312.

Schaller, B. and Graf, R. (2004). Cerebral venous infarction: the pathophysiological concept. Cerebrovasc. Dis. 18: 179–188.

Sejvar, J.J., Labutta, R.J., Chapman, L.E., Grabenstein, J.D., Iskander, J., and Lane, J.M. (2005). Neurologic adverse events associated with smallpox vaccination in the United States, 2002-2004. JAMA 294: 2744–2750.

Shah, S., Patel, J., Alchaki, A.R., Eddin, M.F., and Souayah, N. (2018). Development of transverse myelitis after vaccination, a CDC/FDA vaccine adverse event reporting system (VAERS) study, 1985–2017. Neurology 90: P5.099.

Shaikh, M.F., Baqai, T.J., and Tahir, H. (2012). Acute brachial neuritis following influenza vaccination. BMJ Case Rep. 2012: 1–2.

Sharifian-Dorche, M., Bahmanyar, M., Sharifian-Dorche, A., Mohammadi, P., Nomovi, M., and Mowla, A. (2021). Vaccine-induced immune thrombotic thrombocytopenia and cerebral venous sinus thrombosis post COVID-19 vaccination; a systematic review. J. Neurol. Sci. 428: 117607.

Sharifian-Dorche, M., Huot, P., Osherov, M., Wen, D., Saveriano, A., Giacomini, P.S., Antel, J.P., and Mowla, A. (2020). Neurological complications of coronavirus infection; a comparative review and lessons learned during the COVID-19 pandemic. J. Neurol. Sci. 417: 117085.

Sharma, K., Tengsupakul, S., Sanchez, O., Phaltas, R., and Maertens, P. (2019). Guillain-Barré syndrome with unilateral peripheral facial and bulbar palsy in a child: a case report. SAGE Open Med. Case Rep. 7, 2050313x19838750.

Shaw, F.E., JR., Graham, D.J., Guess, H.A., Milstien, J.B., Johnson, J.M., Schatz, G.C., Hadler, S.C., Kuritsky, J.N., Hiner, E.E., Bregman, D.J., et al. (1988). Postmarketing surveillance for neurologic adverse events reported after hepatitis B vaccination. Experience of the first three years. Am. J. Epidemiol. 127: 337–352.

Shaw, V.C., Chander, G., and Puttanna, A. (2020). Neuromyelitis optica spectrum disorder secondary to COVID-19. Br. J. Hosp. Med. 81: 1–3.

Smarrazzo, A., Mariani, R., Valentini, F., Lombardi, M.H., Sinibaldi, S., Peschiaroli, E., Papa, R.E., and Campana, A. (2021). Three-fold increase in admissions for paediatric febrile convulsions during COVID-19 pandemic could indicate alternative virus symptoms. Acta Paediatr. 110: 939–940.

Sørbø, J.G., Moe, S.E., and Holen, T. (2007). Early upregulation in nasal epithelium and strong expression in olfactory bulb glomeruli suggest a role for Aquaporin-4 in olfaction. FEBS Lett. 581: 4884–4890.

Souayah, N., Ajroud-Driss, S., Sander, H.W., Brannagan, T.H., Hays, A.P., and Chin, R.L. (2009). Small fiber neuropathy following vaccination for rabies, varicella or Lyme disease. Vaccine 27: 7322–7325.

Spencer, J.P., Trondsen Pawlowski, R.H., and Thomas, S. (2017). Vaccine adverse events: separating myth from reality. Am. Fam. Physician 95: 786–794.

Stam, J. (2005). Thrombosis of the cerebral veins and sinuses. N. Engl. J. Med. 352: 1791–1798.

Stone, J., Carson, A., Aditya, H., Prescott, R., Zaubi, M., Warlow, C., and Sharpe, M. (2009). The role of physical injury in motor and sensory conversion symptoms: a systematic and narrative review. J. Psychosom. Res. 66: 383–390.

Stowe, J., Andrews, N., Wise, L., and Miller, E. (2006). Bell's palsy and parenteral inactivated influenza vaccine. Hum. Vaccine 2: 110–112.

Swaddiwuthipong, W., Weniger, B.G., Wattanasri, S., and Warrell, M.J. (1988). A high rate of neurological complications following Semple anti-rabies vaccine. Trans. R. Soc. Trop. Med. Hyg. 82: 472–475.

Takeyama, R., Fukuda, K., Kouzaki, Y., Koga, T., Hayashi, S., Ohtani, H., and Inoue, T. (2021). Intracerebral hemorrhage due to vasculitis following COVID-19 vaccination: a case report. Acta Neurochir. 164: 543–547.

Tian, M., Yang, J., Li, L., Li, J., Lei, W., and Shu, X. (2020). Vaccine-associated neurological adverse events: a case report and literature review. Curr. Pharmaceut. Des. 25: 4570–4578.

Tinazzi, M., Geroin, C., Erro, R., Marcuzzo, E., Cuoco, S., Ceravolo, R., Mazzucchi, S., Pilotto, A., Padovani, A., Romito, L.M., et al. (2021a). Functional motor disorders associated with other neurological diseases: beyond the boundaries of "organic" neurology. Eur. J. Neurol. 28: 1752–1758.

Tinazzi, M., Geroin, C., Marcuzzo, E., Cuoco, S., Ceravolo, R., Mazzucchi, S., Pilotto, A., Padovani, A., Romito, L.M., Eleopra, R., et al. (2021b). Functional motor phenotypes: to lump or to split? J. Neurol. 268: 4737–4743.

