

Rehabilitation of paroxysmal sympathetic hyperactivity secondary to severe brain injury: A case report

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Abstract. Paroxysmal sympathetic hyperactivity (PSH) is a complication of severe brain injury (SBI), characterised by paroxysms of excessive sympathetic nervous system activity, with manifestations such as fever, tachycardia, hypertension, excessive sweating and abnormal high muscle tone. PSH can delay diagnosis and rehabilitation, impacting the functional recovery of patients. The present case report aims to explore rehabilitation management strategies and treatment effects for PSH. The case of a 31-year-old woman who presented with rapid onset of PSH following SBI is included in the report. The patient received comprehensive rehabilitation treatment after transfer to The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine, Hangzhou, China), 5 months after the initial brain injury. Neurological function recovery, symptom relief and changes in functional outcomes were evaluated. Management focused on autonomic nervous system dysfunction and an individualised rehabilitation programme. Following comprehensive rehabilitation, the PSH symptoms of the patient demonstrated notable improvement. The frequency of PSH episodes decreased from several times per week to once every 1-2 months, and episode duration shortened to <1 min. The PSH-assessment measure total score was 26 at initial diagnosis, 24 at rehabilitation admission and 4 after comprehensive rehabilitation treatment. The Glasgow Coma Scale score

improved from E1VTM1 to E4VTM3. Brunnstrom stages of bilateral upper limbs, hands and lower limbs progressed from I-I-I to II-II-II. In conclusion, in the present patient with PSH secondary to SBI, a stepwise, multidisciplinary rehabilitation strategy was temporally associated with symptomatic improvement, recovery of neurological function and improvement in activities of daily living. These findings suggest the potential clinical feasibility of an integrated rehabilitation approach for managing PSH.

Introduction

Severe brain injury (SBI) (1) often leads to severe complications, such as paroxysmal sympathetic hyperactivity (PSH). The clinical features of PSH include tachycardia, hypertension, shortness of breath, elevated body temperature, profuse sweating and postural rigidity. These symptoms may recur frequently, causing notable distress to patients (2,3). Diagnosis relies on the PSH-assessment measure (PSH-AM) score (4). The PSH-AM consists of two components: The clinical feature scale (CFS) and the diagnostic likelihood tool (DLT). The total score is the sum of the two component scores, and a total score >17 supports a definitive diagnosis of PSH. Other conditions, including epilepsy, infection, pulmonary complications, pain and medication effects, must first be systematically excluded (5). The first episode of PSH is typically managed with oral clonazepam and propranolol. Gabapentin, pregabalin and other agents can be used in the maintenance period, with treatment lasting 3 to 6 months (6). The rehabilitation programme includes passive joint mobilisation, tilt table training and hyperbaric oxygen therapy (HBOT), which may reduce the risk of recurrence and improve patient prognosis when initiated (7).

Using a case report of rehabilitation treatment for a patient with PSH following SBI, the present study describes the diagnostic process, clinical course and multidisciplinary management strategy. Clinical observations are summarised regarding the temporal associations between interventions, individualised rehabilitation and patient outcomes, while acknowledging the inherent limitations of single-case evidence.

Case report

A 31-year-old woman was found unconscious at home in February 2024. Emergency head computed tomography (CT) revealed a cerebral haemorrhage in the right basal ganglia

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Abbreviations: SBI, severe brain injury; PSH, paroxysmal sympathetic hyperactivity; PSH-AM, paroxysmal sympathetic hyperactivity-assessment measure; CFS, clinical feature scale; DLT, diagnostic likelihood tool; CT, computed tomography; GCS, Glasgow Coma Scale; EEG, electroencephalogram; fNIRS, functional near-infrared spectroscopy; HBOT, hyperbaric oxygen therapy; TMS, transcranial magnetic stimulation

Key words: brain injury, sympathetic nerve, hyperexcitation, rehabilitation treatment, case report

(Fig. 1). The Glasgow Coma Scale (GCS) score was E1VTM1 (total: 3 points; T indicates tracheal intubation), meeting diagnostic criteria for SBI (8). On day 3 after admission, the patient underwent an intracranial hematoma evacuation, decompressive craniectomy and external ventricular drainage at the Department of Neurosurgery, The First Affiliated Hospital, Zhejiang University School of Medicine (Hangzhou, China). On the 27th day post-onset, the patient suddenly developed a fever (39°C; normal adult range, 36.0-37.2°C), tachycardia (heart rate, 190 bpm; normal adult resting heart rate, 60-100 bpm), hypertension (205/110 mmHg; normal adult blood pressure, <130/80 mmHg), profuse sweating and increased muscle tone. The attending physician systematically excluded pulmonary oedema and severe pneumonia based on chest CT findings, and epilepsy was excluded via electroencephalogram (EEG). The differential diagnosis also considered and excluded infection, medication side effects and pain as contributing causes. PSH was diagnosed using the PSH-AM scoring system. The CFS of the patient had a total score of 17, which was calculated as follows: Heart rate (190 bpm; 3 points) + respiratory rate (42 breaths per min; 3 points) + systolic blood pressure (205 mmHg; 3 points) + body temperature (39°C; 3 points) + severe diaphoresis (3 points) + moderate hypertonia during episodes (2 points). The DLT had a total score of 9, which was calculated as follows: Presence of antecedent acquired brain injury (1 point) + clinical features (fever, tachycardia, hypertension, profuse sweating and increased muscle tone) occurring simultaneously (1 point) + episodes were paroxysmal in nature (1 point) + sympathetic over-reactivity to normally non-painful stimuli (1 point) + features persisting for ≥ 2 weeks post brain injury (1 point) + ≥ 2 episodes per day (1 point) + medication administered to reduce sympathetic features (1 point) + absence of parasympathetic features during episodes (1 point) + absence of other presumed causes of the features (1 point). Therefore, the total score of PSH-AM was 26, and a definitive diagnosis of PSH was made. Treatment with clonazepam at 2 mg every 8 h and propranolol at 10 mg three times daily was initiated, resulting in symptom improvement. On day 30, a PSH episode recurred; 10 mg intravenous diazepam was administered resulting in stabilisation. Over the subsequent weeks, PSH recurred intermittently (~4 additional episodes). Maintenance medication was adjusted to 2 mg clonazepam via nasogastric tube every 8 h, 10 mg propranolol three times daily and 2.5 mg bromocriptine twice daily.

