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Hemodynamic signal changes during saliva and water swallowing: a near-infrared spectroscopy study

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Abstract. Here, we compared the hemodynamic response observed during swallowing of water or saliva using near-infrared spectroscopy (NIRS). Sixteen healthy adults swallowed water or saliva in a randomized order. Relative concentration changes in oxygenated and deoxygenated hemoglobin during swallowing were assessed. Both swallowing tasks led to the strongest NIRS signal change over the bilateral inferior frontal gyrus. Water swallowing led to a stronger activation over the right hemisphere while the activation focus for saliva swallowing was stronger left lateralized. The NIRS time course also differed between both swallowing tasks especially at the beginning of the tasks, which might be a sign of differences in task effort. Our results show that NIRS is a sensitive measure to reveal differences in the topographical distribution and time course of the hemodynamic response between distinct swallowing tasks and might be therefore an adequate diagnostic and therapy tool for swallowing difficulties. [DOI: 10.1117/1.JBO.23.1.015009]

Keywords: deoxygenated hemoglobin; dysphagia; near-infrared spectroscopy; oxygenated hemoglobin; swallowing.
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1 Introduction

Swallowing is a complex motor behavior that requires voluntary movements as well as involuntary reflexes.[1] Accordingly, functional magnetic resonance imaging (fMRI) studies show that a large network of brain areas including motor and sensory areas, frontal and temporal areas, the cerebellum and brain stem is involved in the swallowing process.[2–5] Different brain lesions lead to difficulties in swallowing, so-called dysphagia.[6] Dysphagia often occurs in neurologic patients. 22% to 65% of neurologic patients (e.g., stroke patients, patients with multiple sclerosis, Parkinson's disease, and traumatic brain injury) are affected by dysphagia.[6] Even neurologic healthy elderly people show dysphagia symptoms. The overall prevalence of dysphagia in the population is about 13.5% to 16%.[7–9] Dysphagia reduces quality of life and health of affected people dramatically.[6,8,10] Neuroimaging tools such as fMRI are often used for the diagnosis of dysphagia as well as for the assessment of the recovery of swallowing functions.[11,12] Identifying neuronal correlates of swallowing is important to understand the neuronal underpinnings of dysphagia and might be also relevant for its treatment.[13–16]

Although fMRI has a high spatial resolution, fMRI measurements are associated with some disadvantages. For instance, fMRI measurements are expensive, patients have to lie in a narrow and loud scanner during swallowing, movement artifacts can disturb the signal, and fMRI measurements are restricted to the installation site of the scanner.[17–19] In contrast, near-infrared spectroscopy (NIRS) is a relatively new and noninvasive, cost-sensitive, and portable technique to measure hemodynamic changes in the outer layer of the cortex.[20] NIRS measures concentration changes of oxygenated hemoglobin (oxy-Hb) and deoxygenated hemoglobin (deoxy-Hb) induced by cortical activation in the brain tissue using light in the near-infrared range, whereas fMRI only measures concentration changes in deoxy-Hb.[21] An increase in regional cerebral blood flow (rCBF), which is a sign of neuronal activation, goes along with an increase in oxy- and a decrease in deoxy-Hb concentrations.[21–23] One important advantage of NIRS over fMRI is that the NIRS signal is relatively robust when participants move during the measurement.[24,25] Especially during swallowing, small head movements are inevitable. Furthermore, during swallowing, participants can sit in a normal upright position for NIRS recordings. When dysphagia patients have to lie in an fMRI scanner during swallowing the probability to choke is exorbitantly high.[26] Compared to fMRI, NIRS also has a much higher temporal resolution.[17] Hence, NIRS is an optimal method to measure changes in brain activation patterns during swallowing, even when deeper brain structures such as the brain stem cannot be measured with NIRS.[20]

NIRS studies that investigate the hemodynamic response during swallowing are rare.[14–16,27–29] However, these prior NIRS studies successfully show that changes in cerebral activation during active swallowing can be reliably detected and that the hemodynamic signal changes differ when swallowing distinct fluids (e.g., odorless versus flavored broth,[27] or sour versus sweet versus distilled water[28,29]). The strongest NIRS signal changes during swallowing of either water, saliva, or a sucrose solution were found over the bilateral inferior frontal gyrus (IFG).[14–16,27,29]

In this study, we investigated whether NIRS is also sensitive enough to reveal differences in the hemodynamic response between swallowing saliva and water. Therefore, we directly compared the NIRS signal change during swallowing of

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water and saliva in healthy adults. Prior fMRI studies show that there are some differences in brain activation patterns between swallowing water and saliva.[4,18,30–33] However, the cortical networks activated during water and saliva swallowing are generally overlapping.[18] We hypothesized that NIRS might be sensitive enough to reveal the small differences in the hemodynamic brain response between these two swallowing tasks, which have been found in prior fMRI studies.[4,18,30–33] Identifying the hemodynamic response during different swallowing tasks in healthy individuals might be a first step for the application of NIRS in the diagnostics and treatment of dysphagia.

