Physiology & Behavior 151 (2015) 404–411

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Peripheral and central control of swallowing initiation in healthy humans

Seiya Aida [a], Ryosuke Takeishi [a], Jin Magara [a], Masahiro Watanabe [a], Kayoko Ito [b], Yuki Nakamura [a], Takanori Tsujimura [a], Hirokazu Hayashi [a], Makoto Inoue [a,*]

[a] Division of Dysphagia Rehabilitation, Niigata University Graduate School of Medical and Dental Sciences, 2-5274 Gakkocho-dori, Chuo-ku, Niigata 951-8514, Japan
[b] Oral Rehabilitation, Niigata University Medical and Dental Hospital, 1-754 Asahimachi-dori, Chuo-ku, Niigata 951-8520, Japan

HIGHLIGHTS

- We applied pharyngeal electrical stimulation to the pharynx in healthy humans.
- Peripheral inputs facilitated the central inputs that control voluntary swallowing.
- Swallowing initiation may be attributed to the excitability of the brainstem neural network.
- The neural network associated with chewing may regulate involuntary swallowing initiation.

ARTICLE INFO

Article history:
Received 5 May 2015
Received in revised form 31 July 2015
Accepted 1 August 2015
Available online 4 August 2015

Keywords:
Pharyngeal electrical stimulation
Voluntary swallow
Involuntary swallow
Chewing

ABSTRACT

We investigated (1) how peripheral inputs might assist central inputs in the control of voluntary evoked swallowing, (2) inter-individual variation in involuntary and voluntary swallowing initiation, and (3) whether natural chewing behavior affects the initiation of involuntary swallowing in healthy humans. Eleven participants completed a repetitive saliva swallowing test (RSST), chewing test (CHEW), and rest period (REST). In RSST, participants repetitively swallowed as quickly as possible. In CHEW, subjects chewed gum freely. We delivered pharyngeal electrical stimulation (PEStim) to the laryngopharynx and compared the number of swallows that occurred with and without PEStim. PEStim significantly increased the number of voluntary evoked swallows in RSST, as well as the number of swallows in CHEW and REST trials, although this facilitatory effect was larger in REST trials. We found a positive correlation between the number of swallows at RSST without PEStim and that at REST with PEStim within individuals. Additionally, we found a significant positive correlation between the number of swallows at RSST with PEStim and the sum of that at RSST without PEStim and at REST with PES. Based on the current results, we suggest that (1) peripheral inputs within a certain range appear to facilitate the central inputs that control voluntary swallowing, (2) inter-individual variations in swallowing initiation may arise from differences in the excitability of the common neural network in the lower brainstem, and (3) during chewing, food reduction in the oral cavity is prioritized, such that the neural network associated with chewing may regulate swallowing initiation.

1. Introduction

Swallowing involves complex sensorimotor neural components. The complexity of swallowing may be due to two critical functions of this behavior: 1) propelling the food bolus from the oral cavity into the stomach through the pharynx and the esophagus, and 2) protecting the upper respiratory tract from aspiration or suffocation by secretions or food [1–4]. To complete swallowing, numerous pairs of related muscles must be coordinated such that they are synchronously activated bilaterally [1–3]. The motor patterns underlying swallowing are programed by the central pattern generator (CPG) in the medulla oblongata, and both peripheral and central inputs into the CPG can trigger swallowing [2,3]. In other words, swallowing can be initiated either involuntarily or voluntarily.

The superior laryngeal nerve (SLN), which innervates the laryngopharyngeal and laryngeal mucosa, represents a peripheral input involved in the swallowing reflex. SLN stimulation can readily trigger a swallowing reflex even in anesthetized animals [5–7]. There are two pieces of evidence to suggest that peripheral inputs may play

Abbreviations: CHEW, chewing test; CPG, central pattern generator; EGG, electroglottography; EMG, electromyography; Mas, masseter muscle; PEStim, pharyngeal electrical stimulation; REST, resting; RJM, rhythmic jaw movement; RSST, repetitive saliva swallowing test; SHy, suprahyoid muscle group; SLN, superior laryngeal nerve; STper, stimulus thresholds for perception; STtol, stimulus thresholds for toleration.

