Review

DOI: 10.5582/bst.2025.01029

Post-stroke dysphagia: Neurological regulation and recovery strategies

Xinyue Li[1], Minmin Wu[1], Jiongliang Zhang[1], Donghui Yu[1], Yuting Wang[1], Yumeng Su[1], Xiangyu Wei[1], Xun Luo[2], Qing Mei Wang[3,*], Luwen Zhu[4,*]

[1] Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang, China;
[2] School of Psychiatry, Wenzhou Medical University, Wenzhou, China;
[3] Stroke Biological Recovery Laboratory, Spaulding Rehabilitation Hospital, the Teaching Affiliate of Harvard Medical School, Boston, MA, USA;
[4] The Second Affiliated Hospital of Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang, China.

SUMMARY: Swallowing is a complex process requiring precise coordination of numerous muscles in the head and neck to smoothly guide ingested material from the mouth to the stomach. Animal and human studies have revealed a complex network of neurons in the brainstem, cortex, and cerebellum that coordinate normal swallowing. The interactions between these regions ensure smooth and efficient swallowing. However, the current understanding of the neurophysiological mechanisms involved in post-stroke dysphagia (PSD) is incomplete, and complete functional connectivity for swallowing recovery remains understudied and requires further exploration. In this review, we discussed the neuroanatomy of swallowing and the pathogenesis of PSD and summarized the factors affecting PSD recovery. We also described the plasticity of neural networks affecting PSD, including enhancing activation of neural pathways, cortical reorganization, regulation of extracellular matrix dynamics and its components, modulation of neurotransmitter delivery, and identification of potential therapeutic targets for functional recovery in PSD. Finally, we discussed the therapeutic strategies based on functional compensation and motor learning. This review aimed to provide a reference for clinicians and researchers to promote the optimization of PSD treatments and explore future research directions.

Keywords: stroke, dysphagia, neurological regulation, pathogenesis, recovery mechanisms

1. Introduction

Swallowing is the physiological process of transporting food, drinks, or saliva from the oral cavity through the pharynx and esophagus to the stomach, encompassing three phases: oral, pharyngeal, and esophageal. Dysphagia is the impaired ability to safely and effectively transport food from the mouth to the stomach, caused by structural or functional damage to the jaw, lips, tongue, soft palate, pharynx, esophagus, or other related organs. Symptoms may include choking on water, difficulty swallowing, sore throat, food getting stuck, reflux, or vomiting. Dysphagia can result from various causes, including neurological conditions such as stroke and Parkinson's disease (PD), muscle disorders like amyotrophic lateral sclerosis (ALS), and structural issues including esophageal strictures, tumors, or esophageal tears.

Central nervous system (CNS) disorders are the most common causes of dysphagia, with post-stroke dysphagia (PSD) being the most prevalent. Studies have shown that the incidence of PSD is as high as 80% (*1*), making it one of the most common complications in post-stroke patients, while 13%-18% of patients have persistent dysphagia within 6 months after the onset of the disease (*2*). PSD increases the risk of aspiration pneumonia, respiratory infections, and malnutrition, which in turn leads to prolonged hospital stays, higher post-discharge mortality rates, and significant impacts on patients' physical and mental health, potentially endangering their lives (*3*).

Despite the gradual increase in the understanding and research on PSD, there is still a need to strengthen our knowledge of the influencing factors, recovery mechanisms, and therapeutic approaches, as well as to enhance interdisciplinary cooperation. Currently, the complexity of factors influencing PSD, along with a lack of systematic research and insufficient interdisciplinary cooperation, makes it difficult to establish comprehensive management standards and unified treatment guidelines. This, in turn, affects patients' recovery outcomes and quality of life. Therefore, this review aimed to explore

the pathogenesis of PSD in depth, the factors and mechanisms that affect recovery, and its treatment. We also sought to integrate the concept of interdisciplinary cooperation and propose a future vision for exploring the application of novel technological tools for the assessment and intervention of dysphagia. This review seeks to provide new perspectives and reference points for the management and clinical practice of PSD.

2. About swallowing

2.1. Anatomy and physiological mechanism of swallowing

Swallowing is a complex physiological process that involves the coordinated action of multiple organs, such as the oral cavity, pharynx, and esophagus, to ensure the smooth passage of food and liquid from the oral cavity to the stomach. The swallowing process is divided into three phases: the oral, pharyngeal, and esophageal phases, in which food is first chewed and mixed with saliva to form a bolus in the mouth, while enzymes in the saliva begin to digest the carbohydrates. The tongue then pushes the food bolus from the oral cavity to the pharynx, with the movement of its back helping propel the food mass toward the pharynx. The soft palate rises during this stage, preventing food from entering the nasal cavity. During the pharyngeal phase, the cricopharyngeal muscles of the pharynx, including the superior, middle, and inferior pharyngeal constrictor muscles, begin to contract, pushing the food bolus towards the esophagus. At this point, the epiglottis drops, covering the larynx, and preventing food from entering the trachea. The vocal cords protect the airways and ensure the smooth passage of food. In the esophageal phase, food is propelled toward the stomach by peristaltic movements of the esophagus. The upper esophageal sphincter (UES) relaxes to allow food to enter the esophagus, while the lower esophageal sphincter (LES) opens as the food reaches the stomach, ensuring smooth passage into the stomach (*4*). The coordinated action of these structures and mechanisms allows the swallowing process to proceed smoothly, ensuring the efficient transport of food from the mouth to the stomach, while protecting the respiratory tract from food and fluids.

The swallowing activity is closely associated with the medulla oblongata of the brainstem. The dorsal swallow group (DSG) and ventral swallow group (VSG) of the medulla oblongata constitute the central pattern generator (CPG) of the brainstem. The dorsolateral region includes the nucleus tractus solitarius (NTS) and the rhombencephalic parvicellular reticular formation (RFpc), while the ventrolateral region consists of the nucleus ambiguus (NA) and its surrounding reticular formation. Transsynaptic transmission of both anterograde and retrograde tracer experiments have shown that during swallowing, motor neurons controlled by the NA in the VSG (motor neurons of cranial nerves V, VII, IX, X, and XII) are activated sequentially by the DSG to ensure the completion of physiological swallowing (*5*). The initiation of swallowing is usually triggered by the stimulation of receptors in the oral cavity (*e.g.* taste buds and tactile receptors). When these receptors detect the presence of food or liquid, signals are transmitted to the swallowing centers in the brainstem to initiate the swallowing process (Figure 1) (*6*).

Through electrophysiological and neuroanatomical studies, researchers have found two structures in the brainstem called hemi-CPGs, which are located on both sides of the medulla oblongata and show a symmetrical distribution. When stimulating a peripheral nerve (usually the superior laryngeal nerve) on one side, the ipsilateral hemi-CPG is activated first, and the activation signal is then transmitted to the contralateral hemi-CPG through direct synaptic connections of interneurons to achieve synchronous activation of both sides (*5*). Lang *et al.* (*7*) further demonstrated that the NTS plays a key role in the synchronization of two hemi-CPGs, while injury to the peripheral nerve fibers does not affect this synchronization process. If unilateral damage occurs in the brainstem, or if the NTS on one side is completely damaged, the initiation of swallowing and rhythmic control are consequently lost. However, in this case, stimulation of the superior laryngeal nerve on the other side still triggers a complete swallowing action, suggesting that the regulation of swallowing function may depend on the unilateral control mechanism of the CPG and synchronization between the two halves of the CPG.

The muscles responsible for bolus preparation and formation during the oral phase are controlled by the trigeminal (V), facial (VII), and hypoglossal (XII) nerves (*5*). The trigeminal nerve performs both sensory and motor functions. Its three branches (ophthalmic, maxillary, and mandibular) transmit tactile, temperature, and nociceptive information from the oral cavity and pharynx to the brainstem. This allows the CNS to monitor the location and state of food, ensuring the timely initiation of swallowing reflex. The mandibular branch of the trigeminal nerve also controls the movement of the masticatory muscles, which are crucial for chewing and mixing food into an easy-to-swallow bolus, the effectiveness of which is vital for subsequent swallowing. The facial nerve is primarily responsible for the movement of the facial muscles, aiding in efficiently pushing food onto the tongue and preventing it from being retained in the cheeks. It regulates secretion from the salivary glands, particularly the sublingual and submandibular glands, which are important for lubricating food and facilitating swallowing. Furthermore, the facial nerve is responsible for taste sensation in the anterior two-thirds of the tongue, contributing to the perception of food and the pleasure associated with swallowing. The hypoglossal nerve

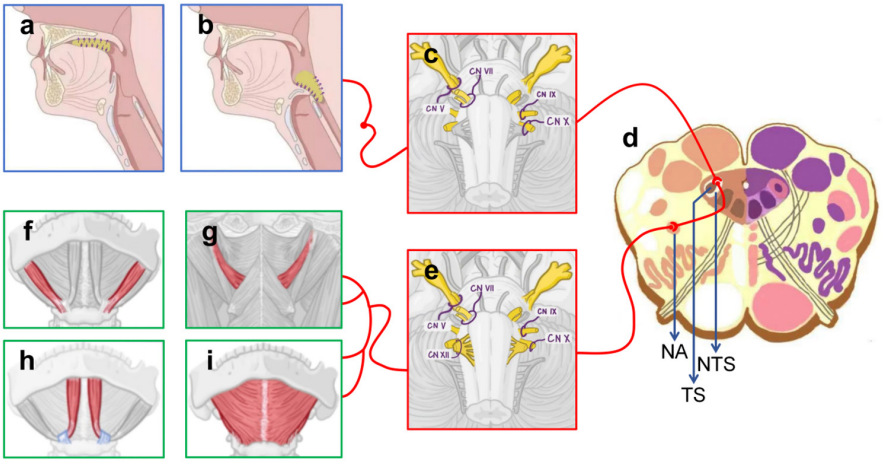

Figure 1. Mechanisms of swallowing. (a) Oral phase; **(b)** Pharyngeal phase; **(c)** Afferent nerves (V, VII, IX, X); **(d)** Medulla oblongata horizontal section; **(e)** Efferent nerves (V, VII, IX, X, XII); **(f)** Stylohyoid muscle; **(g)** Stylopharyngeus muscle; **(h)** Anterior belly of digastric muscle; **(i)** Mylohyoid muscle. When a food bolus stimulates the receptors in the oral and pharyngeal regions, the signal transmission is conveyed by the afferent nerves (cranial nerves V, VII, IX, and X) to the swallowing center in the brainstem, specifically the medulla oblongata. Within the medulla, the signal is transmitted from the NTS and TS in the dorsolateral region to the NA in the ventrolateral region. Activation of the motor neurons (cranial nerves V, VII, IX, X, and XII) controlled by the NA ensues, thereby innervating the muscles associated with swallowing and ensuring the completion of physiological swallowing. NTS: nucleus tractus solitarius; NA: nucleus ambiguous; TS: tractus solitaries.

innervates all movements of the tongue, including the intralingual and extralingual muscles. By controlling the precise movement of the tongue, it processes the chewed food into a bolus and propels it to the pharynx. During the pharyngeal phase, the recurrent laryngeal nerve controls laryngeal elevation and vocal fold closure, while the vagus nerve (X) regulates the downward movement of the epiglottis to cover the larynx. Together, they prevent food from entering the trachea and respiratory tract (*8*). The glossopharyngeal nerve (IX) is primarily responsible for transmitting sensory information from the pharynx to the CNS, initiating the swallowing reflex and ensuring the smooth passage of food into the esophagus. Additionally, at the esophageal stage, the vagus nerve regulates smooth muscle movement in the esophagus and coordinates peristalsis and sphincter activity. Overall, the coordinated action of these nervous systems ensures a smooth and effective swallowing process, preventing food from accidentally entering the trachea and ensuring it reaches the stomach.

2.2. Factors affecting the function of swallowing

Many factors affect swallowing function, including diet, smoking, alcohol consumption, and neurological disorders. Broadly speaking, they can be categorized into physiological, pathological and psychological factors, which interfere with the swallowing function to varying degrees through different pathways (Figure 2).

2.2.1. Physiological factors

The influence of diet on the swallowing function is significant. It is well known that hard, dry, and rough foods (*e.g.* nuts, dried fruits, and whole grains) may cause dysphagia, whereas soft and moist foods (*e.g.* cooked vegetables, soups, and purees) are easier to swallow. In addition, foods that are too hot or cold may cause throat discomfort and complicate swallowing. Moreover, foods high in fiber can lead to the accumulation of food debris, making swallowing difficult. Thin liquids (*e.g.* water) may be challenging for patients with dysphagia but thickeners can adjust the consistency of liquids, enhancing airway protection by promoting more timely laryngeal vestibular closure (*9*), which eases swallowing and reduces the risk of choking.

The effects of smoking and alcohol consumption on swallowing function are similar, and both threaten oral, pharyngeal, and esophageal health. Smoking was confirmed to be a significant predictor of dysphagia and aspiration pneumonia in a study of 189 older individuals with follow-up periods of up to 4 years (*10*). Acute systemic alcohol exposure has been shown to inhibit the pharyngeal-esophageal sphincter contraction reflex (PUCR) and reflex pharyngeal swallowing (RPS) (*11*). Specifically, chronic cigarette smoke, nicotine, and alcohol stimulation can cause oral dryness and reduced salivary secretion, leading to issues such as oral ulcers and gingivitis, which can impair masticatory function (*12*). Long-term smoking and alcohol consumption also lead to tissue and structural changes in the larynx and esophagus, such as mucosal degeneration, hyperplasia, and fibrosis of tissue structures, resulting in a delay in the function of swallowing-related structures and interference with normal swallowing process (*13*). Swallowing is a complex reflex that requires coordination by the CNS. Nicotine and alcohol slow the initiation and execution of the swallowing reflex by inhibiting the CNS, thereby making swallowing sluggish and impairing its coordination (*11*).