After 5 months from the initial onset, the patient was transferred to The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine) for specialised care. On admission, a physical examination revealed: i) A GCS score of E1VTM1; ii) no marked increase in muscle tone in the extremities; and iii) Brunnstrom stages I-I-I for the bilateral upper limbs, hands and lower limbs. Barthel Index score is 0 (9). The EEG (Fig. 2) indicated a severe abnormality in brain function. Functional near-infrared spectroscopy (fNIRS) at rest (10 min quiet-state recording; Fig. 3) indicated an average prefrontal cortex functional connectivity strength of 0.151. In healthy adults, resting-state prefrontal functional connectivity strength is typically reported at 0.40-0.70, and this low value therefore indicates a severe decline in brain function. On the third day of admission to The First Affiliated Hospital

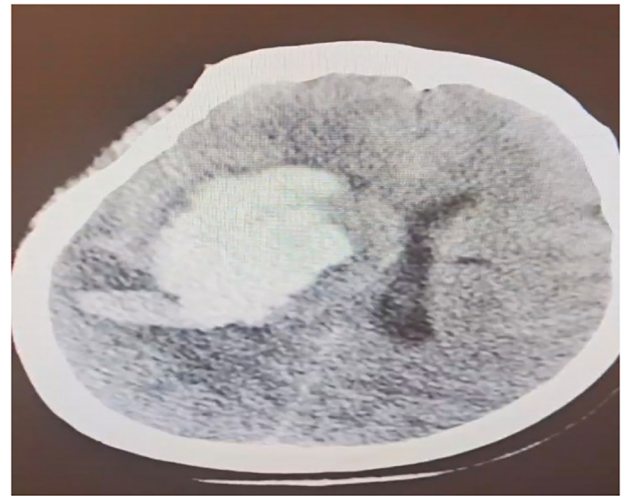


Figure 1. Cerebral haemorrhage in the right basal ganglia, which was a key cause of illness. The right basal ganglia lesion represents the primary structural injury implicated in the development of paroxysmal sympathetic hyperactivity, as this region participates in the cortical-thalamic-basal ganglia autonomic regulatory circuit.

of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine), the patient experienced a PSH episode as follows: Body temperature, 38.6°C; heart rate, 190 bpm; blood pressure, 188/102 mmHg; limb muscle tone, grade 2; and generalised diaphoresis lasting 11 min. Before diagnosing this episode as PSH, the following alternative aetiologies were systematically excluded: Infection (blood cultures and inflammatory markers reviewed), seizures (concurrent EEG monitoring), pulmonary complications (oxygen saturation trend and chest auscultation), pain response and medication effects. The PSH-AM scoring system was applied: The CFS had a total score of 16, which was calculated as follows: Heart rate (190 beats per min; 3 points) + respiratory rate (38 breaths per minute; 3 points) + systolic blood pressure (188 mmHg; 3 points) + body temperature (38.6°C; 2 points) + severe diaphoresis (3 points) + moderate hypertonia during episodes (2 points). The DLT had a total score of 8, which was calculated as follows: Presence of antecedent acquired brain injury (1 point) + clinical features occurring simultaneously (1 point) + episodes were paroxysmal in nature (1 point) + sympathetic over-reactivity to normally non-painful stimuli (1 point) + ≥ 2 episodes per day (1 point) + medication administered to reduce sympathetic features (1 point) + absence of parasympathetic features during episodes (1 point) + absence of other presumed causes of the features (fever, tachycardia, hypertension, generalised diaphoresis and increased limb muscle tone) (1 point). Therefore, the total score of PSH-AM was 24 and a definitive diagnosis of PSH was made. Immediate treatment included 2 mg clonazepam, 50 mg metoprolol, 2.5 mg bromocriptine mesylate and sodium valproate oral solution containing 12 g of active pharmaceutical ingredient in a total volume of 300 ml per bottle, yielding a standardized concentration of 40 mg/ml (12 g/300 ml=0.04 g/ml=40 mg/ml). The clinical regimen was administered via nasogastric tube feeding, with a dosing interval of every 8 h and a single administered volume of 10 ml. Accordingly, the single therapeutic

