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# **Clinical Study**

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# Clinical Outcome and Intraoperative Neurophysiology of the Lance-Adams Syndrome Treated with Bilateral Deep Brain Stimulation of the Globus Pallidus Internus: A Case Report and Review of the Literature

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### **Keywords**

Lance-Adams syndrome  $\cdot$  Myoclonus  $\cdot$  Deep brain stimulation  $\cdot$  Globus pallidus internus  $\cdot$  Microelectrode recording

# Abstract

**Background:** The Lance-Adams syndrome (LAS) is a myoclonus syndrome caused by hypoxic-ischemic encephalopathy. LAS cases could be refractory to first-line medications, and the neuronal mechanism underlying LAS pathology remains unknown. **Objectives:** To describe a patient with LAS who underwent bilateral globus pallidus internus (GPi) stimulation and discuss the pathophysiology of LAS with intraoperative electrophysiological findings. **Patients:** A 79-yearold woman presented with a history of cardiopulmonary arrest due to internal carotid artery rupture following carotid endarterectomy after successful cardiopulmonary resuscitation. However, within 1 month, the patient developed sensory stimulation-induced myoclonus in her face and extremities. Because her myoclonic symptoms were refractory to pharmacotherapy, deep brain stimulation of the GPi was

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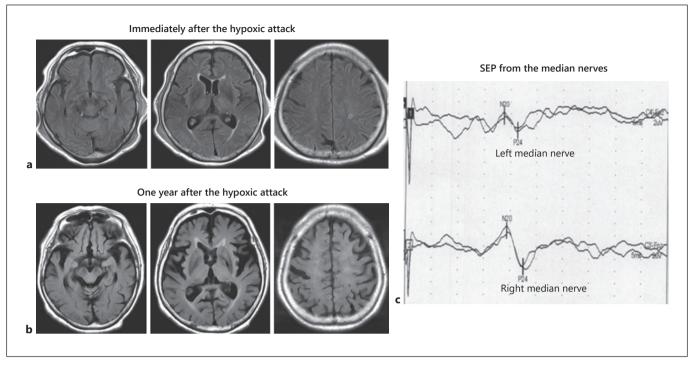
performed 1 year after the hypoxic attack. **Results:** Continuous bilateral GPi stimulation with optimal parameter settings remarkably improved the patient's myoclonic symptoms. At the 2-year follow-up, her Unified Myoclonus Rating Scale score decreased from 90 to 24. In addition, we observed burst firing and interburst pause patterns on intraoperative microelectrode recordings of the bilateral GPi and stimulated this area as the therapeutic target. **Conclusion:** Our results show that impairment in the basal ganglion circuitry might be involved in the pathogenesis of myoclonus in patients with LAS.

## Introduction

The Lance-Adams syndrome (LAS) is a syndrome of action, intention, and/or stimulus-induced myoclonus that occurs in patients in the chronic phase after cerebral

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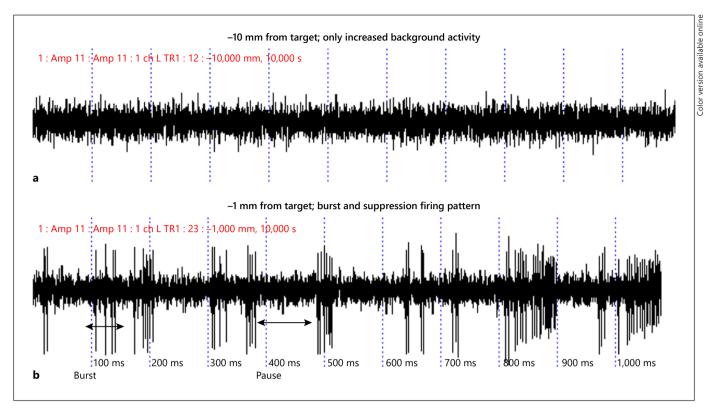


**Fig. 1. a**, **b** MRI acquired immediately and 1 year after the hypoxic event. There was no other abnormality than diffuse atrophy. **c** Somatosensory evoked potentials (SEPs) from the left and right median nerves.

hypoxia. This condition was first described by Lance and Adams in 1963, and only about 150 cases have been reported. Little is known about the pathophysiology of LAS. The first-line treatment of LAS comprises levetiracetam, zonisamide, clonazepam, valproate sodium, 5-hydroxy tryptophan (5-hydroxy tryptamine), y-amino butyric acid, baclofen, and L-dopa [1]. However, LAS generally has limited response to pharmacotherapy. Although recent reports of LAS patients demonstrated successful outcomes after deep brain stimulation (DBS), neurophysiological aspects were not assessed. To better understand the pathophysiology of LAS, we present a case of LAS caused by cardiorespiratory arrest after carotid endarterectomy who was successfully treated with globus pallidus internus (GPi)-DBS. Moreover, we present the findings of intraoperative neuronal cell firing in the basal ganglia.