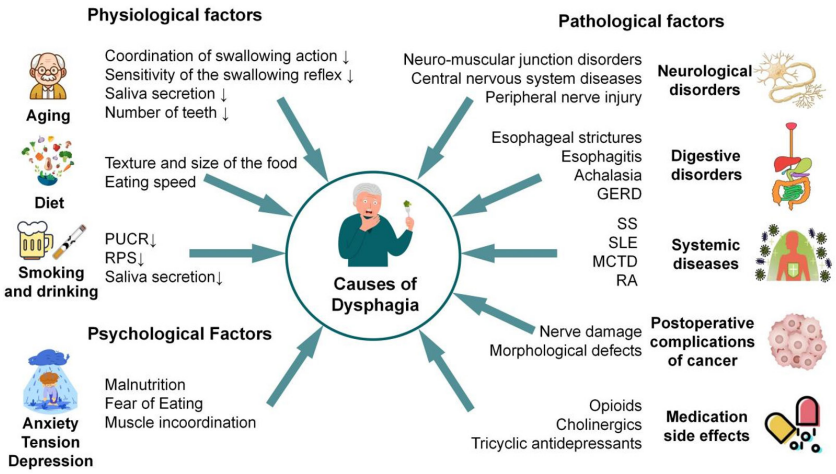

Figure 2. Causes of dysphagia. Factors affecting swallowing function can be categorized into physiological factors, including diet, smoking and alcohol consumption, and aging. And pathological factors, which can be categorized into neurological, digestive, and systemic disorders, as well as postoperative complications of cancer and medication side effects. In addition, psychological factors caused by anxiety, tension, and depression are also included.These factors interfere with swallowing function to varying degrees through different pathways. PUCR: pharyngeal-esophageal sphincter contraction reflex; RPS: reflex pharyngeal swallowing; GERD: gastroesophageal reflux disease; SS: sjögren's syndrome; SLE: systemic lupus erythematosus; MCTD: mixed connective tissue disease; RA: rheumatoid arthritis.

Aging affects the swallowing function both physiologically and structurally, increasing the risk of aspiration, choking, and malnutrition in older adults. The European Union Geriatrics Society White Paper showed that the prevalence of dysphagia in nursing homes exceeds 60%, and up to half of the older population over 60 years of age experience some type of swallowing disorder (*14*). Physiologically, the speed and sensitivity of the swallowing reflex diminish with age, indicating that the initiation of the swallowing maneuver becomes delayed, thereby increasing the risk of aspiration and choking. Simultaneously, aging leads to degeneration of the CNS and peripheral nervous system (PNS), slowing nerve conduction and impairing the coordination of nerves involved in swallowing, making the process more difficult. Additionally, the decline in salivary gland function and reduced salivary secretion in older individuals lead to dry mouth and insufficient lubrication of food, making it harder to form a food mass and increasing the risk of aspiration during swallowing (*15*). Structurally, the number of teeth affects the chewing ability. Multiple regression analysis found that the rates of swallowing problems in older adults with 0-24 and 25-32 remaining teeth were 2.04% and 1.31%, respectively, indicating that tooth loss is associated with reduced swallowing function in this demographic (*16*).

2.2.2. Pathological factors

A wide range of pathological factors affect the swallowing function in adults, including neurological disorders, digestive disorders, systemic diseases, and side effects of neurological medications, all of which may lead to dysphagia. Stroke is the most common neurological condition that causes dysphagia, and damage to areas of the brain that control swallowing can result in a dull or uncoordinated swallowing reflex. Subdural lesions of the brainstem, including the pontine and medulla oblongata, are the most common causes of dysphagia (*17*). Flowers *et al.* (*18*) found that in a randomized sample of 250 patients with stroke, dysphagia prevalence was 37-45% *via* screening, 51-55% through clinical assessment, and 64-78% with instrumental techniques. PD causes the degeneration of motor neurons, affecting the coordination and strength of the swallowing muscles, resulting in stiffness of the muscles in the oral and pharyngeal regions. The basal ganglia are the primary sites of pathology in PD, and videofluoroscopy can reveal oropharyngeal involvement, as evidenced by dysphagia and impaired transit of the meal bolus between the pharynx and proximal esophagus (*19*). A meta-analysis by Kalf *et al.* (*20*) showed that dysphagia occurred in 35% of patients with PD in studies examining subjective outcomes; however, in studies using objective measures, the proportion was as high as 82%. Patients with Alzheimer's disease (AD) experience a progressive loss of swallowing function and cognitive decline (*21*). A scoping review conducted by Affoo *et al.* (*22*) showed that the prevalence of dysphagia in patients with AD ranges from 32% to 45% when assessed clinically and from 84% to 93% when assessed instrumentally. ALS affects motor neurons and leads to weakness, atrophy of the swallowing muscles, and a decrease in the saliva clearance rate (*23*).

Peripheral nerve injuries such as those affecting the trigeminal, facial, and hypoglossal nerves can impair the function of the muscles of the mouth and tongue, leading to difficulties in food processing and propulsion (*24*). Digestive disorders that can cause swallowing difficulties include esophagitis, esophageal stricture,

esophageal cancer, gastroesophageal reflux disease (GERD), and achalasia cardia (*25*). Patients with Sjögren's syndrome (SS), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), and rheumatoid arthritis (RA) experience various degrees of dysphagia (*25*). The anticholinergic and antidopaminergic effects of antipsychotics and tricyclic antidepressants should not be overlooked, as they cause dry mouth, interfering with the lubrication of the food bolus, and reduce the coordination and strength of peristalsis (*26*). Patients who have undergone radiation or chemotherapy for cancer experience prolonged chewing and swallowing owing to dry mouth compared to their condition before treatment (*27*).

2.2.3. Psychological Factors

It is important to note that psychological factors are closely linked to impaired swallowing function. Stressful emotions such as anxiety and tension can not only lead to incoordination of the muscles involved in swallowing but may also trigger spasms, thereby exacerbating symptoms of dysphagia. For instance, patients may experience difficulty swallowing or even choking during meals due to nervousness. The impact of these psychological factors on swallowing function extends beyond the physiological level and can affect social interactions as well. Studies have shown that among patients with dysphagia, 45% consider eating to be a negative experience, 41% feel anxious or panicked during meals, and 36% avoid dining with others due to fear of embarrassing situations (*28*). These emotional and psychological changes not only diminish the quality of life but may also lead to malnutrition, further exacerbating muscle atrophy and swallowing dysfunction, creating a vicious cycle.

Depression is another significant psychological factor contributing to dysphagia. Patients with depression often experience symptoms such as low mood, slowed thinking, and reduced cognitive function. These symptoms can impair the swallowing reflex and the coordination of swallowing actions, leading to prolonged food retention in the oral cavity and increasing the risk of aspiration (*29*). Additionally, persistent loss of appetite, reduced food intake, or even refusal to eat can result in physical weakness, further aggravating swallowing difficulties. Lin *et al.* (*30*) found in a survey of elderly individuals across 18 care facilities that those with depressive symptoms had a higher frequency of dysphagia compared to those without such symptoms. Furthermore, studies on PD (*31*), multiple sclerosis (*32*), and GERD (*33*) have identified a significant positive correlation between depressive symptoms and dysphagia. Moreover, patients with depression may develop a fear of eating, worrying about choking or aspiration during meals. This fear can inhibit swallowing function, worsening dysphagia.

3. Pathogenesis of PSD

The etiology of PSD encompasses a multitude of intricate physiological pathways, which can be categorized into several distinct yet interrelated components. These include impairments to the cortical swallowing center, disruptions to cortical descending fibers, lesions within the brainstem, alterations in the extrapyramidal system and cerebellum, and damage to the cerebral nerves. Dysfunction or injury to any of these neural substrates may precipitate dysregulation of the swallowing process, characterized by impaired coordination, delayed pharyngeal response, and an elevated risk of aspiration during deglutition (Figure 3).

3.1. Cortical swallowing center impairment

Empirical evidence derived from both human and animal studies has delineated the cortical regions primarily implicated in the orchestration of swallowing, which are predominantly localized within the primary motor cortex (M1), primary sensory cortex (S1), insula, cingulate gyrus, supplementary motor area (SMA), and premotor cortex, and other cortical domains. These areas are pivotal in the initiation of deglutition and the regulation of the oropharyngeal phase (*34*). Various cortical lesions result in distinct dysphagic phenotypes, predominantly manifesting as challenges in the initiation of swallowing and delays in pharyngeal reflexes. The primary motor and sensory cortices, collectively referred to as the primary sensorimotor cortex (SM1), are situated within the precentral gyrus of the frontal lobe and the postcentral gyrus of the parietal lobe. SM1 is a well-characterized cortical region that plays a significant role in swallowing, with dysfunction primarily contributing to the impaired control of swallowing movements. Daniels *et al.* (*35*) have demonstrated that lesions within M1 confer a higher risk of aspiration compared to those within S1. Advanced spatial delineation of SM1 *via* diffusion-weighted MRI has revealed that S1 lesions are correlated with impaired laryngeal vestibular closure and pharyngeal residue, while M1 lesions are associated with compromised laryngeal elevation (*36*). The insula, another cortical component, is integral to the initiation of swallowing by processing sensory inputs and interfacing with SM1 across both hemispheres to modulate the timing of swallowing onset following mastication or other oral activities (*37*). Research has indicated that the absence of insular activation is linked to pharyngeal dysphagia, which significantly elevates swallowing thresholds, impairs the patient's capacity to plan swallowing movements, and results in uncoordinated or abnormal swallow completion, thereby heightening the risk of aspiration (*37*). The cingulate gyrus is instrumental in the early stages of swallowing by generating swallowing commands through the retrieval of relevant memories. Consequently, disruptions

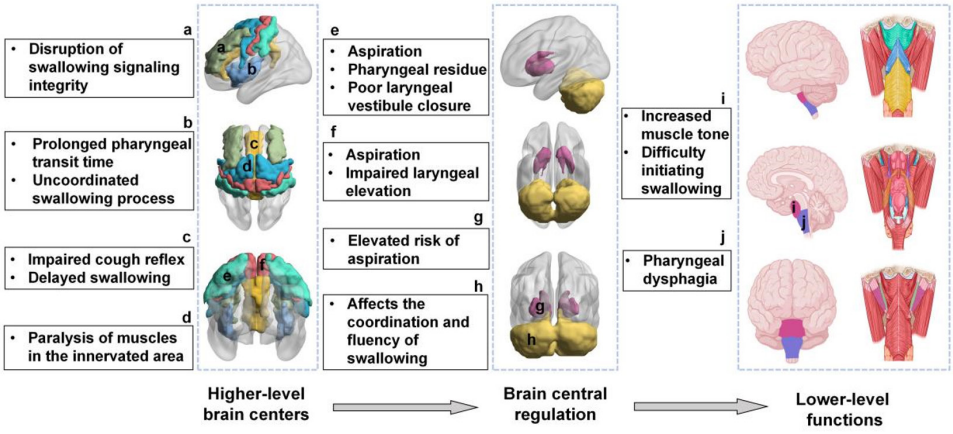

Figure 3. Pathogenesis of PSD. (a) Supplementary motor area (SMA); **(b)** Insula; **(c)** Cingulate gyrus; **(d)** Premotor cortex; **(e)** primary sensory cortex (S1); **(f)** primary motor cortex (M1); **(g)** Basal ganglia; **(h)** Cerebellum; **(i)** Pons; **(j)** Medulla oblongata. In the sections higher-level brain centers and brain central regulation, the lateral, upper and frontal views of the brain are presented from top to bottom. In the lower-level functions, from top to bottom, they are the lateral view, sagittal cut and frontal view of the brain. The swallowing signal can be conducted via the following pathways: M1, S1, insula, cingulate gyrus, SMA, and premotor cortex serve as higher-level central nervous system structures, transmitting swallowing signals to subcortical structures such as the basal ganglia and cerebellum. These subcortical structures, in turn, innervate brainstem nuclei and neural clusters, such as the pons and medulla oblongata, which control muscles associated with swallowing, including the stylohyoid, stylopharyngeus, and the posterior belly of the digastric muscle. Damage to different cortical areas can lead to varied manifestations of dysphagia.

in cingulate gyrus activation can impair the issuance of swallowing commands, leading to delays in swallowing and the potential development of dysphagia (*38*). The SMA, which shares substantial common information with M1 in the cingulate cortex, is crucial in the processing of swallowing motor functions, and damage to this area may result in compromised or delayed swallowing command signals, thereby disrupting the integrity of swallowing signaling and precipitating swallowing disorders (*39*). The premotor cortex projects to both pyramidal and extrapyramidal systems and is tasked with integrating afferents from the frontal cortex, basal ganglia, cerebellum, and other regions, with injuries to this area primarily presenting as muscle paralysis within the innervated region (*34*).

