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Comparison of pseudocontinuous arterial spin labeling perfusion MR images and time-of-flight MR angiography in the detection of periictal hyperperfusion

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ABSTRACT

Background: Magnetic resonance imaging (MRI), including perfusion MRI with three-dimensional pseudo-continuous arterial spin labeling (ASL) and diffusion-weighted imaging (DWI), are applied in the periictal (including ictal and postictal) detection of circulatory and metabolic consequences associated with epilepsy. Our previous report revealed that periictal hyperperfusion can firstly be detected on ASL, and cortical hyperintensity of cytotoxic edema secondarily obtained on DWI from an epileptically activated cortex. Although magnetic resonance angiography (MRA) using three-dimensional time-of-flight is widely used to evaluate arterial circulation, few MRA studies have investigated the detection of periictal hyperperfusion.

Methods: To compare the ability of ASL and MRA to detect the periictal hyperperfusion on visual inspection, we retrospectively selected 23 patients who underwent ASL and MRA examination on both periictal and interictal periods. Patients were divided into the following three groups according to periictal ASL/DWI findings: positive ASL and DWI findings (n = 13, ASL+/DWI+ group), positive ASL and negative DWI findings (n = 5, ASL+/DWI- group), and negative ASL and DWI findings (n = 5, ASL-/DWI- group).

Results: Periictal hyperperfusion on MRA was detected in 6 out of 13 patients (46.2%) in the ASL+/DWI+ group, but not in all patients in the ASL+/DWI- and ASL-/DWI- groups. Furthermore, in 5 out of these 6 patients, the diagnosis of periictal MRA hyperperfusion could not be made without referring to interictal MRA and/or periictal ASL findings, because the periictal MRA findings were so minute.

Conclusion: The minimum requirement for the development of periictal MRA hyperperfusion is that its epileptic event is intense enough to induce the uncoupling between metabolism and circulation, with the induction of glutamate excitotoxity, and severe cytotoxic edema on DWI. ASL is vastly superior to MRA in the detection of periictal hyperperfusion.

1. Introduction

In the clinical field of epilepsy, it is difficult to record electroencephalography (EEG) with exact timing during ictal or peri-ictal periods. In most hospital, without continuous EEG monitoring facilities, routine EEG examination is unavailable outside working hours or on weekends, and the timing of EEG recording is often delayed [4–6,10,11]. Another problem with EEG diagnosis is the sensitivity of peri- or inter-ictal EEG. During the inter-ictal state, paroxysmal activities are not always recorded [4,10]. Furthermore, paroxysmal activities generated in the deep brain structures, such as the hippocampus and the interhemispheric cortex, are difficult to detect from the scalp-recorded EEG, compared with the paroxysms at the cerebral convexity [10].

In contrast, magnetic resonance imaging (MRI) with high magnetic-field scanners has become routinely available in the clinical field of epilepsy. Arterial spin labeling (ASL) is a completely non-invasive and repeatable perfusion MRI technique that uses magnetically-labeled

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Table 1
Clinical profiles, periictal MRA, and EEG findings of patients in the ASL+/DWI+ group.

Patient no	Age Sex	Symptoms	Clinical diagnosis	Epileptogenic lesion	Periictal MRI findings ASL Localization/ DWI		Periictal MRA findings Without ASL/without/with interictal MRA		Periictal EEG findings (interval from MRI)
1	61F	Impaired consciousness, aphasia	SFE, NCSE	Old ICH, Lt fronto-parietal	+ Rt posterior cortex	+	+	+/+	Rhythmic slow waves, Lt occipital (5 days)
2	68F	GTCS	SFE	Old ICH, Lt putamen	+ Lt hemisphere	+	–	+/+	Rhythmic slow waves, Lt occipital (5 days)
3	67 M	GTCS→ Impaired consciousness	SFE, NCSE (Subtle SE)	Resected meningioma, Rt frontal base	+ Rt posterior cortex	+	–	−/+	RIDs, Lt frontal (subsequent)
4	72 M	GTCS→ Impaired consciousness	SFE, NCSE (Subtle SE)	Old ICH, Rt putamen	+ Rt posterior cortex	+	–	−/+	PLEDs, Rt middle temporal (subsequent)
5	85F	Confusion	Dementia related Epilepsy, NCSE	None	+ Bil frontal & Lt parieto-occipital	+	–	−/+	REDs, Lt frontal & parieto-occipital (subsequent)
6	55F	Sensory aphasia	SFE, NCSE	Old ICH, Lt occipito-parietal	+ Lt posterior cortex	+	–	−/+	REDs, Lt posterior temporal (subsequent)
7	87F	Impaired consciousness	Dementia related Epilepsy, NCSE	None (Dementia+)	+ Rt posterior cortex	+	–	−/+	REDs, Rt posterior quadrant (subsequent)
8	87F	Disorientation	SFE, NCSE	Acute infaction. Lt medial fronatal	+ Lt medial frontal	+	–	−/+	REDs, Lt fronto-centaral & temporal (subsequent)
9	78F	Stupor	SFE, NCSE	Rt watershed old infarction	+ Rt frontal & parietal	+	–	−/+	REDs, Lt frontal (subsequent)
10	56 M	Confusion	SFE, NCSE	Old ICH, Lt fronto-parietal	+ Lt posterior cortex	+	–	−/+	RIDs, Lt parietal (subsequent)
11	78 M	Confusion	SFE, NCSE	Old ICH, Rt frontal	+ RT frontal	+	–	−/+	RIDs, Lt frontal (subsequent)
12	92F	GTCS	SFE	Old infarction. Lt Parietal	+ Rt posterior cortex	+	–	−/+	Rhythmic slow waves, Rt parietal (subsequent)
13	68 M	GTCS	SFE	Old ICH, Rt temporal	+ Rt posterior cortex	+	–	−/+	Slow waves, Rt posterior quadrant (1 day)

