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Three cases of paroxysmal alien limb phenomena due to epileptic seizures and review of literatures

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Abstract

Background: The alien hand phenomenon (AHP) is a rare disorder of involuntary limb movement together with a loss of sense of limb ownership. AHP occurs as a consequence of frontal, callosal, or posterior cerebral lesions. To characterize the phenomenon of AHP, three patients with paroxysmal AHP were described and proved to be focal seizures by using video-EEG monitoring.

Method: Clinical history of 3 epileptic patients with AHP was collected. EEG and MRI were performed in each patient. One patient completed EEG monitoring and postoperative pathological examination. We also review the recent literatures and summarize the characteristics, types and hypothetic mechanisms of epileptic AHP.

Results: Case 1 had AHP of the left arm followed by the left arm convulsion or AHP only. MRI imaging showed a lesion in the posterior parietal lobe. After complete resection of the lesion, he remained seizure free for 1.5 years. Cases 2 and 3 had AHP and convulsion. The three cases did not have auto-motor signs, so they were identified to be the posterior type of AHP.

Conclusions: The mechanism underlying AHP remains poorly understood. Currently, little is known for the epileptic paroxysmal AHP, a quite rare form of AHP. AHP can be represented before or immediately after convulsion, or be represented by the paroxysmal symptom only.

Keywords: Epilepsy, Alien hand phenomenon, Seizure, EEG

Background

The alien hand phenomenon (AHP) or alien hand syndrome (AHS) [1, 2] refers to a variety of abnormal motor activity in one hand that is not voluntarily initiated, together with a loss of sense of hand ownership [2, 3]. The AHP sign was first described by Brion and Jedy-nakin in 1972 in a patient with corpus callosum tumour. Since the initial report, several reports have described AHP in frontal strokes, corpus callosum infarction, corpus callosotomy, anterior communicating artery rupture, combination of a posterior callosum lesion and contralateral thalamic sensory lesion, bifrontal

penetrating injury cortico-basal degeneration, Alzheimer's disease, early Creutzfeld-Jakob disease, progressive supranuclear palsy [1–4]. However, the seizure-associated AHP with ictal semiology has been rarely reported [3, 4]. The locations of lesions for AHP are often in the parietal lobe or the mesial frontal lobe including the corpus-callosum [3, 5, 6]. Here we present three patients with paroxysmal AHP that was proved to occur during an epileptic seizure by video-EEG monitoring. One of them then received surgery (resection) and remained seizure free for 1.5 years after surgery.

Methods

Three cases of epileptic patients with AHP who came to our hospital were reported in this study. Clinical history was collected carefully. EEG and MRI were performed in

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each patient. One patient completed EEG monitoring and postoperative pathological examination. All the clinical data were recorded and analyzed in detail. AHP is a rare disorder, especially in the patients with epilepsy. There were only nine cases of epileptic AHP reported before our study. Therefore, we reviewed the related literatures systematically to better understand the characteristics, types, and hypothetic mechanisms of this disorder. This study was approved by the Institutional Ethics Committee of Peking University First Hospital. Informed consent was obtained from all the patients in this report.

Results

Case 1

Case 1 was a 17-year-old left-handed young man who suddenly felt that “the left hand was not mine” and he could not manipulate the computer 2 years ago (2016). The episode lasted for a few minutes, with full awareness. The seizures occurred at an interval of 1–2 days. After more than 1 year (16 days and a year), in 2017, the seizure developed from the initial loss of ownership of the left hand to the left arm clonus and to the sequential

development of generalized tonic clonic seizure (GTCS). Two hours later he suffered a second attack. After that he had episodes at a frequency of 6–7 times/ month.

Magnetic resonance imaging (MRI) showed a very clear lesion (neoplasm) in the posterior right parietal lobe (Fig. 1). Scalp EEG (international 10–20 system) showed regional epileptiform discharges in the left temporal lobe, which was not concordant to the lesion on MRI. Therefore, we repeated scalp EEG with high density international 10% system (Fig. 2). The interictal EEG revealed regional epileptiform discharges in the right parietal and occipital regions (Fig. 3). The ictal EEG also demonstrated that the seizure originated from the right central parietal lobe (Fig. 4).