3.2. Cortical descending fiber impairment

Cortical descending fibers originate from the large pyramidal cells of the cerebral cortex and descend into the spinal cord, ending directly or indirectly at the anterior horn motor neurons of the spinal cord in what is known as the corticospinal fiber, and at the somatomotor nuclei and special visceral motor nuclei within the brainstem in what is known as the corticonuclear fibres. These fibers also synapse with the somatomotor nuclei and special visceral motor nuclei within the brainstem, facilitating the innervation of voluntary musculature involved in the act of swallowing. Disruption of the white matter within the corticospinal fibers can sever the connection between the swallowing center and cortical descending fibers, impairing bilateral cortical connectivity and precipitating dysphagia. The corticonuclear fibre is known to exert a facilitatory influence on the medullary swallowing center, participating in the active swallowing process (*40*). Damage to the corticonuclear fibre can lead to prolongation of the pharyngeal phase of deglutition, while reflexive swallowing activity remains relatively preserved. Further damage affecting inhibitory neuronal loops can result in the loss of high-level inhibition at the medullary swallowing center, preventing the initiation of active swallowing (*41*).

3.3. Brainstem injury

In the context of brainstem injury, the medullary swallowing center is the second largest swallowing center after the cortex and subcortex. It includes the NA, NTS, and surrounding reticular structures, which control and regulate the swallowing reflex. Lesions to the medullary swallowing center can remove the inhibition of the pharyngeal phase, resulting in its prolongation (*42*). Daniels *et al.* (*6*) observed that infratentorial infarcts, particularly those involving the pontine bridges and medulla oblongata, are more likely to cause swallowing deficits compared to supratentorial infarcts, with the medulla oblongata being the most significantly affected. Unilateral damage to the medullary swallowing center can result in unilateral paralysis of the vocal cords, soft palate, and laryngeal muscles, with less severe impairment of swallowing function, whereas bilateral damage can lead to the loss of the pharyngeal reflex (*43*). However, Handy *et al.* (*44*) noted through clinical observation that patients with acute unilateral medullary stroke often exhibit bilateral pharyngeal muscle paralysis, sluggish pharyngeal reflex, and prolonged pharyngeal phase. The underlying mechanisms are not uniform. One possible cause is damage to the medulla oblongata nucleus. When the nucleus of the medulla oblongata is lesioned, the connection between the medulla oblongata

and the thalamus is disrupted, leading to a series of motor, sensory, and cognitive effects, including bilateral pharyngeal muscle paralysis (*45*). Another potential mechanism is that the medullary swallowing center functions as a unified entity. Damage to one side can interrupt the connection with the contralateral center and affect the innervation of contralateral nerve fibers, leading to dysfunction of the entire center. This manifests as uncoordinated muscle activities, prolonged pharyngeal phase, and swallowing dysfunction. However, with active treatment and the body's compensatory mechanisms, intact central neurons on the ipsilateral side can gradually establish contact with the contralateral swallowing center, thereby improving swallowing function.

3.4. Extrapyramidal and cerebellar system impairment

Extrapyramidal and cerebellar system impairments refer to damage to the neurological structures outside the pyramidal system that regulate muscle tone and coordinate muscle activity, enabling the execution of fine and random movements (*46*). Extrapyramidal injuries can lead to dystonia in swallowing muscles, characterized by muscle stiffness or tremor, resulting in inflexible and uncoordinated swallowing movements (*42*). Furthermore, the extrapyramidal system plays a crucial role in the coordination of swallowing movements by influencing and controlling all conduction pathways of somatic movements, including the cerebral cortex, cerebellum, and brainstem reticular formation. Damage to this system can compromise this coordination, leading to impaired food propulsion during swallowing and affecting the smoothness and accuracy of deglutition (*47*).

3.5. Cranial nerve injury

Normal deglutition is facilitated by the coordinated activity of several cranial nerves, predominantly the V, X, and XII nerves. Impairment of these nerves, which are integral to the swallowing process, can result in a spectrum of dysphagic symptoms, including pharyngeal muscle weakness, impaired bolus propulsion, discoordinated soft palate movements, and incomplete closure of the laryngeal orifice, thereby prolonging the pharyngeal phase (*5*). X nerve is particularly crucial, with its dorsal nucleus regulating the majority of the soft palate, pharyngeal, and cricopharyngeal muscles. It is responsible for innervating soft palate elevation, vocal fold closure, and epiglottic reflexion. Dysfunction of the X nerve can severely compromise swallowing function, leading to paralysis of the majority of its innervated muscles, insufficient laryngeal closure, hoarseness, choking, and dysphagia (*48*). Additionally, X nerve damage can diminish sensory feedback during swallowing, reducing sensation at the tongue base and epiglottis, and increasing the risk of aspiration (*24*).

The V nerve, governed by four major nuclei — sensory, pontine, spinal tract, and motor nuclei — plays a pivotal role in swallowing. The trigeminal motor nucleus is the sole motor nucleus among these, receiving and processing afferent impulses from motor neurons in the brainstem and spinal cord. Its dorsal aspect is the reticular formation, which relays and transmits sensory information related to swallowing to the thalamic nuclei, including tactile and gustatory sensations in the pharynx, auditory sensations in the larynx, vocal cord vibrations, and laryngeal muscle tension. Its ventral aspect is part of the cortical-subcortical pathway that governs swallowing. Consequently, the trigeminal nucleus and its surrounding area serve as a relay station. Injury to the ventral aspect of the trigeminal motor nucleus can disrupt the swallowing conduction pathway, leading to paralysis of the oral muscles it innervates, such as the masticatory muscles, stylohyoid muscle, mylohyoid muscle, and the anterior belly of digastric muscle, and consequently prolonging the pharyngeal phase (*49*). The trigeminal spinal fiber nucleus also innervates facial sensation, and damage to this nucleus can reduce sensation in the oral cavity, tongue, and soft palate, potentially delaying swallow triggering and increasing the risk of aspiration (*50*).

The tongue, primarily functioning in the oral phase, also contributes to the pharyngeal phase through the propulsive force generated by its muscular movements. Therefore, damage to the XII nerve can lead to paralysis of the lingual muscles, resulting in poor propulsion of food in the oral cavity and prolonged retention of food, which may cause food to flow out of the oral cavity or prematurely into the pharynx, increasing the risk of aspiration and pharyngeal dysphagia (*24*).

4. Factors affecting recovery from PSD

A variety of factors influence recovery from PSD, including the type and site of stroke, the patient's functional status, the presence of comorbidities, sex differences, the kinematic characteristics of the hyoid bone and epiglottis, and the necessity of performing a tracheostomy. These factors work together to determine the patient's recovery and degree of improvement in the swallowing function (Figure 4).

In terms of the type and site of stroke, patients with hemorrhagic stroke are more likely to develop PSD than those having ischemic stroke (*51*). Hemorrhagic strokes usually involve larger areas of brain damage, and direct hemorrhage and secondary cerebral edema may directly affect the areas in the brainstem and cerebral cortex that control swallowing. In addition, increased intracranial pressure due to hemorrhage disrupts cerebrospinal fluid flow (*52*), which may further impair the neural network involved in swallowing. Swallowing kinematic analysis also demonstrates that the vertical laryngeal movements of patients with hemorrhagic stroke are significantly lower than those of patients with ischemic stroke,

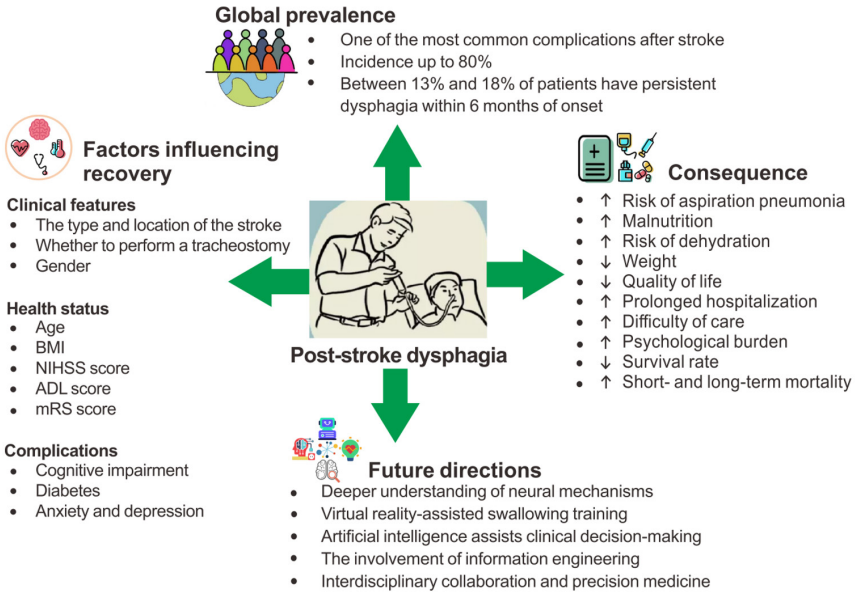

Figure 4. Post-stroke dysphagia. This figure presents a concise summary of PSD, highlighting its global prevalence, factors influencing recovery, consequences, and future research directions. BMI: body mass index; NIHSS: national institutes of health stroke scale; ADL: activity of daily living; mRS: modified Rankin scale.

suggesting that patients with hemorrhagic stroke have a more pronounced reduction in tongue movements and slower recovery during swallowing (*53*). Li *et al.* (*54*) showed that patients with left and right hemisphere stroke may exhibit different swallowing difficulties, with pharyngeal dyskinesia being more prominent in patients with right hemisphere stroke and reduced oral coordination being more prominent in patients with left hemisphere stroke. Additionally, comparative analysis of functional magnetic resonance imaging (fMRI) of brain activation in patients with left and right hemisphere stroke revealed that brain activation during a swallowing task is smaller in patients with left hemisphere damage than in those with right hemisphere damage. This suggests that the left cerebral hemisphere is more dominant in swallowing function and that patients with left hemisphere pathology may experience more severe dysphagia (*54*). The swallowing-related structures, the NA and the NTS, are located in the lateral medulla of the brainstem and control the coordination of the swallowing reflex and associated muscles; thus, brainstem stroke is also a poor prognostic factor for PSD (*55*). Dysphagia is a common clinical feature in patients with lateral medullary syndrome (LMS), with prevalence rates ranging from 51% to 94% (*56*). However, the severity and duration of dysphagia in patients with LMS are highly variable, ranging from very mild and transient to extremely severe and requiring months or even years of nasogastric feeding. Slow recovery is often associated with silent aspiration, which can lead to aspiration pneumonia. Swallowing control mechanisms in the brain require bilateral inputs to maintain normal function. When one side of the brain is injured, the other side can partially compensate for this injury, thus reducing dysphagia (*57*). Bilateral injuries lack this compensatory mechanism and worsen dysphagia compared with unilateral injuries. Cerebellar stroke accounts for approximately 4% of all strokes, and a retrospective cohort study conducted in 2023 showed that 11.45% of patients with cerebellar infarction have dysphagia (*58*). Studies have shown that after an isolated cerebellar stroke, pharyngeal reflexes may disappear, along with tremors, incoordination, and imprecise movements related to swallowing (*46*). This is attributed to the cerebellum's ability to receive information indirectly through the complex spinal cord — medulla oblongata — reticular formation pathway, enabling it to make various motor adjustments with the help of these structures. A cerebellar stroke may result in the disruption of cerebellar function and its connecting structures, such as the reticular formation, leading to the loss of the inhibitory reflex, which, in turn, affects swallowing.

In terms of functional status, advanced age, low Body Mass Index(BMI), high National Institutes of Health Stroke Scale (NIHSS) scores, and low Activity of Daily Living (ADL) scores are negative predictors of PSD recovery, whereas a modified Rankin scale (mRS) score of 0 is a predictor of good prognosis (*59*). As age increases, the neuroplasticity of the brain and swallowing-related muscle tissues declines, requiring more rehabilitative support and a longer period to recover swallowing function. A low BMI indicates malnutrition or reduced muscle mass. The BMI of patients with PSD is positively correlated with swallowing ability at discharge, and those with a low BMI tend to have poorer swallowing rehabilitation. In addition, patients with malnutrition upon admission often exhibit more severe dysphagia (*60*). In recent years, the concept of sarcopenic dysphagia has been proposed, where the reduction in overall muscle mass in patients with stroke

is accompanied by changes in swallowing-related muscle groups. This results in weakened muscle strength, masticatory weakness, muscle contraction disorders, and loss of muscle function, all of which slow down stroke rehabilitation and the recovery of swallowing function (*61*). The NIHSS is a standardized scale used to assess the severity of stroke, evaluating levels of consciousness, speech, motor function, and sensory function. One study found that an NIHSS score > 9 is an early predictor of dysphagia (*62*). High NIHSS scores usually reflect more severe neurological damage, with multiple impaired functions of the brain regions, and dysphagia may coexist with other neurological dysfunctions, increasing the complexity of recovery. ADL and mRS scores assess an individual's independence in daily life. Low ADL and high mRS scores indicate greater dependence and individualized rehabilitation therapy to gradually restore overall function (*17*).