Abbreviations: MRA, magnetic resonance angiography; EEG, electroencephalography; ASL, arterial spin labeling perfusion image; DWI, diffusion weighted image; MRI, magnetic resonance imaging; F, female; M, male; GTCS, Generalized tonic-clonic seizure; SFE, symptomatic focal epilepsy; NCSE, non-convulsive statue epilepticus; SE, status epilepticus; Lt, left; Rt, right; Bil, bilateral; ICH, intracerebral hemorrhage; PLEDs, periodic lateralized epileptiform discharges; REDs, repetitive epileptiform discharges; RIDs, repeated ictal discharges.

Table 2
Clinical profiles, periictal MRA, and EEG findings of patients in the ASL+/DWI- group.

Patient no	Age Sex	Symptoms	Clinical diagnosis	Epileptogenic lesion	Periictal MRI findings ASL Localization/DWI		Periictal MRA findings Without ASL/without/with ASL interictal MRA		Periictal EEG findings (interval from MRI)
14	58 M	Confusion	SFE, NCSE	Lt hippocampal sclerosis	+ Lt. hemisphere	–	–	−/−	RIDs, Lt anterior temporal (subsequent)
15	43F	Confusion	SFE, NCSE	Calcified AVM, Lt frontal	+ Lt hemisphere	–	–	−/−	PLEDs, Lt frontal (subsequent)
16	59 M	Impaired consciousness	Situation-related epilepsy, NCSE	None	+ Bil. frontal lobes	–	–	−/−	RIDs, Bil frontal (subsequent)
17	83 M	Confusion	Situation-related epilepsy, NCSE	None	+ Bil. frontal lobes	–	–	−/−	RIDs, Bil frontal (subsequent)
18	62F	Aphasia	Acute symptomatic seizure	ICH, Lt parietal	+ Rt posterior cortex	–	–	−/−	Rhythmic slow waves, Lt occipital (1 day)

Abbreviations: MRA, magnetic resonance angiography; EEG, electroencephalography; ASL, arterial spin labeling perfusion image; DWI, diffusion weighted image; MRI, magnetic resonance imaging; F, female; M, male; GTCS, Generalized tonic-clonic seizure; SFE, symptomatic focal epilepsy; NCSE, non-convulsive statue epilepticus; Lt, left; Bil, bilateral; AVM, arterio-venous malformation; ICH, intracerebral hemorrhage; PLEDs, periodic lateralized epileptiform discharges; RIDs, repeated ictal discharges.

water in the blood as an endogenous tracer. Our recent studies have demonstrated that combined use of three-dimensional pseudocontinuous ASL and diffusion-weighted imaging (DWI) can provide valuable information about the circulatory and metabolic consequences associated with epilepsy during ictal [11,16] and periictal periods [4,10,12]. During ictal periods, the epileptogenic cortex is in an extreme electrophysiological state, with the activated cortex exhibiting increased glucose and oxygen usage, thereby causing compensatory regional hyperperfusion. This “ictal hyperperfusion” is primarily detected by ASL [4,5,9–12,16]. When this hyperperfusion is no longer sufficient to supply the hyperactive cortical area, with the induction of glutamate excitotoxity, pathophysiological changes leading to cytotoxic edema in epileptic cortical neurons can occur. The affected areas are secondarily detected as an abnormally high signal in the cortical

Table 3
Clinical profiles, periictal MRA, and EEG findings of patients in the ASL-/DWI- group.

Patient no	Age Sex	Symptoms	Clinical diagnosis	Epileptogenic lesion	Periictal MRI findings ASL location/DWI		Periictal MRA findings Without ASL/without/with interictal MRA		Periictal EEG findings (interval from MRI)
19	64F	GTCS	SFE	Old ICH, Lt frontal	–	–	–	−/−	Generalized slow waves (subsequent)
20	68 M	GTCS	SFE	Old ICH, Rt frontal	–	–	–	−/−	Sporadic spikes, Rt frontal (1 day)
21	17 M	Impaired consciousness	SFE	Cavernoma, Rt temporal	–	–	–	−/−	Nothing particular (subsequent)
22	55 M	Impaired consciousness	SFE	Old ICH, Lt putamen	–	–	–	−/−	Slow waves, Lt hemisphere (subsequent)
23	68 M	Impaired consciousness	SFE	Old ICH, Lt putamen	–	–	–	−/−	Slow waves, Lt centro-parietal (2 days)

Abbreviations: MRA, magnetic resonance angiography; EEG, electroencephalography; ASL, arterial spin labeling perfusion image; DWI, diffusion weighted image; MRI, magnetic resonance imaging; F, female; M, male; GTCS, Generalized tonic-clonic seizure; SFE, symptomatic focal epilepsy; Lt, left; Rt, right; Bil, bilateral; ICH, intracerebral hemorrhage.

lamina, designated “cortical hyperintensity” on DWI [4,5,9–12,16]. The decreased apparent diffusion coefficient in the area corresponding to that of the cortical hyperintensity on DWI is noted, but generally mild, probably because these epilepsy-associated changes are reversible [9,10,11].

