Dissociating the spatio-temporal characteristics of cortical neuronal activity associated with human volitional swallowing in the healthy adult brain

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Abstract

Human swallowing represents a fundamental but understudied feeding behaviour, which is essential for life. The effortless and natural manner in which we prepare and initiate a volitional swallow, comprising a series of oral and pharyngoesophageal peristaltic events, belies the complex interaction of cortical and sub-cortical structures involved in ensuring its optimal performance (Miller, 1982). Moreover, to initiate and regulate safe swallowing, an intricate combination of sensory feedback and motor planning/programming is critical (Jean, 1990).

Swallowing dysfunction (dysphagia) is a clinically common problem, which can develop as a result of lesions in apparently disparate cortical regions, for example, following stroke (Smithard et al., 1996). However, due to our incomplete understanding of the spatial and temporal characteristics of cortical processing during swallowing, insight into the mechanisms explaining dysphagia after brain injury has been limited. Some aspects of the neuroanatomical representation of the cortical network that control swallowing have been identified in man using functional brain mapping techniques, including functional Magnetic Resonance Imaging (fMRI) (Hamdy et al., 1999a,b; Hartnick et al., 2001; Kern et al., 2001b; Martin et al., 2001; Mosier and Bereznaya, 2001; Suzuki et al., 2003), transcranial magnetic stimulation (TMS) (Hamdy et al., 1996), and positron emission tomography (PET) (Hamdy et al., 1999a,b). These studies confirm that this seemingly simple task recruits many discrete regions of the brain. However, to delineate the functional connectivity between cortical regions and dissociate their specific contributions to the different aspects of swallowing, it is essential to directly record neural activity dynamically with high temporal resolution.

Until recently, such detailed brain measurements have only been possible in experimental animal models since traditional human brain-imaging techniques such as PET and fMRI reflect changes in cortical function that are secondary consequences to alterations in regional cerebral blood flow and have poor temporal resolution (Aine, 1995). However, magnetoencephalography (MEG) has started to resolve some of these limitations. MEG...
detects the post-synaptic magnetic fields generated by active populations of cortical neurons with millisecond temporal resolution and has a comparable spatial resolution to PET and fMRI. Nevertheless, until now, technical limitations in MEG data acquisition and analysis have prevented its use in exploring the cortical activation patterns during complex sensorimotor tasks such as swallowing (Loose et al., 2001).

Synthetic aperture magnetometry (SAM) (Robinson and Vrba, 1999) is a new method based on spatial filtering techniques (Van Veen et al., 1997) for analysing MEG signals that overcomes many previous limitations. These have included the requirement to analyse phase locked data (averaged evoked responses) and the use of a priori estimates of numbers of equivalent active dipoles to explain the data.

SAM can reveal significant changes in power of non-phase-locked data within selected frequency bands in cortical areas activated during a task. The technique requires no a priori estimates of numbers or approximate locations of sources. This so-called Event-Related Desynchronisation (ERD)/Synchronisation (ERS) is a correlate of increased neural activation within the cortex (Pfurtscheller and Lopes da Silva, 1999). A recent study has shown that SAM can be used to detect non-phased locked cortical activity during complex language and visual paradigms (Singh et al., 2002) and that the activation patterns demonstrated are spatially coincident with fMRI data acquired using identical experimental paradigms. The main assumption behind SAM is that all electrical sources are uncorrelated and is an optimal technique with which to identify small high amplitude regions of activation (Hillebrand and Barnes, 2002). Importantly, SAM retains the millisecond temporal resolution needed to unravel the cortical dynamics of swallowing.