In the PSD recovery process, the presence of comorbidities significantly affects the effectiveness of rehabilitation, particularly in patients with cognitive impairment, diabetes, and psychiatric conditions such as anxiety and depression. Studies have found a correlation between cognitive impairment and dysphagia — the presence of cognitive impairment on admission is associated with a poor outcome of dysphagia at discharge (*21*). At this stage, cognitive problems in patients with PSD are still not adequately addressed, yet improvements in cognitive function are important for the recovery of swallowing ability. Cognitive deficits can affect dysphagia through various mechanisms, including attention, awareness, planning and organizational skills, memory, language skills, and behavioral and psychological states. The impairment of these cognitive functions makes swallowing recovery more difficult and increases the risk of aspiration and other complications. For example, when cognitive impairment affects behavioral control, patients may exhibit inappropriate behaviors such as impatient or unconscious rapid swallowing during the deglutition process, which can lead to dysphagia and aspiration (*63*). Therefore, improving the patients' cognitive function, especially by enhancing the cognitive control of swallowing maneuvers, can improve their control, coordination, and safety during swallowing, thereby reducing dysphagia and improving food intake. Several studies have demonstrated the negative effects of diabetes on PSD recovery (*64,65*), showing that diabetes is more strongly associated with ischemic stroke in women than in men, with a more pronounced difference in patients with type 1 diabetes (*66*). Neurological factors associated with diabetes contribute to the increased risk of PSD by elevating the incidence of stroke (*64*). The hyperglycemic state, accompanied by microvascular and macrovascular damage in patients with diabetes, is thought to affect neuroplasticity and impair the ability to recover from injury (*65*). Depression and anxiety have been associated with dysphagia. Studies have found that anxiolytics, antidepressants, and sedative medications are used more frequently in older adults with dysphagia than in those without swallowing problems (*67*). Rudolph *et al.* (*68*) used a case-control study to explore the effects of psychotropic medications on swallowing function and found that swallowing function is diminished in patients using these medications and that higher dosages are associated with worse swallowing function. Drugs such as loxapine and phenazopyridine have also been shown to have deleterious effects on swallowing function in older individuals (*69*), with the anticholinergic effects of the drugs potentially leading to dry mouth and reduced salivation, thus affecting food lubrication. The effects of these drugs on the nigrostriatal pathway can lead to extrapyramidal symptoms and delayed dyskinesia, including dysphagia.

There is a link between PSD severity and sex; in general, women have more severe strokes and poorer swallowing functions (*70*). The International Stroke Trial showed a higher mortality rate in women, with 8003 women and 9367 men randomly assigned to the aspirin or heparin group, with a 14-day mortality rate of 11.0% in women versus 8.7% in men and a 6-month mortality rate of 24.5% in women versus 19.3% in men (*71*). In addition, women performed worse than men in stroke-related outcomes and measured dimensions such as disability, quality of life, anxiety, and depression (*72*). Some scholars have different perceptions regarding the association between PSD and sex. Renoux *et al.* (*73*) found no difference in stroke severity and degree of swallowing dysfunction between men and women after adjusting for age and premorbid mRS scores, suggesting that differences between men and women may be due to age and premorbid functional status rather than sex itself. We believe that the sex difference is justified owing to significant physiological differences in muscle strength, bone structure, and hormone levels, which may affect the recovery of swallowing muscle groups and the efficiency of neural repair after a stroke. This can lead to slower recovery of swallowing functions in women with stroke.

The kinematic parameters of the hyoid and epiglottis include movement trajectory, velocity, amplitude, and onset position, which are potentially useful in predicting PSD recovery. Lee *et al.* (*74*) analyzed a video fluoroscopic swallowing study (VFSS) and concluded that altered initial posterior movement of the hyoid and reduced horizontal forward movement during swallowing may be new kinematic indicators of poor prognosis for PSD. These changes in hyoid motion trajectory can lead to poor relaxation of the UES, accumulation of residue in the piriform sinus, and an increased risk of aspiration. In addition, movement of the epiglottis is recognized as an important mechanism for airway protection during swallowing. During normal swallowing, the epiglottis moves from a vertical resting position to a full downward tilt and then returns to the resting position. Frame-by-frame tracking of the hyoid position revealed that

when food reaches the pharynx, reduced and sluggish movement of the epiglottis leads to incomplete laryngeal protection, thereby causing aspiration and delaying the recovery process (*9*).

It is worth noting that most previous studies predicting the prognosis of swallowing function excluded patients who underwent tracheostomy, probably to improve the manageability of the study and the reliability of the results. Tracheal intubation or tracheotomy in the acute phase of stroke has more significant adverse effects on swallowing improvement (*75*), and invasive maneuvers may damage the muscles and nerves controlling the swallowing process, causing biomechanical alterations in the trachea, which can result in altered pharyngeal phases.

In conclusion, we described the multiple factors that influence recovery from PSD, and a comprehensive understanding of these factors may help develop a more individualized and precise rehabilitation intervention strategy, which can significantly improve the recovery of patients with dysphagia and their quality of life.

5. Mechanisms of recovery from PSD

Recovery from PSD is mainly based on neural remodeling and redistribution mechanisms. Neural remodeling refers to the nervous system's adaptation to new functional demands after an injury by altering synaptic connections and neural circuits. Synaptic plasticity is one of the mechanisms underlying neural remodeling. Damaged neural circuits can facilitate learning, memory, and recovery by strengthening synaptic connections that allow neural networks to adjust to experiences and environmental changes. Simultaneously, other regions of the brain and spinal cord can take over the functions of the damaged regions, and this functional redistribution often relies on the reorganization of neural networks. For example, in patients with PSD, the lateral brain regions may compensate for the damaged prefrontal regions, partially restoring impaired swallowing through the synergistic and compensatory effects of different brain regions to enhance the control and regulation of the swallowing process.

Neuroplastic mechanisms ensure the coordination and smoothness of swallowing process by enhancing neural pathway activation and cortical reorganization. These processes promote repair and support functional recovery by mediating the interrelated effects of the extracellular matrix (ECM) and peripheral neuronal network (PNN), while improving signaling efficiency through modulation of neurotransmitter levels, all of which significantly enhance swallowing recovery in post-stroke patients.

5.1. Activation of neural pathways and cortical reorganization of the brain

Swallowing involves the coordination of multiple neural pathways, including the cortical, brainstem, vagus, trigeminal, and hypoglossal nerves. When an individual performs a specific swallowing function, the relevant neural networks in the brain are activated and coordinated to ensure a smooth and effective swallowing process. After a stroke, damage to brain areas responsible for swallowing can reduce the signaling efficiency of neural pathways, impair swallowing sensation, and hinder muscle control, resulting in weakened swallowing function that compromises both the safety and effectiveness of swallowing. According to the principles of neuroplasticity, swallowing-related neural networks can be activated through constant practice or external stimulation, which promotes the frequent activity of undamaged neurons, enhancing the connections between neurons and the efficiency of information transmission. In a study using blood oxygen level-dependent fMRI to examine brain activity during different swallowing maneuvers before and after treatment in patients with dysphagia caused by medullary infarction revealed that in the acute phase of stroke, only partial activation of the bilateral precentral gyrus and left lingual gyrus occurred during saliva swallowing. Forceful swallowing of saliva increased the activation of the bilateral auxiliary motor area, posterior central gyrus, and right insular cortex and increased thalamic activation after swallowing rehabilitation training (*37*). In addition, repetitive transcranial magnetic stimulation (rTMS) (*76*) and motor-evoked potentials (MEP) (*54*), as observed in MRI studies, have shown hyperactivation of the contralateral hemisphere in patients with PSD during functional recovery. This suggests that the improvement of dysphagia in patients with stroke may be related to compensatory brain mechanisms and the activation of regions bilaterally involved in the cortical representation of swallowing.

Simultaneously, cortical areas of the brain reorganize, with undamaged regions redistributing functions to compensate for the damaged areas. Patients with higher stroke severity have increased levels of default mode network (DMN) connectivity, reflecting a compensatory strategy for the function of the damaged part of the brain. Additionally, higher functional connectivity between brain networks decreases as patients with stroke recover (*77*). Prolonged compensatory brain activity is thought to reflect maladaptive brain plasticity, which can lead to poorer functioning in patients with stroke. Similarly, Huang *et al.* (*78*) proposed that improved swallowing function in these patients after swallowing training, as observed in MRI studies, is associated with reduced brain functional network connectivity. This suggests that the brain becomes less reliant on internal thought and more focused on the swallowing process during automated swallowing tasks. A cross-sectional study showed that enhanced resting-state functional connectivity between the precuneus, left and right anterior central gyri, and right para-motor area is negatively associated

with the Rosenbek penetration aspiration scale (PAS) and positively correlated with UES opening duration (UOD), suggesting that patients with stronger functional connectivity between the anterior central gyrus and medulla oblongata have a lower risk of penetration and aspiration and a longer UOD (*79*). Further studies have found that brain fMRI in patients with hemispheric and brainstem stroke showed different neurological changes. In patients with hemispheric stroke, improvement in the Functional Oral Intake Scale (FOIS) is associated with reduced functional brain connectivity in the ventral DMN of the precuneus, as observed on fMRI. Conversely , in patients with brainstem stroke, improvement in FOIS is linked to reduced functional brain connectivity in the left sensorimotor network of the posterior central region, as characterized by brain fMRI (*78*).

In summary, recovery from PSD is a complex process involving neural reorganization and functional connectivity changes at multiple levels. Modulation of cortical–medulla functional connectivity and changes in swallowing-related brain networks can serve as biomarkers for characterizing the recovery of swallowing function. By combining advanced neuroimaging techniques with behavioral assessments, we can further precisely assess the dynamic changes in these connections during swallowing and their clinical relevance, providing important clues for understanding the mechanisms of activation and cortical reorganization of neural pathways in the brain after PSD. However, given the limited published literature on the subject and the small number of included patients, the available data are insufficient for predictive modeling of swallowing function measures. In future studies, the predictive value of cortical–medulla connectivity for swallowing function and recovery should be further investigated, with the aim of revealing its mechanism of action in neural remodeling.

5.2. Regulatory role of the ECM and its members

The ECM is a structural scaffold embedded in brain cells and the vascular system, consisting of a variety of proteins (*e.g.* collagen, fibronectin, and glycosaminoglycans) and cytokines, which provide the support and signals required for cell growth, migration, and differentiation. The ECM in the CNS exhibits diverse morphologies, including diffuse, homogeneous, amorphous, and nearly ubiquitous substrates, as well as highly organized structures. Highly reticulated extracellular matrices known as PNNs typically encase neurons and serve supportive, protective, and regulatory functions during neuronal activity (*80*). A study of PNNs in the M1 of male PSD mice showed that electroacupuncture (EA)-induced increased c-Fos expression, enhanced spike firing, and potentiated excitatory postsynaptic currents (sEPSCs) in excitatory neurons, which improved swallowing function. However, after the removal of PNNs in the contralateral M1, stroke-induced swallowing dysfunction occurred, and the effect of EA disappeared, suggesting that PNNs may be involved in stroke pathogenesis and EA-mediated improvement in swallowing function (*81*). Meanwhile, the structure of PNNs changes rapidly after stroke onset, facilitating more efficient γ-aminobutyric acid (GABA) signaling and enhancing the dynamic reorganization of interneurons. The remodeling of PNNs and their associated synapses occurs earlier than the recovery of function, suggesting that remodeling of PNNs is an early and critical step in the recovery of function (*82*). This may indicate that dynamic changes in the PNN affect the survival and regeneration of neurons associated with swallowing, modulate inhibitory signaling between neurons, and promote the recovery of swallowing function.

In the ECM, proteases and protease inhibitors aid in post-stroke recovery by regulating their own activities to maintain basement membrane integrity. This remodeling and regulation of the ECM is experience-dependent (*83*). Enhanced activity of ECM proteases, such as tissue plasminogen activator (tPA) and matrix metalloproteinase-9 (MMP-9), has been observed in the brain tissues of both mice and patients after stroke in response to enriched environmental interventions. Meanwhile, the expression of a disintegrin and metalloproteinase with thrombospondin motifs 4 (ADAMTS4) and its inhibitor, tissue inhibitor of matrix metalloprotease-1 (TIMP1), tends to remain balanced (*84*). This suggests that swallowing-related skill training and physical therapy may promote neuroplasticity by modulating the activity of proteases and protease inhibitors and enhancing the ability of the nervous system to self-adjust and adapt to the environment and experiences, which in turn may influence the recovery of swallowing function.

After stroke, ECM members regulate the migration and activation of inflammation-related factors, thereby affecting the healing and repair processes of the injured area (*83*). It is hypothesized that the PSD recovery process is also related to the inflammatory regulatory effects of the ECM. In preclinical studies of ischemic stroke, tenascin-C in the ECM, which is mainly expressed during embryonic CNS development and at lower levels in adults, reappears after brain injury. Tenascin-C mitigates astrogliosis following ischemic stroke in mice and modulates the interaction between microglia and astrocytes, thereby promoting the proliferation of the microvasculature and neural stem cells in the penumbra, reconstruction of the neurovascular unit, and neural repair (*85*). Fibronectin is highly expressed in animal models of ischemic stroke, with its expression level peaks in the infarct region 7 days after middle cerebral artery occlusion (MCAO) (*86*). Fibronectin enhances the local immune response by promoting the migration of immune cells to the site of inflammation, and its

upregulation contributes to neuronal cell adhesion and migration in the injured region, thereby supporting neural regeneration (*83*). In clinical studies of ischemic stroke, polymerase-associated factor 1 (PAF1) supports regeneration by enhancing the activity of regulatory T cells and inhibiting the synthesis of pro-inflammatory cytokines. Elevated levels of PAF1 are associated with a better prognosis after ischemic stroke (*87*).

In ischemic stroke, there is limited data on changes in the ECM and its components in human subjects from clinical studies, compared to the more extensive findings in preclinical research. Further studies are necessary to elucidate the changes and functions of other ECM members in the brain and circulation of patients. Furthermore, in the context of hemorrhagic stroke, there is a scarcity of experimental and clinical data regarding changes in the ECM and its components within the interstitial matrix, basement membrane, and perineuronal nets. Consequently, further comprehensive research is necessary to assess alterations in the ECM and its constituents in hemorrhagic stroke.

