



# Brain perfusion single photon emission computed tomography abnormality in MRI-negative stroke-like patients post COVID-19 vaccination

Supatporn Tepmongkol, MD<sup>a,b,c,d,\*</sup> , Nijasri C. Suwanwela, MD<sup>c,e,f</sup>, Nattiya Hirankarn, MD<sup>g</sup>, Sookjaroen Tangwongchai, MD<sup>c,d,h</sup> , Pongpat Vorasayan, MD<sup>c,e,f</sup>, Chanan Sukprakun, MD<sup>a</sup>, Natakorn Siritaranon, MD<sup>i</sup>, Naruchorn Kijpaisalratana, MD<sup>c,f,j</sup>, Wasan Akarathanawat, MD<sup>e,f</sup>, Aurauma Chutinet, MD<sup>c,e,f</sup>, Jarturon Tantivatana, MD<sup>c,k</sup>

## Abstract

Stroke-like symptoms after COVID-19 vaccination was thought to be functional if there was no anatomical image abnormality. We aimed to analyze brain perfusion changes in these patients. A case-control study of brain perfusion single photon emission computed tomography (SPECT) of 12 vaccinated patients with left-sided stroke-like symptoms were compared with 12 age- and gender-matched normal interictal brain SPECTs using voxel-based analysis. Significant hyperperfusion was seen on the right side in postcentral, inferior parietal, mid temporal, parahippocampal, and caudate regions, and on the left side in the thalamus, hippocampus, and mid temporal areas. In addition, there were hypoperfused bilateral superior frontal gyri and right mid/posterior cingulate cortex (Family-wise-error corrected  $p$ -values  $< .05$ ). Both hypoperfusion and hyperperfusion in the brain are demonstrated. We hypothesize that these findings might be the result of the functional neurological disorder. However, based on other previous studies, circulating spike protein in the patients' plasma early after vaccination might also be the cause.

**Abbreviations:** ACE2 = angiotensin-converting enzyme 2, COVID-19 = Coronavirus disease 2019, CT = computed tomography, MRA = magnetic resonance angiography, MRI = magnetic resonance imaging, SPECT = single photon emission computed tomography, SPM = statistic parametric mapping.

**Keywords:** COVID-19, functional neurological disorder, immunization stress-related response (ISRR), SARS-CoV-2, SPECT, stroke

## 1. Introduction

Since the Severe acute respiratory syndrome Coronavirus 2 pandemic or coronavirus disease (COVID-19) in 2019, COVID-19 vaccination in Thailand has started in February 2021. There have been many transient focal neurological symptoms after CoronaVac® (Vero cell, inactivated, Sinovac Life Sciences, China) and Oxford/ChAdOx (Non-replicating viral vector, University of Oxford, Astra Zeneca, UK) Covid-19 vaccine administration. According to our post-vaccination surveillance record, 49 of the total 15,747 patients (0.31%) were reported to have focal neurological symptoms 4 months after starting vaccination in our hospital. In addition, we have

reported the first case and a descriptive case series with neurological symptoms post-COVID-19 vaccination in those who did not show an abnormality on magnetic resonance imaging (MRI).<sup>[1,2]</sup> Although there have been many reports regarding neurological complications following COVID-19 vaccination with a spectrum from mild to devastating,<sup>[3–8]</sup> a small percentage of 3.5% and 1% were reported to have transient sensory symptoms and weakness.<sup>[5]</sup> Only 1 report mentioned advanced brain imaging beyond MRI.<sup>[4]</sup> For those who did not have computed tomography (CT)/MRI abnormalities, patients were usually diagnosed with immunization stress-related response<sup>[9]</sup> or The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition functional neurological

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

<sup>a</sup> Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, <sup>b</sup> Chulalongkorn University Biomedical Imaging Group (CUBIG), Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, <sup>c</sup> Chula Neuroscience Center, King Chulalongkorn Memorial Hospital, Bangkok, Thailand, <sup>d</sup> Cognitive Impairment and Dementia Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, <sup>e</sup> Division of Neurology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, <sup>f</sup> Chulalongkorn Comprehensive Stroke Center, King Chulalongkorn Memorial Hospital, Bangkok, Thailand, <sup>g</sup> Center of Excellence in Immunology and Immune-mediated Diseases, Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, <sup>h</sup> Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, <sup>i</sup> Division of Nuclear Medicine, Department of Radiology, King Chulalongkorn Memorial Hospital, Bangkok, Thailand, <sup>j</sup> Division of Academic Affairs, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, <sup>k</sup> Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