### Table 1

<table>
<thead>
<tr>
<th>Cortical area</th>
<th>Mean peak Talairach coordinate</th>
<th>Active volume (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precentral gyrus (L)</td>
<td>−55.2, 2.0, 31.0</td>
<td>5.22</td>
</tr>
<tr>
<td>Inferior frontal gyrus (L)</td>
<td>−52.2, 1.0, 34.0</td>
<td>1.43</td>
</tr>
<tr>
<td>Middle frontal gyrus (L)</td>
<td>−52.2, 4.0, 37.0</td>
<td>0.09</td>
</tr>
<tr>
<td>Tongue phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precentral gyrus (L)</td>
<td>−34.1, 23.1, 64.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Postcentral gyrus (R)</td>
<td>53.2, 20.1, 43.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Precentral gyrus (L)</td>
<td>−64.3, 2.0, 20.0</td>
<td>0.05</td>
</tr>
<tr>
<td>Precentral gyrus (R)</td>
<td>35.1, −17.1, 64.0</td>
<td>0.03</td>
</tr>
<tr>
<td>Swallow phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus (R)</td>
<td>47.2, −25.1, 66.0</td>
<td>5.53</td>
</tr>
<tr>
<td>Inferior parietal lobule (R)</td>
<td>38.1, −56.2, 37.0</td>
<td>2.94</td>
</tr>
<tr>
<td>Paracentral lobule (L)</td>
<td>−7.0, −35.1, 64.0</td>
<td>1.75</td>
</tr>
<tr>
<td>Angular gyrus (R)</td>
<td>38.1, −56.2, 36.0</td>
<td>1.09</td>
</tr>
<tr>
<td>Supramarginal gyrus (R)</td>
<td>39.2, −56.2, 36.0</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Fig. 1. Statistical non-Parametric Permutation Testing Maps (SnPM). Group SAM results. Significant ERD effects ($P < 0.05$) revealed by the Active–Passive comparison in: (A) 25–40 Hz band for Water infusion, (B) 5–15 Hz band for Tongue thrust, and (C) Swallowing (5–15 Hz). Blue/Pink colours represent ERD (i.e., negative) group scores.
This fundamental shift in the MEG paradigm away from phase-locked, evoked response studies has greatly enhanced its utility as a brain-imaging technique.

Therefore, it was the aim of this study to use this novel technique to, first, dissociate the relative cortical contributions of each of the separable components of swallowing in the sensorimotor sequence, and second, to identify the spatio-temporal characteristics of cortical activation during swallowing. Such an understanding would greatly enhance our appreciation of the relevance of cortical regions to swallowing and would provide insight into the mechanisms underlying dysphagia after cerebral injury.

Materials and methods

Subjects

Eight healthy right-handed individuals (6 males and 2 females, age range 26–45 years) gave informed consent to participate in the study, approved by the local regional ethics committee. Each had a structural MRI brain volume acquired before the experiment using a 1.5-T Philips ACS-NT MRI scanner (Imaging Science and Biomedical Engineering, Manchester University, Manchester, England, UK).

Magnetoencephalography

MEG data were collected using a 151 channel CTF Omega system (CTF Systems Inc, Post Coquitlam, Canada) in a magnetically shielded environment (Vacuumschmelze).

Intraoral infusion

To facilitate swallowing, mineral water was infused into the oral cavity via a plastic catheter attached to a fluid reservoir, positioned 50 cm above the mastoid process of each subject when seated. The reservoir was calibrated to deliver 5 ml of water over 2 s, using a standard intravenous infusion catheter valve, and controlled by a single operator seated outside of the shielded room.

Protocol

Subjects were seated in an upright position and three electromagnetic coils were located on a headband to enable determination

![Fig. 2. Comparison of time–frequency plots calculated for all subjects from left caudolateral precentral gyrus. MRI-SAM group mean images for all eight subjects (right) show each active phase versus rest phase for the 15- to 25-Hz bands. Time 0 on the x-axis corresponds to the onset of the visual cue for each condition. Colours represent the level of frequency power difference between the active and passive phases, with blues/purples indicating a decrease in power (ERD) and reds/yellows an increase in power (ERS). The time–frequency wavelet plots were derived from a virtual electrode placed in precentral gyrus (as indicated by the dot and arrows in the group SAM brain images). Averaged time–frequency wavelet plots were obtained from this site in each individual and then averaged across the group to provide a group mean time–frequency plot.](image-url)
of the head position within the MEG helmet. Subjects were asked to visually fixate a previously explained task-coded coloured shape in the middle of a computer monitor located outside the shielded environment but visible through a portal. To simulate normal swallowing and tongue behaviour, subjects were instructed to perform four tasks; firstly, to fixate the target and remain still; secondly, to receive 5 ml of water through the delivery tube and to hold it within the mouth; thirdly, to swallow the water on receipt of a visual cue; fourthly, to gently press their tongue against the junction of their front teeth and upper palate. Instruction for each command was achieved through changing the shape and colour of the fixation cue. The inter-stimulus interval of cues was 6 s and the four-phase sequence was repeated 20 times.

