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# Speech-language performance and comorbid disorders in children with perisylvian syndrome induced by viral encephalitis

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## ABSTRACT

**Importance:** Viral encephalitis is one of the main causes of the perisylvian syndrome, which can cause damage to children's language-speech, feeding, and swallowing functions. Comprehensive assessment of language-speech and swallowing function and comorbidity research on these children will help children's rehabilitation workers to better understand the disease and strengthen the systematic management of comorbid disorders.

**Objective:** To describe speech and language pathology and the occurrence of comorbid disorders in children with perisylvian syndrome induced by viral encephalitis.

**Methods:** Twenty-two children with acquired perisylvian syndrome were recruited in this study. Language and speech functions, including oral motor function, swallowing function, language ability, and dysarthria were assessed in these patients. Craniocerebral magnetic resonance imaging (MRI), electroencephalogram examination, and intelligence evaluation were performed to determine brain lesions and comorbid disorders.

**Results:** All children exhibited different degrees of oral movement, dysphagia, and speech and language disorders. There was a significant difference between expressive and receptive language ability ($P < 0.05$). There were 10, 8, and 12 children who had an intellectual disability, limb disability, and epilepsy, respectively. In addition to the damage of the peri-tegmental cortex found in MRI, thalamus lesions occurred in 19 cases and white matter involvement in six cases.

**Interpretation:** Children with acquired perisylvian syndrome caused by viral encephalitis are characterized by persistent pseudobulbar dysfunction, speech and language impairment, and orofacial diplegia. They have a high probability of secondary epilepsy and are prone to motor and cognitive impairment, which need systematic management.

**KEYWORDS**
Perisylvian syndrome, Speech, Language, Feeding disorder, Viral encephalitis

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# INTRODUCTION

Perisylvian syndrome comprises a variety of clinical manifestations due to lesions in the perisylvian or opercular regions, which is characterized by pseudobulbar paralysis caused by the loss of voluntary movements that control the face, tongue, pharynx, and masticatory muscles.[1,2] The etiology of perisylvian syndrome is multiple and heterogeneous, including congenital or acquired, persistent or intermittent. In adults, the etiology is mostly secondary to cerebrovascular diseases.[3] In childhood, it can be due to congenital malformations such as polymicrogyria, meningitis and encephalitis, and epilepsy originating within the central temporal region.[4–6] In 1953, Worster Drought pointed out for the first time that perisylvian syndrome was the sequelae of childhood encephalitis.[7]

Perisylvian syndrome does great harm to feeding and speech function. Congenital perisylvian syndrome in children, including congenital bilateral perisylvian polymicrogyria and bilateral perisylvian dysplasia have been studied comprehensively, and the major phenotypes are the defects in speech production, language, and oral movement function,[8,9] but the studies on acquired perisylvian syndrome secondary to childhood viral encephalitis are limited to case reports and lack objective evaluation.

This study aims to comprehensively evaluate the speech and language performance in children with acquired perisylvian syndrome due to viral encephalitis and to study the occurrence of comorbid disorder and its potential correlation with brain magnetic resonance imaging (MRI). In this way, deeper insights are given into the daily functions of these patients, so as to improve the understanding of the professionals involved in the treatment.

# METHODS

## Ethical approval

The study was approved by the medical ethics committee of Qingdao University Women and Children's Hospital (No. QFELL-YJ-2023-202) and all parents provided informed consent.

## Patients

A total of 22 children with perisylvian syndrome treated in the Neurorehabilitation Department of Qingdao University Women and Children's Hospital from January 2015 to June 2020 were recruited in this study. The eligibility criteria are 1) Perisylvian syndrome was caused by viral encephalitis; 2) The core clinical manifestation was pseudobulbar palsy (i.e. motor speech impairment and feeding problems as the main symptoms); 3) Brain MRI showed lesions around bilateral operculum. All patients underwent physical and neurologic examinations. A standardized and itemized questionnaire was used to collect information with an emphasis on feeding, oral movement and speech characteristics, and accompanying disorders.

## Measurements of speech and language performance and mental performance

Children were examined by members of the same research group and standardized neurolinguistic assessments were performed in our rehabilitation center. In order to evaluate speech and language functions, the patients were asked to take neurolinguistic tests. Speech, language, and oral motor and swallowing function were assessed by speech therapists, and intellectual function was evaluated by professional psychologists.

