



# Nonspecific effects of gap paradigm on swallowing☆☆☆☆☆



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## HIGHLIGHTS

- Initiation of visually guided swallowing is enhanced using the gap paradigm.
- The gap effects are significant on a delay from muscle contraction to action.
- This effect covers voluntary motions in general, unlike a gap effect on saccade.

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## ABSTRACT

**Objective:** Analogous to the gap paradigm in experiments for saccadic eye movements with very short reaction times, we hypothesized that the initiation of oropharyngeal swallowing movements guided by visual cues are encouraged under experimental conditions using a similar gap paradigm.

**Methods:** A red visual cue indicating to hold a bolus in the mouth and a blue one indicating to swallow the bolus were sequentially provided on a computer display to 11 healthy participants. The gap period between these cues varied from 0 to 800 ms. Swallowing kinetics and kinematics were recorded using surface electromyography and a laser displacement sensor, respectively.

**Results:** In comparison with the no-gap paradigm, the delay from the onset of muscle activities to initiation of movement significantly decreased with a 100- ( $p < 0.01$ ) and 200-ms ( $p < 0.005$ ) gap period. With other gap periods, no significant change was detected in the delay.

**Conclusions:** Initiation of visually guided swallowing was enhanced by a gap paradigm of 100–200 ms. Wrist flexion was boosted in a similar manner. Thus, the gap effect may be a generalized warning effect.

**Significance:** Our findings might provide insights into the contribution of the basal ganglia to volitional swallowing.

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## 1. Introduction

The pharyngeal phase of swallowing is driven by the convergence of peripheral sensory inputs on the swallowing center in the brainstem, including inputs from the pharyngeal mucosa [14], plate [9,10], and masticatory muscles [24]. Recent advances on functional brain imaging techniques, however, have revealed that widely distributed brain regions are involved in the initiation and execution of swallowing movements [4–6,18–20,28]. These regions include not only the primary motor and sensory cortices but also the insula, operculum, anterior

cingulate cortex, supplementary motor area, cerebellum, thalamus, and basal ganglia. Activities in these regions during swallowing are considerably modulated by multiple factors such as age [11,27], bolus type [11], and sensory modalities [13]. In addition, the type of swallowing task, e.g., volitional swallowing [5,18,20], reflexive swallowing [18], covert swallowing [17], and making a decision on whether to swallow [12, 25], makes a marked difference on brain activities. Consequently, it is sometimes difficult to interpret the brain activity as having a definitive role in swallowing.

The basal ganglia are a key structure in decision making and control of action [2,3,23]. It is logical to believe that they greatly contribute to swallowing, in particular, to the initiation of volitional swallowing. In practice, some studies have clearly detected activities in the putamen and globus pallidus during swallowing [4,5,19,20,22,28], which are input and output nuclei of the basal ganglia, respectively. Nevertheless, correspondence between these activities and multiple aspects of swallowing is still obscure [16]. This is partly due to limitations associated with current brain imaging studies; further advances in technology are required. Therefore, using a methodology that has elucidated the

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contribution of the basal ganglia to other volitional movements may help determine the functional role of the basal ganglia in swallowing.

Motor function of the basal ganglia regarding saccadic eye movements has been extensively investigated [7,8]. Similar to the pharyngeal phase of swallowing, saccade is a centrally programmed and ballistic movement; it enables us to maintain focus on an interesting object by putting it precisely on the center of retina. In an experiment, monkeys were trained to orient their eyes from a centrally situated target (fixation point) to a visual target illuminated around the fixation point. When a gap of approximately 200 ms was provided between extinction of the fixation point and illumination of the new visual target (gap paradigm), the reaction time of the saccadic eye movement significantly shortened (express saccade) in comparison with that when the visual target was given immediately provided after extinction of the fixation point (no-gap paradigm) [1]. The neural basis for express saccade has been associated with neural networks comprising the basal ganglia, superior colliculus, and oculomotor center in the brainstem [15]. Given that the basal ganglia also play a crucial role in the initiation of swallowing, we expect subjects to execute “express swallowing” under experimental conditions using the gap paradigm, analogous to express saccade.

In this study, we recorded the kinetics and kinematics of visual cue-guided swallowing movements to elucidate the impact of the gap paradigm on reaction time of swallowing.

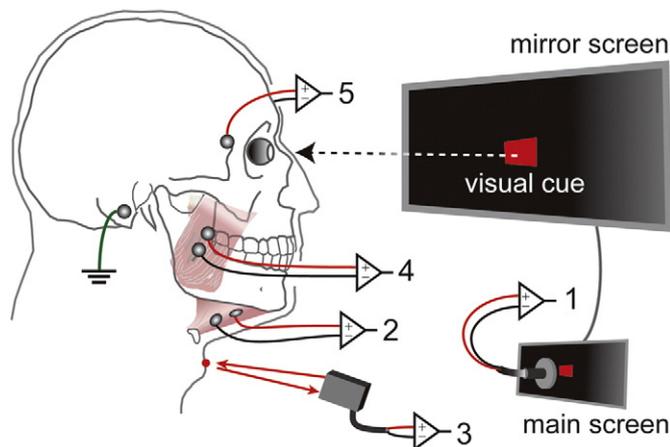
## 2. Materials and methods

Two experiments were performed, both in conformity with the Declaration of Helsinki. The study was approved by the Ethical Committee of Faculty of Education of Kumamoto University, and all participants provided their written informed consent.