\* Correspondence: Supatporn Tepmongkol, Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine, Chulalongkorn University, Rama IV Rd., Pathumwan, Bangkok 10330, Thailand (e-mail: Supatporn.t@chula.ac.th).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and build up the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Tepmongkol S, Suwanwela NC, Hirankarn N, Tangwongchai S, Vorasayan P, Sukprakun C, Siritaranon N, Kijpaisalratana N, Akarathanawat W, Chutinet A, Tantivatana J. Brain perfusion single photon emission computed tomography abnormality in MRI-negative stroke-like patients post COVID-19 vaccination. *Medicine* 2022;101:47(e31965).

Received: 13 October 2022 / Received in final form: 1 November 2022 / Accepted: 1 November 2022

<http://dx.doi.org/10.1097/MD.00000000000031965>

symptom disorder.<sup>[10]</sup> We thus aimed to explore if there is any specific brain perfusion change in patients who experienced transient stroke-like symptoms (sensory and/or motor dysfunction) without MRI and/or magnetic resonance angiography (MRA) abnormality and was sent for further investigation with single-photon emission computed tomography (SPECT) by comparing patients' SPECT images with age- and gender-matched controls.

## 2. Methods and materials

### 2.1. Patients

Twelve patients who had stroke-like symptoms within 7 days after COVID-19 vaccine injection with negative CT, MRI, and MRA and were sent for brain perfusion SPECT from February to July 2021 in our hospital were enrolled. History, clinical presentations, neurological examination by neurologists were retrospectively reviewed by accessing the Hospital information system. A radiologist (J.T.) reviewed CT and MRI retrieved from the picture archiving system.

This study was conducted retrospectively from data obtained for clinical purposes and the study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (COA no. 917/2021). Informed consent was obtained from all patients.

### 2.2. Brain perfusion SPECT imaging protocol and analysis

SPECT was performed during focal neurological symptoms by intravenous injection of 11.1 Megabecquerel per kilogram (0.3 MilliCurie per kilogram) Tc-99m ethylcysteinate dimer. Patients were placed in a dimly lit room with low noise and were instructed to rest with their eyes open for 30 minutes. Acquisition started 30 minutes after injection using a dual-headed GE Discovery 670 (Chicago) SPECT/CT machine equipped with low energy, high resolution, parallel hole collimators. The zoom factor was 1.5. Images were acquired in 120 views with 3 degrees/steps. Reconstruction was done using filtered back projection with Chang's attenuation correction and a Butterworth filter (0.55 Nyquist frequency and power 10). SPECT images of all 12 patients in the vaccinated group were compared with 12 age- and gender-matched interictal state epilepsy patients who did not have a seizure for at least 24 hours and visually showed symmetric uptake on both cerebral hemispheres (control group) using Statistical Parametric Mapping, statistic parametric mapping (SPM) 12 (Wellcome Trust Centre for Neuroimaging, UCL, UK) running under MATLAB 7.10.0. All SPECTs in this control group were performed before the COVID-19 period. Preparation of the patient before scan and image acquisition were identical for both groups. Brain images of vaccinated patients who had symptoms on the right body side were flipped on the *x*-axis so that all patients would have symptoms on the same left body side. All images were co-registered, realigned, and spatially normalized to Montreal Neurological Institute space. Smoothing was performed using an isotropic 3D-Gaussian kernel of 16 mm full-width-at-half maximum. Dose correction for all images was done by equating global counts. We used a 2-sample *t*-test for the comparison of vaccinated and control groups. Statistical significance was defined as the combination of uncorrected  $P < .001$  at the voxel level, and family-wise error (FWE) corrected  $P < .05$  at the cluster level. Hyperperfusion (vaccinated-control) and hypoperfusion (control-vaccinated) clusters were determined. The anatomical location from the resulting Montreal Neurological Institute coordinates was identified by using the automated anatomical labeling 3 atlas in the SPM toolbox.<sup>[11]</sup>

## 3. Results

Twelve patients (9 females and 3 males) with a median age of 37.5 years (range 24–50 years) were right-handed and had COVID-19 vaccine intramuscular injection in the left arm. The symptoms ranged from mono- or hemi-hypesthesia/paresthesia/paresis or abnormal sensation and motor function. The symptoms onset was 15 minutes to 7 days after receiving the COVID-19 vaccine. There was no obvious abnormality seen on MRI and MRA in all patients. The symptoms' duration ranged from 2 days to 1 month. Patient characteristics are shown in Table 1.