5.3. Role of neurotransmitters

Neurotransmitters are chemicals that transmit signals between neurons and play important roles in the recovery of the swallowing function after stroke.

Substance P (SP), a neuropeptide widely found in the CNS and PNS, promotes nerve repair, enhances neuroplasticity, and regulates neuroinflammation by binding to its receptor neurokinin-1 (NK1), which positively contributes to PSD recovery. After a stroke, cerebral damage often leads to diminished swallowing reflexes. Capsaicin, by stimulating unmyelinated C-fibers and releasing tachykinins such as SP, promotes the reconstruction of neural pathways and enhances the swallowing reflex through activation of the NK1 receptor on the glossopharyngeal nerve (*88*). The SP can also facilitate the neural circuit of swallowing control. The release of transient receptor potential vanilloid subtype 1 (TRPV1) agonists can enhance the sensitivity of the brainstem and cortical regions to sensory inputs from the oral cavity and pharynx, enhancing the brain's perception of these signals and promoting the initiation of the swallowing reflex. This facilitates the initiation and execution of the swallowing reflex (*89*). Neuroinflammation often accompanies stroke, exacerbates neurological damage, and delays functional recovery. SP regulates the neuro-immune system feedback mechanism by interacting with the NK1 receptor, which helps to balance the local inflammatory response, promotes neuroprotection, attenuates neurological damage, and facilitates the neural repair process to some extent (*90*). Clinical and animal experimental studies have shown that the level of SP can be used as a potential biomarker for predicting swallowing recovery, as higher concentrations of SP suggest better recovery of the swallowing reflex and more pronounced improvement in swallowing function (*91,92*). Pharmacological modulation of the action of SP or modulation of NK1 receptor activation may help accelerate the recovery of the gag reflex and reduce dysphagia, providing a new target for the clinical treatment of PSD.

Glutamate, the main excitatory neurotransmitter, promotes communication between neurons. It can enhance the activity of swallowing-related neural circuits and help re-establish swallowing function in both the oropharyngeal and complete swallowing phases (*5*). Studies have shown that swallowing behavior can be effectively induced by microinjections of glutamate at the NTS site in the brain, and that the process is similar to electrical or mechanical stimulation, suggesting that excitatory amino acid (EAA) receptors play an important role in inducing swallowing during the oropharyngeal phase (*93*). The key role of EAA in the complete swallowing phase was further confirmed by their ability to initiate specific esophageal peristaltic contractions by injecting glutamate and EAA agonists into the subcentral nuclear region of rats (*94*). It is worth emphasizing that specific neurons in the NTS are responsible for initiating and patterning the processes of swallowing and esophageal peristalsis. Therefore, the response produced by glutamate injection results in coordinated muscle activity, rather than haphazard movement (*5*). In addition, experimental results with agonists and antagonists of EAA receptors have revealed that activation of either N-methyl-D-aspartate (NMDA) receptors or non-NMDA receptors triggers swallowing and esophageal contractions; however, activation of NMDA receptors is more effective than that of non-NMDA receptors, which is related to the high-density distribution of NMDA receptors in the NTS region (*5*).

Inhibitory phenomena also play important roles in swallowing. The neurotransmitter GABA is a major mediator of synaptic inhibition. It helps to regulate homeostasis in the body, prevents neuronal overexcitation, and protects the stability of the swallowing center. During the swallowing process, GABA controls the different phases of swallowing by inhibiting the transmission of nerve signals. The swallowing preparation phase prevents non-target activities from interfering with the initiation of the swallowing reflex. During swallowing, it coordinates the actions of different muscle groups to ensure smooth passage of food through the esophagus. In the recovery phase, it helps the neural network restore baseline activity and prevents overexcitation from triggering secondary muscle spasms or overreactivity (*5*). Similarly, Wang and Bieger (*95*) showed that the local injection of GABA or a GABA agonist such as muscimol inhibits motor events associated with swallowing and esophageal peristalsis. When swallowing involves only the oropharyngeal phase, it can proceed normally with the local administration of

a subthreshold dose of the GABA receptor antagonist bicuculline. This allows the oropharyngeal phase to follow primary peristalsis (*95*). In contrast, during rapid rhythmic swallowing, the administration of bicuculline can release inhibition, preventing the initiation of the esophageal phase, and thus the completing rhythmic swallowing process (*95*). This suggests that GABA plays a key role in coordinating swallowing by regulating its rhythm and phases, inhibiting neural activity to ensure efficient coupling between the oropharyngeal phase and esophageal peristalsis.

Acetylcholine is responsible for transmitting neural signals from the brain to the pharynx and esophagus. Thus, the release of acetylcholine and the enhancement of its receptor activity during swallowing recovery can promote the contraction of the pharyngeal and esophageal muscles, helping the swallowing process proceed smoothly. During swallowing, striated muscles actively push food through the mouth and into the pharynx, while smooth muscles push food from the esophagus to the stomach. Acetylcholine responds heterogeneously to different muscle types by acting on striated muscles through motor neuron activation of nicotinic acetylcholine receptors (nAChRs) to accomplish the swallowing maneuver and on smooth muscles through parasympathetic activation of muscarinic acetylcholine receptors (mAChRs) to propel food to the stomach (*5*). Additionally, the involvement of acetylcholine receptors in the coupling process between the oropharynx and esophagus may vary among species; systemic injections of the anticholinergic drug atropine have been found to block the esophageal phase of swallowing in sheep (*96*), whereas in cats and humans, atropine injections do not block esophageal peristalsis (*97*). Based on the heterogeneity of the response to acetylcholine in different muscle types, the clinical treatment of dysphagia should be based on an in-depth understanding of the specific pathomechanisms and the development of drugs with a high degree of selectivity to avoid unnecessary interference with healthy swallowing muscle groups. Furthermore, in cross-species drug development and clinical trials, differences in the responses of different species to acetylcholine and its receptors need to be fully considered. Even within the same species, differences in the response to acetylcholine may exist between individuals owing to genetic variation, receptor subtype distribution, drug metabolism, and other factors, requiring adjustment of the drug dosage or selection of different therapeutic strategies based on individual patient characteristics.

Stimulation of GABA receptors in the vagal nucleus can modulate the excitatory effects of glutamate and acetylcholine (*98*), suggesting a dynamic balance between these neurotransmitters. This balance ensures an appropriate ratio of excitability to inhibition, facilitating the fine regulation of neural activity and promoting orderly neural function. A lack of such a regulatory mechanism can lead to dysregulation of the balance between excitability and inhibition in the nervous system, thus affecting the coordination of swallowing. Over-excitability may lead to aspiration and choking, while under-excitability can cause delayed or incomplete swallowing responses. Therefore, the activity of glutamate, GABA, and acetylcholine and the balanced relationship among the three may be important biomarkers for assessing the recovery of swallowing function. Drugs and neuromodulation techniques targeting EAA, GABA, and acetylcholine receptors may be an effective means of treating PSD. In the future, brain imaging techniques, such as electroencephalography (EEG) or fMRI, can be used to observe the activity patterns of different neurotransmitters and changes in related neural circuits in animal models or patients with stroke. The extent of recovery of the swallowing function can be predicted by assessing the relationship between neurotransmitter receptor activity and swallowing behavior.

6. Treatment strategies based on functional compensation and motor learning

Functional compensation refers to adapting environments, tools, or strategies to help patients overcome dysphagia and ensure that they can safely ingest food and fluids. Motor learning involves the improvement of the coordination and efficiency of swallowing movements through practice and training. In patients with PSD, a combination of compensatory and motor learning approaches can effectively promote recovery of swallowing function. This can be achieved through proper food selection; control of dose and viscosity; the use of various swallowing techniques, movements, and exercises to strengthen the swallowing muscles and improve sputum production; and the application of various neural stimuli to swallowing-related muscles to increase prehyoid bone movement. In 2024, Bendix *et al.* published an article in *The Lancet* illustrating intervention strategies and treatment methods for dysphagia (*99*). Herein, we discuss several additional treatment methods, including noninvasive approaches like vacuum swallowing and acupuncture, as well as invasive treatments such as botulinum toxin A (BTX-A) injections, balloon catheter dilatation, cricopharyngeal muscle myotomy (CPM), and cricopharyngeal peroral endoscopic myotomy (CP-POEM) (Table 1).

6.1. Non-invasive methods

Non-invasive Brain Stimulation (NIBS) is a sophisticated and multi-dimensional strategy for modulating brain activity, holding broad potential in the therapeutic management of PSD. NIBS facilitates the initiation of neuroplastic changes by modulating the excitability of cerebral hemispheres, specifically reducing excitability

in the compromised hemisphere while enhancing that of the contralateral, unaffected hemisphere, through the application of electric or magnetic fields. The principal modalities of NIBS employed in PSD treatment are tDCS and rTMS. These two methodologies differ subtly in their approach to eliciting excitatory or inhibitory effects. The tDCS modulates neuronal activity by altering electrode positions, whereas rTMS achieves this by adjusting stimulation frequency. Specifically, tDCS enhances brain plasticity through the application of a mild electrical stimulation *via* a constant, low-intensity direct current. The anodal stimulation results in the depolarization of the resting membrane potential, thereby augmenting neuronal excitability, while cathodal stimulation induces hyperpolarization, diminishing neuronal excitability. While rTMS influences cerebral metabolism and neural activity by generating induced currents through magnetic fields that act upon the cerebral cortex, with high frequencies employed to augment cortical excitability and stimulate localized neuronal activity, and low frequencies used to reduce cortical excitability and inhibit neuronal cell function. A network meta-analysis has demonstrated that rTMS outperforms tDCS in enhancing swallowing function and diminishing aspiration risk in PSD patients (*100*). This superiority may stem from rTMS's enhanced capacity to penetrate the skull and access the cerebral cortex through magnetic field action, coupled with its precise localization. Furthermore, tDCS induces only local neuronal currents, which are incapable of spontaneous neuronal firing, and thus cannot elicit movements by activating the motor cortex of the intact efferent pathway, as rTMS can (*101*). It is noteworthy that, in terms of adverse effects, rTMS carries a risk of inducing epilepsy (*101*), dizziness (*102*), headaches (*102*), or epistaxis (*103*), while tDCS predominantly results in transient dizziness and mild headaches (*104*). Consequently, in clinical practice, physicians must balance the therapeutic benefits against the potential adverse effects, evaluate the efficacy and safety profiles of rTMS and tDCS for PSD, and choose the most appropriate treatment plan for patients.

Vacuum swallowing is a novel, noninvasive approach for compensatory swallowing. A case report suggests that patients with LMS, who have weak pharyngeal contractions and impaired UES function, involuntarily achieve vacuum swallowing through diaphragm contraction during swallowing. This approach also creates negative pressure in the esophagus and increases pressure in the LES, improving the pharyngeal passage of food through compensatory swallowing operations (*105*). Furthermore, patients can modulate the intensity of the negative pressure within the esophagus by voluntarily controlling the contraction of the primary and accessory respiratory muscles during the swallowing process (*56*). Velopharyngeal contractile integral (VPCI) measures pharyngeal contractility, or "vigor", including contraction pressure, duration, and frequency. An increase in VPCI can be observed during vacuum swallowing, which results in an involuntary prolongation of swallowing time and enhanced contraction. This is similar to the effects of the Mendelsohn maneuver, where the larynx is elevated for a few seconds by forcefully pushing against the palate during swallowing, and the Shaker exercise, where the head is lifted through repetitive head-lifting movements in the supine position (*105*). Vacuum swallowing provides an effective compensatory strategy for the recovery of swallowing function in patients with dysphagia by promoting changes in physiological mechanisms and increasing pharyngeal contractility.

Acupuncture, a traditional treatment, has shown potential effectiveness in the rehabilitation of PSD and has been recommended by the World Health Organization as an alternative and complementary therapy for the treatment of stroke and the improving its sequelae (*106*). Acupuncture can reduce dysphagia by stimulating specific acupoints, modulating nervous system function, and improving nerve signaling during swallowing. In addition, acupuncture helps relax the pharynx and related muscles, reducing tension and spasms, thus facilitating smoother swallowing and playing a compensatory role. Excitatory neurons in layer 5 (L5) of the M1 control swallowing activity. EA stimulation of the CV23 acupoint (EA-CV23), as a peripheral stimulation strategy, has been demonstrated to improve swallowing function in PSD model mice by activating motor cortical inputs to the NTS *via* the parabrachial nuclei (PBN) (*107*). These findings highlight the crucial role of the M1-PBN-NTS neural pathway in mediating the protective effects of EA-CV23 against swallowing disorders, thereby suggesting a promising therapeutic approach for the treatment of dysphagia. However, there is a lack of high-quality RCTs that comprehensively assess the efficacy of acupuncture for PSD. Wu *et al.* identified the core acupoints most strongly correlated with PSD — GB20, CV23, EX-HN14, Gongxue, MS6, SJ17, EX-HN12, and EX-HN13 — utilizing data mining techniques. Through complex network, correlation, and cluster analyses, they identified GB20, CV23, and MS6 as the most evidence-supported acupoints for PSD (*108*). These results provide scientific evidence and clinical support for the use of acupuncture to improve PSD by modulating neural networks and stimulating specific acupoints. As part of a comprehensive treatment program, acupuncture is expected to help patients regain their swallowing ability more effectively in the future.

6.2. Invasive methods

BTX-A is a neurotoxin that inhibits the release of acetylcholine from presynaptic cholinergic nerve endings, blocks neuromuscular transmission, reduces overactive muscle tone, and aids in the relaxation of the UES and other swallowing-related muscles (*109*).