According to prior NIRS studies, we expected that both swallowing tasks generally lead to strong NIRS signal changes over the bilateral IFG.[14–16,27,29] According to the results of prior fMRI studies, we hypothesized that water swallowing should lead to stronger activation patterns over the right hemisphere, whereas saliva swallowing should lead to a more pronounced activation over the left hemisphere.[18,32,33] In this context, a meta-analysis by Sörös et al. shows that water swallowing leads to stronger activation patterns over the right hemisphere, e.g., the right insula, compared to saliva swallowing.[18] In contrast, there is evidence that neuronal activation during saliva swallowing is more left lateralized.[32] Furthermore, prior fMRI studies report on an overall greater neural activation in association with voluntary swallowing of saliva compared to water swallowing.[4,30,31] Hence, we also expected differences in the extent of the NIRS signal change between the two swallowing tasks especially over the IFG.[4]

2 Methods

2.1 *Participants*

Sixteen right-handed, healthy young adults (eight male, eight female, mean age = 23.81 years, SE = 0.53) took part in this study. The sample size of the present study is comparable to the sample size of a prior NIRS study, which investigated cortical correlates of execution and imagination of swallowing, that found large effects of $\eta^2 > 0.4$ with power values of >99%.[14] The sample sizes of prior fMRI studies that investigated neuronal responses during swallowing water and saliva ranged from 8 to 14 participants.[30–33] Only Humbert et al. measured 23 participants.[4] Hence, with $N = 16$ as in the present NIRS study, we should be able to reach comparable power values than these prior fMRI studies.

All participants gave written informed consent. They had normal or corrected-to-normal vision. The study was approved by the Ethics Committee of the University of Graz, Austria (reference number GZ. 39/25/63 ex 2013/14) and is in accordance with the ethical standards of the Declaration of Helsinki.

2.2 *Swallowing Tasks*

Participants should either swallow water or saliva in a randomized order. For the water swallowing task, room-temperature water was drawn through a 3-mm-diameter flexible tubing attached to a 1-l bottle of still mineral water. During the saliva swallowing task, participants were instructed to swallow saliva. The swallowing trials had a duration of 15 s. During this time period, participants swallowed five to six times in average. In sum, 20 water and 20 saliva swallowing trials were performed in a randomized order. Between swallowing trials, a fixation cross appeared at the screen with a variable duration of 28 to 32 s. During these resting trials, participants were instructed to relax and avoid swallowing as much as they could. At the beginning of the experimental session, participants were trained shortly in both swallowing tasks to accustom oneself to the timing of the trials before starting the tasks.

2.3 *NIRS Recordings and Analysis*

Relative concentration changes of oxy- and deoxy-Hb were assessed with a continuous wave system (ETG-4000, Hitachi Medical Co., Japan) using two 4×4 optode probe sets (consisting of 16 photodetectors and 16 light emitters) resulting in a total of 48 channels (see Fig. 2). The ETG-4000 uses two different wavelengths (695 ± 20 and 830 ± 20 nm). The distance between the mounted optodes was 3 cm. The sampling rate of the NIRS system was set to 10 Hz. Based on previous NIRS studies that investigated hemodynamic signal changes during swallowing,[14,16] the probe set was positioned over motor areas and the IFG. Channels 1, 4, 27, and 31 corresponded to the bilateral IFG (Brodmann areas BA 44 and 45), channels 5 to 8, 10, 28 to 30, 32, and 34 to the premotor and supplementary motor cortex (BA 6 and 8), channels 14 and 35 to the primary motor cortex (BA 4), channels 13, 16, 17, 21, 36, 39, 40, and 42 to the somatosensory cortex (BA 3, 5, and 40), and channels 12, 15, 18 to 20, 37, 41, and 43 to 45 to the supramarginal gyrus (BA 7, 22, and 40).[14,16] These brain labels from the 1988 Talairach Atlas, called the Talairach Daemon,[34,35] were retrieved by MNI coordinates of the NIRS channels, which were assessed using ELPOS (zebris Medical GmbH), a system to determine three-dimensional coordinates of head positions with high accuracy based on the run time measurement of ultrasonic pulses.

Preprocessing of the NIRS raw signal included an artifact correction (criterion for rejection: amplitude of Hb-signal $> \pm 3$ SD; visual inspection) and data filtering with a 0.01-Hz high pass filter to remove baseline drifts and a 0.90-Hz low pass filter to remove cardiac pulsation.[36] Task-related concentration changes of oxy-Hb and deoxy-Hb were referred to a 5-s baseline interval prior to the task (seconds −5 to 0).

2.4 *Statistical Analysis*

The NIRS time series of the two swallowing tasks were segmented and averaged separately. For statistical analysis, oxy-Hb and deoxy-Hb during the task condition were averaged for the time intervals of 0 to 5 s, 5 to 10 s, 10 to 15 s, 15 to 20 s, and 20 to 25 s after task onset.