Tregoning, J.S., Brown, E.S., Cheeseman, H.M., Flight, K.E., Higham, S.L., Lemm, N.M., Pierce, B.F., Stirling, D.C., Wang, Z., and Pollock, K.M. (2020). Vaccines for COVID-19. Clin. Exp. Immunol. 202: 162–192.

Trimboli, M., Zoleo, P., Arabia, G., and Gambardella, A. (2021). Guillain-Barré syndrome following BNT162b2 COVID-19 vaccine. Neurol. Sci. 42: 4401–4402.

Tsai, L.K., Hsieh, S.T., Chao, C.C., Chen, Y.C., Lin, Y.H., Chang, S.C., and Chang, Y.C. (2004). Neuromuscular disorders in severe acute respiratory syndrome. Arch. Neurol. 61: 1669–1673.

Tsetsos, N., Poutoglidis, A., Vlachtsis, K., Kilmpasanis, A., and Gougousis, S. (2021). Sudden sensorineural hearing loss following the second dose of COVID-19 vaccine. Cureus 13: e17435.

Tsui, P., Deptula, A., and Yuan, D.Y. (2017). Conversion disorder, functional neurological symptom disorder, and chronic pain: comorbidity, assessment, and treatment. Curr. Pain Headache Rep. 21: 29.

Tullu, M.S., Rodrigues, S., Muranjan, M.N., Bavdekar, S.B., Kamat, J.R., and Hira, P.R. (2003). Neurological complications of rabies vaccines. Indian Pediatr. 40: 150–154.

van den Berg, B., Walgaard, C., Drenthen, J., Fokke, C., Jacobs, B.C., and Van Doorn, P.A. (2014). Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat. Rev. Neurol. 10: 469–482.

Vanood, A. and Wingerchuk, D. (2019). Systematic review investigating relationship between neuromyelitis optica spectrum disorder (NMOSD) and vaccination (P1.2-003). Neurology 92: P1.2-003.

Vellozzi, C., Iqbal, S., and Broder, K. (2014). Guillain-Barre syndrome, influenza, and influenza vaccination: the epidemiologic evidence. Clin. Infect. Dis. 58: 1149–1155.

Vodicka, J., Jelínková, H., and Chrobok, V. (2010). Smell impairment after tick-borne encephalitis vaccination: case report. Vaccine 28: 886–888.

Vojdani, A. and Kharrazian, D. (2020). Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases. Clin. Immunol. 217: 108480.

Voon, V., Brezing, C., Gallea, C., Ameli, R., Roelofs, K., Lafrance, W.C., Jr., and Hallett, M. (2010). Emotional stimuli and motor conversion disorder. Brain 133: 1526–1536.

Waheed, W., Carey, M.E., Tandan, S.R., and Tandan, R. (2021). Post COVID-19 vaccine small fiber neuropathy. Muscle Nerve 64: E1–E2.

Warner, M.J., Hutchison, J., and Varacallo, M. (2021). *Bell palsy*. StatPearls. StatPearls Publishing LLC, Treasure Island (FL, USA).

Whittaker, A., Anson, M., and Harky, A. (2020). Neurological Manifestations of COVID-19: a systematic review and current update. Acta Neurol. Scand. 142: 14–22.

Wildemann, B., Jarius, S., Hartmann, M., Regula, J.U., and Hametner, C. (2009). Acute disseminated encephalomyelitis following vaccination against human papilloma virus. Neurology 72: 2132–2133.

Willison, H.J., Jacobs, B.C., and Van Doorn, P.A. (2016). Guillain-Barré syndrome. Lancet 388: 717–727.

Woo, E.J., Mba-Jonas, A., Dimova, R.B., Alimchandani, M., Zinderman, C.E., and Nair, N. (2021). Association of Receipt of the Ad26.COV2.S COVID-19 vaccine with presumptive Guillain-Barré syndrome. Jama 326: 1606–1613.

World Health Organization (2021). COVID-19 vaccine tracker and landscape, Available at: <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>.

Yachou, Y., El Idrissi, A., Belapasov, V., and Ait Benali, S. (2020). Neuroinvasion, neurotropic, and neuroinflammatory events of SARS-CoV-2: understanding the neurological manifestations in COVID-19 patients. Neurol. Sci. 41: 2657–2669.

Yazdanpanah, N. and Rezaei, N. (2022). Autoimmune complications of COVID-19. J. Med. Virol. 94: 54–62.

Yazdanpanah, N., Saghazadeh, A., and Rezaei, N. (2020). Anosmia: a missing link in the neuroimmunology of coronavirus disease 2019 (COVID-19). Rev. Neurosci. 31: 691–701.

Yeh, E.A., Collins, A., Cohen, M.E., Duffner, P.K., and Faden, H. (2004). Detection of coronavirus in the central nervous system of a child with acute disseminated encephalomyelitis. Pediatrics 113: e73–6.

Yonee, C., Toyoshima, M., Maegaki, Y., Kodama, Y., Hayami, H., Takahashi, Y., Kusunoki, S., Uchibori, A., Chiba, A., and Kawano, Y. (2013). Association of acute cerebellar ataxia and human papilloma virus vaccination: a case report. Neuropediatrics 44: 265–267.

Zamani, R., Pouremamali, R., and Rezaei, N. (2021). Central neuroinflammation in Covid-19: a systematic review of 182 cases with encephalitis, acute disseminated encephalomyelitis, and necrotizing encephalopathies. Rev. Neurosci., https://doi.org/10.1515/revneuro-2021-0082.