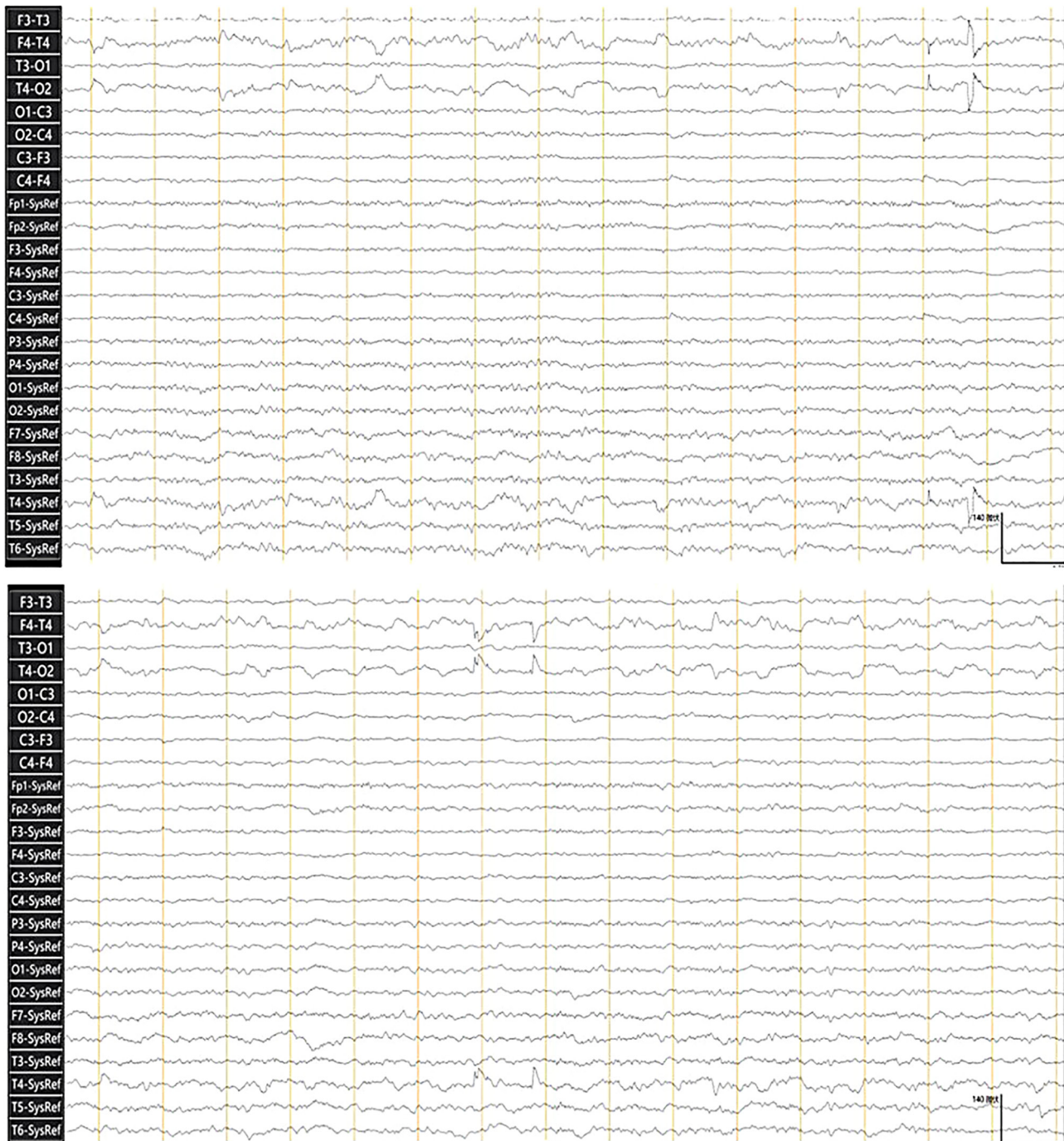


Figure 2. Electroencephalogram at rehabilitation admission (~5 months post-onset; July 2024). θ activity and rhythm were predominant at 6 Hz, with amplitudes as low as $35 \mu\text{V}$. The two sides were symmetrical, and a small amount of low- and medium-amplitude noise predominated at 8 Hz. The θ activity at 4-5 Hz and the δ at 2-3 Hz at $60 \mu\text{V}$, were scattered. Severe brain function abnormalities were indicated. The predominance of slow-wave (θ and δ) activity, with the absence of a normal α rhythm, is consistent with severe encephalopathy. The absence of epileptiform discharges supports the exclusion of seizures as a cause of the paroxysmal episodes.

dose of sodium valproate was calculated as 400 mg (10 ml x 40 mg/ml). Following treatment, blood oxygen saturation recovered to $\geq 95\%$, heart rate normalised to ~ 100 bpm, respiratory rate to 30-40 breaths/min, limb muscle tone decreased and diaphoresis gradually resolved. Thereafter, comprehensive rehabilitation therapy was combined with ongoing pharmacological management, as detailed in Table I. The rehabilitation programme was specifically differentiated as follows: i) PSH-targeted pharmacotherapy consisting of

clonazepam, propranolol/metoprolol, sodium valproate and bromocriptine; ii) neurological rehabilitation consisted of HBOT, high-frequency transcranial magnetic stimulation (TMS), auricular vagus nerve electrical stimulation and motor training; and iii) supportive/preventive care consisting of seizure prophylaxis, spasticity management, consciousness promotion and nutritional support. After comprehensive treatment, the frequency of PSH episodes decreased to once every 1-2 months, with episode duration shortened to < 1 min.

Table I. Comprehensive treatment measures.