In two of the subjects, repeat identical studies were performed 8 weeks after the initial recordings to assess reproducibility.

Data analysis

**MEG acquisition and analysis**

MEG data were sampled at 625 Hz and an anti-aliasing filter with a cutoff of 200 Hz was used. After data acquisition, a 3-D digitiser (Polhemus Isotrak™) was used to digitise the shape of the subjects head and localise the electromagnetic head coils with respect to that shape. The software Align (www.ece.drexel.edu/ICV/Align/align11.html) was used to match each subject’s anatomical head surface extracted from the MRI with that achieved by the digitiser to enable MRI co-registration with the MEG data.

The phases of volitional swallowing and the sensory input modulation of these phases are complex and do not reveal highly synchronous evoked responses using conventional signal averaging paradigms. A non-linear beamformer technique, synthetic aperture magnetometry, was therefore used to analyse the MEG data (Robinson and Vrba, 1999; Van Veen et al., 1997). This technique has been used recently to study sensorimotor cortex function (Hirata et al., 2002; Taniguchi et al., 2000). Singh et al. (2002) have also described spatially coincident activation of group MEG/SAM data with group functional MRI data sets using cognitive paradigms.

SAM analysis can be used in a ‘box-car’ design, with epochs designated as Passive or Active. The Passive epochs were defined as the 5-s period after the cue to rest. To prevent temporal overlap, the three Active epochs were defined as 5 s windows following the cues to receive water, swallow or produce a tongue thrust. Fourier analysis, using a Hanning window, was used to calculate the spectral power in specified frequency bands. The difference between these spectral power estimates for the Active and Passive states was then assessed using a pseudo t statistic calculation (Robinson and Vrba, 1999) over all blocks. Frequency bands selected for analysis were 5–15, 15–25 and 25–40 Hz.

**Statistical non-parametric permutation testing**

The functional volumes computed with SAM were aligned with the individual anatomical MRI’s and using SPM99 (Friston et al., 1995), these volumes were spatially normalised into a standard template space (Singh et al., 2002).

It was essential to reveal areas of cortex yielding statistically significant activation across the subject group. Given the low subject numbers, possible deviation from normal distribution, problems of multiple comparisons and possible statistical distortion of the data from strong activation in one individual, Non-Parametric Permutation testing was therefore applied (Nichols and Holmes, 2001; Singh et al., 2003). Probability maps for voxel level effects ($P < 0.05$ corrected) were computed and visualised as group statistical non-parametric maps (SnPM) using mri3dX (http://www.aston.ac.uk/lhs/staff/singhkd/mri3dX).

Approximate neuroanatomical localisations of these voxels were determined using a Talairach database (Lancaster et al., 2000). Together with the computed volumes of significant voxel clusters (mri3dX), data are detailed in Table 1.

Once identified, Talairach coordinates of voxels of statistical significance ($P < 0.05$ corrected, detailed in Table 1) within the group were located as regions of interest (ROI) for further analysis within individual subjects.

**Time–frequency plots**

To examine the temporal sequencing of activation within ROIs, time–frequency plots were calculated using wavelet analysis. For some analysis of each ROI, the power at a given latency and frequency bin of each passive and active phase was expressed as a percentage change from the mean power in that frequency bin in the passive period. Statistical significance of the power changes was assessed using a bootstrap-based technique (Graimann et al., 2002). Only those changes that were significant at the $P < 0.05$ level were displayed. This was repeated for all latencies and frequency bins.