* Corresponding author at: Division of Dysphagia Rehabilitation, Niigata University Graduate School of Medical and Dental Sciences, 2-5274 Gakkocho-dori, Chuo-ku, Niigata 951-8514, Japan.
E-mail address: inoue@dent.niigata-u.ac.jp (M. Inoue).

http://dx.doi.org/10.1016/j.physbeh.2015.08.003
0031-9384/

a major role in initiating swallowing within the neural circuitry in the brainstem: 1) the nucleus tractus solitarii, which is part of the swallowing CPG, directly receives rich inputs from afferent fibers of the SLN, and 2) initiation of the swallowing reflex is not interrupted after ablation of the cortex [6]. In addition, repetitive pharyngeal electrical stimulation (PEStim) has been found to evoke a swallowing reflex and can facilitate voluntary swallowing in conscious humans [8]. This result was expected because the stimulated areas are innervated by the SLN. However, initiation of swallowing using this method was likely less successful than that in anesthetized animals using SLN stimulation. Additionally, in terms of swallowing frequency, a wide inter-individual variation in both voluntary and involuntary swallowing initiation has been reported among subjects [8,9].

The potentials required to initiate voluntary swallowing have been found to vary greatly from subject to subject, even in healthy humans [10–12]. Human brain imaging has exposed the cortical representation of voluntary swallowing [13–18]. Specifically, activation of the intermediate and caudal anterior cingulate cortex, as well as lateral cortical activation in the insula, may be implicated in the activation of the swallowing CPG in the brainstem [15]. Although it is possible that inter-individual variations in the time interval between voluntary swallows may be due to differences in the excitability of such brain areas, the ways in which the neural network is involved in this variation have not been clarified. Kitada et al. and Yahagi et al. [10,12] proposed that chemosensory input, such as water stimulation, facilitates the initiation of voluntary swallowing via the supramedullary neural mechanism and compensates for difficulties initiating voluntary swallowing. Thus, unhindered initiation of voluntary swallowing requires information from both supramedullary and peripheral inputs. Additionally, inter-individual variability in swallowing initiation is dependent on the excitability of supramedullary neural components, brainstem neurons, or both.

Other oral behaviors, such as chewing, may also affect the initiation of the swallowing reflex. When humans eat solid foods in a natural manner, a triturated bolus is transported from the oral cavity to the oropharynx before swallowing [19–21]. In this situation, chewing continues after the bolus reaches the epiglottic vallecula. This phenomenon suggests that the swallowing reflex is inhibited during chewing, because mechanical or chemical stimulation applied to the pharyngeal regions is known to immediately initiate the swallowing reflex [22]. Although we have previously shown that the swallowing reflex is inhibited during cortically evoked rhythmic jaw movements in anesthetized rats [23], whether this is also the case during natural mastication in humans is unclear.

In the present study, we used PEStim to study the influence of peripheral inputs on the initiation of swallowing. We also employed the repetitive saliva swallowing test (RSST, which measures the number of rapid voluntary swallows in 30 s) to study the influence of central inputs. The aim of the present study was to investigate (1) how peripheral inputs contribute to central inputs controlling voluntary evoked swallowing, (2) what causes inter-individual variations in swallowing initiation, and (3) whether natural chewing affects the initiation of involuntary swallowing in healthy humans.

2. Materials and methods

2.1. Participants

Eleven healthy male adults (mean age ± SD: 32.4 ± 1.4 years; age range: 22–37 years) participated in the study. Informed consent was obtained from all participants, and no subject had a history of alimentary disease, pulmonary disease, neurological disease, musculoskeletal disorders, speech disorders, voice problems, or dental, masticating, or swallowing problems. No smokers participated in the present study. The experiments were approved by the Ethics Committee of the Faculty of Dentistry, Niigata University (25-R33-11-25).