Table 1. Treatment of PSD

Category	Intervention Method	Specific Practices	Advantages	Disadvantages	Results
Protective Intervention	Dietary adjustment	Using concentrated liquid, soft food, pureed food, *etc.*	Oral food residue↓	Palatability and appetite↓	Aspiration↓
	Oral hygiene	Gargle method, negative pressure brushing, hot and cold oral brushing, *etc.*	Oral comfort↑	Difficult to implement in patients with impaired consciousness.	Oral pathogens↓, Aspiration pneumonia↓
	Nutritional supplementation	Nasogastric tube or gastrostomy tube (PEG) if necessary	Suitable for long-term use	Risk of blockage	BMI↑, total protein↑, albumin↑, hemoglobin↑
Rehabilitative Intervention	Behavioral strategies	1. Maintaining a sitting or semi-reclining position while eating 2. Using specialized feeding tools to enable self-feeding	Eating autonomy and sensation↑	Nursing complexity↑	Aspiration pneumonia↓, nutrition↑, quality of life↑
	Sensory training	Including vibration stimulation, ice acid stimulation, K point stimulation, *etc.*	Personalized treatment and high safety	Long training duration, significant individual variability	Swallowing reflex↑, initiation time of pharyngeal swallowing↓
	Swallowing training	Including oral motor exercises, tongue retraction exercises, swallowing reflex training, *etc.*			Coordination of swallowing muscles↑, muscle strength↑
Pharmacological Treatment	TRPV-1 receptor agonists	Such as capsaicin, piperine, resiniferatoxin	Multimodal stimulation with a wide range of options	Possible adverse effects: oral pain, discomfort	Pharyngeal sensation↑
	GABA medications	Such as baclofen	Muscle spasms↓	Possible adverse effects: cognitive impairment	Regulation of excitatory amino acids and acetylcholine excitability
	ACE inhibitors	Such as captopril, enalapril, benazepril	Multitarget action	Possible adverse effects: dry cough, angioedema	Substance P↑, cough reflex↑
	Anticholinergic drugs	Such as clonazepam, tiotropium	Saliva secretion↓, relaxation of smooth muscles	Possible adverse effects: dry mouth, constipation	Aspiration and cough↓
	Dopaminergic drugs	Such as levodopa, dopamine receptor agonists, benserazide	Latency of swallowing response↓	Possible adverse effects: gastrointestinal discomfort, orthostatic hypotension	Swallowing safety↑
	Gastrointestinal prokinetic drugs	Such as domperidone, mosapride, itopride	Gastrointestinal motility↑	Possible adverse effects: gastrointestinal discomfort	Nutrient absorption↑

TRPV1: transient receptor potential vanilloid subtype 1; GABA: γ-aminobutyric acid; ACE: angiotensin Converting Enzyme; tDCS: transcranial direct current stimulation; rTMS: repetitive transcranial magnetic stimulation; PES: pharyngeal electrical stimulation; NMES: neuromuscular electrical stimulation; UES: upper esophageal sphincter; CPA: cricopharyngeal achalasia; BTX-A: botulinum toxin A; CPM: cricopharyngeal muscle myotomy; CP-POEM: cricopharyngeal peroral endoscopic myotomy.

Table 1. Treatment of PSD (continued)

Category	Intervention Method	Specific Practices	Advantages	Disadvantages	Results
Neurostimulation Techniques	tDCS	Anodal stimulation increases the excitability of the affected side, while cathodal stimulation decreases the excitability of the healthy side	Non-invasive, high safety, flexible regulation, sustained effects	Device dependency, stimulation discomfort, significant individual variability, requires continuous treatment	Cortical excitability↑
	rTMS	High frequency stimulation enhances the excitability of the affected side, while low frequency stimulation reduces the excitability of the healthy side			Neural plasticity↑
	PES	High frequency (5.0 Hz) stimulation can extend swallowing response time, low frequency (0.2 Hz) stimulation can increase cortical excitability			Motor cortex reorganization↑
	NMES	Low frequency stimulation of the healthy side, high frequency stimulation of the affected side			Strength↑, endurance↑and activity↑ of swallowing muscles
Traditional Chinese Medicine Treatment	Acupuncture	The strongest evidence for acupoints is GB20, CV23, and MS6	High safety, individualized treatment protocols	Requires continuous treatment	Swallowing nerve signal transmission↑
Invasive Methods (mainly for treating UES dysfunction and CPA)	BTX-A injection	Injection site is the cricopharyngeus muscle, dosage range varies and is individual	Multiple localization techniques, significant efficacy	Significant individual variation in dosage, limited duration of efficacy	Tension of UES and other swallowing-related muscles↓
	Balloon catheter dilatation	Start with a small volume balloon and gradually increase	Simple procedure, significant therapeutic outcomes	Strict indications, repeated treatments may be required	Rhythmicity and timing of swallowing↑
	CPM and CP-POEM	Direct action on the cricopharyngeus muscle or lower esophageal sphincter through surgery	Good long-term effects	Surgical risk↑, postoperative care requirements↑	Muscle tension↓, esophageal diameter↑

TRPV1: transient receptor potential vanilloid subtype 1; GABA: γ-aminobutyric acid; ACE: angiotensin Converting Enzyme; tDCS: transcranial direct current stimulation; rTMS: repetitive transcranial magnetic stimulation; PES: pharyngeal electrical stimulation; NMES: neuromuscular electrical stimulation; UES: upper esophageal sphincter; CPA: cricopharyngeal achalasia; BTX-A: botulinum toxin A; CPM: cricopharyngeal muscle myotomy; CP-POEM: cricopharyngeal peroral endoscopic myotomy.

BioScience Trends. 2025; 19(1):31-52. www.bioscience trends.com

BTX-A is minimally invasive, safe, and reproducible and is often used in clinical practice to treat UES dysfunction and cricopharyngeal achalasia (CPA). Schneider *et al.* first reported the use of BTX-A to treat swallowing dysfunction in 1994 (*110*). After BTX-A injection, the nervous system adapts to a new swallowing mechanism, enabling patients to learn new swallowing patterns and strategies through repetitive practice, thereby performing swallowing maneuvers more smoothly. However, current clinical studies are limited by small sample sizes, lack of standardized injection protocols, and inconsistent therapeutic outcomes. Therefore, larger studies with clear injection methods, subject criteria, and outcome definitions are needed to further investigate the therapeutic value of BTX-A in dysphagia.

The basic principle of balloon catheter dilatation is to insert a controllable inflatable balloon catheter into the patient's oral cavity under endoscopic guidance, confirm that the balloon catheter is located at the exact position of the stricture through endoscopic observation, and utilize its dilatation to gradually increase the esophageal lumen and promote smooth passage of food. Sensory input from balloon-guided active repetitive swallowing can influence the swallowing CPG and motor responses, enhancing plasticity in the swallowing centers of the brainstem, associated cortical areas, and subcortical structures, thereby improving or restoring the swallowing rhythm (*111*). However, current clinical applications have found that the presence of an endoscope during dilatation may reduce the efficacy of dilatation therapy and that the discomfort and trauma caused by the endoscope may increase the risk of perforation, bleeding, and aspiration. Compared to traditional balloon dilation, videofluoroscopy-guided balloon dilation is an innovative technique that allows esophageal dilation under visualization, offering enhanced visual control and reducing the risk of perforation and other complications. Both active and passive modes of balloon catheter dilatation have been shown to be effective; however, active balloon dilatation allows flexibility in adjusting the dilatation regimen and pressure settings according to the patient's actual situation, and data at the FOIS level has shown that active dilatation is more effective (*112*). Despite published guidelines (*113*), balloon catheter dilatation protocols have not been standardized across institutions. Balloon diameters and pressures, as well as the duration of each dilation, vary significantly depending on the operator's personal preference and experience. Currently, the universal standard recommends a maximum balloon diameter of 20 mm for symptomatic relief in adults and 10 mm in children. Therefore, future studies should focus on determining the optimal balloon diameter, dilation pressure, and duration, as well as establishing standardized operating practices to improve treatment outcomes and minimize the risk of complications.

When conservative therapies such as medication and swallowing training are ineffective, CPM can be performed to improve the patient's ability to swallow by relieving the excessive tension of the cricopharyngeal muscles. In 2016, Nair *et al.* (*114*) reported on a patient with dysphagia lasting more than 1.5 years who showed no improvement after BTX-A injection. After undergoing CPM, the patient was able to eat orally, had the original PEG tube removed, and experienced significant improvements in nutritional status and mood. CP-POEM is an emerging minimally invasive endoscopic procedure for patients with UES dysfunction and CPA. The first retrospective study of CP-POEM for the treatment of oropharyngeal dysphagia demonstrated clinical and technical success in all 27 patients who underwent the procedure, showing improvement in dysphagia scores. During a median follow-up of 42.3 months, only one patient experienced reflux recurrence without dysphagia (*115*). This suggests that CP-POEM is a safe and effective alternative treatment option with low recurrence rates and favorable long-term outcomes. However, due to the limited number of current studies, the long-term outcomes of CP-POEM should be further evaluated through prospective studies.

Aging, functional decline, and comorbid conditions are common in older adults, and age-related changes in swallowing function may precede dysphagia. In patients with PSD and comorbid sarcopenia, addressing muscle loss and reduced swallowing muscle mass can help accelerate the recovery of swallowing function. In addition to regular swallowing rehabilitation training and physical therapy, it is necessary to ensure adequate protein and energy intake. This underscores the importance of an interdisciplinary team in managing and treating PSD. Effective collaboration among neurologists, speech therapists, physical therapists, dietitians, and caregivers, along with multifaceted interventions such as speech therapy, nutrition support, and physical therapy, helps manage PSD more systematically and effectively, ultimately improving the function and quality of life of older adults.

These integrative treatment strategies offer diverse pathways for the recovery of patients with PSD, emphasizing the importance of personalized medicine and the need for multidisciplinary collaboration. However, we must recognize the existing problems. First, because the site, directionality, and hemispheric coordination of the swallowing network are not fully understood, the lack of knowledge limits the optimization of neuromodulatory procedures, and the current study design and methodology lack uniform standards and norms, making it difficult to compare and generalize the results. Therefore, future studies should aim to establish standardized study designs and assessment indices to improve the reproducibility of the studies and the validity of the results, which, in turn, will provide a more solid scientific basis for clinical practice. Second, many studies have focused on the short-term efficacy of

PSD, while less attention has been paid to the long-term effects of treatment and its impact on the quality of life; thus, long-term follow-up studies are needed. Finally, different treatments may operate through various neural mechanisms; however, the current understanding of the neurobiological mechanisms of dysphagia remains limited. Systematic basic research is needed to clarify the mechanisms of action of these treatments.

7. Future directions

Owing to the bilateral innervation characteristics and neuroplasticity of the swallowing function, there is a certain potential for recovery of the swallowing function in post-stroke patients. Promoting the plasticity of neural networks by enhancing neural pathway activation, cortical reorganization, mediating ECM dynamics and its components, and modulating neurotransmitter transmission are key therapeutic targets for recovering swallowing function in patients with PSD. However, studies on the specific neural mechanisms and brain regions involved in swallowing recovery are limited. Although the cerebral cortex, brainstem, and cerebellum play important roles in the swallowing process, researchers have yet to identify the specific brain regions crucial for swallowing recovery and how these regions contribute to functional recovery through neural connections and network reorganization. In addition, existing studies tend to focus on specific regions of the cerebral cortex such as the motor and perceptual cortices, whereas relatively little research has been conducted on the brainstem and its downstream structures. Due to this lack of in-depth understanding of these neural mechanisms, clinical interventions often lack relevance and effectiveness.

In future management and treatment of PSD, information engineering will drive technological innovation and facilitate diagnostic advances, enabling the management of individual-based dysfunction patterns and their susceptibility risk factors through digital means. For example, wearable devices can monitor the swallowing process of patients in real time; collect physiological data such as heart rate, swallowing frequency, and hyoid trajectory; and analyze changes in swallowing function using intelligent algorithms, thus enabling personalized swallowing assessment and prediction. Meanwhile, virtual reality technology can simulate the swallowing environment to help patients perform swallowing training in a safe environment and provide real-time feedback to guide patients in improving their swallowing skills and dietary choices, thereby improving their swallowing ability and confidence. Additionally, AI-based assessment systems have been developed to analyze large amounts of patient swallowing video or audio data through machine learning to identify patterns of swallowing disorders, thereby providing accurate support for clinical decision-making. Interdisciplinary collaboration not only promotes technological innovation but also better meets the individualized needs of patients and promotes the development of precision medicine. The combination of medicine and engineering has become an important driving force for medical innovation.

8. Conclusion

This review thoroughly explored the neurophysiological mechanisms, influencing factors, recovery mechanisms, and therapeutic strategies of PSD and proposed a series of integrated therapeutic approaches based on functional compensation and motor learning. Neural remodeling and functional redistribution mechanisms are central to PSD recovery and involve a wide range of brain regions and neural networks. Activation of damaged neural pathways, enhanced cortical reorganization of the brain, and modulation of the ECM and neurotransmitters are critical steps in the recovery process. Research suggests that effective PSD management requires a multidisciplinary approach incorporating physical therapy, speech therapy, acupuncture, and other emerging medical and industrial techniques. Future research should focus on precise neurobiological mechanisms to develop more effective therapeutic strategies, especially by applying modern technologies such as artificial intelligence and virtual reality to personalized medicine to provide optimal rehabilitation for patients with PSD.