After complete removal of the neoplasm, the patient was seizure free for 1.5 years under the oxcarbazepine therapy. The neoplasm was pathologically determined to be ganglioglioma. Microscopic examination revealed proliferative neuronal and glial cells arranged without normal architecture in the brain parenchyma of the parietal lobe. Some neurons exhibited eosinophilic cytoplasm. There were dysplastic neurons but not ballon cells. The neoplasm tissue had a prominent capillary

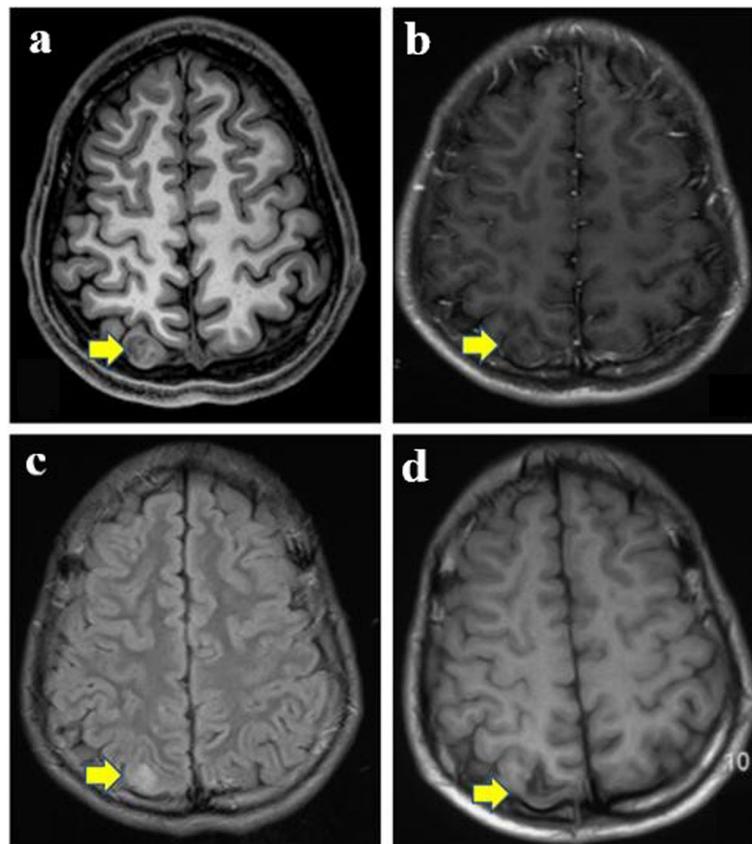


Fig. 1 Brain MRI. Yellow arrows indicate the lesion in the right parietal lobe. The lesion showed mixed signal with very clear boundary, without edema or signal enhancement. **a** T1-weighted image, **b** T1 enhancement, **c** T2 Flair image, **d** post-operative T1 weighted image

