Specific areas of cortical activity during solid bolus swallowing in humans are unknown. We tested the hypothesis that cortical representations of swallowing in humans may vary by bolus type. Twenty-one normal subjects swallowed three kinds of food: agar (solid), a capsule and water. We followed the same countdown method for identification of the cortical representations during swallowing performances as a previous study (Tanaka et al., 2006). Functional magnetic resonance imaging (fMRI) showed that the precentral gyrus, postcentral gyrus, medial temporal gyrus, superior temporal gyrus and cingulate gyrus were activated when swallowing an agar bolus (p<0.001). The subcortex was not activated. The cerebellum was activated only during capsule swallowing (p<0.001). Water bolus swallowing activations were similar to agar bolus swallowing. The cluster size of water swallowing was larger than the agar swallowing. We conclude that the cortical representations for swallowing are variable by food type.

Key words: swallowing, cortical activation, solid bolus, functional MRI

Introduction

Swallowing is a complex physiological process involving voluntary and reflexive motor activity. Current research indicates, from both clinical evidence following cerebral vascular disease and functional studies of the human brain, that cerebral cortical activities are crucial to successful human swallowing. The cortical representations of swallowing have been investigated using functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and transcranial magnetic stimulation (TMS) techniques. These investigations have demonstrated that the insular region of the cortex, the deep aspects of the premotor cortex, the sensorimotor cortex and the anterior cingulatgy gyrus appear to participate in the normal pharyngeal swallow response. However, conclusions from these investigations were only based on either a dry swallow or a small water bolus. The cortical activities associated with solid food swallowing and capsule swallowing have not been fully investigated. The aim of the present study was to elucidate the cortical representations of the oropharyngeal phase of swallowing using blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI) technique with three different bolus types: agar, a capsule and 5ml of water.

Materials & Methods

Subjects.

Twenty-one healthy adult volunteers (9 male, 12
female) participated in this study. All subjects were right handed (average age of 29.2 years; range, 23-38). All subjects provided written informed consent and completed a brief health-related questionnaire before participation. None of the subjects had any history of swallowing difficulty or other neurological or gastrointestinal disease. The study protocols were approved by the Clinical Research Review Committee of the Seirei Hamamatsu General Hospital.

Study task and materials.

The experimental tasks included swallowing three bolus materials. Prior to the study, all subjects were given general information on MRI scanning and the study methods. Each subject was asked to swallow the test materials prior to fMRI recording. Only subjects who did not cough in the supine position or were able to swallow in this position were included. Two subjects were eliminated from the study. The experiment was begun after the subjects understood all sequences and performed all activities without any problems.

Subjects swallowed each material in the following order; 5ml water, a capsule and agar. The agar was 8 X 8 X 8 mm cube and given without water. Subjects were allowed to mash the bolus in their mouth before they swallowed. A standard #5 capsule (11mm X 2mm, columnar) filled with lactose was also given without water. Subjects were told to swallow the capsule without chewing. The water boluses were given in 5ml amounts at 15 °C. Subjects were told to swallow the water normally. All boluses were delivered through a plastic cylinder that was placed between the lips. The examiner placed each bolus into the cylinder with a long-handled plastic spoon. Each subject’s head was held in place, however, the jaw was allowed to move for delivering the bolus into the pharynx.

As in our previous study15, each swallowing cycle began with an 18-second rest period (OFF) followed by a six-second count down for swallowing preparation, followed by a six-second window for swallowing (ON) (Fig 1). One study consisted of 8 swallowing cycles.

OFF: rest, ON: swallowing preparation and swallowing

cerebral images at one time point consisting of 12 axial images interspersed with two millimeter inter-slice gaps. Images at 82 time points were obtained repetitively. Each scanner was equipped with a QD head coil.

Data Analysis.