Thus, the development of the ictal ASL/DWI findings depends on the magnitude and duration of epileptic activity during ictal periods [4,9–12]. When the epileptic activities do not have enough intensity to induce the uncoupling between metabolism and circulation, no signs of cortical DWI hyperintensity are found, whereas ictal ASL hyperperfusion is obtained [9–12]. Conversely, the electrophysiological intensity of the epileptic activities can be roughly estimated with the detection of these ASL/DWI findings [10,16]. An epileptic event with positive ASL and DWI findings is estimated to be the strongest in intensity, that with negative ASL and DWI findings the mildest, and an event with positive ASL and negative DWI findings intermediate between the two [9–12].

Such ictal MRI findings on ASL/DWI are reversible in most cases; however they can persist during postictal periods, and are then considered as “periictal (ictal + postictal)” MRI findings [4,6,9–12]. Furthermore, postictally, increased ASL signals persist for longer than DWI hyperintensities [4,9–12]. Thus, periictal ASL hyperperfusion is superior to DWI hyperintensity in the periictal detection of epileptic events [4,6,9–12]. The detection of “periictal” MRI findings obviously depends on the time interval between the cessation of the ictus and MRI examination, in addition to the magnitude and duration of the epileptic activity [6,8,12].

Magnetic resonance angiography (MRA) using three-dimensional time-of-flight is widely used to evaluate arterial circulation; however, few studies have investigated the ability of MRA to detect periictal hyperperfusion [2,13]. In the present study, we compared the ability of ASL and MRA to detect periictal hyperperfusion on visual inspection.

2. Methods

2.1. Subjects

From May 2011 to May 2018, 284 patients were admitted to Kyushu Rosai Hospital for the control of epileptic ictus as neuroemergency cases. Most patients underwent an initial emergent neuroradiological examination, such as a computed tomographic (CT) scan and/or “conventional” MR examination, including T1/T2 weighted images, images with fluid attenuated inversion recovery and DWI on arrival, with a subsequent routine electroencephalography (EEG) scheduled within several hours or days. In 87 (30.6%) of the 284 patients, ASL and/or MRA examinations were added at the first conventional MRI examination on arrival or the second MRI examination for clinical purposes, depending on the patient's condition and at the discretion of attending physicians.

Among these patients, we retrospectively selected 23 patients (12 women, 11 men, mean age 67 years, range 17–92 years) who underwent both ASL and MRA examinations during both periictal and interictal periods, and an EEG examination during a periictal period. These 23 patients were divided into the following three groups according to their periictal ASL/DWI findings: the ASL+/DWI+ group, which included patients with positive ASL and DWI findings (n = 13, Patients 1–13; Table 1); the ASL+/DWI-, which included patients with positive ASL and negative DWI findings (n = 5, Patients 14–18; Table 2); and the ASL-/DWI- group, which included patients with negative ASL and DWI findings (n = 5, Patients 19–23; Table 3).

On the basis of subsequently performed comprehensive examinations, 18 patients (Patients 1–4, 6, 8–15, and 18–23) were diagnosed as having symptomatic focal epilepsies associated with an epileptogenic lesion, including old intracerebral hemorrhage, acute or old cerebral infarction, resected meningioma, hippocampal sclerosis, calcified arterio-venous malformation, and cavernous angioma. Two patients (Patients 5 and 7) without epileptogenic lesions were diagnosed having dementia-associated epilepsy. Patients 16 and 17 were diagnosed as having situation-related seizure, which is a ‘de novo’ non-convulsive status epilepticus (NCSE) of frontal origin, as described by Thomas et al. [14,15]. Possible causative factors in these two patients included the association of hyponatremia (Patients 16 and 17, who had 123 and 124 mEq/l, respectively), chronic alcoholism (Patient 16), and non-ketotic hyperglycemia (Patient 17, 264 mg/dl). Patient 18 was diagnosed having acute symptomatic seizures associated with the onset of intracerebral hemorrhage.

Ten patients (Patients 1, 3–11) in the ASL+/DWI+ group and four patients (Patients 14–17) in the ASL+/DWI- group were diagnosed as having NCSE, based on the clinical, EEG, and ASL/DWI findings [11].

We retrospectively analyzed the relationship between periictal development of ASL/DWI and MRA findings. Informed consent was obtained from the patients or their families.

Ethical approval was obtained from the institutional review board of Kyushu Rosai Hospital and written informed consent was obtained from all patients or their families.

2.2. MRI

MRI was performed using a 3-T scanner (HDxt Signa; GE Healthcare, Milwaukee, WI) equipped with an 8-channel receive-only head coil for signal reception.