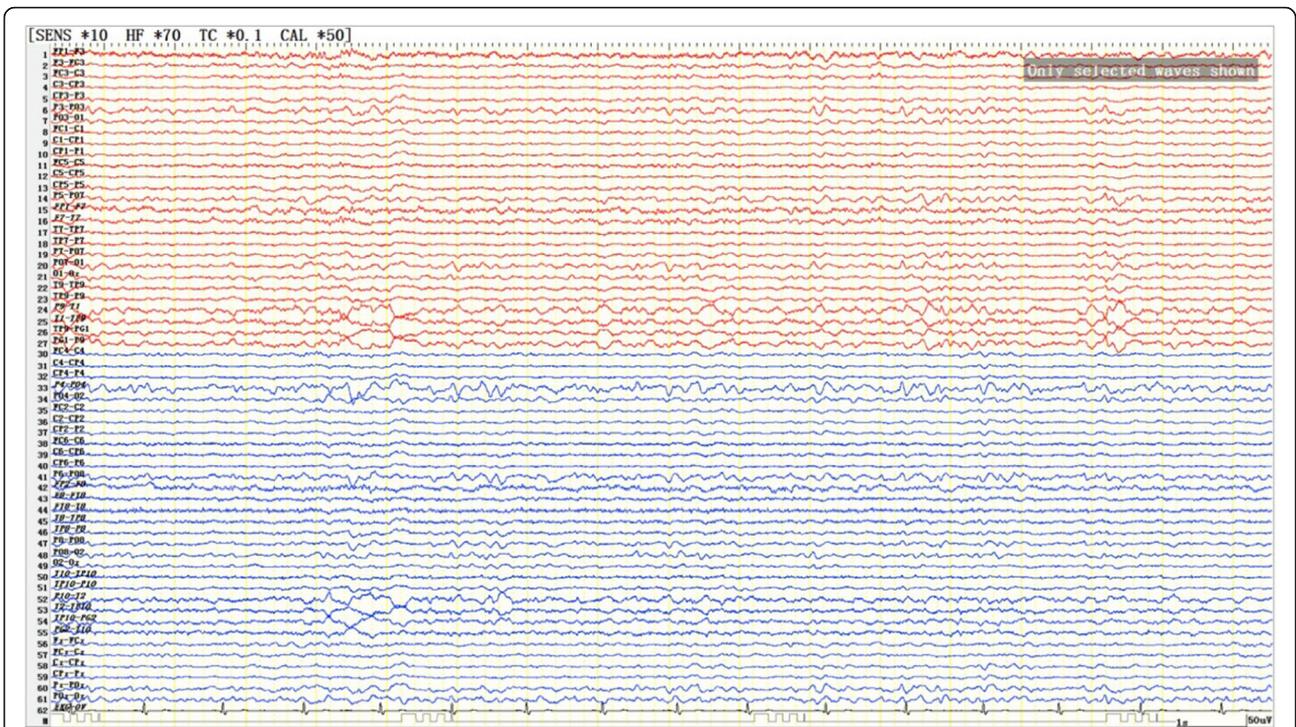


Fig. 2 The interictal EEG with high-density international 10% system

network. Immunohistochemical staining showed positive signals for neuron-specific nucleoprotein (NeuN), synaptophysin and chromogranin A in the neuron component, and positive immunoreactivity for glial fibrillary acidic

protein (GFAP), olig2, neurofilament protein (NFP) and SOX10 in the glial component. The Ki-67 proliferation index was low (3%). Immunostaining resulted in negative signals for R132H-mutant IDH1 and P53, and the

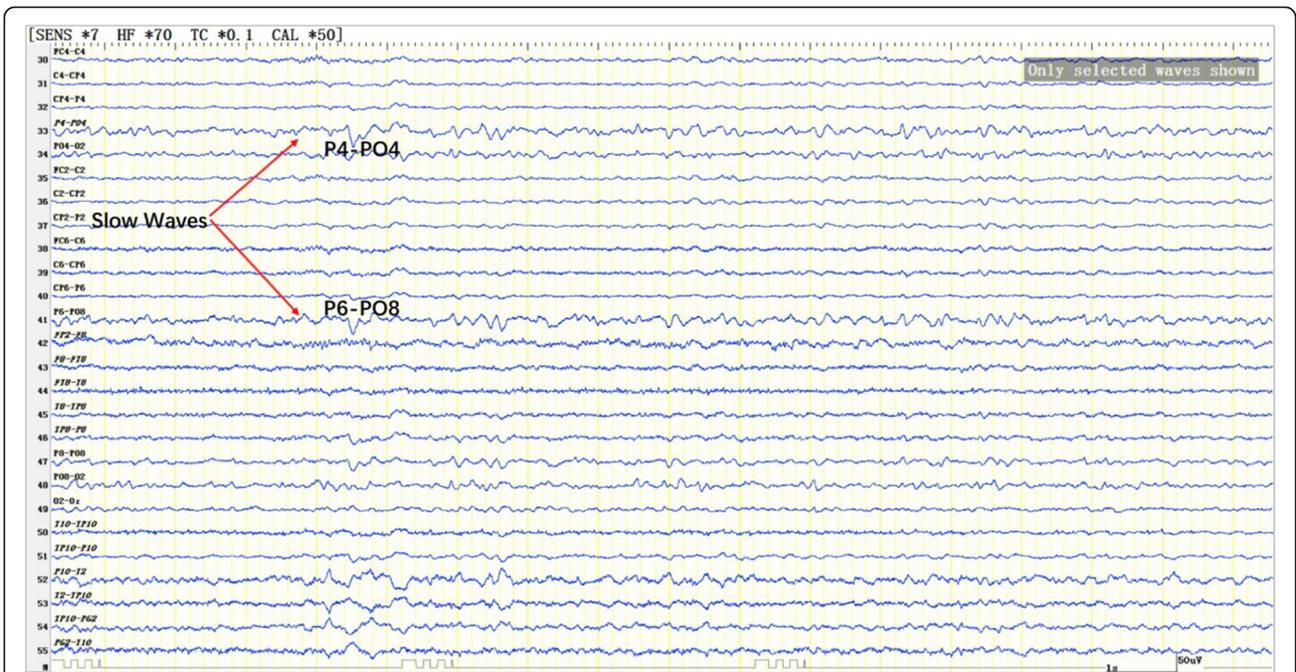
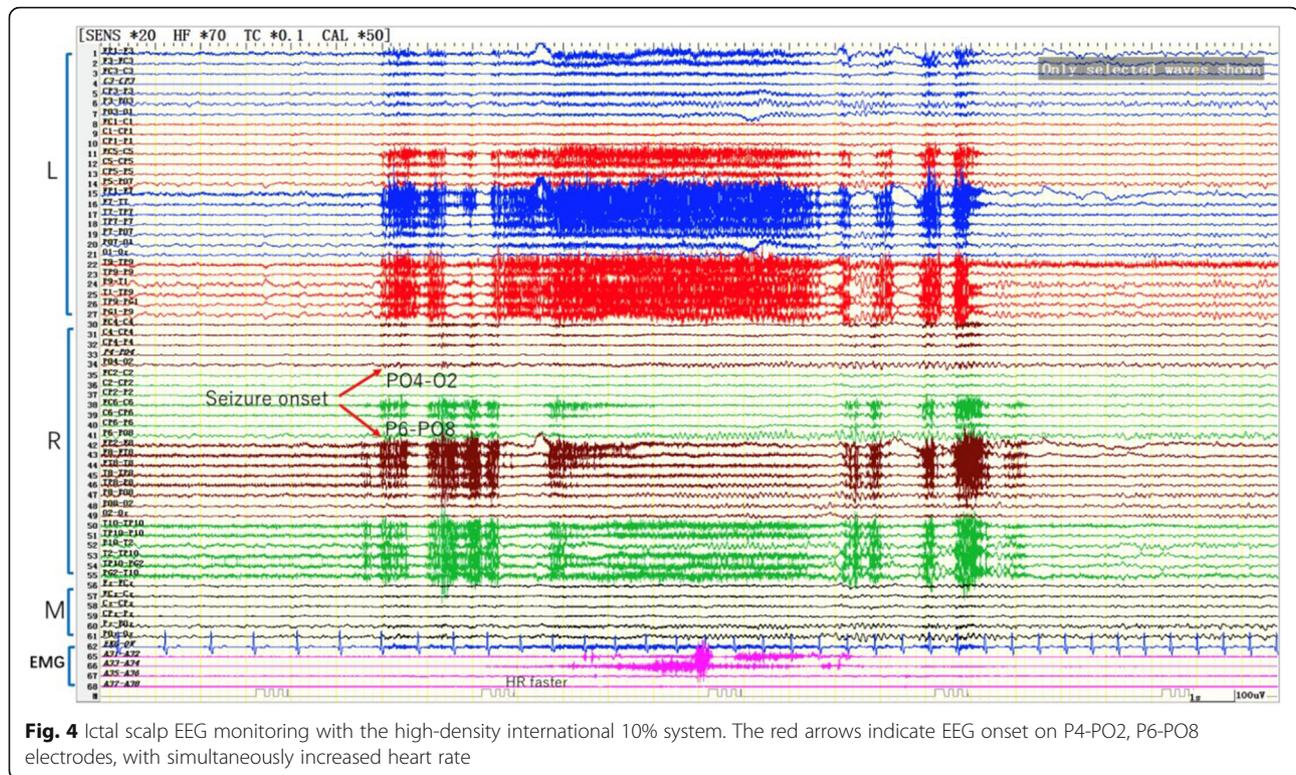