Correlation statistics and image registration were facilitated by the Statistical Parametric Mapping (SPM99) software written by the Wellcome Department of Cognitive Neurology (University College, London, UK) and implemented in the Matlab v.5.3 (Mathworks, Natick, MA, USA)16. Data preprocessing included realignment of the images to the first image of the series to adjust for motion artifact and stereotactictic normalization into a standard space using the EPI template of the Montreal Neurological Institute (MNI, Canada) approximating that of Talairach and Tournoux17. Subsequently, the normalized data were smoothed using a Gaussian Kernel, 7.5 X 7.5 X 7.5 mm, in order to improve the signal to noise ratio. We correlated the swallowing cycle with the MRI images using SPM99 software. Only the MRI scans for the swallowing were used in our analysis. A statistical parametric map of the t statistic was generated for each voxel. The individual z score contrast images were analyzed for uncorrected height with the threshold at a p value of 0.001 in each sequence for each subject. In order to make group mean statistical parametric map-

---

**Fig. 1. Task Paradigm**

The block-trial task paradigm was used in the present study. The swallowing experiment began with an 18-second rest period (OFF) followed by a six-second count down for swallowing preparation, followed by a six-second period for swallowing (ON). One swallowing cycle included the “OFF” period and “ON” period. One study consisted of 8 swallowing cycles.

OFF: rest, ON: swallowing preparation and swallowing

---

**Task Paradigm**

The block-trial task paradigm was used in the present study. The swallowing experiment began with an 18-second rest period (OFF) followed by a six-second count down for swallowing preparation, followed by a six-second period for swallowing (ON). One swallowing cycle included the “OFF” period and “ON” period. One study consisted of 8 swallowing cycles.

OFF: rest, ON: swallowing preparation and swallowing

---

A 1.5 Tesla MRI (Signa 1.5, GE Medical Systems, Wauwatosa, WI., USA) was used. A one shot echo planar imaging (EPI) sequence was used with the following settings: repetition time (TR) 3000 msec, echo time (TE) 60 msec, field of view (FOV) 24 cm, 8 mm thickness, 64x64 matrix. It took three seconds to obtain
ping maps, one sample t-test of the z score images from the all subjects (p=0.001) was applied for three sequences of the study. The regions of cortical signal changes associated with swallowing are shown graphically as color overlaid images stereotaxically mapped on the anatomic images into the Talairach and Tournoux space\textsuperscript{16,18}.

Results

Areas of increased cerebral activation.

Multiple regions of increased brain activity were observed in all sequences during oropharyngeal swallowing. The regions of the right precentral gyri (Brodmann's Area: BA, 6 & 4), left inferior parietal lobe (BA 40), right and left medial temporal gyri (BA 21), left superior temporal gyri (BA 22 & 42) and right cingulate gyrus were activated during the agar swallowing (p < 0.001, uncorrected) (Table 1). In the capsule swallowing, the right and left precentral gyri (BA 6), right cingulate gyrus right and left and cerebellum were activated (p < 0.001, uncorrected) (Table 1 & Fig 2). With the 5ml water bolus the right and left precentral gyri (BA 6), left inferior frontal gyri (BA 47), left medial temporal gyrus (BA 21), left superior temporal gyri (BA 22, 44), right postcentral gyrus (BA 40), right cingulate gyrus and the right insular regions were activated (p < 0.001, uncorrected) (Table 1). The cluster size of each sequence is shown in Table 1. The cluster size of the 5ml water swallowing is much larger than the agar swallowing. Large clusters of brain activation areas in the water bolus swallowing are shown in Fig 3.

Discussion

The present study has provided the first trial of how

<table>
<thead>
<tr>
<th>Table 1. Areas with stronger activation during the agar, capsule, and water bolus swallowing</th>
</tr>
</thead>
<tbody>
<tr>
<td>cluster</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Agar</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Capsule</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Water</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Coordinates x, y, z express the position of the voxel with peak activation level (p < 0.001, uncorrected, extent threshold 10 voxels) with the cluster (in mm) relative to the anterior commissure (AC) in the stereotactic space (Talairach and Tournoux, 1988). Coordinates: x, lateral distance from the midline (+ right, - left); y, anteroposterior distance from the AC (+ anterior, - posterior); z, height relative to the AC line (+ height, - below). p < 0.05 small volume corrected for multiple spatial comparisons. Lt., left; Rt., right.
swallowing is processed in the human cerebral cortex using solid food and capsules. It is also the first study to compare the cerebral representation of swallowing on a liquid versus a solid bolus.