# **Case Report**

A 79-year-old woman in the chronic phase after hypoxic-ischemic encephalopathy presented with involuntary movements in her extremities. One year ago, she underwent a left carotid endarterectomy at another hospital. Four days postoperatively, she experienced left carotid artery bleeding, which resulted in cardiopulmonary arrest due to hematoma-induced tracheal compression. Although she was successfully revived by cardiopulmonary resuscitation, she experienced continuous disturbance of consciousness. Her Glasgow Coma Scale (GCS) score was 8 (E3VTM5), and myoclonic seizures established on her face and extremities. The myoclonic seizures were triggered by sensory stimulation and spontaneous movements, such as opening or closing of the eyes and mouth. Combined treatment with levetiracetam (3,000 mg/ day), clonazepam (1.5 mg/day), and phenobarbital (160 mg/day) was administered, but the myoclonic seizure was medically intractable. The patient could not maintain a sitting position and was mostly bedridden because of persistent myoclonus, which rendered her incapable to participate in rehabilitation therapy (see www.karger.com/doi/10.1159/000509318 for the online suppl. Video). She was referred to our hospital for further evaluation of the indication of DBS surgery. Magnetic resonance imaging revealed diffuse brain atrophy without any other abnormalities (Fig. 1a, b). A resting electroencephalogram (EEG) demonstrated a generalized, slow activity in her reference electrodes without any epileptic discharges. Somatosensory evoked potential (SEP) from her median nerves is shown in Figure 1c. Although P24 amplitude increased, the difference between the amplitudes of P24 and N20 was <10 µV; therefore, P24 was not considered as a predominant SEP [2-4]. These results suggested that her myoclonic seizure was not a cortical myoclonus [2-5]. Three previously published case reports have described successful treatment of myoclonic seizure in patients with LAS with GPi-DBS [6-8]. Her myoclonic seizure did not permit ambulation, and her family strongly hoped for a



**Fig. 2.** Intraoperative microelectrode recordings of the globus pallidus (GP): –10 mm from the GP externus (GPe) and –1 mm from the GP internus (GPi). These recordings showed increased background activity in GPe and burst firing and interburst pause patterns in GPi.

surgical intervention. Therefore, we performed GPi-DBS for her intractable myoclonic seizure. Figure 2a, b shows the intraoperative microelectrode recordings of the GPi. The external segment of the globus pallidus (GPe) showed increased background activity, but there were abnormal bursts and interburst pauses, indicative of dystonia, in the GPi. The patient was implanted with a quadripolar electrode and an implantable pulse generator (Brio; St. Jude Medical, St. Paul, MN, USA). Postoperatively, her myoclonic seizure reduced remarkably; she could now keep a sitting position and undergo rehabilitation (see online suppl. Video). We used bipolar stimulations on both GPi. The following parameters were used: 237 µs, 110 Hz, 4.25 mA on the left side and 212 µs, 110 Hz, and 2.50 mA on the right side (Table 1). The patient still remains in a minimally conscious state; however, suppression of the action myoclonus remains stable 2 years after GPi-DBS. Her preoperative Unified Myoclonus Rating Scale (UMRS) score [9] of 90 preoperatively and was reduced to 24 postoperatively at the 2-year follow-up (Table 1).

# Discussion

The mechanism underlying the pathogenesis of LAS remains unknown. Lance and Adams indicated that abnormal synchronous and recurrent excitation of the ven-

trolateral thalamic nucleus and cerebral cortex pathways causes LAS [10]. Fluorodeoxyglucose-positron emission tomography study revealed saccharometabolic acceleration in the ventrolateral thalamic nucleus and pontine tegmentum in a patient with LAS [11]. Biochemical investigation revealed that the concentrations of serotonin and dopamine metabolites decreased in the cerebrospinal fluid of patients with LAS, indicating that both the serotonergic and dopaminergic systems were depressed in these patients [12]. Recently, a case study reported the use of ventral intermediate nucleus (Vim) DBS for LAS after cerebral infantile palsy [13], while 3 cases reported on the use of GPi-DBS for LAS [6-8, 13] (Table 1). From these reports, GPi-DBS showed improvement in UMRS by 63% on average; in addition, Vim-DBS improved UMRS by 81%. The present case also had a 73% improvement in UMRS, comparable to previous reports, suggesting that DBS is effective for myoclonus in LAS. The programming parameters for these prior cases, except for a study by Ramdhani et al. [8], utilized a bipolar configuration to achieve therapeutic gain, and amplitudes tend to be >2.5 V/mA. Yamada et al. [6] and the present case