Fig. 3 The interictal EEG monitoring with high density international 10% system. The red arrows indicate slow waves on P4-PO4 and P6-PO8



oncofetal marker CD34. Therefore, a final pathological diagnosis was made as ganglioglioma (WHO grade 1) (Fig. 5).

Case 2

Case 2 was a 30-year-old right-handed woman. The first episode occurred when at the age of 6 years, with symptoms of forced turning of the head and eyes to the left, and secondary GTCS. She had one episode per month. In the last year, she experienced diplopia during episodes, and thereafter she “suddenly lost all notion of where her right face and upper and lower limbs were” and that “the right limbs were not her own when looking at it”. These episodes occurred once every 1–2 months. Neurological and general examinations were normal. Scalp EEG showed normal background activity, and sharp waves were observed on bilateral occipitals and posterior temporal regions, otherwise on the bilateral central regions. The abnormality was more severe in the left than in the right side, and the right post temporal region had continuous sharp waves (Fig. 6). Computerized tomography (CT) scanning showed a metal foreign matter under the scalp. She was treated with tegretal and remained seizure free after the treatment.

Case 3

Case 3 was a 28-year-old right-handed man. When he was 15 years old, he had episodes of head turning to the

right, which recurred briefly. He suffered several episodes on that day. He was treated with valproate, but his seizure was not completely controlled.