Treatment method	Comprehensive treatment measure
Environmental requirements	Avoid strong light and noise stimulation, maintain a constant room temperature of 22-24°C and control humidity at 50-55%.
Sodium valproate oral solution	10 ml every 8 h, administered via nasal feeding.
Metoprolol tartrate tablets	25 mg every 8 h, administered via nasal feeding.
Clonazepam tablets	1 mg every 8 h, administered via nasal feeding.
Bromocriptine mesilate tablets	2.5 mg twice daily, administered via nasal feeding.
Levetiracetam tablets	0.5 g twice daily, administered via nasal feeding.
Eperisone hydrochloride tablets	50 mg three times a day, administered via nasal feeding.
Rehabilitation therapy	Transcranial magnetic stimulation uses 10 Hz high-frequency stimulation on the left dorsolateral prefrontal cortex, delivering 1,200 pulses per treatment session, lasting 15 min, 5 times a week. Vagus nerve electrical stimulation in the left ear concha is performed at a frequency of 25 Hz and a current of 0.5-1.0 mA for 20 min per session, 5 times a week. The electric standing bed starts at an initial tilt angle of 30° and gradually increases to 90°, used once daily for 20 min, 5 times a week. In joint mobilisation training, the therapist supports the patient's elbow, knee, shoulder and hip joints, and performs small range flexion and extension (5-30° along the anatomical axis, speed ≤10°/sec), twice daily for 30 min, 5 times a week.
Hyperbaric oxygen therapy	0.1 Megapascal for 60 min, once a day, 5 times a week.
Nursing interventions	Turn the patient every 2 h to prevent pressure sores, keep the skin dry and breathable, maintain oral hygiene for local cleanliness, and monitor vital signs daily.

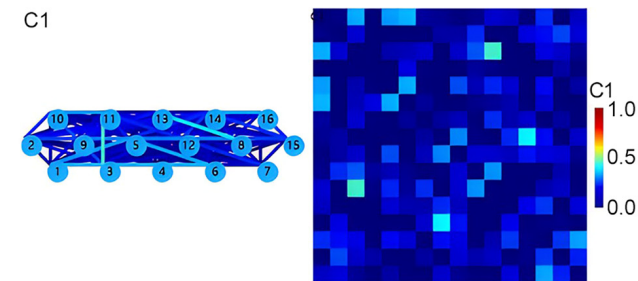


Figure 3. fNIRS at rehabilitation admission (~5 months post-onset; July 2024). Acquisition: fNIRS, resting-state recording; 10-min quiet-state measurement; prefrontal cortex channels. Functional connectivity strength is calculated as the mean correlation coefficient across channel pairs. Average prefrontal cortex functional connectivity strength was 0.151. The clinical interpretation was a severe decline in prefrontal cortex functional connectivity, consistent with the depressed level of consciousness of the patient (Glasgow Coma Scale, E1VTM1). This value serves as the base-line for assessing treatment response. fNIRS, functional near-infrared spectroscopy.

After 2 months of comprehensive rehabilitation in the Department of Rehabilitation Medicine, The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine), the re-examination findings were as follows: Body temperature, 36.6°C; respiratory rate, 18 breaths per min; heart rate, 87 bpm; blood pressure, 116/76 mmHg; and limb muscle tone, grade 0. For the PSH-AM scoring: The CFS had a total score of 0 and the DLT had a total score of 4, which was calculated as follows: Presence of antecedent acquired brain injury (1 point) + medication administered to reduce sympathetic features (1 point) + absence of parasympathetic features during episodes (1 point) + absence of other

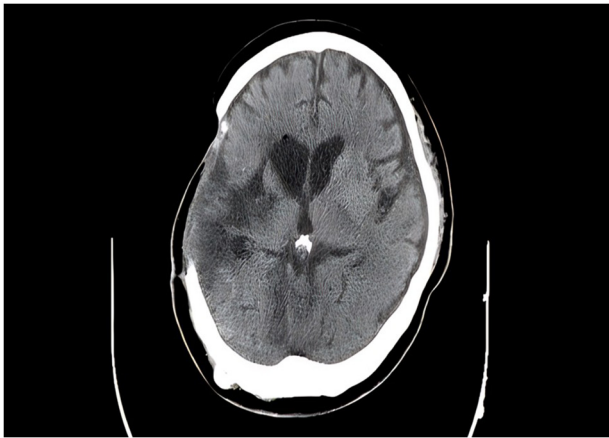


Figure 4. Head CT at the 2-month re-examination (~7 months post-onset; September 2024). Acquisition: Non-contrast axial head CT. Acquired ~2 months after rehabilitation admission (~7 months after initial brain injury). Resolution of the right basal ganglia haemorrhage. Low-density changes in the prior haemorrhage region are consistent with post-resorption encephalomalacia. The CT indicated improvement compared with the CT scan at onset. The radiological resolution of haemorrhage temporally coincided with clinical improvement (change in paroxysmal sympathetic hyperactivity-assessment measure score from 24 to 4 and Glasgow Coma Scale from E1VTM1 to E4VTM3). CT, computed tomography.

presumed causes of the features (1 point). Therefore, the total score of PSH-AM was 4. No PSH episodes were observed during the follow-up period (2 months of in-hospital rehabilitation plus 1 month of post-discharge observation). The GCS score improved to E4VTM3. Direct and consensual pupillary light reflexes were intact. The patient opened their eyes spontaneously without external stimulation. No notable increase in limb muscle tone was