Because most patients with perisylvian syndrome suffered from dysfunctional movements of lips, tongue, and jaw, the Oral Motor Score[10] was used to score the aspects of lips, tongue, and jaw movements separately. A total of 14 items were evaluated, including mandibular opening, closing, moving to the left, moving to the right, and protruding; lip abduction, pinching, closing, and lip-smacking; tongue protruding, left pendulum, right pendulum, lifting, and bouncing. Each item was scored according to the 0–5 six-grade scoring system. A total score of 70 is regarded as a normal function.

Swallowing function was evaluated by the dysphagia disorders survey (DDS),[11] including the oral stage, pharyngeal stage, and esophageal stage. A total of eight aspects were assessed for hard, soft, and liquid food. Performance for each task component and each food type is scored as 0 for competent function and 1 for deficient function or need of compensatory support. The total score ranges from 0 to 22. The higher the scores are, the more severe the dysphagia is. Dysphagia severity scale (DSS) was used to grade the severity of dysphagia.

Language ability was assessed using sign-significate relations (S-S)[12] for diagnosis of language development delay, and developmental characteristics of children were recorded meanwhile. S-S was developed by the Subcommittee on Language Development Delay of the Japanese Phonetics and Speech Medicine Association. This test is standardized by the Language Department of the China Rehabilitation Research Center based on the Chinese population. S-S test was performed to assess language comprehension, language expression, basic learning ability, and communicative attitude, for calculation of corresponding developmental ages and developmental quotients (DQ). DQ [(developmental age/actual age) × 100)] of receptive

language and expressive language < 75 is diagnosed as developmental delay.

Dysarthria was evaluated using the Chinese version of dysarthria examination,[10] which was compiled by the China Rehabilitation Research Center based on the characteristics of Mandarin Chinese and with reference to the Japanese dysarthria test. The assessment consisted of two parts. One part was the evaluation of articulation organs, including functional examinations of breathing, larynx, face, mouth, hard palate, tongue, mandible, and reflexes. The other part was articulation assessment, including conversation, words, syllable retelling, article reading, and articulation imitation movement examination. The limitation of active movement of vocal organs with decreased speech articulation was diagnosed as motor dysarthria.

Some children in this study developed cognitive impairment. We employed two test systems for a robust assessment of cognitive capacity in these patients. The Chinese version of Gesell Development Diagnosis Scale (GDDS)[13] was used for children under 3 years and 10 months, Wechsler nonverbal intelligence quotient (IQ) test[14] was performed for children over 3 years and 10 months, and developmental age was assessed for each child. Intellectual disability was diagnosed by nonverbal IQ < 70 or DQ < 75.

### Brain MRI and video-electroencephalogram recordings

All patients had cranial MR examinations. Brain MRI was carried out with a 1.5 or 3.0 T Siemens Verio scanner (Siemens Healthcare) to obtain $T_1$- and $T_2$-weighted images and fluid-attenuated inversion recovery images. The configuration of the sylvian and opercular regions was studied in detail.

All patients were examined by video-electroencephalogram (VEEG) at least once. VEEG was measured in the state of wakefulness and sleep. VEEG leads include two unipolar ones, three bipolar ones (longitudinal, horizontal, and circular), and sphenoid electrodes. The whole recording process lasted for 60–120 min. Epilepsy was diagnosed and treated accordingly based on seizure manifestations and electroencephalogram (EEG) characteristics. In the case of epilepsy, particular attention was given to seizure history, seizure type, frequency, course of treatment, and response to treatment.

### Statistics

Descriptive statistics were used. Paired-sample *t*-tests were used to compare the difference between receptive and expressive DQ scores. *P*-values of less than 0.05 were regarded as statistical significance.