Eight years later when he was 23 years old, his episodes had some change. He had GTCS in episodes, and immediately after that, the patient “I suddenly had a strange feeling on the right arm that I could not recognize the right arm as my own”, and he could realize the ownership of the right arm after looking at the right arm. Neurological and general examinations were normal. Scalp EEG showed background slowing. There were 2-Hz slow waves on the bilateral occipital and posterior temporal regions, and slowing was more severe in the right than in the left (Fig. 7). MRI showed a cystiform lesion under the right insular cortex (Fig. 8). However, the patient refused to receive a presurgical evaluation.

In this report, we described three patients who experienced paroxysmal episodes of “one limb was not mine” or “was lost”, who were confirmed to be AHP. They all experienced convulsions, but the convulsions had different relationships with AHP among them. In case 1, the AHP of the left arm was followed by the left arm convulsion or only the AHP occurred; In case 2, the episodes switched from GTCS to AHP 4 years later; in case 3, the AHP occurred immediately after GTCS. All the 3 patients had hand convulsions and AHP. Case 1 received resection, while cases 2 and 3 were treated with anti-

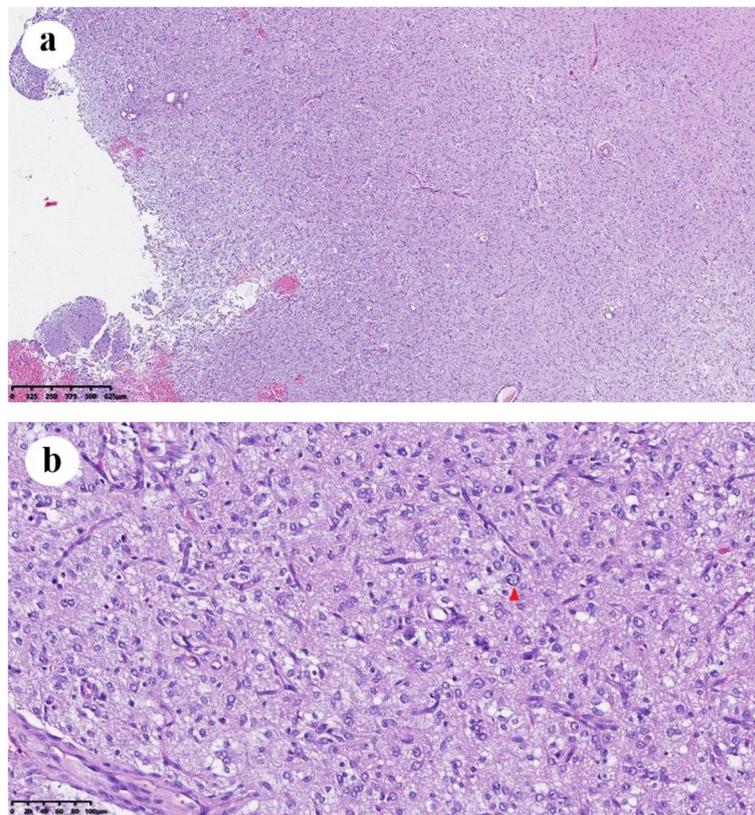


Fig. 5 Pathological examination revealed features of ganglioglioma. **a** Proliferative neuronal and glial cell elements arranged with abnormal architecture, with prominent capillary network (H&E staining, $\times 40$), **b** Dysplastic neurons (arrow, H&E staining, $\times 200$)

epileptic drugs. The phenomenon of case 3, i.e., GTCS followed immediately by AHP, had not been reported in the literature.

Discussion

AHP was originally identified to be the “failure to identify an upper limb as one’s own on palpating it behind the back or with eyes closed” [4]. Thereafter, the definition was added to include one limb having unintended motor activity. AHP comprises at least two essential components: the dissociation of intention and the presence of semipurposeful or pseudovolitional movement. Some patients also show nonrecognition of the limb [3, 7]. Some definitions put emphasis on the automotor component, i.e., the dissociation between the individual’s intention and action, and that the action of the limb is driven by somebody else [1, 8]. Dood and Jankovic [2] have proposed a new definition: “AHP includes failure to recognize ownership of one’s limb, a feeling that one body part is foreign, personification of the affected body part, and autonomous activity which is perceived and outside voluntary control.”