Additionally, for selected ROIs, time–frequency plots for the active epochs were averaged for each individual and averaged across the group to provide an analysis of the common temporal changes in oscillatory power.

Fig. 3. SnPM results for the Active phase of tongue thrust. The EMG resulting from the tongue itself produced significant activation in the 25- to 40-Hz bands. Note how this activity is external to brain tissue and localises to the tongue region positioned under the glass brain. This demonstrates that MEG can localise distant sources providing the signal-to-noise ratio is high.
Fig. 4. Time–frequency wavelet plots calculated for multiple cortical sites in one representative individual. Spectrograms calculated for a single subject for voxels in positions E0 (precentral gyrus), E1 (inferior parietal lobule), E2 (postcentral gyrus Brodmann area 2) and E3 (postcentral gyrus, Brodmann area 5) simultaneously. MRI-SAM images (right) for the active water phase versus rest in 25–40 Hz bands (upper right image), and for the swallow phase (middle right) and tongue thrust phase (lower right) in the 15- to 25-Hz bands. Time 0 on the x-axis indicates the end of the 5 s of the Passive period and 0 s for the commencement of the 5 s of the Active phase. Significant changes in power ($P < 0.05$) with respect to the mean level in the Passive phase are indicated. Colours represent the level of significant percentage ERD/ERS with blues/purples indicating a decrease in power (ERD) and reds/yellows an increase in power (ERS) with respect to the Passive phase.
Results

Group results

Fig. 1 shows the SnPM group SAM data for each active state compared to the passive state. Talairach coordinates and neuro-anatomical locations of areas of significant activation (P < 0.05) in the group mean data for each active state are summarised in Table 1.

Fig. 2 shows the group mean data for each active state compared to the passive state before non-parametric statistical analysis, together with group mean time–frequency plots from caudolateral precentral gyrus.

Spatial characteristics

Water infusion phase

Group SnPM data (Fig. 1A) showed significant activation in left caudolateral pericentral cortex (BA 4, 6, 9 and 43) in the 25- to 40-Hz frequency bands. A lower level of activation was observed in similar cortical areas in the right hemisphere (Figs. 1 and 2) but did not reach group significance. In addition, an area in left prefrontal cortex revealed significant group activation.

Tongue thrust phase

Group SnPM data (Fig. 1B) showed significant activation within the left and right superior precentral gyrus (BA 4) together with the right postcentral gyrus in the 5–15 Hz frequency band. A small area of significance in inferior precentral cortex was also evident on the left, though a larger area of activation at this location can be seen in the group mean SAM images and appears bilaterally (Fig. 2).

Swallow phase

Group SnPM data (Fig. 1C) for the 5–15 Hz frequency bands showed significant activation in the right superior postcentral gyrus (BA 3, 1, 2) and the left paracentral lobule (BA 6). The inferior parietal lobule (BA 40) in the right hemisphere was also significantly activated, as were the angular gyrus and supramarginal gyrus.

Temporal characteristics

By selecting voxels from regions of cortex representing significant ERD/ERS in the above-described active states, the temporal patterns of activation could then be examined through time–frequency plots using wavelet analysis.

Individual spectrograms

To investigate the patterns of temporal activity within the cortex to swallowing tasks, regions of interest (ROI) comparable with those identified from the SnPM group SAM data (Table 1) were identified from individual data sets in both hemispheres. Time–frequency wavelet plots for each of the active–passive state comparisons for ROIs were calculated.

Highly significant Event-Related Synchronisation (ERS) was observed in an antero-caudal area external to the brain in the higher frequency bands (25–70 Hz) for the active states of swallowing and tongue thrust (Fig. 3). This distant source was subsequently shown to represent EMG activity generated by the tongue and orofacial musculature.