## RESULTS

### Clinical features

The development of 22 children (six males, 16 females; mean age 42 months; standard deviation 20 months; age range 16–84 months) prior to encephalitis was normal. Encephalitis started at the mean age of 26 months with a standard deviation (SD) of 18 months. All 22 children had fever and convulsions at the acute stage, of which 15 cases had focal seizures with the involvement of unilateral oral, facial, and labial muscles, and nine cases had status convulsions. According to the etiological examination of encephalitis, there were eight cases of herpes simplex virus encephalitis, three cases of enterovirus-associated encephalitis, and 11 cases of unknown etiology. The children received more than 3–6 months of rehabilitation therapy, including speech therapy, swallowing therapy, oral and facial acupuncture, and neuromodulation therapy.

### Neuro-imaging

All 22 patients were examined by MRI at least twice, of which the first and the last examination were performed within one week of and one month after the symptom onset respectively. We observed the brain injury of children with the last MR examination. The MRI findings of all children were mainly destructive lesions of the cortex around the operculum, including abnormal signals in the frontal lobe, temporal lobe, insular lobe, and parietal lobe, as well as secondary atrophy and necrotic malacia. The lesions in the frontal lobe and temporal lobe were observed in 22 cases, the insular lobe in eight cases, the parietal lobe in four cases, and the occipital lobe in one case. Thalamic lesion was observed in 19 cases, including four cases of unilateral thalamus, 15 cases of bilateral thalamus, three cases of the putamen, and 22 cases of thalamic involvement as shown in Table 1. White matter abnormal signal, malacia, or ventricular dilatation were found in six cases. No cerebellar or brainstem lesions were revealed in any of the children. High intensity in the bilateral operculum, insular lobe, and thalamus, and the bilateral lesions were asymmetrical in a child with herpes simplex encephalitis as shown in Figure 1.

### Speech and language performance

The speech and language evaluation is listed in Table 1. The 22 children were varied in oral movement and dysphagia. Most of them could eat soft food but had weaknesses related to chewing strength. Some patients could bite and cut harder foods using their teeth but exhibited poor chewing ability. Two cases were able to bite, chew, and swallow peanuts and carrots. The score range of oral movement is 5–42 points, with an average score of 21.63 (SD = 11.70). Specifically, the average scores of mandibular movement, lip movement, and tongue movement are 7.93 (SD = 3.49)

**TABLE 1** Clinical characteristics of participants with perisylvian syndrome after viral encephalitis

| Patient no. | Sex/Age (month) | Oral motor score[a] | Dysphagia severity score[b] | DQ of receptive speech | DQ of expressive speech | Seizures[c] | Cognition disability[d] | Limb paralysis[e] | MRI[f] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | F/20 | NR | NR | 38 | 38 | + | + | 0 | 1 |
| 2 | F/34 | 26 | 1 | 87 | 49 | + | − | 1 | 2 |
| 3 | F/66 | 27 | 2 | 44 | 40 | + | + | 1 | 2 |
| 4 | M/56 | 31 | 1 | 80 | 25 | − | − | 0 | 2 |
| 5 | M/74 | 25 | 1 | 70 | 50 | + | + | 1 | 2 |
| 6 | F/28 | 25 | NR | 86 | 24 | − | − | 1 | 2 |
| 7 | M/48 | 20 | 2 | 49 | 24 | SEDs | + | 0 | 0 |
| 8 | F/26 | 36 | 2 | 90 | 60 | − | − | 0 | 2 |
| 9 | M/54 | 6 | NR | 42 | 40 | + | + | 2 | 2 |
| 10 | F/26 | 5 | 1 | 27 | 27 | + | + | 0 | 2 |
| 11 | F/72 | 17 | 1 | 90 | 30 | − | − | 0 | 1 |
| 12 | F/18 | NR | NR | 75 | 20 | + | + | 1 | 2 |
| 13 | M/60 | NR | NR | 80 | 35 | SEDs | − | 0 | 0 |
| 14 | M/16 | 20 | 2 | 80 | 57 | − | − | 0 | 0 |
| 15 | F/29 | 25 | 1 | 92 | 19 | SEDs | − | 0 | 2 |
| 16 | F/29 | 42 | 1 | 96 | 55 | − | − | 0 | 2 |
| 17 | F/35 | 9 | 1 | 81 | 32 | + | − | 0 | 1 |
| 18 | F/30 | 11 | 1 | 95 | 41 | SEDs | − | 1 | 2 |
| 19 | F/31 | 38 | 1 | 42 | 15 | + | + | 0 | 2 |
| 20 | M/57 | NR | 1 | 60 | 17 | + | + | 0 | 2 |
| 21 | F/26 | NR | 1 | 95 | 20 | + | − | 0 | 1 |
| 22 | F/84 | 8 | 2 | 8 | 4 | + | + | 1 | 2 |