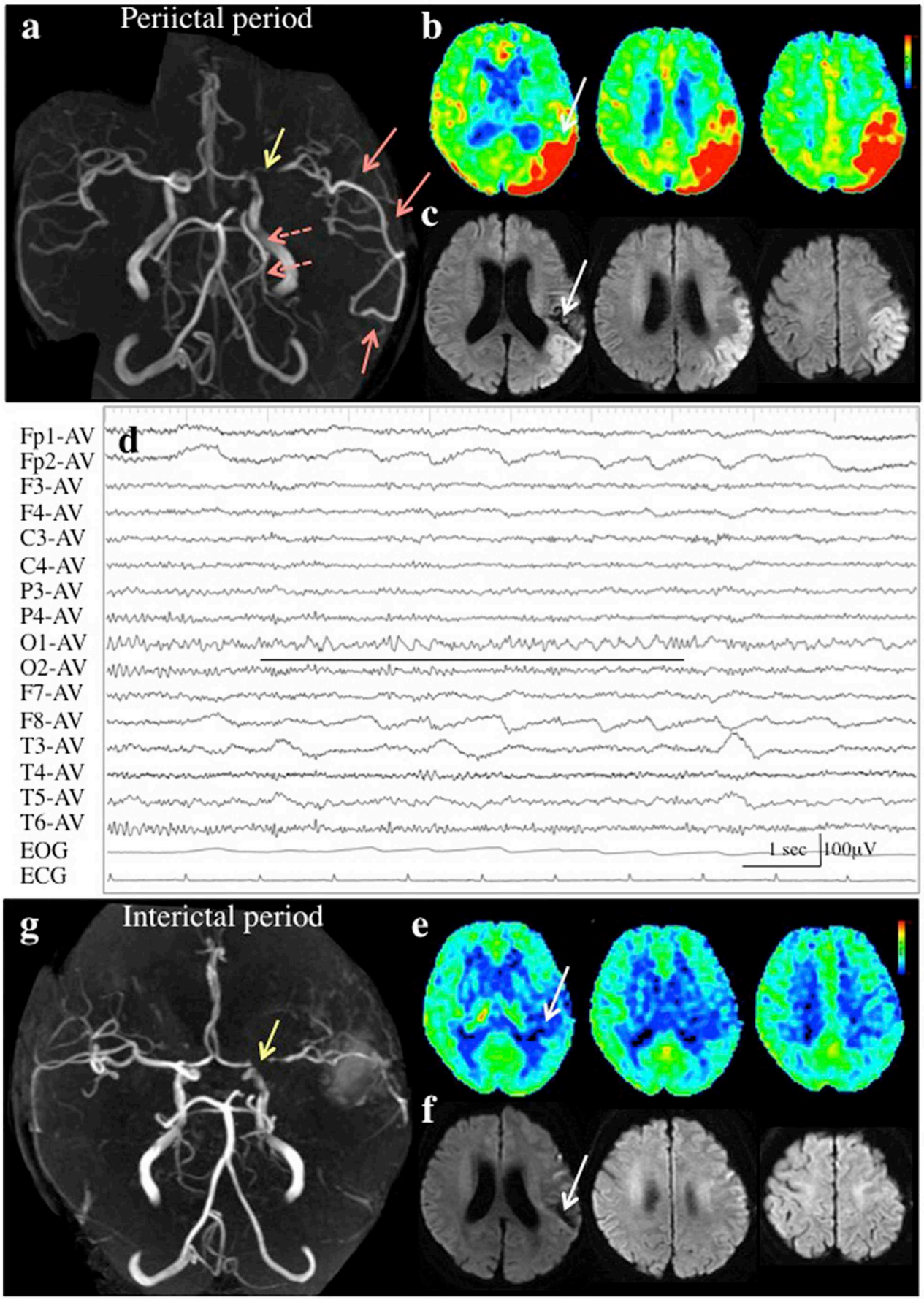

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Fig. 1. Patient 1.(a) At the periictal period of non-convulsive status epilepticus, time-of-flight MR angiography (MRA) showed apparent hyperperfusion in the periphery of the left middle cerebral artery (MCA) (red arrows). Compared with interictal MRA (g), hyperperfusion in the periphery of posterior cerebral artery (PCA) was also noted (red dashed arrows). Yellow arrows indicate the artifact of the aneurysmal clip. (b) Magnetic resonance (MR) perfusion images with three-dimensional pseudocontinuous arterial spin labeling (ASL) revealed marked hyperperfusion in the left posterior cortex (parietal, occipital, and posterior temporal lobes), postero-dorsal to the old hematoma in the left fronto-parietal lobe (white arrow). (c) Diffusion weighted imaging (DWI) revealed gyriform cortical hyperintensity in the area corresponding to that of the hyperintensity on ASL, around the old hematoma (white arrow). (d) The electroencephalogram (EEG) with an averaged reference (AV), performed 5 days after the MR examination, indicated rhythmic slow waves over the left occipital region (the O1 electrode of the international EEG 10–20 system, black line). (e) During interictal states, hyperperfusion was not noted on the ASL. The old hematoma (white arrow) was depicted as no signal area. (f) On DWI, there was no cortical hyperintensity area around the old hematoma (white arrow). (g) MRA showed a markedly decreased flow in the periphery of the left MCA and PCA. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

The ASL was prepared using a three-dimensional spiral fast-spin echo sequence with background suppression for perfusion imaging covering the entire brain, as previously described [3–5,11,12,16]. A pseudocontinuous labeling was employed. The acquisition parameters were as follows: 4 arms with 1004 points in each spiral arm, phase encoding in the z direction = 32, section thickness = 4 mm, time to repeat (TR) = 4728, and number of excitation (NEX) = 2. The labeling duration was 1.5 s. Post-labeling delays (PLDs) of 1.5 s (1.525 s) was chosen. Acquisition time was 1 min 44 s.