2.2. Electrophysiological procedure

To assess swallowing events, we recorded electromyographic (EMG) and electroglottographic (EGG) activities according to our previous procedure [11,24–26]. To record activity in the masseter muscle (Mas), we bilaterally attached bipolar surface EMG electrodes (ZB-150H; Nihon Kohden, Tokyo, Japan) to the skin over the center of the masseter. To record activity in the suprahyoid muscle group (SHy), we bilaterally attached electrodes to the anterior surface of the digastric muscle. The former and latter are known to be the jaw closer and hyoid elevator, respectively. Detected EMG signals were filtered and amplified (low, 30 Hz and high, 2 kHz) (WEB-1000; Nihon Kohden, Tokyo, Japan) to remove movement-related artifacts. We also positioned bipolar surface EGG electrodes on either side of the thyroid cartilage (EGG-D200; Laryngograph, London, UK). Amplified EMG and EGG signals were stored via an interface board (PowerLab; ADInstruments, Colorado Springs, CO, USA) on a personal computer. The sampling rate was 10 kHz. Data analysis was performed using the PowerLab software package (LabChart6; ADInstruments, Colorado Springs, CO, USA). We also recorded button-pressing behavior. During the trials, the subjects were instructed to hold a button in their hand and press it immediately after each swallow.

In a portion of the trials, we delivered PEStim to the laryngopharynx. To deliver PEStim, we developed stimulus electrodes (TK210-107b; Unique Medical Co., Ltd., Tokyo, Japan). The catheter made of silicon was 50 cm long, 3 mm in outer diameter and 2 mm in inner diameter with two ring electrodes made of platinum; the distal electrode was positioned 3 mm from the tip of the catheter, with a distance of 13 mm between the electrodes (Fig. 1). In our preliminary experiment, we confirmed that catheter was reasonably thin and soft and was not painful. The stimulation site was at the lateral wall of the laryngopharynx, at the level of the pyriform sinus. This was confirmed by videoendoscopy. We delivered bipolar surface electrical stimulation (1-ms pulse duration; 5 Hz) through cables connected to an electrical stimulator (SEN3401, Nihon Kohden, Tokyo, Japan). To determine the intensity of the stimulus, we increased the current by 0.1 mA every 5 s. Once stimulus thresholds for perception (STper) and tolerability (STtol) were determined according to cues given by the subject, the stimulus intensity was calculated as STper + 0.75 (STtol − STper).

2.3. Experimental protocol

To reduce the possible influence of the environment on swallowing performance, experiments were performed in an air-conditioned room with a constant temperature of 20–24 °C and humidity of 40–70%. Subjects were asked to refrain from eating, drinking, smoking, and brushing

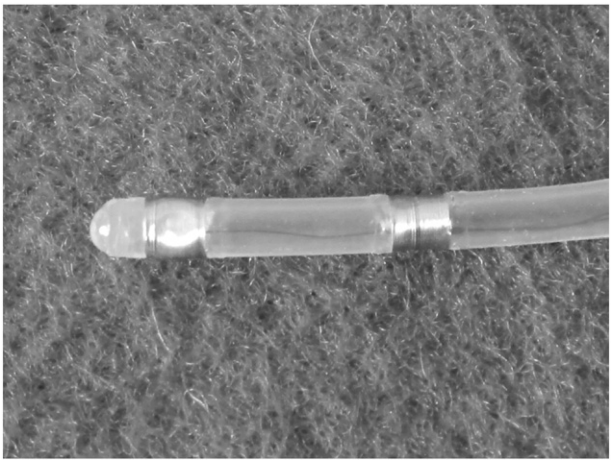

Fig. 1. Photograph of tip of catheter used for electrical stimulation.