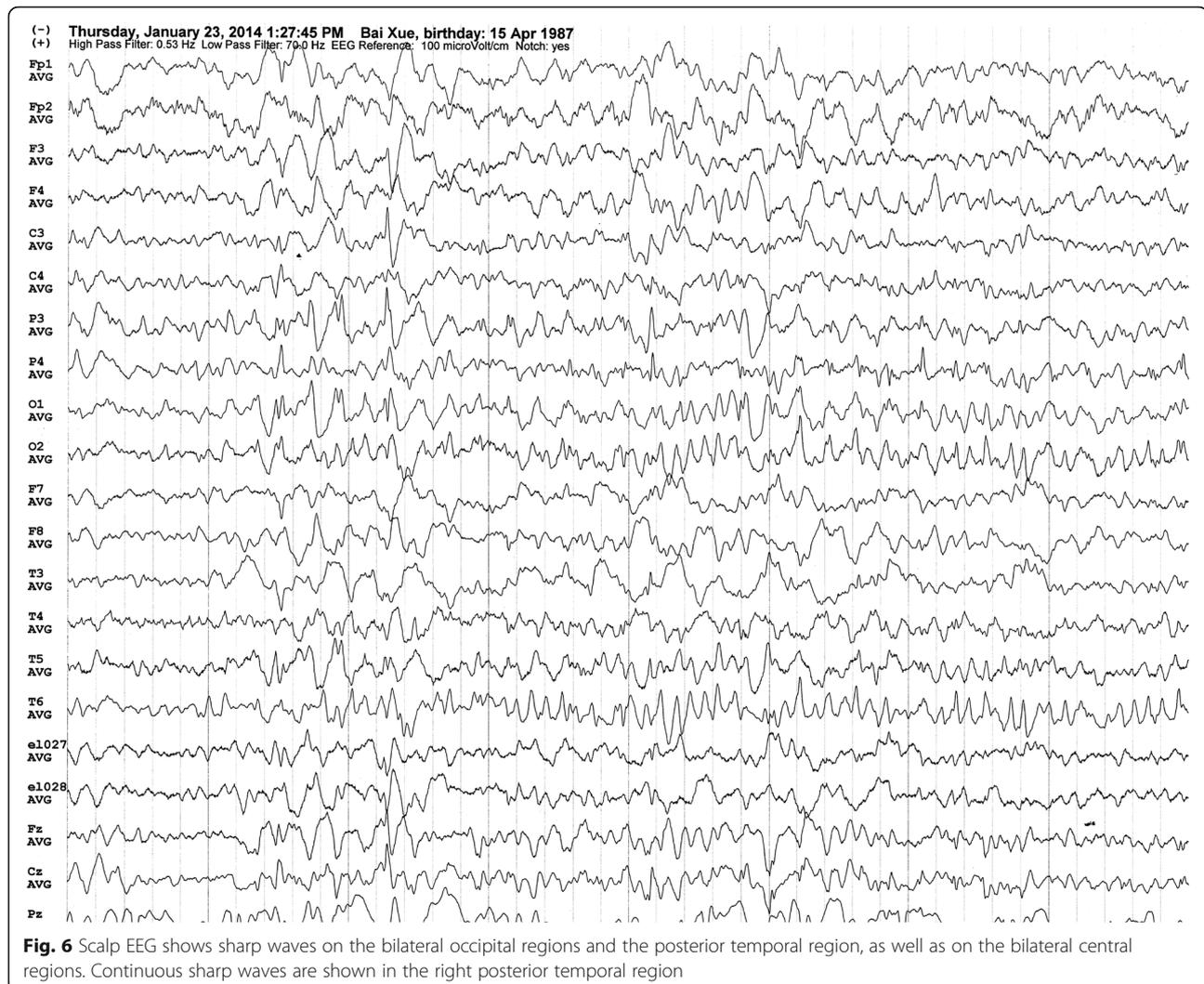
Recently, the AHP has been divided into two types: the anterior and the posterior AHP. The anterior AHP

includes the frontal type associated with reflexive grasping, groping and the compulsive manipulation of tools, and the callosal type characterized by intermanual conflict and the absence of frontal features. The posterior AHP is associated with prominent estrangement from the limb, rigidity, apraxia, cortical sensory findings and neglect [2, 9].

From the nosological perspective, Aboitiz [10] classified AHP into the following five classes: (1) diagnostic dyspraxia and intermanual conflict; (2) alien hand signs; (3) syndrome of the anarchic hand or way-ward hand; (4) supernumerary hands; and (5) agonistic dypraxia.

In this report, all the three cases of AHP had no signs of auto-motor, therefore they belonged to the posterior type [9], or the second class of Aboitiz classification [10]. The case 3 experienced AHP immediately after ictals, which may be attributed to the Todd’s paralysis.