All signals were digitized (sampling rate, 10 kHz) using PowerLab 8/30 (AD INSTRUMENTS, Bella Vista, NSW, Australia) and were captured on a personal computer for off-line analysis. Statistical analyses were executed using a computer statistical package (R version 3.2.3, free software).

### 2.1. Experiment 1: gap effects on swallowing

Eleven volunteers (six men and five women, mean age 20.6 years, age range 20–22 years) with no clinical history of difficulty in swallowing were invited to participate in Experiment 1.

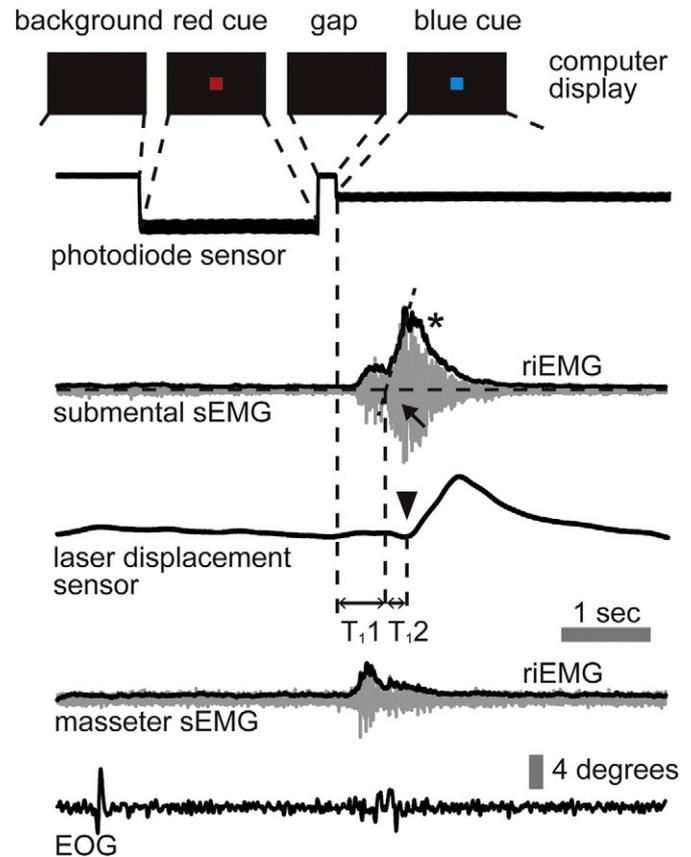


**Fig. 1.** Experimental arrangement. Participants sat in front of a mirror computer screen on which the appearance of a visual cue was turned on and off. The timing of the cue was detected using a silicon photodiode (1) placed at the center of the main computer screen. Surface electromyogram signals were recorded from the submental area (2). Movements of the thyroid cartilage were detected using a laser displacement sensor (3). Surface electromyogram signals from the masseter muscle (4) and electrooculogram (5) were also recorded to detect undesirable movements.

The participants were seated upright in front of a computer screen at a distance of 60 cm (Fig. 1). Nothing was shown on the computer screen (black background) at the beginning of experiment. Five seconds later, a visual cue (a red square of 2.1 cm corresponding to 2° both in width and height on the mirror screen) was displayed at the center of both the main and mirror computer screens for 2 s. After the red cue disappeared, a blue square of the same size was displayed at the same place (Fig. 2, uppermost row).

The participants were instructed to stare at the red cue throughout its illumination while keeping 5 ml of jelly (Aqua Gelée Pouch, Foodcare TMF, Kanagawa, JAPAN) on their tongue, and they were then asked to swallow the jelly as soon as possible after the blue cue appeared. Gap periods of 0, 50, 100, 200, 300, 400, and 800 ms between the extinction of the red cue and illumination of the blue cue were assigned pseudo-randomly four times each, for a total of 28 trials for each participant.

The illumination and extinction of visual cues were detected using a silicon photodiode (100 mm<sup>2</sup> in the photodetector area, Edmund Optics Japan, Tokyo, Japan) placed at the center of the main computer screen (1 in Fig. 1). The change in illumination was amplified using a 57–601 photodiode amplifier (Edmund Optics Japan).



**Fig. 2.** An example of visually-guided swallowing under the gap paradigm (gap period = 200 ms) in Experiment 1. The top row shows thumbnail images of the computer display in a chronological sequence. Submental surface electromyographic recordings (sEMG, gray trace) were rectified and integrated (riEMG, black trace) for further analysis. Submental riEMG generally shows two upward deflections. The point of intersection (arrow) between the approximately straight line of the second deflection (asterisk) and baseline was taken to approximate the onset of swallowing reflex. Initiation of the anterior shift of the thyroid cartilage was determined by the onset of the upper deflection of the displacement signals of the larynx (indicated by arrowhead). EOG = electrooculography; riEMG = rectified and integrated surface electromyography; sEMG = surface electromyography; T<sub>1</sub> = the time from the illumination of the blue cue to second deflection of the submental riEMG; T<sub>2</sub> = the delay from the onset of the second deflection of the submental riEMG to initiation of the anterior shift of the thyroid cartilage.

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