The acquisition parameters of MRA were as follows: TR = 26 ms, TE = 3.8 ms, flip angle = 18 degrees, FOV = 22 cm, matrix = 384 × 160, section thickness = 1.2 mm, NEX = 1, acquisition time = 3 min 49 s. Three-dimensional reconstructed images were used to evaluate the periictal hyperperfusion.

Evaluation of ASL/DWI and MRA findings was based on visual inspection by two radiologists (H.N. and A.N.) who were blinded to the clinical data. Evaluation of periictal MRA findings was performed three times; first, periictal MRA was evaluated without referring to periictal ASL and interictal MRA findings; second, periictal MRA was evaluated with periictal ASL findings but without interictal MRA findings; third, periictal MRA was evaluated with periictal ASL and interictal MRA findings. An increased vascularity in MRA was defined as “MRA hyperperfusion”. No differences in the radiologists' interpretations were noted on independent assessments (*kappa* = 1) [7].

2.3. EEG

Subsequent routine EEG recordings were obtained using an 18-channel digital EEG machine (Neurofax; Nihon-Kohden, Tokyo, Japan) with electrode placement according to the International EEG 10–20 system, as described previously [4,11,12,16]. Evaluation of the EEG findings was based on visual inspection by two board certified electroencephalographers (T.M. and A.S.) who were blinded to the clinical data. No differences in the electroencephalographers' interpretations were noted on independent assessments (*kappa* = 1) [7]. As previously described [11], three kinds of EEG findings, namely, repeated ictal discharges, repetitive epileptic discharges, and periodic lateralized epileptic discharges were included in the ongoing ictal EEG findings.

3. Results

3.1. Evaluation of periictal MRA findings without periictal ASL and interictal MRA findings

Of the 23 patients included in the current study, Patient 1 in the ASL +/DWI+ group was the only patient diagnosed as having periictal hyperperfusion on MRA without referring to periictal ASL and interictal MRA findings (Table 1).

Patient 1 was a 61-year-old woman who had an old hematoma in the left fronto-parietal lobe as the epileptogenic lesion. The hematoma occurred in association with vasospasm following ruptured aneurysm of the left internal carotid-posterior communicating arteries (IC-PC), which had been successfully clipped. In the postoperative 9 months, she developed NCSE. On MRA, apparent hyperperfusion was detected at the periphery of the left middle cerebral artery (MCA) (Fig. 1a, red arrows) without periictal ASL and interictal MRA findings, while an aneurysmal clip artifact was noted around the IC-PC (Fig. 1a, yellow arrow). A marked increase in ASL signals was found in the left posterior cortex, postero-dorsal to the old hematoma cavity (Fig. 1b white arrows). DWI clearly showed cortical hyperintensity in the area corresponding to that of the ictal ASL hyperperfusion (Fig. 1c). Although subsequent EEG could not be performed on the weekend, routine EEG, performed 5 days after the MRI examination, failed to reveal ongoing ictal discharges, but depicted the rhythmic slow waves over the left occipital region (the O1 electrode of the International EEG 10–20 system; Fig. 1d, black line), which confirmed the presence of an irritative zone in the left posterior region. During the interictal state when neither ASL hyperperfusion nor cortical DWI hyperintensity was noted (Fig. 1e, f), visualization of the left MCA periphery on MRA was markedly decreased compared with that on periictal MRA (Fig. 1g). A retrospective comparison with interictal MRA revealed that periictal MRA also demonstrated hyperperfusion in the periphery of the posterior cerebral artery (PCA) (Fig. 1a, red dotted arrow), in addition to the MCA periphery.

3.2. Evaluation of periictal MRA findings with periictal ASL but without interictal MRA findings

With periictal ASL but without interictal MRA findings, Patient 2 in the ASL+/DWI+ group was the only patient diagnosed as having periictal MRA hyperperfusion (Table 1).

Patient 2 was a 69-year-old woman who underwent evacuation of the left huge putaminal hematoma extending to the left fronto-parietal and temporal lobes. In the postoperative 4.5 years, she developed generalized seizure that lasted approximately 1 h and emergent MRI examination was performed within 1 h of cessation of her seizure. ASL and DWI clearly demonstrated marked periictal hyperperfusion (Fig. 2a) and cortical hyperintensity (Fig. 2b), respectively, in the cortex of the left hemisphere, except for a surgical defect of the hematoma (Fig. 2a, b, indicated with white arrows). With the periictal ASL findings, on MRA, increased branches of the left MCA periphery compared with those of the right was noted (Fig. 2c). Subsequent EEG showed frequent paroxysmal activities over the left temporal region with continuous slow wave activities over the left hemisphere (Fig. 2d, black arrows). Interictally, ASL hypoperfusion was noted in the entire left hemisphere (Fig. 2e). Cortical DWI hyperintensity was not noted (Fig. 2f). On interictal MRA, visualization of the left MCA periphery was markedly decreased on the left and increased on the contralateral side (Fig. 2g), compared with that of periictal MRA.