[a]Oral motor score ranging from 0 (very severe oral motor dysfunction) to 70 (normal oral motor function).
[b]Dysphagia severity score ranging from 0 (no dysphagia) to 3 (extremely severe dysphagia).
[c]Seizures noted as present (+), absent (−), subclinical epileptiform discharges as SEDs.
[d]Cognition disability given as nonverbal IQ < 70 or receptive DQ < 75 or absent as (−).
[e]Limb paralysis noted as absent (0), hemiplegia (1), and bilateral paralysis(2).
[f]Intensity of thalamus lesions on T2 weighted MR images depicted as absent (0), unilateral (1), and bilateral (2).
Abbreviations: DQ, developmental quotient; F, female; M, male; MRI, magnetic resonance imaging; NR, not recorded; SEDs, subclinical epileptiform discharges.

(normal total score is 25), 8.80 (SD = 5.63) (normal total score is 20), and 5.81 (SD = 4.43) (normal total score 25), respectively. Tongue range of the motor was frequently limited, including reduced protrusion and lateral movements. Seventeen cases were evaluated by DDS and DSS. The score of dysphagia ranged from 3 to 12 points in the patients, including 12 cases of mild dysphagia and five cases of moderate and severe dysphagia. The speech and language function was evaluated. The average DQ scores of receptive language were 68.50 (SD = 25.50) for all patients, of which eight cases were above 85 (within or above the average range), five cases between 75 and 84 (borderline level), and nine cases lower than 75 (low average). Expressive DQ is low with an average DQ of 32.82 (SD = 15.04). On a paired-sample *t*-test, there was a significant difference between receptive and expressive DQ scores ($t = 7.009$, $P < 0.001$). Among them, 11 cases could pronounce words or a handful of single words; four cases could communicate with simple sentences; all of them had dysarthria; the other seven cases could not speak at all and communicated only by visual and body signals.

## Comorbid disorders

Table 1 shows the occurrence of other comorbid disorders. Ten out of 22 cases suffered from intellectual disability. There were eight cases of limb motor disability, seven cases of hemiplegia, and one case of quadriplegia. Twelve cases had epilepsy and five cases showed subclinical epileptiform discharges. No antiepileptic drugs were given after the acute phase. Of 10 cases of intellectual disability, nine were accompanied by seizures, of which four cases had refractory epilepsy that was difficult to control by the combination of multiple drugs. The onset of epilepsy occurred in nine cases within 6 months after the acute encephalitis and three cases after 6 months. The types of

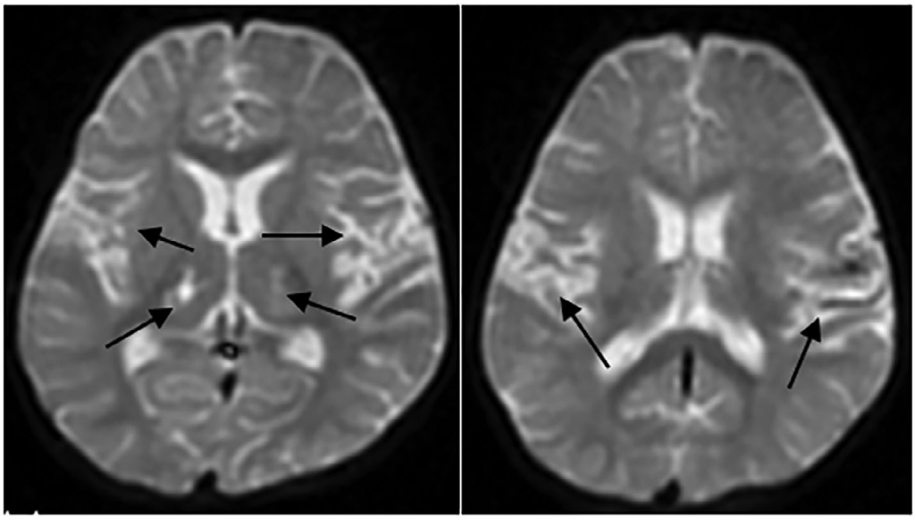

**FIGURE 1** Magnetic resonance imaging (MRI) of a child with herpes encephalitis. MRI (T2-weighted axial image) reveals bilateral opercular, insular, and thalamic hyperintensities (shown with single arrows).