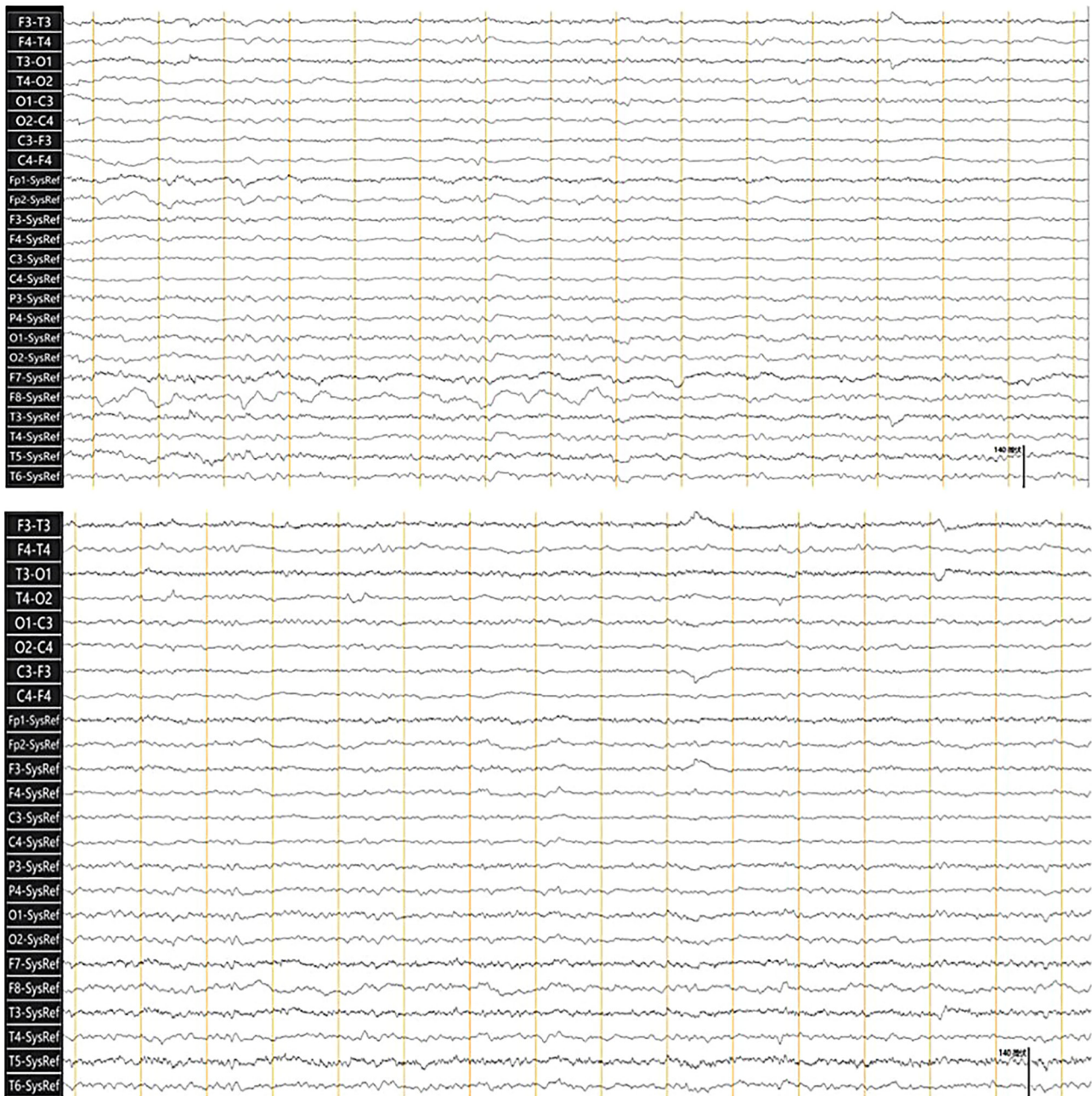


Figure 5. EEG at the 2-month re-examination (~7 months post-onset; September 2024) Acquisition: Resting-state scalp EEG, using the same electrode placement and protocol as in Fig. 2. Recorded ~2 months after admission for rehabilitation. Findings present low-amplitude 6.5-7 Hz θ activity and rhythm, with a small amount of low-amplitude 8 Hz α activity scattered throughout. Minor to moderate low-amplitude θ activity (4-6 Hz) and low-amplitude δ activity (2-3 Hz), combined with low-amplitude δ activity (70 μ V), were scattered. Improvement in brain function compared with admission. The increase in θ frequency (6 Hz to 6.5-7 Hz) and the appearance of scattered α activity are consistent with improved consciousness. These EEG changes are compatible with published associations between EEG frequency progression and recovery from brain injury. EEG, electroencephalogram.

observed. Brunnstrom stages of the bilateral upper limbs, hands and lower limbs progressed to II-II-II. Head CT re-examination (Fig. 4) indicated resolution of the right basal ganglia haemorrhage with improvement compared with admission imaging. EEG re-examination (Fig. 5) revealed low-amplitude ($\leq 35 \mu$ V) 6.5-7 Hz θ activity, scattered low-amplitude ($\leq 35 \mu$ V) 8 Hz α activity and decreased scattered low-to-moderate-amplitude (peak 70 μ V) 2-3 Hz δ activity. In awake healthy adults, dominant posterior α rhythm ranges from 8-13 Hz with amplitudes of 20-100 μ V; θ activity is minimal during wakefulness and δ activity is typically absent. These electrographic changes indicated improvement in

brain function. fNIRS re-examination (Fig. 6) showed the average prefrontal cortex functional connectivity strength increased to 0.551, a 0.4-unit increase from admission. At the 2-month reassessment following admission to the rehabilitation department (7 months after the initial brain injury), the patient regained the ability to move the limbs independently and demonstrated spontaneous emotional responses (tears and smiling). The Barthel Index score improved from 0 at admission for rehabilitation to 25 at the 2-month follow-up (7 months after initial brain injury). Specifically, bowel and bladder control each scored 10 points, and transfer ability scored 5 points, indicating improvement in daily