When swallowing a solid (agar) bolus, cerebral activation was seen in the precentral gyri, inferior parietal lobe, cingulate gyrus and the medial and superior temporal gyri. These areas of activation are consistent with previous studies[19,20]. In the present study, no activation was observed in subcortical regions. Activation of subcortical regions during swallowing has been reported in previous studies[8,21]. According to those results, the basal ganglia (putamen) and thalamus were activated during repetitive salliva or water swallowing. They concluded that volitional swallowing activity was influenced by the activation of the basal ganglia. During the agar swallowing in the present study, subjects allowed to mash the bolus in their mouth before swallowing. In this condition, swallowing is more natural compared to the repetitive saliva or water swallows done in previous studies[22,23]. Mastication, combined with a solid bolus swallow clearly activates different cortical areas than water or dry swallowing.

Activation of the premotor cortex and cerebellum was observed during the capsule swallowing. Cerebellar activation during swallowing was found in some studies[7,8,10], but not in others[9,24]. However, the swallowing tasks were different. Mosier[7], Suzuki[8] and Zald[10], used repetitive saliva swallowing for their tasks, whereas Hartnick[9] and Kern[24] did not. In addition, Mosier[7] studied single water swallowing and repetitive saliva swallowing; the cerebellum was activated only on repetitive saliva swallowing. Our data show that the cerebellum was only activated when taking the capsule without water. It may be that this task involved more coordination of the motor component for succession to swallow safely because of no water. Similarly, repetitive

![Fig. 2. Brain regions showing significantly stronger activation in the cerebellum during the capsule swallowing. Clusters of significant activation (p < 0.001, uncorrected) are overlaid on consecutive axial, sagittal, and coronal slices of a T1 anatomic MRI that was normalized stereotactically into the Montreal Neurological Institute (MNI, Canada) standard space. Color scale indicates z score.](image)

![Fig. 3. Similar cerebral activation areas were observed during agar bolus swallowing and liquid bolus swallowing. The cluster size of the liquid bolus is larger than agar bolus.](image)
swallowing placed increased demands on the swallowing network. We believe that this extra effort activated cortical and cerebellar structures.

During liquid bolus swallowing, areas of cerebral activation were similar to the agar bolus. However, the cluster size of brain activation for the liquid bolus was larger than solid bolus (Table 1, Fig 3). This finding suggests that water swallowing requires the coordination of many regions in the cerebral cortex and subcortex. It has been suggested that patients with oropharyngeal swallowing disorders may have more difficulty with liquids than other bolus types. Perhaps this is because more regions of the brain must be activated to achieve a successful liquid swallowing. Because of generalized brain decompensation, these multiple sites are more difficult to access.

Our methodology in this study divided swallowing into two phases, oral and pharyngeal transport. To interpret the data one must differentiate between oral activity associated with swallowing and oral activity not associated with swallowing. For instance, Kern reported that the movement of the lips and tongue during nonswallowing movements produced different cortical activation patterns during deglutition. Our block design methodology avoids confusing non-swallow lip closure and tongue movement from real swallowing performance. Using this method, we feel we have captured the oropharyngeal stage of swallowing. However, swallowing while laying on one’s back is unusual, but it’s the only way to gather information using fMRI. Further investigations, using an older population that isolate each phase of swallowing and their corresponding cortical representation with different kinds of solid food and bolus volume are needed.

In conclusion, solid and liquid bolus swallowing tasks are represented cortically and subcortically at multiple sites. The cortical representation of a solid bolus swallowing task showed cortical activation similar to previous studies. Unlike previous study, however, subcortical activation was not seen. The premotor cortex and cerebellum were activated when swallowing a capsule. This task may require more swallowing and oral motor coordination than solid food or liquid swallowing. The cortical representations for swallowing are variable by food type and may explain the variable responses in swallowing performance we see in patients who have oropharyngeal dysphagia.

Acknowledgments

We thank the staff of the Department of Rehabilitation Medicine, Department of Radiology and Department of Nutrition at Seirei Hamamatsu General Hospital for their corporation on our research project. We also thank Dr. M. E. Groher for his great comments on this research. This manuscript was part of an oral presentation given at the 28th meeting of The Society of Swallowing and Dysphagia of Japan on Feb. 5, 2005.

References