Since the 1990s, nine cases have been reported with AHP. Eight of them had seizure onset area in the right hemisphere, and one case had seizure onset area in the left hemisphere. Here, two of the three cases had seizure onset area in the left hemisphere, while one case in the right. All together, these 12 cases could be classified into the following types:

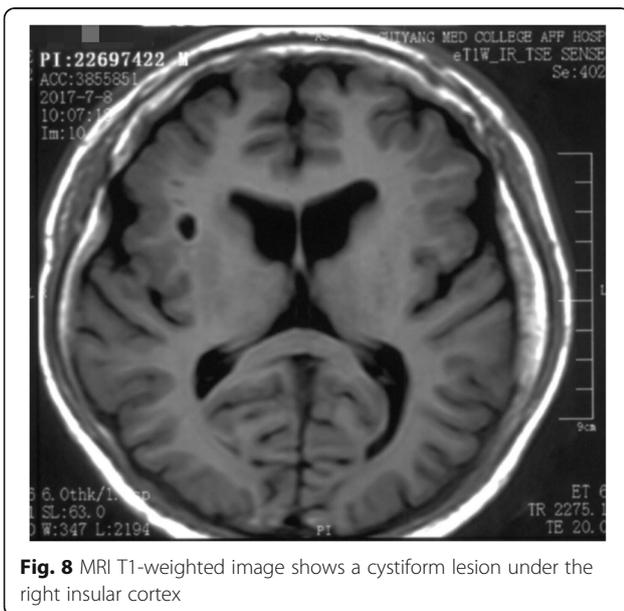
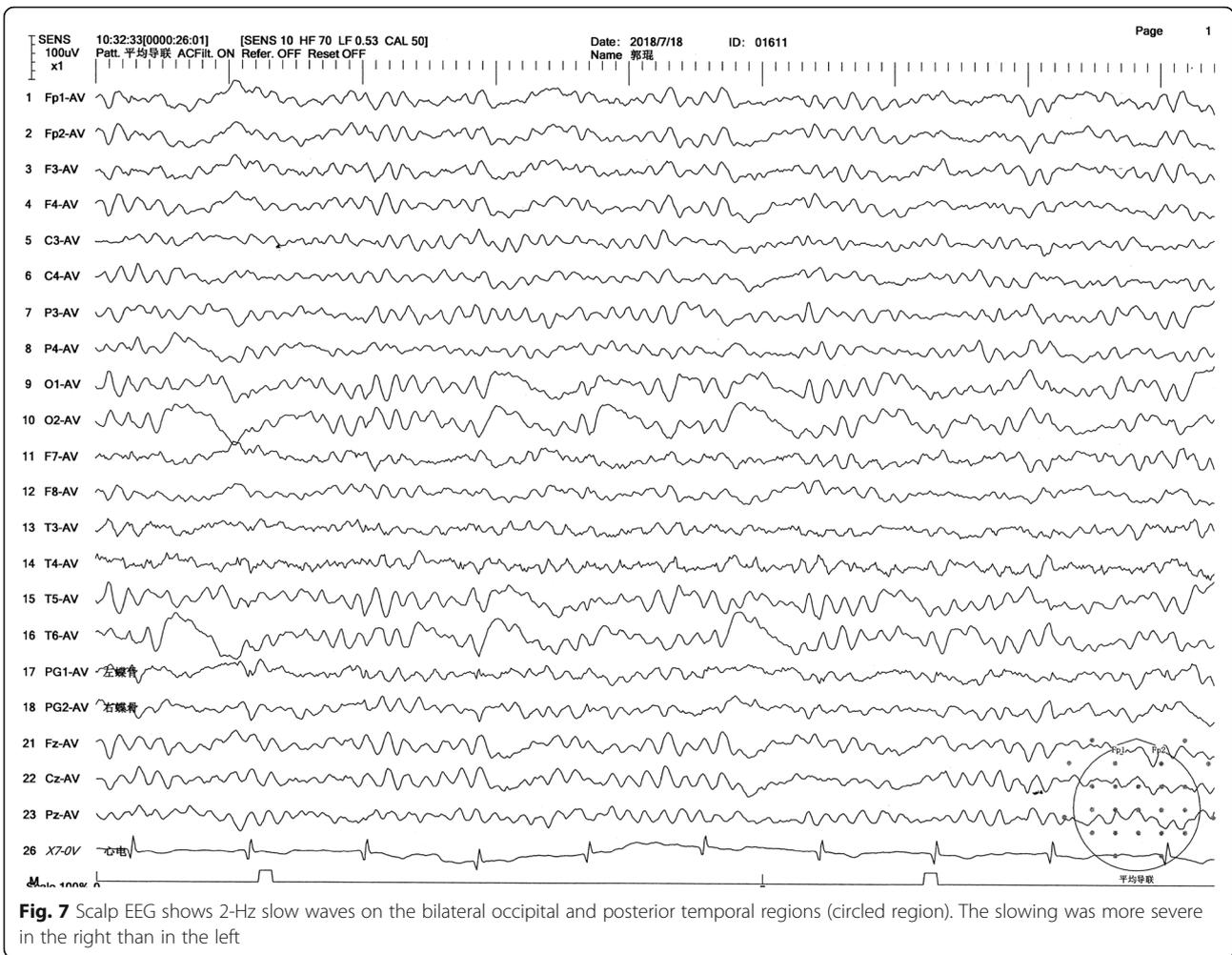