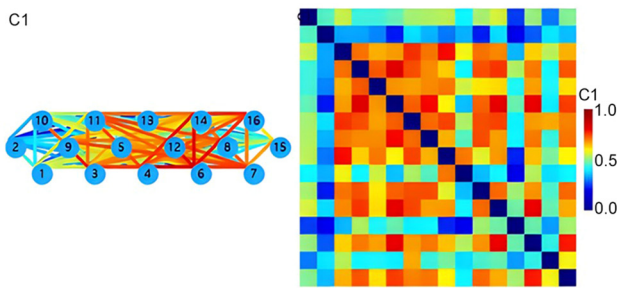


Figure 6. fNIRS at 2-month re-examination (~7 months post-onset; September 2024). Acquisition: fNIRS, resting-state recording and 10-min quiet-state measurement. Recorded ~2 months after admission for rehabilitation. Average prefrontal cortex functional connectivity strength: 0.551 (an increase of 0.4 from the admission value of 0.151). Substantial improvement in prefrontal cortex functional connectivity. This increase temporally coincided with clinical improvement in Glasgow Coma Scale (E1VTM1 to E4VTM3) and paroxysmal sympathetic hyperactivity-assessment measure score (24 to 4). The data are consistent with, but do not prove, the hypothesis that functional reorganisation of the prefrontal cortex contributes to improved top-down sympathetic regulation. fNIRS, functional near-infrared spectroscopy.

living activities. Major clinical, neurophysiological and imaging parameters across the clinical course are summarised in Fig. 7. Key outcome indicators before and after comprehensive rehabilitation are summarised in Table II.

At the 2-month reassessment following admission for rehabilitation (7 months after severe brain injury), the patient demonstrated partial neurological and functional recovery. The patient achieved spontaneous eye-opening with intact pupillary light reflexes, exhibited primitive emotional responses and regained limited independent limb movement. Motor function reached Brunnstrom stage II in bilateral upper limbs, hands and lower limbs, while activities of daily living remained severely impaired, reflected by a Barthel Index score of 25. Although paroxysmal sympathetic hyperactivity symptoms were well-controlled pharmacologically, the patient still required ongoing multidisciplinary rehabilitation support. Given that the patient was within the sub-acute recovery phase of severe brain injury, further functional improvements in consciousness, motor performance and activities of daily living might be anticipated with continued targeted rehabilitation intervention. Nevertheless, the long-term prognosis remains uncertain, considering the substantial structural brain damage secondary to right basal-ganglia haemorrhage. Persistent neurological deficits, including disorders of consciousness and motor impairment, cannot be excluded.

Discussion

The pathophysiological mechanisms of PSH mainly include the following aspects: i) The central autonomic network imbalance mechanism. In the present case, the right basal ganglia haemorrhage may have affected the autonomic regulation pathway between the diencephalon and brainstem. When damaged, the basal ganglia, the core structure of the cortico-thalamic-basal ganglia loop, can disrupt the inhibitory projections mediated by γ -aminobutyric acid, leading to disinhibition of the sympathetic excitation centre in the posterior hypothalamus. Functional near-infrared imaging revealed that the connectivity strength of

the prefrontal cortex increased from 0.151 to 0.551 before and after treatment, indicating that the functional reorganisation of the prefrontal cortex and limbic system may improve the symptoms of the patient by enhancing top-down sympathetic regulation (10). ii) The neurotransmitter storm hypothesis (11-13). The recurring sympathetic storms of the patient (such as increased heart rate and blood pressure) may be related to the dysfunction of presynaptic norepinephrine transporters. Animal experiments indicate that after brain injury, the glutamate uptake capacity of astrocytes decreases, leading to excessive activation of N-methyl-D-aspartate receptors, triggering calcium influx and promoting the release of large amounts of catecholamines. iii) Neuro-immune-endocrine axis disorder. Previous studies found that abnormal activation of the IL-6/Jak2/STAT 3 pathway in brain endothelial cells can change blood-brain barrier permeability. This allows peripheral inflammatory factors to directly affect the paraventricular nucleus of the hypothalamus, thus forming an ‘inflammation-sympathetic hyperactivity’ cycle (14,15).

According to the auxiliary examination results, the post-treatment head CT showed improved findings compared with the previous CT, with resolution of the haemorrhage and low-density shadows. The frequency of θ waves in the electroencephalogram was higher than that at admission. The frequency of θ waves increased from 6 to 6.5-7 Hz, and scattered α activity appeared. Previous literature has shown that the θ wave primarily appears in the medial part of the cerebral cortex, especially in the hippocampus, and that it is the primary mode of brain activity during relaxation and recovery. It is also closely related to cognitive and conscious functions (16). Modulation of hippocampal-medial cortical θ oscillations supports arousal maintenance, attentional processing and memory-related neuronal coordination; in patients with severe brain injury, an increase in θ frequency and the emergence of α -band activity reflect partial restoration of thalamocortical circuitry, which correlates with improved consciousness and cognitive performance (17). Studies have shown that as patients recover from brain injury, particularly with regard to motor and cognitive functions, the frequency of θ waves on the EEG may increase. The appearance of the α wave indicates that consciousness has improved, reflecting the gradual recovery of the brain's capacity for consciousness (18,19).