The median age of the control group was 37.5 years (range 24–50 years). The gender of each individual in the control group was matched to the patients. No obvious brain perfusion abnormality was detected in this control group's cortical and subcortical regions.

SPM revealed both hypoperfusion and hyperperfusion in the patient group compared to age- and gender-matched controls (Fig. 1, Table 2). Significant hyperperfusion was seen on the right cerebral hemisphere in the postcentral gyrus, inferior parietal, mid temporal, parahippocampal regions, caudate, and on the left hemisphere in the left thalamus, hippocampus, and mid temporal regions (Family-wise-error corrected  $p$ -values  $< .05$ ). In addition, there were hypoperfused bilateral superior frontal gyri and right mid/posterior cingulate cortex (Family-wise-error corrected  $p$ -values  $< .05$ ).

## 4. Discussion

Although many types of neurological manifestations have been reported as complications of COVID-19 vaccination,<sup>[3–8,12–16]</sup> most patients reported were thought to be functional neurological disorders, and the symptoms were usually reversible. It is thus a condition, until now, that has an unproven cause with an unclear explanation. We encountered many cases of individuals who had COVID-19 vaccination with stroke-like manifestation. Patients were immediately sent for brain perfusion SPECT after negative MRI results for an explanation of this phenomenon. Our study has proven that there are indeed some perfusion abnormalities in the brain.

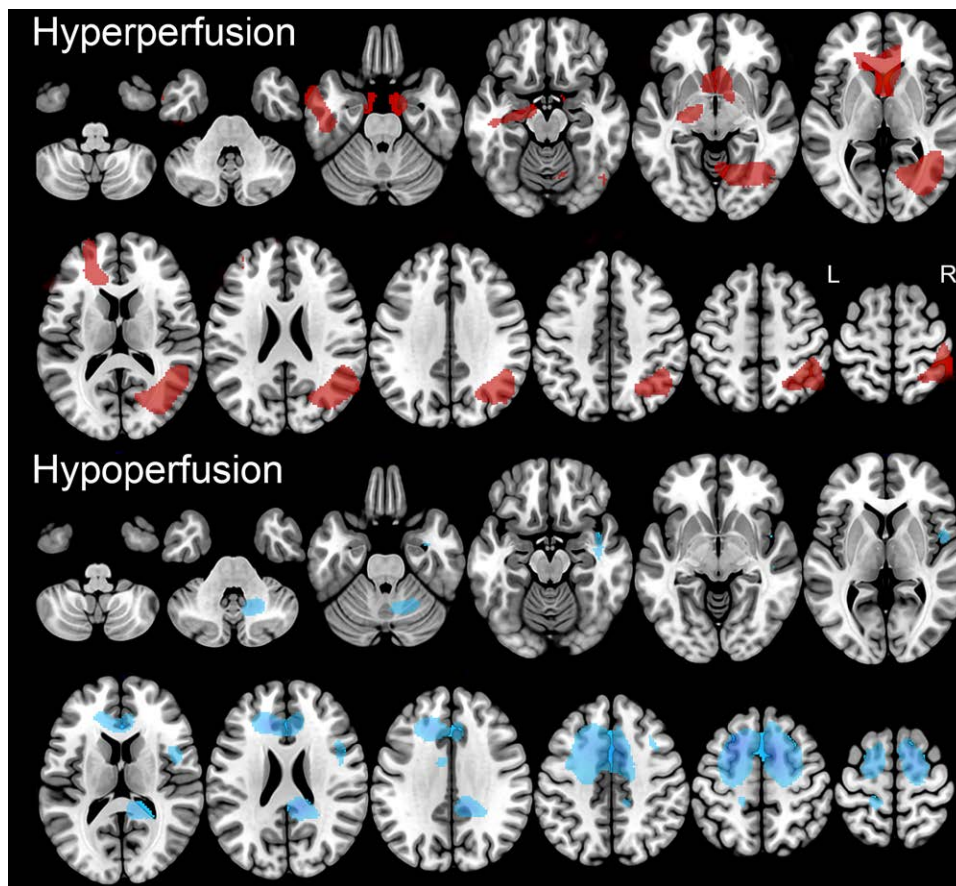
As shown in Figure 1 and Table 2, both hyperperfusion and hypoperfusion are demonstrated. Hyperperfusion is located mainly at the right post-central gyrus and inferior parietal/supramarginal gyrus, the primary somatosensory cortex, and the area responsible for sensorimotor integration and spatial attention of the left body side, respectively. As we flipped the brain of the patients who had signs and symptoms on the right side of the body to be on the same side as those with signs/symptoms on the left body side, hyperperfusion seen can explain the tingling sensation and numbness of the left body side in our patients. The underlying cause for this finding may be due to blood vessel inflammation caused by the interaction of spike protein with Angiotensin-converting enzyme 2 (ACE2) on endothelial cells, which causes loss of blood-brain-barrier integrity as explained in neurological conditions of COVID-19 infection.<sup>[17–19]</sup> Recently, a report found an S1 fragment of spike protein in the plasma of some individuals from day 1 to 14 after COVID-19 vaccination.<sup>[20]</sup> Since all vaccines against COVID-19 contain spike protein, thus there is a possibility that some individuals receiving COVID-19 vaccine may experience the effect of spike protein-endothelial interaction. Vasculitis induced by the interaction of spike protein with ACE2 on vascular endothelial cells is probably the cause of hyperperfusion in some brain regions. However, the reason why there is more vulnerable vasculitis in the parietal region or other particular areas is unknown.