As can be seen in Fig. 4, in a representative subject, direct measurements of neuronal activity in real time revealed highly significant and sustained decreases in power in the 15–25 Hz frequency bands within precentral gyrus (Brodmann area 4, virtual electrode E0), postcentral gyrus (Brodmann area 2, virtual electrodes E2), inferior parietal lobule (Brodmann area 40, virtual electrode E1) and postcentral gyrus Brodmann area 5 (virtual electrode E3) simultaneously. This ERD was observed throughout the water infusion and tongue thrust phases. The ERS was also observed through the initiation phase of swallowing for each of these sites but disappeared immediately following the volitional swallowing phase. The implication from these data is that all the sampled cortical loci become excited at the onset of receipt of the bolus, despite the shifting spatial patterns of activations during the separate tasks for swallowing. This temporal pattern was a consistent feature across subjects and was robust on a trial–retrial basis (Fig. 2).

Group-averaged time–frequency plots

Fig. 4 reveals the pattern of activation over time at an inferior precentral gyrus site. This site was chosen because of precentral cortex involvement in all three active phases across all subjects.

In common with many previous reports, the precentral site had a dominant resting frequency in the 15- to 25-Hz band (Salmelin and Sams, 2002). Power in this frequency band was reduced throughout the water infusion and tongue thrust phases. This is clearly reflected in the pattern of event-related desynchronisation (ERD) seen in the corresponding group SAM brain images. The 15- to 25-Hz resting oscillations were again reduced in power during the swallowing phase, with a rebound ERS observed upon completion, consistent with previous reports associated with motor tasks (Pfurtscheller and Lopes da Silva, 1999; Salmelin and Sams, 2002).

Discussion

Synthetic aperture magnetometry, event-related desynchronisation/ synchronisation and cortical neuronal activity

Previously, studies that have attempted to dynamically image human cortical neuronal activity during complex sensorimotor tasks, such as swallowing, have been fraught with technical limitations (Loose et al., 2001) and subsequently nearly all of our current knowledge has been gleaned from invasive animal studies using intra-cortical micro-recording techniques (Martin et al., 1997).

Utilising a new technique for analysing the brain’s neuro-magnetic signals, synthetic aperture magnetometry (SAM), we have demonstrated that changes in the spectral power of neuronal activity (ERD/ERS) can be used to dissociate both the spatial and temporal characteristics of cortical activity within an interconnected cortical swallowing network. Uniquely, this novel utilisation of SAM allows us to make direct comparisons between the animal and human brain. SAM has recently been compared with the BOLD response measured with fMRI where excellent concordance of the spatial ERD/ERS activations was reported (Singh et al., 2002). Our data demonstrate that SAM analysis can clearly delineate the neural correlates of the differing phases of human swallowing, from the receipt of the bolus, to the post-swallow phases, with preferential activation of superior sensorimotor cortex occurring during volitional swallowing and tongue movement and caudolateral sensorimotor cortex during water
infusion. Moreover, spatially, the cortical loci of ERD/ERS associated with swallowing identified in our study are broadly similar to those described by other functional imaging techniques, lending further evidence to support the utility of this novel approach.

Spatial characteristics of human swallowing

Water infusion

The water infusion phase is characterised by activation of the predominantly left caudolateral frontal opercular cortex. These loci are consistent with the observations of a PET study by Zald and Pardo (2000) who in addition described insular and cerebellar cortex activation with intra-oral stimulation of deionised distilled water. This region also encompasses the cortical areas previously implicated in gustation (Cerf-Ducastel and Murphy, 2001; Cerf-Ducastel et al., 2001; Frey and Petrides, 1999; Kobayakawa et al., 1996). The functional relevance of this caudal region of motor cortex to swallowing has also been investigated by Narita et al. (1999), where swallowing difficulties could be induced in monkeys upon cold-block of the same area. Thus, this caudal region (associated in our study with oral receipt of the food bolus) appears critically important in the initiation of the swallow. Indeed, Martin and Sessle (1993) have speculated that this region may have importance to swallowing because thermosensory inputs from tongue, which ascend to the lateral sensorimotor cortex, might additionally facilitate other cortical regions linked to swallowing.