In the present case, the Brunnstrom stage of the patient progressed from stage I to stage II, indicating some functional recovery in the cortical-basal ganglia-thalamic loop. The intracerebral haemorrhage affected the neuroregulatory pathway between the cortex, thalamus and basal ganglia, thereby inducing PSH. The GCS score increased from E1VTM1 to E4VTM3, reflecting greater consciousness (20). The emotional responses (such as crying and smiling) that appeared later in the patient may indicate functional reorganisation of the posterior nodes of the default mode network, consistent with imaging evidence showing a 0.4-unit increase in resting-state functional connectivity strength (21). HBOT may promote angiogenesis by upregulating hypoxia-inducible factor-1 α , thereby providing a structural basis for improving consciousness and motor function (22). High-frequency TMS can inhibit the excessive activation of the amygdala (23). Motor training and electrical stimulation of the auricular vagus nerve exert arousal-promoting effects simultaneously (24). Clonazepam enhances the inhibitory effect of central γ -aminobutyric acid neurotransmission

Time Point	Phase	Clinical Event	Key Findings / Assessments	Interventions
Feb 2024 (Day 0)	Initial Injury	Onset of severe brain injury; a 31-year-old woman was found unconscious at home	CT: right basal ganglia haemorrhage; GCS E1V1M1; diagnostic criteria for SBI met	Emergency admission; supportive care
Day 3 post-onset	Surgery	Neurosurgical intervention	Intracranial hematoma evacuation, decompressive craniectomy, and external ventricular drainage	Surgical decompression; ICU monitoring
Day 27 post-onset	First PSH	First PSH episode: fever, tachycardia, hypertension, diaphoresis, hypertonia	T 39°C, HR 190 bpm, BP 205/110 mmHg, RR 42/min; PSH-AM = 26 (CFS 17 + DLT 9); excluded: pneumonia (chest CT), epilepsy (EEG), infection, drug effects, pain	Clonazepam 2mg q8h PO; Propranolol 10mg TID -> symptom improvement
Day 30 post-onset	Recurrence	PSH episode recurrence	Acute sympathetic storm; stabilisation achieved post-intervention	IV diazepam 10mg -> stabilisation
Day 30+ (subsequent weeks)	Recurrence	Intermittent PSH recurrences (~4 additional episodes)	Recurrent sympathetic hyperactivity despite initial treatment	Medication adjustment: Clonazepam 2mg NG q8h; Propranolol 10mg TID; Bromocriptine 2.5mg BID
~5 months post-onset (Jul 2024)	Rehab Admission	Transfer to a rehabilitation hospital for specialised care	GCS E1VTM1; Brunnstrom I-I-I; CT: residual hemorrhage; EEG: theta 6Hz (<=35uV), severe abnormality; fNIRS: 0.151 (severe decline)	Comprehensive admission assessment; baseline functional evaluation
Rehab Day 3	Rehab Intervention	PSH episode on 3rd day of rehab admission (11 min duration)	T 38.6°C, HR 190 bpm, BP 188/102 mmHg, muscle tone grade 2, generalised diaphoresis; PSH-AM = 24 (CFS 16 + DLT 8); excluded: infection, seizures, pulmonary complications, pain, drug effects	Immediate: NG clonazepam 2mg, metoprolol 50mg, bromocriptine 2.5mg, sodium valproate 10mg -> SpO2 >=95%, HR ~100. Comprehensive rehab: (1) PSH pharmacotherapy, (2) Neuro rehab (HBOT, high-freq TMS, vagus nerve stim, motor training), (3) Supportive care
During rehab period	Rehab Intervention	Progressive symptom reduction during comprehensive rehabilitation	PSH frequency decreased from several times/week to ~once/1-2 months; episode duration shortened to < 1 min	Ongoing multidisciplinary rehabilitation + pharmacological management
~7 months post-onset (Sep 2024)	Re-examination	2-month re-evaluation after comprehensive rehabilitation	T 36.6°C, HR 87, BP 116/76, tone grade 0; PSH-AM = 4 (CFS 0 + DLT 4) - no active PSH; GCS E4VTM3; Brunnstrom II-II-II; CT: haemorrhage resolved; EEG: theta 6.5-7Hz + scattered alpha; fNIRS: 0.551 (+0.4)	Continued maintenance therapy; outcome assessment
Long-term follow-up	Follow-up	Functional recovery and emotional responsiveness	Independent limb movement; spontaneous emotional responses (tears and smiling); sustained PSH control	Ongoing supportive rehabilitation

Figure 7. Clinical timeline of paroxysmal sympathetic hyperactivity secondary to severe brain injury. SBI, severe brain injury; PSH, paroxysmal sympathetic hyperactivity; PSH-AM, paroxysmal sympathetic hyperactivity-assessment measure; CFS, clinical feature scale; DLT, diagnostic likelihood tool; CT, computed tomography; GCS, Glasgow Coma Scale; EEG, electroencephalogram; fNIRS, functional near-infrared spectroscopy; HBOT, hyperbaric oxygen therapy; TMS, transcranial magnetic stimulation; BI, Barthel Index; T, body temperature; HR, heart rate; bpm, beats per minute; BP, blood pressure; RR, respiratory rate; ICU, intensive care unit; TID, three times daily; IV, intravenous; NG, nasogastric (tube); q8h, every 8 h; BID, twice daily; SpO₂, peripheral oxygen saturation (pulse oxygen saturation); PO, by mouth.