Hypoperfusion is mainly seen in bilateral supplementary motor areas, right mid/posterior cingulate gyrus, and left medial frontal gyrus. This finding can explain motor symptoms by two hypotheses. Firstly, it can be a functional motor disorder defined

**Table 1**  
**Patient characteristic and MRI/MRA results.**

Characteristics	Patient number											
	1	2	3	4	5	6	7	8	9	10	11	12
Age (yr)	24	24	42	48	47	29	29	50	37	35	38	45
Gender	Female	Male	Female	Female	Male	Female	Female	Female	Female	Male	Female	Female
Medical history	-	-	-	-	Hypertension	Graves' Disease	Endometriosis	Dyslipidemia	-	deficiency, Traumatic splenectomy	-	Thyrototoxicosis
History of migraine	Yes	Yes	Yes	No	No	No	No	No	Yes	No	No	No
Symptom onset after vaccination	20 mins	4 h	7 h	1 d	2 h	7 d	6 d	20 mins	40 mins	1 d	40 mins	15 mins
Type of vaccine	CoronaVac	CoronaVac	CoronaVac	CoronaVac	CoronaVac	CoronaVac (2 <sup>nd</sup> dose)	CoronaVac	CoronaVac (2 <sup>nd</sup> dose)	CoronaVac	CoronaVac	CoronaVac	AstraZeneca
Side of neuro. deficit	Left	Left	Right	Left	Right	Right	Left	Left	Left	Left	Bilateral	Left
<b>Symptoms &amp; signs</b>												
Sensory	Tingling at Lt. hand progressed to numbness at Lt. arm, leg	Tingling at Lt. arm followed by numbness at Lt. side of face, neck, leg	-	Numbness Lt. side of face, neck, arm	Tingling at Lt. hand and foot progressed to numbness at Rt. hand, perioral, foot	Numbness at Rt. side of face (perioral) and Rt. leg	Tingling at Lt. hand progressed to arm, face, and leg	Numbness Lt. side of face, arm, leg	Tingling at Lt. hand progressed to arm	Tingling at Lt. temporal area	Numbness Lt. side of arm and bilateral leg	Numbness Lt. side of face, arm, leg
Motor	Lt. hemiparesis grade 3	Lt. hemiparesis grade 4	Rt. hemiparesis grade 4	Lt. arm monoparesis grade 4	-	Asymmetric nasolabial folds	-	Rt. Leg weakness grade 4	-	Lt. facial weakness	Lt. arm weakness	Lt. hemiparesis grade 3
Headache	Lt. temporal pulsatile headache 1 d after sensory symptom	Lt. temporal & occipital headache 1 d after sensory symptom	Rt. temporal & periorbital headache 1 d after weakness	Occipital headache on the same d	-	-	-	-	-	-	Generalized headache	-
Nausea/vomiting	Yes	Yes	No	No	No	No	No	No	No	No	No	No
Visual phenomena	Flashing light	Blurred vision	No	No	No	No	No	No	No	No	No	No
Symptom duration (d)	10	2	3	10	4	4	2	5	2	4	30	2
MRI	No infarction	No infarction	No infarction	No infarction	No infarction	No infarction	No infarction	No infarction	No infarction	No infarction	No infarction	No infarction
MRA	Mild irregularity	No abnormalities	No abnormalities	No abnormalities	No abnormalities	No abnormalities	No abnormalities	No abnormalities	No abnormalities	No abnormalities	No abnormalities	No abnormalities