- (1) Paroxysmal AHP, followed by ipsilateral upper limb convulsion. Three cases, including cases 1 and 4 in Leiguarda's report [1], and the case in Brázdil's report [5];
- (2) Paroxysmal AHP followed by ipsilateral upper limb convulsion and then GTCS. Three cases, including case 2 in Leiguarda's report [1], one case in Feinberg's and our reports, respectively;
- (3) Partial or generalized convulsion followed by AHP. One case, i.e., case 2 in our report;
- (4) AHP associated with automatism. Three cases, including case 3 in Leiguarda's report [1], and cases 1 and 2 in Boecebeck's report [10];
- (5) Initial partial seizures, followed by AHP after partial seizure remission. One case, i.e., the case in Kim's report [8];
- (6) Generalized convulsion immediately followed by AHP. One case, i.e., case 3 in our report.

The location of AHP has been identified in the supplementary motor area, the anterior cingulate gyrus, the anterior corpus callosum or the callosal genu, the posterior primary sensory cortex, the tertiary somatosensory cortex in the superior parietal lobule and the posterior post-central gyrus [3, 5, 6]. The involvement of the occipital lobe and thalamus are rarely reported [6, 9, 11]. Unfortunately, no studies have addressed the onset zone of epileptic AHP episode.

The mechanisms of AHP have been reported in studies on non-epileptic diseases. The hypothetical mechanisms are as follows:

- (1) SMA is involved in motor planning and initiation, as well as inhibition [6], and in the control and execution of internally generated motor sequences [1]. On the other hand, the inferior parietal lobule is a multi-modal association area that contributes to



and modulates the origin of other motor systems [1]. Dysfunction of the two areas may be the basis of AHP [1].

- (2) The AHP is characterized by the coexistence of automotor activity and partial asomatogenesis [1]. This may be explained by the functional dissociation of the primary and supplemental association areas and simultaneous inhibition of the primary sensory cortex and primary motor cortex [7], simultaneous activation and inhibition of two or more cortical areas, as well as functional disassociation of the primary sensory cortex (S1) and supplementary sensory area (S2) [3, 10].
- (3) If AHP is caused by a callosal lesion, the abnormal auto-motor activity would be dissociated from conscious volition due to the interhemispheric disconnection [1].
- (4) The interhemispheric disconnection hypothesis. The corpus callosum connects both hemispheres and relays information between them. In a healthy subject, one hemisphere controls the activity of the

contralateral limb, while simultaneously suppressing the contralateral hemisphere through corpus callosal connections. Damage to the connections can result in unwanted motor activity of the limbs. Damage to the function of the posterior region may result in a variant of a neglect syndrome (e.g. the loss of sense of ownership of the limb) [6].

- (5) Resting-state fMRI findings. Ridley [12] reported a patient with developmental diagonistic dyspraxia (DD) during status epilepticus, which resolved over 2 years. Comparison of the whole-brain functional connectivity during acute DD with that after remission revealed that during the period of acute DD, the efficiency of salience and the right fronto-parietal networks were impaired, involving the frontal superior and midline structures, while after remission the network changes resolved.

In conclusion, the mechanism underlying AHP, particularly the rare epileptic paroxymal AHP, is poorly understood [4]. AHP can be represented before or immediately after convulsion, or be represented by the paroxysmal symptom only.

Abbreviations

AHP: Alien hand phenomenon; ALH: Alien limb phenomena; DD: Diagonistic dyspraxia; EEG: Electroencephalogram; MRI: Magnetic resonance imaging; GTCS: Generalized tonic clonic seizure; WHO: World health organization

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Authors' contributions

WWW and XW designed the review, and revised the manuscript. Other authors conducted the systematic search and extracted the eligible studies. WWW drafted the study. All the authors read and approved the final manuscript.

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Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Ethics Committee of Peking University First Hospital. Informed consent was obtained from all the patients in this report.

Consent for publication

All authors and patients agreed to publish the study.

Competing interests

The authors declare that they have no competing interests.

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