Funding: This work was supported by a grant from the National Natural Science Foundation of China (No.82174477) and the Heilongjiang Key R&D Program (2022ZX06C24).

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Takizawa C, Gemmell E, Kenworthy J, Speyer R. A systematic review of the prevalence of oropharyngeal dysphagia in stroke, Parkinson's disease, Alzheimer's disease, head injury, and pneumonia. Dysphagia. 2016; 31:434-441.
2. Mann G, Hankey GJ, Cameron D. Swallowing function after stroke: Prognosis and prognostic factors at 6 months. Stroke. 1999; 30:744-748.
3. Martin SS, Aday AW, Almarzooq ZI, *et al.* 2024 heart disease and stroke statistics: A report of US and global data from the American Heart Association. Circulation. 2024; 149:e347-e913.
4. Sasegbon A, Cheng I, Hamdy S. The neurorehabilitation of post-stroke dysphagia: Physiology and pathophysiology. The Journal of physiology. J Physiol. 2025; 603:617-634.
5. Jean A. Brain stem control of swallowing: Neuronal network and cellular mechanisms. Physiol Rev. 2001; 81:929-969.
6. Daniels SK, Pathak S, Mukhi SV, Stach CB, Morgan RO,

Anderson JA. The relationship between lesion localization and dysphagia in acute stroke. Dysphagia. 2017; 32:777-784.
7. Lang IM. Brain stem control of the phases of swallowing. Dysphagia. 2009; 24:333-348.
8. McCarty EB, Chao TN. Dysphagia and swallowing disorders. Med Clin North Am. 2021; 105:939-954.
9. Nagy A, Molfenter SM, Péladeau-Pigeon M, Stokely S, Steele CM. The effect of bolus consistency on hyoid velocity in healthy swallowing. Dysphagia. 2015; 30:445-451.
10. Langmore SE, Terpenning MS, Schork A, Chen Y, Murray JT, Lopatin D, Loesche WJ. Predictors of aspiration pneumonia: How important is dysphagia? Dysphagia. 1998; 13:69-81.
11. Dua KS, Surapaneni SN, Santharam R, Knuff D, Hofmann C, Shaker R. Effect of systemic alcohol and nicotine on airway protective reflexes. Am J Gastroenterol. 2009; 104:2431-2438.
12. Ebihara S, Izukura H, Miyagi M, Okuni I, Sekiya H, Ebihara T. Chemical senses affecting cough and swallowing. Curr Pharm Des. 2016; 22:2285-2289.
13. Chebib N, Cuvelier C, Malézieux-Picard A, Parent T, Roux X, Fassier T, Müller F, Prendki V. Pneumonia prevention in the elderly patients: The other sides. Aging Clin Exp Res. 2021; 33:1091-1100.
14. Baijens LW, Clavé P, Cras P, Ekberg O, Forster A, Kolb GF, Leners JC, Masiero S, Mateos-Nozal J, Ortega O, Smithard DG, Speyer R, Walshe M. European Society for Swallowing Disorders - European Union Geriatric Medicine Society white paper: Oropharyngeal dysphagia as a geriatric syndrome. Clin Interv Aging. 2016; 11:1403-1428.
15. Peyron MA, Woda A, Bourdiol P, Hennequin M. Age-related changes in mastication. J Oral Rehabil. 2017; 44:299-312.
16. Shimazaki Y, Saito M, Nonoyama T, Tadokoro Y. Oral factors associated with swallowing function in independent elders. Oral Health Prev Dent. 2020; 18:683-691.
17. Ko N, Lee HH, Sohn MK, *et al.* Status of dysphagia after ischemic stroke: A Korean nationwide study. Arch Phys Med Rehabil. 2021; 102:2343-2352.e3.
18. Flowers HL, Silver FL, Fang J, Rochon E, Martino R. The incidence, co-occurrence, and predictors of dysphagia, dysarthria, and aphasia after first-ever acute ischemic stroke. J Commun Disord. 2013; 46:238-248.
19. Perry L, Love CP. Screening for dysphagia and aspiration in acute stroke: A systematic review. Dysphagia. 2001; 16:7-18.
20. Kalf JG, de Swart BJ, Bloem BR, Munneke M. Prevalence of oropharyngeal dysphagia in Parkinson's disease: A meta-analysis. Parkinsonism Relat Disord. 2012; 18:311-315.
21. Castagna A, Ferrara L, Asnaghi E, Rega V, Fiorini G. Functional limitations and cognitive impairment predict the outcome of dysphagia in older patients after an acute neurologic event. NeuroRehabilitation. 2019; 44:413-418.
22. Affoo RH, Foley N, Rosenbek J, Kevin Shoemaker J, Martin RE. Swallowing dysfunction and autonomic nervous system dysfunction in Alzheimer's disease: A scoping review of the evidence. J Am Geriatr Soc. 2013; 61:2203-2213.
23. James E, Ellis C, Brassington R, Sathasivam S, Young CA. Treatment for sialorrhea (excessive saliva) in people with motor neuron disease/amyotrophic lateral sclerosis. Cochrane Database Syst Rev. 2022; 5:Cd006981.
24. Tsujimura T, Suzuki T, Yoshihara M, Sakai S, Koshi N, Ashiga H, Shiraishi N, Tsuji K, Magara J, Inoue M. Involvement of hypoglossal and recurrent laryngeal nerves on swallowing pressure. J Appl Physiol (1985). 2018; 124:1148-1154.
25. Philpott H, Garg M, Tomic D, Balasubramanian S, Sweis R. Dysphagia: Thinking outside the box. World J Gastroenterol. 2017; 23:6942-6951.
26. Aldridge KJ, Taylor NF. Dysphagia is a common and serious problem for adults with mental illness: A systematic review. Dysphagia. 2012; 27:124-137.
27. Nakajima Y, Tsujimura T, Tsutsui Y, Chotirungsan T, Kawada S, Dewa N, Magara J, Inoue M. Atropine facilitates water-evoked swallows *via* central muscarinic receptors in anesthetized rats. Am J Physiol Gastrointest Liver Physiol. 2023; 325:G109-G121.
28. Ekberg O, Hamdy S, Woisard V, Wuttge-Hannig A, Ortega P. Social and psychological burden of dysphagia: Its impact on diagnosis and treatment. Dysphagia. 2002; 17:139-146.
29. Zeng H, Zeng X, Xiong N, Wang L, Yang Y, Wang L, Li H, Zhao W. How stroke-related dysphagia relates to quality of life: The mediating role of nutritional status and psychological disorders, and the moderating effect of enteral nutrition mode. Front Nutr. 2024; 11:1339694.
30. Lin LC, Wang TG, Chen MY, Wu SC, Portwood MJ. Depressive symptoms in long-term care residents in Taiwan. J Adv Nurs. 2005; 51:30-37.
31. Miller N, Allcock L, Hildreth AJ, Jones D, Noble E, Burn DJ. Swallowing problems in Parkinson disease: Frequency and clinical correlates. J Neurol Neurosurg Psychiatry. 2009; 80:1047-1049.
32. Ranucci D, Falco F, Nicolella V, Di Monaco C, Migliaccio L, Lamagna F, Caracciolo F, Eliano M, Petracca M, Moccia M, Brescia Morra V, Carotenuto A, Lanzillo R. Dysphagia assessment in patients with multiple sclerosis - an additional piece to disability burden. Ann Clin Transl Neurol. 2024; 11:2958-2966.
33. Zamani M, Alizadeh-Tabari S, Chan WW, Talley NJ. Association between anxiety/depression and gastroesophageal reflux: A systematic review and meta-analysis. Am J Gastroenterol. 2023; 118:2133-2143.
34. Cheng I, Takahashi K, Miller A, Hamdy S. Cerebral control of swallowing: An update on neurobehavioral evidence. J Neurol Sci. 2022; 442:120434.
35. Daniels SK, Foundas AL. Lesion localization in acute stroke patients with risk of aspiration. J Neuroimaging. 1999; 9:91-98.
36. Wilmskoetter J, Bonilha L, Martin-Harris B, Elm JJ, Horn J, Bonilha HS. Mapping acute lesion locations to physiological swallow impairments after stroke. Neuroimage Clin. 2019; 22:101685.
37. Gu F, Han J, Zhang Q, Li X, Wang Y, Wu J. Cortical compensation mechanism for swallowing recovery in patients with medullary infarction-induced dysphagia. Front Neurol. 2024; 15:1346522.
38. Qin Y, Tang Y, Liu X, Qiu S. Neural basis of dysphagia in stroke: A systematic review and meta-analysis. Front Hum Neurosci. 2023; 17:1077234.
39. Choi S, Pyun SB. Repetitive transcranial magnetic stimulation on the supplementary motor area changes brain connectivity in functional dysphagia. Brain Connect. 2021; 11:368-379.

40. Jang SH, Lee J, Kim MS. Dysphagia prognosis prediction *via* corticobulbar tract assessment in lateral medullary infarction: A diffusion tensor tractography study. Dysphagia. 2021; 36:680-688.
41. Im S, Han YJ, Kim SH, Yoon MJ, Oh J, Kim Y. Role of bilateral corticobulbar tracts in dysphagia after middle cerebral artery stroke. Eur J Neurol. 2020; 27:2158-2167.
42. Ertekin C, Aydogdu I, Tarlaci S, Turman AB, Kiylioglu N. Mechanisms of dysphagia in suprabulbar palsy with lacunar infarct. Stroke. 2000; 31:1370-1376.
43. Cho YJ, Ryu WS, Lee H, Kim DE, Park JW. Which factors affect the severity of dysphagia in lateral medullary infarction? Dysphagia. 2020; 35:414-418.
44. Singh S, Hamdy S. Dysphagia in stroke patients. Postgrad Med J. 2006; 82:383-391.
45. Numasawa Y, Hattori T, Ishiai S, Kobayashi Z, Kamata T, Kotera M, Ishibashi S, Sanjo N, Mizusawa H, Yokota T. Depressive disorder may be associated with raphe nuclei lesions in patients with brainstem infarction. J Affect Disord. 2017; 213:191-198.
46. Hajipour M, Sobhani-Rad D, Zainaee S, Farzadfar MT, Khaniki SH. Dysphagia following cerebellar stroke: Analyzing the contribution of the cerebellum to swallowing function. Front Neurol. 2023; 14:1276243.
47. Rangarathnam B, Kamarunas E, McCullough GH. Role of cerebellum in deglutition and deglutition disorders. Cerebellum. 2014; 13:767-776.
48. Prescott SL, Liberles SD. Internal senses of the vagus nerve. Neuron. 2022; 110:579-599.
49. Kecskes S, Matesz C, Birinyi A. Termination of trigeminal primary afferents on glossopharyngeal-vagal motoneurons: Possible neural networks underlying the swallowing phase and visceromotor responses of prey-catching behavior. Brain Res Bull. 2013; 99:109-116.
50. Capra NF. Mechanisms of oral sensation. Dysphagia. 1995; 10:235-247.
51. Krekeler BN, Schieve HJP, Khoury J, *et al.* Health factors associated with development and severity of poststroke dysphagia: An epidemiological investigation. J Am Heart Assoc. 2024; 13:e033922.
52. Wilmskoetter J, Martin-Harris B, Pearson WG Jr, Bonilha L, Elm JJ, Horn J, Bonilha HS. Differences in swallow physiology in patients with left and right hemispheric strokes. Physiol Behav. 2018; 194:144-152.
53. Seo HG, Oh BM, Han TR. Swallowing kinematics and factors associated with laryngeal penetration and aspiration in stroke survivors with dysphagia. Dysphagia. 2016; 31:160-168.
54. Li S, Luo C, Yu B, Yan B, Gong Q, He C, He L, Huang X, Yao D, Lui S, Tang H, Chen Q, Zeng Y, Zhou D. Functional magnetic resonance imaging study on dysphagia after unilateral hemispheric stroke: A preliminary study. J Neurol Neurosurg Psychiatry. 2009; 80:1320-1329.
55. Lee WH, Lim MH, Seo HG, Seong MY, Oh BM, Kim S. Development of a novel prognostic model to predict 6-month swallowing recovery after ischemic stroke. Stroke. 2020; 51:440-448.
56. Jang SH, Kim MS. Dysphagia in lateral medullary syndrome: A narrative review. Dysphagia. 2021; 36:329-338.
57. Beharry A, Michel P, Faouzi M, Kuntzer T, Schweizer V, Diserens K. Predictive factors of swallowing disorders and bronchopneumonia in acute ischemic stroke. J Stroke Cerebrovasc Dis. 2019; 28:2148-2154.
58. Huang L, Wang Y, Sun J, Zhu L, Liu J, Wu Y, Shan C, Yan J, Wan P. Incidence and risk factors for dysphagia following cerebellar stroke: A retrospective cohort study. Cerebellum. 2024; 23:1293-1303.
59. Wang L, Qiao J, Sun F, Wei X, Dou Z. Demographic and clinical factors associated with recovery of poststroke dysphagia: A meta-analysis. Brain Behav. 2023; 13:e3033.
60. Shimizu A, Maeda K, Koyanagi Y, Kayashita J, Fujishima I, Mori N. The global leadership initiative on malnutrition-defined malnutrition predicts prognosis in persons with stroke-related dysphagia. J Am Med Dir Assoc. 2019; 20:1628-1633.
61. Fujishima I, Fujiu-Kurachi M, Arai H, *et al.* Sarcopenia and dysphagia: Position paper by four professional organizations. Geriatr Gerontol Int. 2019; 19:91-97.
62. Jeyaseelan RD, Vargo MM, Chae J. National Institutes of Health Stroke Scale (NIHSS) as an early predictor of poststroke dysphagia. PM R. 2015; 7:593-598.
63. Qiao J, Wu ZM, Ye QP, Dai Y, Dou ZL. Relationship between post-stroke cognitive impairment and severe dysphagia: A retrospective cohort study. Brain Sci. 2022; 12:803.
64. Yang C, Pan Y. Risk factors of dysphagia in patients with ischemic stroke: A meta-analysis and systematic review. PloS One. 2022; 17:e0270096.
65. Banda KJ, Chu H, Kang XL, Liu D, Pien LC, Jen HJ, Hsiao SS, Chou KR. Prevalence of dysphagia and risk of pneumonia and mortality in acute stroke patients: A meta-analysis. BMC Geriatr. 2022; 22:420.
66. Rexrode KM, Madsen TE, Yu AYX, Carcel C, Lichtman JH, Miller EC. The impact of sex and gender on stroke. Circ Res. 2022; 130:512-528.
67. Karisik A, Dejakum B, Moelgg K, *et al*. Association between dysphagia and symptoms of depression and anxiety after ischemic stroke. Eur J Neurol. 2024; 31:e16224.
68. Rudolph JL, Gardner KF, Gramigna GD, McGlinchey RE. Antipsychotics and oropharyngeal dysphagia in hospitalized older patients. J Clin Psychopharmacol. 2008; 28:532-535.
69. Miarons Font M, Rofes Salsench L. Antipsychotic medication and oropharyngeal dysphagia: Systematic review. Eur J Gastroenterol Hepatol. 2017; 29:1332-1339.
70. Phan HT, Reeves MJ, Blizzard CL, *et al.* Sex differences in severity of stroke in the INSTRUCT study: A meta-analysis of individual participant data. J Am Heart Assoc. 2019; 8:e010235.
71. Niewada M, Kobayashi A, Sandercock PA, Kamiński B, Członkowska A; International Stroke Trial Collaborative Group. Influence of gender on baseline features and clinical outcomes among 17,370 patients with confirmed ischaemic stroke in the international stroke trial. Neuroepidemiology. 2005; 24:123-128.
72. Reeves MJ, Bushnell CD, Howard G, Gargano JW, Duncan PW, Lynch G, Khatiwoda A, Lisabeth L. Sex differences in stroke: Epidemiology, clinical presentation, medical care, and outcomes. Lancet Neurol. 2008; 7:915-926.
73. Renoux C, Coulombe J, Li L, Ganesh A, Silver L, Rothwell PM. Confounding by pre-morbid functional status in studies of apparent sex differences in severity and outcome of stroke. Stroke. 2017; 48:2731-2738.
74. Lee WH, Lim MH, Seo HG, Oh BM, Kim S. Hyoid kinematic features for poor swallowing prognosis in patients with post-stroke dysphagia. Sci Rep. 2021;