MRA = magnetic resonance angiography, MRI = magnetic resonance imaging.



**Figure 1.** Areas of hyperperfusion (upper 2 rows) and hypoperfusion (lower 2 rows) in vaccinated stroke-like patients compared to controls (N = 12/group). The right hemisphere (R) is contralateral to the body side of neurological symptoms and the left hemisphere (L) is ipsilateral to the symptoms.

previously by Edwards MJ, et al,<sup>[21]</sup> caused by pathology of precision. Abnormality of an intermediate-level motor area or supplementary motor area resulted in the abnormal prior expectation of scaling of movement and consequently caused a failure to realize movement. Since this loop of precision error involves attention, hypoperfusion seen at the right posterior cingulate gyrus can explain this phenomenon, as the posterior cingulate gyrus was shown to be deactivated, or in our study, shown as hypoperfusion, during the attentionally demanding task.<sup>[22]</sup> This disorder was recently redefined as a functional neurological disorder, (a subset of immunization stress-related response or immunization

stress-related response) related to vaccination.<sup>[23]</sup> Sensory symptoms usually preceded motor symptoms in our patients, so we hypothesize that spike protein-induced vasculitis causing hyperperfusion to the parietal lobe might start first, followed by Functional neurological disorder in some patients who had an imbalance of prior beliefs (in the vaccine) and sensory evidence, which is mediated by attention, symptom expectations, experiences and their illness beliefs.<sup>[21]</sup> However, hemiparesis did not have preceding sensory symptoms in one patient (patient no.3). Thus, the underlying cause may be due to the direct effect of spike protein on ACE2 vascular smooth muscle cells since there was evidence that

**Table 2**

**Areas of hyperperfusion and hypoperfusion in patients compared to controls (N = 12/group).**

Cluster $p$ (FWE-corrected)	Number of voxels	Peak $p$ (FWE-corrected)	T	x	y	z	Anatomical location (within 10 mm distance)
<i>Hyperperfusion</i>							
.000	289	.000	9.93	4	18	2	Right caudate/Right olfactory
.000	1178	.001	8.76	36	-54	6	Right mid temporal/Right calcarine
		.001	8.34	42	-40	58	Right postcentral/Right inferior parietal
		.034	6.33	42	-52	42	Right inferior parietal/Right angular gyrus
.021	14	.025	6.52	14	-4	-28	Right parahippocampus/Right hippocampus
.010	35	.026	6.48	-18	-14	-6	Left thalamus
		.046	6.15	-16	-12	-16	Left hippocampus/Left amygdala
.016	22	.028	6.44	-58	-2	-26	Left mid temporal/Left inferior temporal
<i>Hypoperfusion</i>							
.000	335	.002	7.96	-16	18	70	Left superior frontal gyrus/Left supplementary motor area
.000	386	.004	7.64	14	12	68	Right superior frontal gyrus/Right supplementary motor area
.007	50	.012	6.95	-12	38	44	Left superior frontal gyrus/Left medial frontal gyrus
.003	77	.013	6.92	14	-28	32	Right mid/posterior cingulate

$p$  =  $P$ -value, FWE = family-wise error.