and reduces symptoms of sympathetic nervous system hyperactivity (25). β -blockers relieve tachycardia and hypertension by blocking β -adrenergic receptors and reducing the effects of norepinephrine and epinephrine on peripheral target organs (26). Sodium valproate inhibits excessive activation of the central sympathetic pathway by enhancing the inhibitory effect of γ -aminobutyric acid (27). Bromocriptine activates

the dopaminergic inhibitory pathway and indirectly inhibits the overactivation of the midbrain sympathetic centre (28). Levetiracetam regulates synaptic vesicle glycoprotein 2A, which may have unique value in preventing the recurrence of a sympathetic storm (29).

Several key limitations of the present case report must be acknowledged. First, since this is a single-patient report,

Table II. Outcome comparison before vs. after comprehensive rehabilitation.

Parameter	At admission/first episode	At re-examination/follow-up
PSH-AM total score	26 (CFS 17 + DLT 9)	4 (CFS 0 + DLT 4)
PSH episode frequency	Several times per week	~Once every 1-2 months
PSH episode duration	>11 min	<1 min
GCS score	E1VTM1	E4VTM3
Brunnstrom stage (UL/hand/LL)	I-I-I	II-II-II
Limb muscle tone (modified Ashworth scale)	Grade 2 (during episodes)	Grade 0
Body temperature	38.6-39°C (during episodes)	36.6°C (stable)
Heart rate	190 bpm (during episodes)	87 bpm (stable)
Blood pressure	188/102-205/110 mmHg	116/76 mmHg
Head CT	Right basal ganglia haemorrhage	Haemorrhage resolved
EEG	θ 6 Hz ($\leq 35 \mu V$); severe abnormality	θ 6.5-7 Hz + scattered α , improved
fNIRS (prefrontal connectivity)	0.151 (severe decline)	0.551 (+0.4 improvement)
Eye opening (0 points)	None (E1)	Spontaneous (E4)
Pupillary light reflex	Not assessed	Intact (direct and consensual)
Emotional response	Absent	Present (tears and smiling)
Limb movement	None	Independent movement

UL, upper limb; LL, lower limb; fNIRS, functional near-infrared spectroscopy; GCS, Glasgow Coma Scale; PSH-AM, paroxysmal sympathetic hyperactivity-assessment measure; EEG, electroencephalogram; CFS, clinical feature scale; DLT, diagnostic likelihood tool. MAS, modified Ashworth scale.

causal relationships between any specific intervention and the observed clinical improvements cannot be established. Second, no control condition was available; spontaneous neurological recovery, known to occur following SBI (30), cannot be excluded as a contributor to observed outcomes. Third, multiple rehabilitation and pharmacological interventions were implemented simultaneously, making it impossible to attribute improvements to any particular treatment component. Fourth, the patient was transferred to The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine) 5 months after initial injury, limiting the validity of 'rehabilitation' claims as applied to the period of early rehabilitation. Fifth, the generalizability of single-case findings is inherently limited. Sixth, formal quality-of-life instruments were not administered; outcome data were based solely on objective clinical scales (such as GCS and Brunnstrom). Future prospective, controlled studies with larger cohorts and standardised protocols are needed to validate these preliminary observations.

The present case report describes the clinical course of PSH following SBI, from acute onset through chronic management, with pathological mechanisms involving multi-level neural circuit dysregulation. A stepwise, multidisciplinary treatment strategy encompassing targeted pharmacotherapy, neurological rehabilitation and supportive care was temporally associated with symptomatic improvement, neurological recovery and improved functional status. EEG frequency progression and changes in fNIRS-measured prefrontal functional connectivity strength provided objective biomarker data for monitoring treatment response. These observations suggest the potential clinical value of integrated multidisciplinary management for PSH following SBI. Future research should prioritize: i) Prospective,

controlled studies with larger cohorts to evaluate the comparative effectiveness of specific PSH treatment components; ii) serial neuroimaging and neurophysiological monitoring at multiple time points to characterize recovery trajectories; iii) biomarker studies (such as neurotransmitter assays and inflammatory markers) to test mechanistic hypotheses directly; iv) standardized patient-reported outcome measures; and v) long-term follow-up studies to assess PSH recurrence rates, medication tapering strategies and ultimate functional outcomes.

In summary, the present case suggests the potential clinical feasibility of an integrated, multidisciplinary approach to PSH management following SBI, while underscoring the need for higher-quality evidence to guide treatment decisions in this challenging condition.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

ZZ, SX and ZG contributed to the conception and design of the present case report, the analysis and interpretation of

data, and manuscript revision. ZZ and SX contributed to the acquisition of the data. All authors have read and approved the final manuscript. ZZ and SX confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The study was conducted in accordance with the guidelines of the Declaration of Helsinki and received ethical approval on 24 April 2024 from the First Affiliated Hospital of Zhejiang Chinese Medical University Ethics Committee (approval no. 2024-KLS-498-01).

Patient consent for publication

The patient's family provided written informed consent during their first consultation, agreeing for the patient to receive care and authorizing the use of their anonymized clinical data, including images and videos, for medical, academic and research purposes.

Competing interests

The authors declare that they have no competing interests.

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