11:1471.
75. Tsuzuki K, Mori N, Hayami Y, Oshima O, Sugawara H, Tsuji T. Predictors of complete oral intake in patients with stroke after tracheostomy. J Am Heart Assoc. 2024; 13:e000180.
76. Hamdy S, Aziz Q, Rothwell JC, Power M, Singh KD, Nicholson DA, Tallis RC, Thompson DG. Recovery of swallowing after dysphagic stroke relates to functional reorganization in the intact motor cortex. Gastroenterology. 1998; 115:1104-1112.
77. Wang Y, Lu M, Liu R, Wang L, Wang Y, Xu L, Wu K, Chen C, Chen T, Shi X, Li K, Zou Y. Acupuncture alters brain's dynamic functional network connectivity in stroke patients with motor dysfunction: A randomised controlled neuroimaging trial. Neural Plast. 2023; 2023:8510213.
78. Huang YC, Hsu TW, Leong CP, Hsieh HC, Lin WC. Clinical Effects and Differences in Neural Function Connectivity Revealed by MRI in Subacute Hemispheric and Brainstem Infarction Patients With Dysphagia After Swallowing Therapy. Frontiers in neuroscience. 2018; 12:488.
79. Dai M, Qiao J, Wei X, Chen H, Shi Z, Dou Z. Increased cortical-medulla functional connectivity is correlated with swallowing in dysphagia patients with subacute infratentorial stroke. Neuroimage Clin. 2022; 35:103104.
80. Dong Y, Zhao K, Qin X, Du G, Gao L. The mechanisms of perineuronal net abnormalities in contributing aging and neurological diseases. Ageing Res Rev. 2023; 92:102092.
81. Yuan S, Shi J, Tang X, Deng B, Wu Z, Qiu B, Lin S, Ji C, Wang L, Cui S, Xu N, Yao L. The role of perineuronal nets in the contralateral hemisphere in the electroacupuncture-mediated rehabilitation of poststroke dysphagia mice. eNeuro. 2023; 10:ENEURO.0234-23.2023.
82. Dzyubenko E, Willig KI, Yin D, Sardari M, Tokmak E, Labus P, Schmermund B, Hermann DM. Structural changes in perineuronal nets and their perforating GABAergic synapses precede motor coordination recovery post stroke. J Biomed Sci. 2023; 30:76.
83. Li H, Ghorbani S, Ling CC, Yong VW, Xue M. The extracellular matrix as modifier of neuroinflammation and recovery in ischemic stroke and intracerebral hemorrhage. Neurobiol Dis. 2023; 186:106282.
84. Quattromani MJ, Pruvost M, Guerreiro C, Backlund F, Englund E, Aspberg A, Jaworski T, Hakon J, Ruscher K, Kaczmarek L, Vivien D, Wieloch T. Extracellular matrix modulation is driven by experience-dependent plasticity during stroke recovery. Mol Neurobiol. 2018; 55:2196-2213.
85. Dzyubenko E, Manrique-Castano D, Pillath-Eilers M, Vasileiadou P, Reinhard J, Faissner A, Hermann DM. Tenascin-C restricts reactive astrogliosis in the ischemic brain. Matrix Biol. 2022; 110:1-15.
86. Wu CT, Chen MC, Liu SH, Yang TH, Long LH, Guan SS, Chen CM. Bioactive flavonoids icaritin and icariin protect against cerebral ischemia-reperfusion-associated apoptosis and extracellular matrix accumulation in an ischemic stroke mouse model. Biomedicines. 2021; 9:1719.
87. Al Qawasmeh M, Alhusban A, Alfwaress F. An evaluation of the ability of thrombospondin-1 to predict stroke outcomes and mortality after ischemic stroke. Int J Neurosci. 2020; 1-4.
88. Jin Y, Sekizawa K, Fukushima T, Morikawa M, Nakazawa H, Sasaki H. Capsaicin desensitization inhibits swallowing reflex in guinea pigs. Am J Respir Crit Care Med. 1994; 149:261-263.
89. Suntrup-Krueger S, Muhle P, Kampe I, Egidi P, Ruck T, Lenze F, Jungheim M, Gminski R, Labeit B, Claus I, Warnecke T, Gross J, Dziewas R. Effect of capsaicinoids on neurophysiological, biochemical, and mechanical parameters of swallowing function. Neurotherapeutics. 2021; 18:1360-1370.
90. Safwat A, Helmy A, Gupta A. The role of substance P within traumatic brain injury and implications for therapy. J Neurotrauma. 2023; 40:1567-1583.
91. Ikeda J, Kojima N, Saeki K, Ishihara M, Takayama M. Perindopril increases the swallowing reflex by inhibiting substance P degradation and tyrosine hydroxylase activation in a rat model of dysphagia. Eur J Pharmacol. 2015; 746:126-131.
92. Niimi M, Hashimoto G, Hara T, Yamada N, Abo M, Fujigasaki H, Ide T. Relationship between frequency of spontaneous swallowing and salivary substance P level in patients with acute stroke. Dysphagia. 2018; 33:414-418.
93. Kessler JP, Jean A. Evidence that activation of N-methyl-D-aspartate (NMDA) and non-NMDA receptors within the nucleus tractus solitarii triggers swallowing. Eur J Pharmacol. 1991; 201:59-67.
94. Hashim MA, Bieger D. Excitatory amino acid receptor-mediated activation of solitarial deglutitive loci. Neuropharmacology. 1989; 28:913-921.
95. Wang YT, Bieger D. Role of solitarial GABAergic mechanisms in control of swallowing. Am J Physiol. 1991; 261:R639-R646.
96. Car A, Roman C, Zoungrana OR. Effects of atropine on the central mechanism of deglutition in anesthetized sheep. Exp Brain Res. 2002; 142:496-503.
97. Greenwood B, Blank E, Dodds WJ. Nicotine stimulates esophageal peristaltic contractions in cats by a central mechanism. Am J Physiol. 1992; 262:G567-G571.
98. Bieger D. Neuropharmacologic correlates of deglutition: Lessons from fictive swallowing. Dysphagia. 1991; 6:147-164.
99. Labeit B, Michou E, Trapl-Grundschober M, Suntrup-Krueger S, Muhle P, Bath PM, Dziewas R. Dysphagia after stroke: Research advances in treatment interventions. Lancet Neurol. 2024; 23:418-428.
100. Li L, Huang H, Jia Y, Yu Y, Liu Z, Shi X, Wang F. Systematic review and network meta-analysis of noninvasive brain stimulation on dysphagia after stroke. Neural Plast. 2021; 2021:3831472.
101. Nyffeler T, Müri R. Comment on: Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research, by Rossi *et al.* (2009). Clin Neurophysiol. 2010; 121:980.
102. Zhong L, Rao J, Wang J, Li F, Peng Y, Liu H, Zhang Y, Wang P. Repetitive transcranial magnetic stimulation at different sites for dysphagia after stroke: A randomized, observer-blind clinical trial. Front Neurol. 2021; 12:625683.
103. Ünlüer NÖ, Temuçin ÇM, Demir N, Serel Arslan S, Karaduman AA. Effects of low-frequency repetitive transcranial magnetic stimulation on swallowing function and quality of life of post-stroke patients. Dysphagia. 2019; 34:360-371.
104. Nitsche MA, Liebetanz D, Antal A, Lang N, Tergau F, Paulus W. Modulation of cortical excitability by weak direct current stimulation--technical, safety and functional aspects. Suppl Clin Neurophysiol. 2003; 56:255-276.
105. Kunieda K, Sugiyama J, Nomoto A, Ohno T, Shigematsu

T, Fujishima I. Compensatory swallowing methods in a patient with dysphagia due to lateral medullary syndrome-vacuum and prolonged swallowing: A case report. Medicine (Baltimore). 2022; 101:e28524.
106. World Health Organization. Acupuncture: Review and analysis of reports on controlled clinical trials. World Health Organization. 2003; pp.1-81.
107. Yao L, Ye Q, Liu Y, *et al.* Electroacupuncture improves swallowing function in a post-stroke dysphagia mouse model by activating the motor cortex inputs to the nucleus tractus solitarii through the parabrachial nuclei. Nat Commun. 2023; 14:810.
108. Wu M, Song W, Wang X, Tang Q, Gao W, Zhu L. Exploring the rules of related parameters in acupuncture for post-stroke dysphagia based on data mining. Front Neurol. 2024; 15:1394348.
109. Terré R, Panadés A, Mearin F. Botulinum toxin treatment for oropharyngeal dysphagia in patients with stroke. Neurogastroenterol Motil. 2013; 25:896-e702.
110. Schneider I, Thumfart WF, Pototschnig C, Eckel HE. Treatment of dysfunction of the cricopharyngeal muscle with botulinum A toxin: introduction of a new, noninvasive method. Ann Otol Rhinol Laryngol. 1994; 103:31-35.
111. Dodds WJ. The physiology of swallowing. Dysphagia. 1989; 3:171-178.
112. Dou Z, Zu Y, Wen H, Wan G, Jiang L, Hu Y. The effect of different catheter balloon dilatation modes on cricopharyngeal dysfunction in patients with dysphagia. Dysphagia. 2012; 27:514-520.
113. Standards of Practice Committee; Egan JV, Baron TH, *et al*. Esophageal dilation. Gastrointest Endosc. 2006; 63:755-760.
114. Nair SS, Surendaran AJ, Menon JR, Sreedharan SE, Sylaja PN. Persistent post-stroke dysphagia treated with cricopharyngeal myotomy. Ann Indian Acad Neurol. 2016; 19:249-251.
115. Al Ghamdi SS, Bejjani M, Hernández Mondragón OV, Parsa N, Yousaf MN, Aghaie Meybodi M, Ghandour B, Krustri C, Phalanusitthepha C, Ngamruengphong S, Nieto JM, Khashab MA. Peroral endoscopic myotomy for management of cricopharyngeal bars (CP-POEM): A retrospective evaluation. Endoscopy. 2022; 54:498-502.

Received January 24, 2025; Revised February 10, 2025; Accepted February 17, 2025.

**Address correspondence to:*
Luwen Zhu, The Second Affiliated Hospital of Heilongjiang University of Chinese Medicine, 411 Guogeli Street, Nangang District, Heilongjiang Harbin, China.
E-mail: zhuluwen1983@126.com

Qing Mei Wang, Stroke Biological Recovery Laboratory, Spaulding Rehabilitation Hospital, the Teaching Affiliate of Harvard Medical School, Boston, MA, USA.
E-mail: Wang.Qingmei@mgh.harvard.edu

Released online in J-STAGE as advance publication February 22, 2025.