ACE2 is expressed in the vascular smooth muscle cell in the brain and neurons (mainly in the motor cortex and raphe).<sup>[24,25]</sup> This finding can be used to explain motor symptoms in other patients as well. Neurons of the motor cortex (bilateral superior frontal gyri in our study), which expresses more ACE2 than other brain regions,<sup>[25]</sup> might be affected by the spike protein, thereby resulting in vasoconstriction (hypoperfusion) and suppression of the neuronal function. This causes paresis to the efferent contralateral body side with more predominance on the left side due to the affected right mid-cingulate gyrus. The mid-cingulate gyrus is responsible for the orientation of the head and body in space, thus controlling the force and direction of movement.<sup>[26]</sup> The impeded function of the right mid cingulate therefore results in a less controllable left body side, thus accentuating the effect of neuronal dysfunction at the right superior frontal gyrus/right supplementary motor area. The mid-cingulate gyrus also controls response to nociceptive stimuli.<sup>[26]</sup> This finding may also explain hypesthesia on the left body side. However, as mentioned earlier, the hyperperfused right postcentral gyrus caused by an inflamed vessel feeding this area can be an additional explanation of hypesthesia. The explanation for those who did not demonstrate stroke-like symptoms may be due to; No interaction of spike protein on endothelium in those patients, or; No pathology of precision, thus no functional neurological disorder.

In clinical practice, although there are proven brain perfusion changes, if there is no MRI abnormality, the patient can be reassured that the symptoms are likely to be transient as shown in all our patients.

In conclusion, hypoperfusion and hyperperfusion in various brain areas are demonstrated in patients with neurological manifestations after COVID-19 vaccination of COVID-19. Sensory dysfunction is postulated to be caused by hyperperfusion resulting from possible spike protein-induced vasculitis at the contralateral sensory region or hypoperfusion induced by the interaction of spike protein on ACE2 at the contralateral mid cingulate gyrus. The motor dysfunction is probably caused by functional neurological disorder or interaction of spike protein on abundant ACE2 at motor cortices and contralateral mid cingulate gyrus. However, we did not examine the presence of spike protein in the serum or in the brain in this study. Further study is needed to prove these hypotheses.

## Author contributions

**Conceptualization:** Supatporn Tepmongkol, Nijasri C. Suwanwela, Nattiya Hirankarn, Sookjaroen Tangwongchai.

**Data curation:** Supatporn Tepmongkol, Nijasri C. Suwanwela, Pongpat Vorasayan, Naruchorn Kijpaisalratana, Wasan Akarathanawat, Aurauma Chutinet.

**Formal analysis:** Supatporn Tepmongkol, Chanan Sukprakun, Natakorn Siritaranon, Jarturon Tantivatana.

**Investigation:** Supatporn Tepmongkol, Chanan Sukprakun.

**Methodology:** Supatporn Tepmongkol, Nijasri C. Suwanwela, Jarturon Tantivatana.

**Project administration:** Pongpat Vorasayan.

**Validation:** Supatporn Tepmongkol, Nijasri C. Suwanwela, Nattiya Hirankarn, Pongpat Vorasayan, Naruchorn Kijpaisalratana, Wasan Akarathanawat, Aurauma Chutinet.

**Visualization:** Supatporn Tepmongkol, Jarturon Tantivatana.

**Writing – original draft:** Supatporn Tepmongkol, Nijasri C. Suwanwela, Nattiya Hirankarn.

**Writing – review & editing:** Supatporn Tepmongkol, Nijasri C. Suwanwela, Nattiya Hirankarn, Sookjaroen Tangwongchai, Chanan Sukprakun, Jarturon Tantivatana.