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GPi-DBS for Lance-Adams Syndrome

	Age/ conder	Etiology	Dystonic body region	Preoperative modioation	UMRS		Improvement, %	DBS target	DBS parameters, contectos consultanda/nulso ucidibi/frecurance:
	Suma		10231 (000		pre	post			for the state of t
Yamada et al. [6]	71 M	Putaminal hemorrhage and CPA	Right hemibody	Clonazepam, valproate, gabapentin	52	15	71	Left GPi	L: 1–2+, 1.8 V/450 µs/130 Hz
Kobayashi et al. [13]	36 M	Perinatal anoxia	Upper limbs	N/A	21	4	81	Bilateral Vim	Bilateral: 1–3+ settings unavailable
Asahi et al. [7]	54 M	CPA	Generalized	Valproate, clonazepam, baclofen (intrathecal)	25	5	80	Bilateral GPi	R: 1–2+, 2.5 V/1+0–, 2.0 V, 60 µs/125 Hz L: 1–2+, 3.0 V/1+0–, 2.5 V, 60 µs/125 Hz
Ramdhani et al. [8]	26 M	Asthmatic attack and CPA	Generalized	Gabapentin, levetiracetam, valproate	52	32	38	Bilateral GPi	R: C+3-, 2.8 V/90 µs/130 Hz L: C+3-2-1-, 2.5 V/60 µs/130 Hz
Current case	79 F	ICA rupture and CPA	Generalized	Clonazepam, levetiracetam, phenobarbital	06	24	73	Bilateral GPi	R: 3+2-1-, 2.5 mA/212 µs/110 Hz L: 3+2-1-, 4.25 mA/237 µs/110 Hz
CPA, cardi	lopulmonar	y arrest; Gpi, globus pallidus inter	nus; ICA, internal cá	CPA, cardiopulmonary arrest; Gpi, globus pallidus internus; ICA, internal carotid artery; pre/post, pre-/postoperatively; UMRS, Unified Myoclonic Rating Scale; Vim, ventral intermediate nucleus of thalamus.	atively; U	MRS, UI	aified Myoclonic Rating	g Scale, Vim, ventra	intermediate nucleus of thalamus.

Table 1. Cases of Lance-Adams syndrome treated with deep brain stimulation

produced robust responses using long pulse widths (>200  $\mu s).$ 

In addition, 6 cases of myoclonus dystonia, a syndrome which presents myoclonus, showed abnormal neuronal activity in the GPi with faster and shorter bursts, and shorter pauses at DBS surgery [14], in comparison with what is typically observed in pure idiopathic or hereditary dystonia. Vitek et al. [15] first reported irregular neuronal activity in the form of intermittent grouped discharges and pauses in the pallidum in patients with dystonia and hemiballismus; therefore, it is believed that this abnormal discharge pattern in GPi may be associated with the generation of abnormal movements [15–18]. The findings of microelectrode recordings in myoclonic dystonia are very similar to our case. Myoclonic dystonia is typically characterized by childhood-onset subcortical myoclonus that predominates over dystonia with prominent upper body involvement [1, 19]. SGCE is the main causative gene [20]. Therefore, LAS differs from myoclonic dystonia both etiologically and clinically. Although, in myoclonic dystonia, basal ganglia and cortical pathogenic mechanisms are implicated from neurophysiological findings [14, 19], LAS is also potentially related to basal ganglion abnormality. To the best of our knowledge, this is the first report of neuronal activity in the globus pallidus in a patient with posthypoxic myoclonus. The electrophysiological findings and the efficacy of GPi-DBS in the present case suggests that myoclonus in LAS could be due to abnormalities in the basal ganglion circuitry [1].

# Conclusions

We successfully treated a case of severe myoclonic seizure in a patient with LAS using GPi-DBS. GPi-DBS may be an effective and safe treatment option for LAS. The intraoperative burst firing with interburst pauses detected by microelectrode recordings of the GPi and the efficacy of GPi-DBS for our patient suggest the involvement of the basal ganglion circuity in the pathogenesis of myoclonic seizures in a patient with LAS.

# **Statement of Ethics**

The published research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient provided informed consent for participation in this study. Formal ethical approval for this type of study was not required (per University guidelines).

# **Conflict of Interest Statement**

The authors declare no conflict of interest associated with this manuscript.

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### **Author Contributions**

Conception and design: H.M.; acquisition of data: H.M., N.T., R.M.; analysis and interpretation of data: all authors; drafting of the article: N.T.; critically revising the article: K.F., Y.T.; review of the submitted version of the paper: all authors; approval of the final version of the paper on behalf of all authors: H.M.

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