seizures included focal seizures (six cases), spasm seizures (four cases), tonic-spasm (two cases), tonic seizures (two cases), tonic clonus seizures (two cases), myoclonus (two cases), atypical absence (two cases). Among those seizure cases, six patients suffered from more than two types of seizures. The seizure patients were treated with a single drug (three cases), different antiepileptic drugs combination (nine cases), methylprednisolone and prednisone (two cases), or ketogenic diet (two cases). The seizures in four cases could not be prevented by the treatments.

## DISCUSSION

Viral encephalitis was reported as the major acquired etiology of children's perisylvian syndrome. Most of the reports are case studies, lacking systematic evaluation of the status of speech disorders in the patients. To the best of our knowledge, this is the first study to comprehensively describe the speech pathology of children with acquired perisylvian syndrome induced by viral encephalitis and to analyze the comorbid disorders and imaging characteristics of the child patients. Detailed knowledge of language development and eating disorders has potential benefits for optimizing early speech and language therapy.

### Neuro-imaging and motor performance

Perisylvian syndrome secondary to encephalitis represents the cortical (opercular) type of suprabulbar paralysis,[7] as distinguished from subcortical and pontine types. In the pontine type, pathological laughter and crying as well as emotional disorder are usually additional symptoms caused by disinhibition. In our cases, the main lesion is the involvement of the operculum cortex. The cortical structures surrounding the insula, including the frontal operculum and temporal operculum, were involved in MRI findings. Other lobes such as the insular lobe were involved in eight cases, the parietal lobe in four cases, and the occipital lobe in relatively rare cases. Thalamus may play a role in spontaneous speech production and tongue movements, and its lesion could contribute to anarthria.[15] Theys et al.[16] reported a case of right thalamocapsular hemorrhage presented with bilateral perisylvian syndrome. In our study, in the condition that thalamic lesion plays a role in oral movement and language-speech impairments, more advanced imaging techniques such as diffusion tensor imaging (DTI) are needed to track corresponding functional fiber bundles for functional analysis. In addition, destruction of the thalamus or thalamic cortical ring may lead to unilateral limb paralysis. In this study, we found eight cases of limb paralysis, including seven cases of hemiplegia and one case of bilateral paralysis among the 19 thalamic-involved patients. All these cases were accompanied by bilateral thalamic lesions. Among the 22 cases, three cases were not associated with thalamic involvement or limb paralysis. It is notable that there is a correlation between the severity of thalamic lesions and limb paralysis, indicating hemiplegia may be related to the asymmetry of bilateral thalamic lesions.

### Speech and language performance

Bilateral lesions of the operculum can cause automatic motor control disorder and loss of voluntary motor function of the facial, tongue, and pharyngeal muscles, leading to eating difficulty, weak chewing power, and speech disorder. The range of mandibular movement was dramatically limited. Compared to the closing function, the mandibular opening function was less impaired. Some children need to control the mandibular movement by hand to reduce salivation and food spillover. The movement ability of lips and tongue is limited, resulting in serious drooling and

food-mixing dysfunction. In addition, reflex and involuntary functions are preserved. Although a few children failed to follow the instructions to imitate mouth movements due to severe limitations in oral movement, they were able to smile spontaneously, yawn, and keep the actions such as cutting and grinding. Dysphagia was mild in the patients, occurring mainly at the oral stage. Children with dysphagia had poor oromotor control, slow intraoral transport, weak chewing force, and even choking cough while eating. Some children needed to have their food adjusted and some required tube feeding. With the eating and swallowing rehabilitation therapy, most children could eat orally. In contrast to the improvements in oral feeding, dysarthria persisted as a long-term primary speech disorder ranging in severity from anarthria to impaired but with good intelligibility with familiar listeners. These cases of dysarthria require ongoing, long-term speech therapy. Dysarthria is related to deficits across speech subsystems of respiration, articulation, resonance, and phonation. The subjects in our study presented with varied deviant speech characteristics, including omissions, distorted pronunciation, nasal compensation, unintelligible speech, and monotone prosody.