3.3. Evaluation of periictal MRA findings with periictal ASL and interictal MRA findings

With periictal ASL and interictal MRA findings, 4 patients (Patients 2–5) in the ASL+/DWI+ group were diagnosed as having periictal

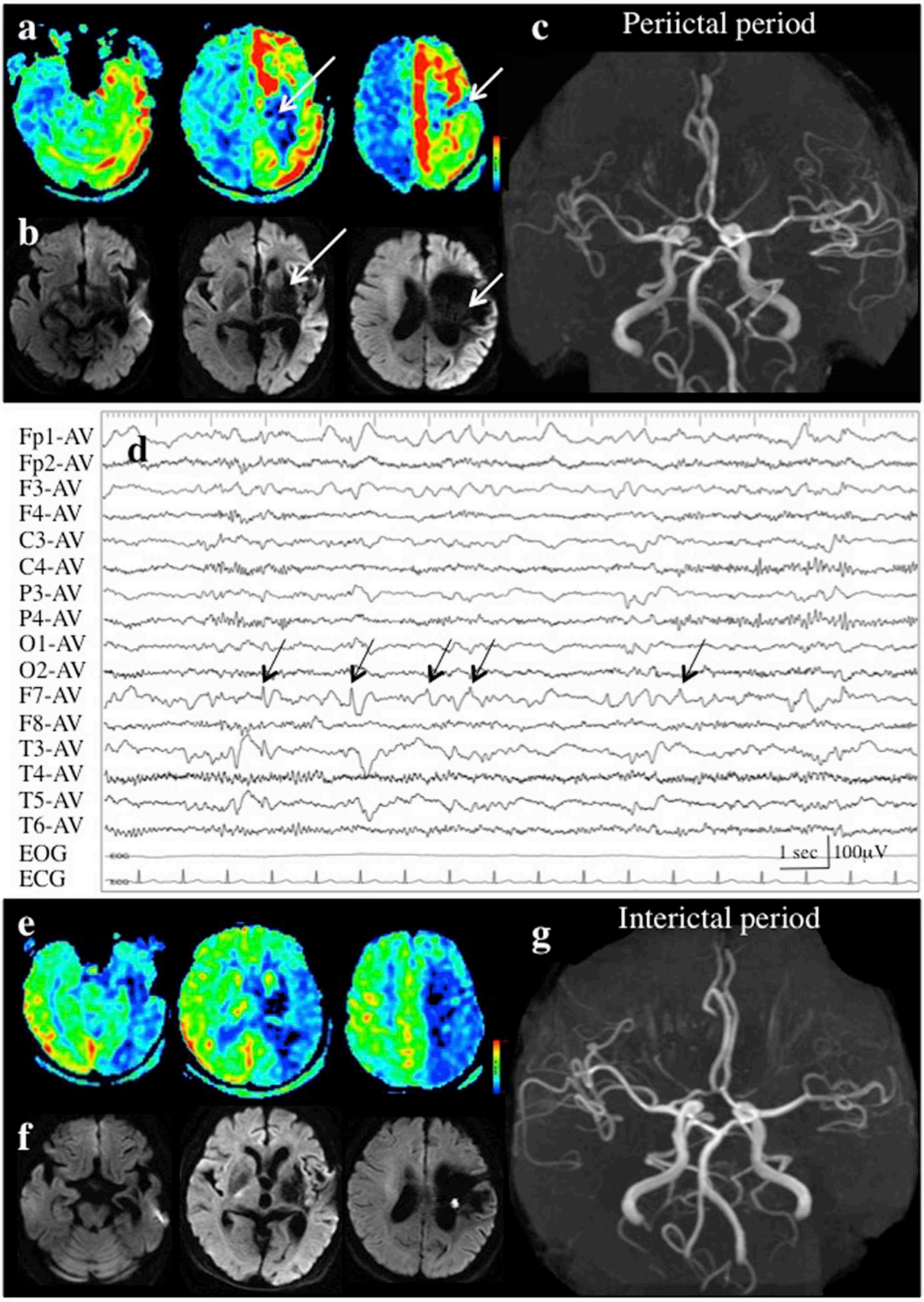

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Fig. 2. Patient 2. Patient 2 was partly reported as Case 1 in our previous report [12]. In this figure, different slices of ASL and DWI and different parts of the EEG from those in the previous report are shown. (a) During the periictal period, ASL showed a marked hyperperfusion in the cortex of the left hemisphere, except for a large surgical defect of the left putaminal hemorrhage (white arrow). (b) DWI demonstrated cortical hyperintensity in the area corresponding to that of the hyperintensity on ASL around the old hematoma (white arrow). (c) MRA indicated an enhanced flow in the left MCA periphery compared with the right side. (d) Subsequent EEG showed frequent paroxysmal activities on the left temporal region (black arrows) with continuous slow wave activities on the left hemisphere. (e) During interictal states, ASL showed hypoperfusion in the entire left hemisphere. (f) On DWI, cortical hyperintensity was not noted. (g) On MRA, visualization of the left MCA periphery was decreased on the left and increased on the contralateral side, compared with periictal MRA.