In considering why tongue/oral sensory input might be crucial to cortical swallowing, it is important to appreciate the role of sensation in the regulation of swallowing. Sensation from the tongue and oropharynx is conveyed via cranial nerves V, IX, X and XII (Kennedy and Kent, 1988; Miller, 1982). This sensory input displays extensive brainstem convergence, with trigeminal (and vagal) afferent fibres terminating within the trigeminal spinal nuclei and nucleus of the tractus solitarius (NTS) of the dorsal region of the brainstem swallowing centre (Jean, 1990). These afferent fibres are capable of influencing brainstem motoneurone and interneuron circuitry, but crucially also circuitry higher in the cerebral cortex. For example, previous studies in man have shown that excitation of afferent pathways of cranial nerves V and X, in the face or neck, produce reflex responses in the pharynx and oesophagus which are likely to be generated via neurons within the brainstem swallowing centre (Hamdy et al., 1997). When combined with cortical input, stimulation of these afferents can produce short-term (100–200 ms) facilitation of cortically evoked swallowing responses, suggesting that both pathways involve the same population of neurones (Diamant, 1995). Moreover, sustained sensory stimulation has been shown to produce longer-term changes in motor cortical excitability: a 10-min period of pharyngeal stimulation increased pharyngeal cortical excitability for at least 30 min after the input, not associated with changes in brainstem excitability (Hamdy et al., 1998). By contrast, a reduction in human oropharyngeal sensation, by local anaesthesia (Mansson and Sandberg, 1974) or afferent nerve damage (logemann, 1985), can disrupt the normal pattern of volitionally initiated swallowing as measured by manometry or videofluoroscopy. Thus, sensation has a major role in central regulatory feedback of swallowing, acting at both brainstem and cortical levels. Our findings with oral infusion of water consolidate this view, but in addition demonstrate that the whole cortical network for swallowing may be highly dependent on this modulation, both for priming the system and in generating the swallow and post-swallow phases.

Swallow

Our data for the “motor” phase of the swallowing sequence show that activity, which initially resides in the caudal region of the pericentral cortex, shifts rostrally to superior postcentral gyri and the paracentral lobule. The shift in topography indicates that in addition to the inferior pericentral gyrus, regions of the sensorimotor cortex, more typically associated with neck movements (Penfield and Boldery, 1937) become increasingly active. This area of cortex is broadly similar to the region of cortex demonstrated to be the representative field of the pharynx and oesophagus, studied with TMS (Hamdy et al., 1996). By contrast, most fMRI and PET studies of volitional and reflexive swallowing have reported significant activation primarily of the lateral (caudal) precentral gyrus for both tasks (Hamdy et al., 1999a,b; Kern et al., 2001b; Martin et al., 2001). Interestingly, an event-related fMRI study (Hamdy et al., 1999a,b) also showed activation of superior premotor cortex (BA areas 6, 8). Given the nature of the oral component to swallowing, it is not surprising that the caudal area is often reported as the main motor cortex region for swallowing. However, it is difficult to dissociate cortical areas associated with the differing phases of swallowing in block trial designs. This may be less of a problem with event-related paradigms, and thus may explain the more superior precentral activation seen in the latter fMRI study.

In contrast to the former studies, our data have now been able to separate the differing components of swallowing with the consequence that the superior regions of precentral cortex are revealed as an important contributor to swallowing. This supports previous TMS studies of pharyngeal motor cortex as a projection relevant to functional swallowing (Hamdy et al., 1996).

Tongue

Another important finding from our study was that tongue movement activates common pericentral cortical loci seen with swallowing. The implication from this observation is that a significant cortical contribution of tongue action during swallowing is sensory (or at least activates sensory cortex), and that this again is in both the superior region of pericentral cortex and the more caudal regions “tongue” motor cortex. These data are consistent with the MEG findings of Salmelin and Sams (2002) using a task where the tongue pressed the teeth. They described motor cortex involvement characterised by suppression and subsequent rebound of the 20-Hz activity. The observed modulation was concentrated to two sites along the central sulcus, identified as the motor face and hand representations.