The Operculum area is the center of language production and processing. There is an association between the extent of operculum involvement and the severity of language impairment.[17] Operculum area was found to be lesioned in all the children in this study. Accordingly, we observed that language disorders occurred in all patients and that expressive language ability was affected more than receptive language. Our findings are consistent with some studies on congenital perisylvian syndrome,[17,18] suggesting the disorders may be related to oral motor function defect due to anterior operculum lesion. In contrast to the study, Braden et al.[9] reported similar severity across both expressive and receptive language in patients with perisylvian polymicrogyria, which may be that their patient cohort had a higher incidence of cognitive abilities (79%) and some patients may have intact receptive language abilities, but only 18 patients (18/54, 33.3%) performed accurate testing. These findings suggest a more thorough assessment of language and cognition should be undertaken in order to accurately determine the language characteristics of each patient.

Among the 22 children, seven cases had difficulty in speech production, and 11 cases were able to express some simple words. Only four cases had short-sentence communication but exhibited dysarthria. If children are largely unintelligible or anarthric but have relatively preserved receptive language abilities, it is recommended that augmentative and alternative communication be introduced as soon as possible to promote communication and social participation.

Perisylvian regions are involved in speech production and development. Both functional and morphological anomalies are found in those regions for some children with speech disorders and language disorders.[19,20] As the major language tract, the arcuate fasciculus (AF) was reported to be unilateral or bilateral loss or hypoplasia in congenital perisylvian syndrome.[21,22] DTI and fiber tractography indicated that bilateral absence of AF could correlate with more severe speech dysfunction in patients with congenital perisylvian syndrome. To better understand the agenesis of AF in perisylvian syndrome, the application of DTI and fiber tracking can help to investigate the role of the AF in the clinical heterogeneity of the perisylvian syndrome. This may help the evaluation of perisylvian syndrome in conjunction with clinical and neurolinguistic findings.

## Other comorbid disorders

More than half of the children in this study presented with seizures that primarily occurred within 6 months of acute encephalitis. The manifestations of seizures are diverse, not limited to salivation, chewing, swallowing, laryngeal symptoms, speech cessation, taste hallucinations, and autonomic nerve signs of insular epilepsy and tegmental epilepsy. Two or more antiepileptic drugs were applied for the combination therapy in seizure patients, of which four cases (30.0%, 4/12) failed to control the seizures. The 10 children without epilepsy basically had normal intelligence, while the children with epilepsy and epileptic discharge of EEG had low intelligence levels and poor speech ability. Epilepsy, especially cases in which there are uncontrolled seizures and abnormal EEG patterns, can exacerbate language and intellectual disability and worsen prognosis.

## Study limitations

This study has several limitations. Firstly, our sample size was relatively small, and the study was performed in a single-center study. Due to the limited number of cases, statistical analysis of subgroups was not performed. Secondly, some children's data were from retrospective studies, which cannot ensure a comprehensive functional assessment of each child. Thirdly, we did not carry out a tracer examination of functional fasciculus related to language function in order to explore the anatomical basis of the lesion and related functional relationships. Advanced imaging techniques such as diffusion tensor tractography examination are needed.

## Conclusion

In summary, our study provides firsthand information on speech and language profiles and comorbid disorders in a cohort of children with acquired perisylvian syndrome induced by encephalitis. Almost all children had varying degrees of oral movement, eating and swallowing disorders, and speech-language disorders, which affected their ability

to communicate and feed in daily life. Half of the children have limb motor disorders, indicative of the correlation between limb paralysis and thalamic lesions. Hemiplegia may be related to the asymmetry of bilateral thalamic lesions. More than half of the children were accompanied by different types of seizures, occurring in all the children with intellectual impairment. Seizures can aggravate the poor prognosis of language and cognition function. Comprehensive and detailed characterization will benefit early identification and further targeted treatment, which may lead to better long-term outcomes.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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