MRA hyperperfusion (Table 1). In these 4 patients, periictal MRA findings were so minute that they could only be detected when comparing with interictal MRA findings. Even with periictal ASL and interictal MRA findings, 7 (Patients 7–13) out of 13 patients in the ASL +/DWI+ group could not be diagnosed as having periictal MRA hyperperfusion.

Patient 3 is a representative case that had meningioma of the right frontal base (Fig. 3 a, b, white arrows). He developed generalized seizure followed by prolonged unconsciousness. Emergent MRI showed marked ictal ASL hyperperfusion (Fig. 3a) and cortical DWI hyperintensity (Fig. 3b) surrounding the meningioma. The meningioma itself had an increased signal on ASL (Fig. 3a, white arrow) and hyperintensity with a surrounding vasogenic edema on DWI (Fig. 3b, white arrow). On MRA, apparent hyperperfusion was not estimated at that time (Fig. 3c). Subsequent EEG depicted the frequent ictal discharges, which originated from the right frontal region with secondary generalization (F4, Fig. 3d, arrow). Based on these findings, a diagnosis of subtle status epilepticus, which is a persistent NCSE after the cessation of convulsive seizures, was made. After control of NCSE, the meningioma was successfully removed. Interictal MRI at postoperative year one, neither ASL hyperperfusion nor cortical DWI hyperintensity was noted (Fig. 3e, f). Retrospectively comparing with interictal MRA findings (Fig. 3g), a small branch of the right ACA was noted on periictal MRA (Fig. 3c, yellow arrow) and was considered to be a sign of ictal MRA hyperperfusion. This branch of the right ACA did not feed the meningioma on preoperative digital subtraction angiography and was not sacrificed during the operation.

In all 5 patients (Patients 14–18) of the ASL+/DWI- group, periictal hyperperfusion was not demonstrated on MRA, while ASL showed hyperperfusion (Table 2). All 5 patients (Patients 19–23) of the ASL-/DWI- group could not be diagnosed as having periictal MRA hyperperfusion (Table 3).

4. Discussion

In the present study, the sensitivity of MRA in the detection of periictal hyperperfusion was obviously inferior to that of ASL. Periictal MRA hyperperfusion was detected in only 6 out of 13 patients (46.2%) of the ASL+/DWI+ group, but not in all patients in the ASL+/DWI- and ASL-/DWI- groups. This indicates that a minimum requirement for the development of periictal MRA hyperperfusion is that its epileptic event is intense enough to induce severe cytotoxic edema in the epileptically activated cortical neurons of the perfused area [4,9–12].

Furthermore, there is a difficulty in the diagnosis of periictal MRA hyperperfusion. In 5 out of these 6 patients, the diagnosis of periictal MRA hyperperfusion could not be made without referring to periictal ASL findings. When the epileptically hyperperfused area was apparent on ASL, by focusing on the arteries that perfuse the area, the diagnosis of MRA hyperperfusion could be made, as demonstrated in Fig. 2. In 4 cases, the periictal MRA findings were so minute that they could only be detected in comparison with interictal MRA findings, as shown in Fig. 3. The most probable cause of the different sensitivities in the detection of periictal hyperperfusion is that the MRA signal is derived from blood flow in the main trunk of proximal artery, while that of the ASL is mainly derived from blood flow in the cortical tissue [1,3,12]. Periictal hyperperfusion is compensatory regional hyperperfusion in the epileptically activated cortical tissue, and thus it is understandable that ASL is superior to MRA in the detection of the circulatory consequences associated with epilepsy.

The clinical implication of ASL is that the tight topographical relationship between the epileptogenic lesion and epileptically induced hyperperfused area can be clearly demonstrated [4,5,10–12,16], while MRA alone cannot be documented the pathophysiological mechanism of the symptomatic local epilepsy in each patient. However, combined use with periictal ASL and periictal and interictal MRAs can depict a marked hemodynamic change between interictal and periictal periods, as shown in Fig. 2. Decreased flow in the MCA periphery on the lesioned side during the interictal state showed an exponential increase in the periictal state, which shows that strong electrophysiological power of the ictus resulted in the generation of the steal phenomenon of blood flow from the non-lesioned side to the lesioned side. However, these MRI findings reveal only the metabolic and circulatory consequences of the epileptic events and it is therefore hard to localize the epileptogenic focus or area [11]. However, the cortical area involved by the spread of the epileptic activities in prolonged epilepsy can be clearly localized [4,5,11,12,16].

The present study has some limitations. First, the data analysis in our study was retrospectively performed via visual inspection. With a small number of patients under a variety of treatment protocols, quantification of ASL and MRA findings could not be performed. Second, because not all patients with epileptic ictus underwent ASL and MRA both in periictal and interictal states during the study period, it is impossible to calculate the diagnostic accuracy of ASL or MRA. Third, continuous EEG monitoring, which should be the reference point of the ictal activities, was not performed.