## References

- [1] Rattanawong W, Akaratanawat W, Tepmongkol S, et al. Acute prolonged motor aura resembling ischemic stroke after COVID-19 vaccination (CoronaVac): the first case report. *J Headache Pain.* 2021;22:93.
- [2] Suwanwela NC, Kijpaisalratana N, Tepmongkol S, et al. Prolonged migraine aura resembling ischemic stroke following CoronaVac vaccination: an extended case series. *J Headache Pain.* 2022;23:13.
- [3] Garg RK, Paliwal VK. Spectrum of neurological complications following COVID-19 vaccination. *Neurol Sci.* 2022;43:3–40.
- [4] Siripongsatian D, Kunawudhi A, Promteangtrong C, et al. Alterations in 18F-FDG PET/MRI and 15O-Water PET brain findings in patients with neurological symptoms after COVID-19 vaccination: a pilot study. *Clin Nucl Med.* 2022;47:e230–9.
- [5] García-Grimshaw M, Ceballos-Liceaga SE, Hernández-Vanegas LE, et al. Neurologic adverse events among 704,003 first-dose recipients of the BNT162b2 mRNA COVID-19 vaccine in Mexico: a nationwide descriptive study. *Clin Immunol.* 2021;229:108786.
- [6] Sharifian-Dorche M, Bahmanyar M, Sharifian-Dorche A, et al. Vaccine-induced immune thrombotic thrombocytopenia and cerebral venous sinus thrombosis post COVID-19 vaccination; a systematic review. *J Neurol Sci.* 2021;428:117607.
- [7] Waheed S, Bayas A, Hindi F, et al. Neurological complications of COVID-19: Guillain-Barre syndrome following Pfizer COVID-19 vaccine. *Cureus.* 2021;13:e13426.
- [8] Corrêa DG, Cañete LAQ, Dos Santos GAC, et al. Neurological symptoms and neuroimaging alterations related with COVID-19 vaccine: cause or coincidence?. *Clin Imaging.* 2021;80:348–52.
- [9] Immunization Stress-Related Responses: a manual for program managers and health professionals to prevent, identify and respond to stress-related responses following immunization. World Health Organization; 2019. Available from: <https://apps.who.int/iris/handle/10665/330277>.
- [10] Demartini B, D'Agostino A, Gambini O. From conversion disorder (DSM-IV-TR) to functional neurological symptom disorder (DSM-5): when a label changes the perspective for the neurologist, the psychiatrist and the patient. *J Neurol Sci.* 2016;360:55–6.
- [11] Rolls ET, Huang C-C, Lin C-P, et al. Automated anatomical labelling atlas 3. *NeuroImage.* 2020;206:116189.
- [12] Ercoli T, Lutzoni L, Orofino G, et al. Functional neurological disorder after COVID-19 vaccination. *Neurol Sci.* 2021;42:3989–90.
- [13] Goss AL, Samudralwar RD, Das RR, et al. ANA investigates: neurological complications of COVID-19 vaccines. *Ann Neurol.* 2021;89:856–7.
- [14] Walter U, Volmer E, Wittstock M, et al. [Cerebral venous sinus thrombosis after COVID-19 vaccination: neurological and radiological management]. *Radiologe.* 2021;61:923–32. Hirnvenen- und Sinusthrombose nach COVID-19-Schutzimpfung: Neurologisch-radiologisches Prozedere.
- [15] Singh Malhotra H, Gupta P, Prabhu V, et al. COVID-19 vaccination-associated myelitis. *QJM.* 2021;114:591–3.
- [16] Lu L, Xiong W, Mu J, et al. The potential neurological effect of the COVID-19 vaccines: a review. *Acta Neurol Scand.* 2021;144:3–12.
- [17] Buzhdygan TP, DeOre BJ, Baldwin-Leclair A, et al. The SARS-CoV-2 spike protein alters barrier function in 2D static and 3D microfluidic in-vitro models of the human blood-brain barrier. *Neurobiol Dis.* 2020;146:105131–105131.
- [18] Rhea EM, Logsdon AF, Hansen KM, et al. The S1 protein of SARS-CoV-2 crosses the blood-brain barrier in mice. *Nat Neurosci.* 2021;24:368–78.
- [19] Bernard I, Limonta D, Mahal LK, Hobman TC. Endothelium infection and dysregulation by SARS-CoV-2: evidence and caveats in COVID-19. *Viruses.* 2020;13:29.
- [20] Ogata AF, Cheng C-A, Desjardins M, et al. Circulating severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) vaccine antigen detected in the plasma of mRNA-1273 vaccine recipients. *Clin Infect Dis.* 2022;74:715–8.
- [21] Edwards MJ, Adams RA, Brown H, et al. A Bayesian account of “hysteria.” *Brain.* 2012;135(Pt 11):3495–512.
- [22] Leech R, Sharp DJ. The role of the posterior cingulate cortex in cognition and disease. *Brain.* 2013;137:12–32.
- [23] Taylor S, Asmundson GJG. Immunization stress-related responses: implications for vaccination hesitancy and vaccination processes during the COVID-19 pandemic. *J Anxiety Disord.* 2021;84:102489.
- [24] Hamming I, Timens W, Bulthuis ML, et al. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol.* 2004;203:631–7.
- [25] Doobay MF, Talman LS, Obr TD, et al. Differential expression of neuronal ACE2 in transgenic mice with overexpression of the brain renin-angiotensin system. *Am J Physiol Regul Integr Comp Physiol.* 2007;292:R373–81.
- [26] Vogt BA. Midcingulate cortex: Structure, connections, homologies, functions and diseases. *J Chem Neuroanat.* 2016;74:28–46.