Nakasato et al. (2001), in an MEG-evoked response paradigm using tongue protrusions, reported motor evoked field dipoles localised on the central sulcus, 14.4 ± 6.1 mm inferior and 7.6 ± 6.9 mm anterior to the ECD for the N20m in the somatosensory evoked fields for median nerve stimuli. The latter two studies, in common with this study, have used tongue movements that differ significantly from the type of movement occurring during swallowing and may account in part for differences between these two conditions.

Previous fMRI studies of tongue movement have predominantly highlighted caudolateral sensory motor cortex activation (Corfield et al., 1999; Kiecker et al., 2000; Stippich et al., 2002).

Kern et al. (2001a) described common cortical activation during both swallowing and swallow-related motor tasks (including tongue rolling), in the anterior cingulate, motor/premotor cortex, insula and operoparietal regions. It is interesting to note that
Martin et al. (1997), using intracortical microstimulation and recording techniques in primates, suggested that many swallow-related tongue-MI neurons have an orofacial mechanoreceptive field, supporting the view that tongue afferent inputs are involved in the regulation of swallowing. Our data confirm that significant sensorimotor cortex activation occurs as a result of tongue activation, with a much greater sensory contribution than previously reported.

**Temporal characteristics of swallowing**

Perhaps, the most important observations from our study were those made during the temporal analysis of ROI. Following water infusion, the caudolateral pericentral cortex showed significant ERD throughout the period that the water bolus remained in the mouth. Spectrographic analysis of individual data sets revealed equivalent temporal patterns of activation in superior sensory cortex, supramarginal gyrus (BA40) and superior parietal lobule (BA5) during the water bolus phase, despite a lack of clear (significant) activation during statistical group mapping. Moreover, the same temporal patterns were observed across the active sites for both swallowing and tongue movement. This indicates that caudolateral sensorimotor cortex, superior sensory cortex, inferior and superior parietal lobule form a functionally active ‘module’, with co-incident temporal activity being generated during the sensory-motor sequence associated with all phases of volitional swallowing. Thus, whilst there are distinct cortical loci for the sensory pre-swallow phase and the sensory-motor swallow phase, there is a clear temporal concordance between each of these loci. This latter observation may be primarily driven by the strong sensory input from the tongue, which appears to engage the whole cortical swallowing network, before any motor associated activity. In support of this notion, Mosier and Bereznaya (2001) used statistical modelling of fMRI data to explore the relationships between different cortical aggregates in the whole brain swallowing network. From their data, they proposed that the sensorimotoric implementation of swallowing in the volitionally initiated condition utilises several functionally connected cortical areas. From our data, it appears that a significant proportion of this activation is sensory in nature, and is co-incident, and whilst activation of the superior and inferior parietal lobule was significantly greater across the group in the swallow phase in comparison with tongue thrust, each region appears to be highly dependent on this sensory input.

From a therapeutic perspective, given the importance our data place on sensory input, it seems that future treatments of swallowing problems after stroke might be more effective if sensory stimulation techniques are employed. This may be particularly relevant if the recovery depends upon accessing and exciting brain regions, which may compensate for the loss of function. In this regard, recent studies of pharyngeal stimulation in dysphagic stroke have shown promise as a therapy for accelerating swallowing recovery (Fraser et al., 2002). Indeed, given our observations, it may be that some forms of oral/tongue stimulation may also be beneficial, if appropriately delivered. Perhaps, future studies, assessing the relative merits of oral stimulation in patients with neurogenic dysphagia, will help to answer this question more definitively.

In conclusion, our data have defined the spatio-temporal patterns of activity associated with volitional swallowing. We have demonstrated that these regions are spatially distinct for each swallow phase, but are temporally co-incident and thus act as a functional module, being highly dependent on sensory input from the tongue. Our ability to simultaneously image the spatio-temporal pattern of cortical activity during a functional task (in this case swallowing) provides new insights into the functional relevance and connectivity within complex cortical networks.

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