5. Conclusion

Our findings show that ASL is vastly superior to MRA in detecting periictal hyperperfusion. Further studies with more sophisticated methods, such as simultaneous examination of continuous EEG monitoring and ASL/MRA examination, and larger numbers of patients are required.

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Declaration of Competing Interest

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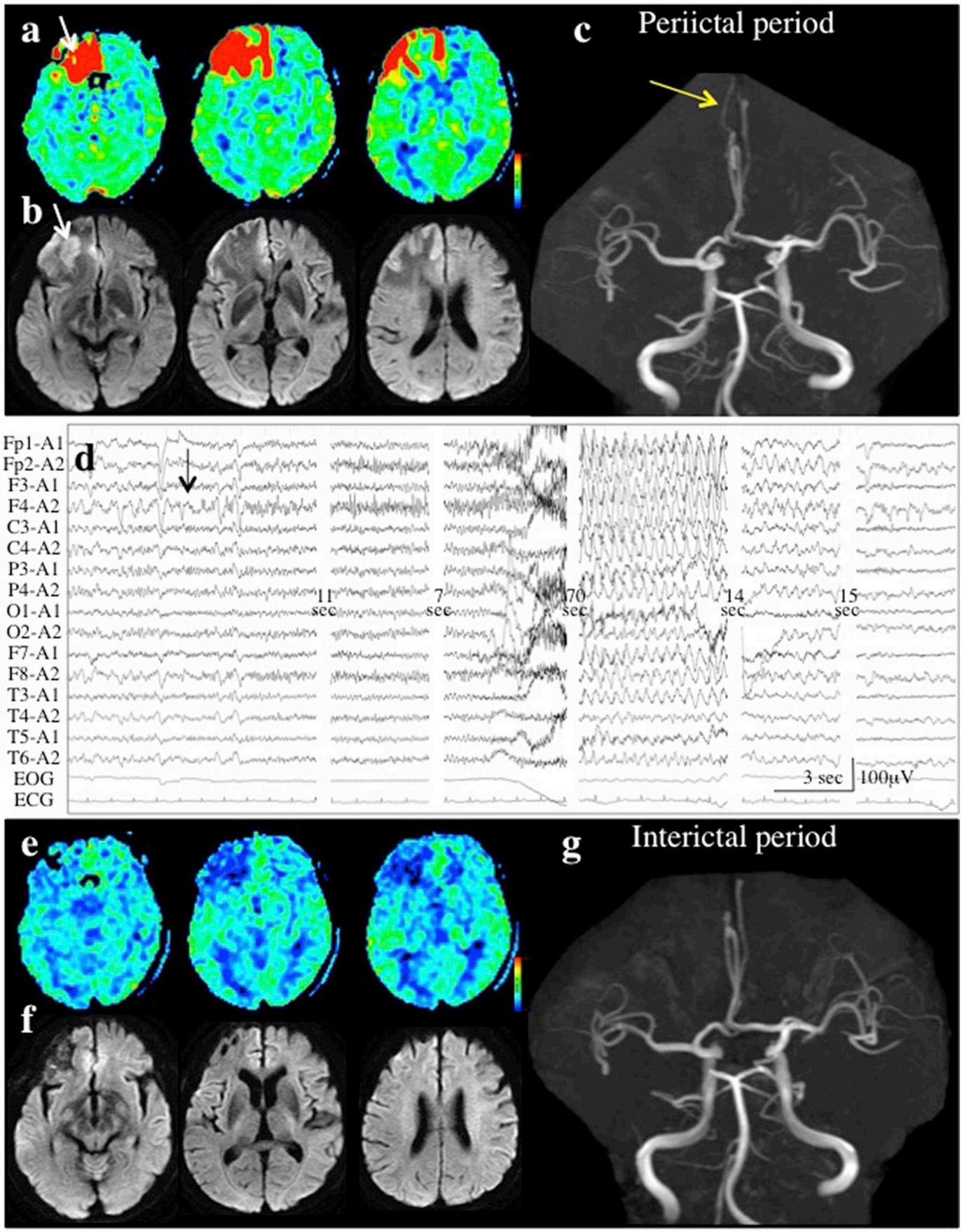

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Fig. 3. Patient 3. During the periictal period, ASL (a) and DWI (b) showed hyperperfusion and cortical hyperintensity around the meningioma of the right frontal fossa, respectively. The meningioma itself was apparent as an increased signal on ASL (a, white arrow) and hyperintensity with surrounding vasogenic edema on DWI (b, white arrow). (c) MRA revealed a small branch of the periphery of the right anterior cerebral artery (ACA) (yellow arrow), compared with the interictal MRA. (d) Subsequent EEG showed ictal discharges that originated from the right frontal region (F4, black arrow) with secondary generalization. (e) Following the removal of the meningioma, during interictal states, the right frontal lobe was depicted as a hypoperfused area on ASL. (f) On DWI, cortical hyperintensity was not noted. (g) On MRA, a small branch of the right ACA had disappeared.

manuscript. The authors have no conflicts of interest to declare. We thank Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

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