In a first step, we wanted to know which brain areas were most active (indicated by an increase in oxy-Hb and/or a decrease in deoxy-Hb relative to the baseline interval) during swallowing saliva and water and whether the activation foci varied over time. Therefore, we identified NIRS channels with the strongest signal change during the different swallowing tasks separately for the different time intervals and oxy- and deoxy-Hb. The averaged oxy- and deoxy-Hb values per time interval were used and statistically compared among all 48 NIRS channels. Simultaneous testing of such a large number of channels escalates the risk of a type I error, and therefore, the proportion of false positives among the channels that are detected as significant was corrected by the false discovery rate (FDR) method.[37] For the FDR analysis, the averaged NIRS signals were z-transformed per channel based on the mean and SD

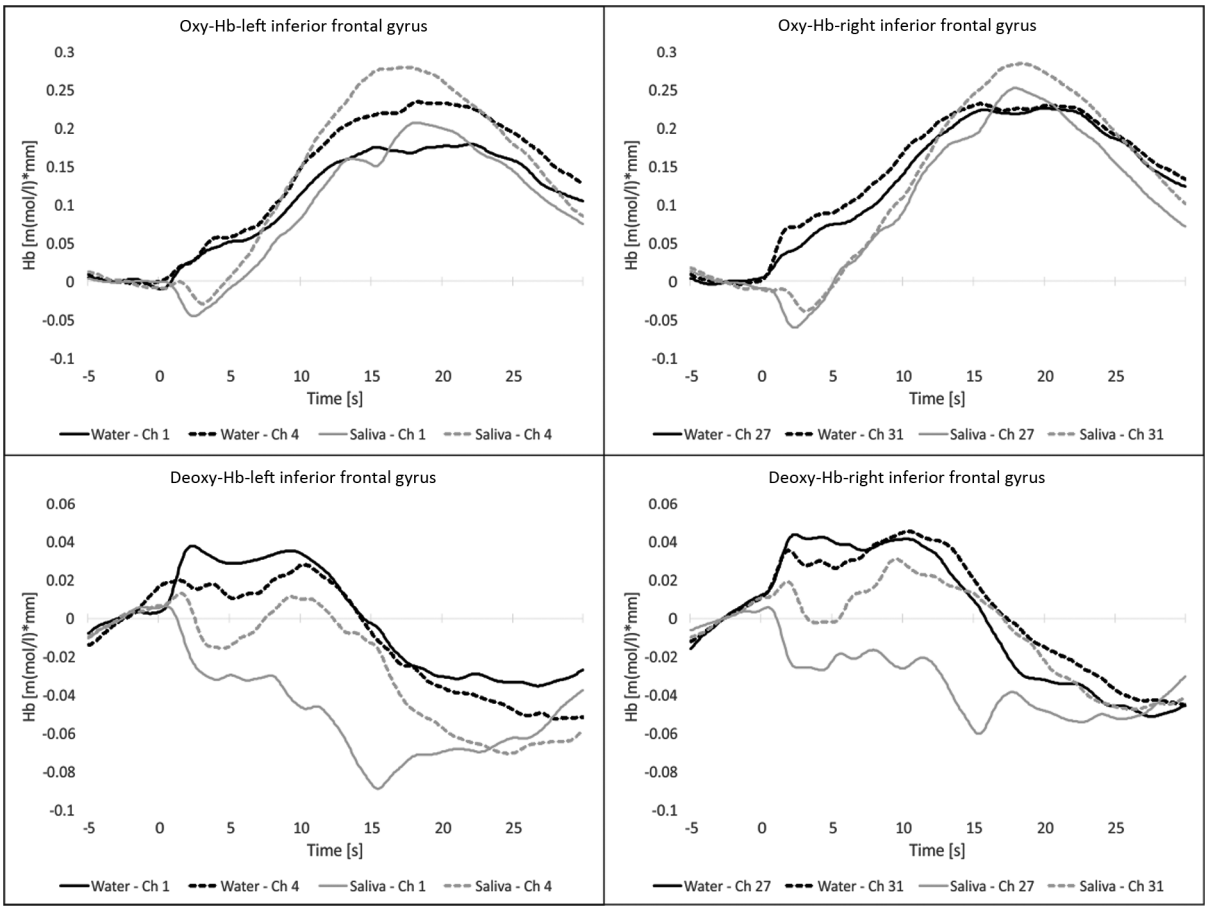

Fig. 1 NIRS time course. Mean activation changes in oxy- (upper panel) and deoxy-Hb (lower panel) during water (black lines) and saliva (gray lines) swallowing, presented separately for channels in the left (channels 1 and 4) and right (channels 27 and 31) IFG, which showed the strongest signal changes during the tasks compared to all other NIRS channels.

of the NIRS signals of all 48 NIRS channels, separately for each of the averaged time intervals and oxy- and deoxy-Hb. The resulting p-values that were calculated from the z-values of each channel were then arranged in ascending order and compared with the critical p-values adjusted in accordance to the FDR method.[37] NIRS channels with p-values smaller than the critical p-values ($p <$ FDR 0.10) were considered as significant. Using the FDR method, we identified NIRS channels that showed the strongest NIRS signal change during the water and saliva swallowing tasks separately for the different time intervals.

In a second step, we investigated event-related signal changes of the NIRS signal (temporal analysis of oxy- and deoxy-Hb). Hence, we did not only focus on the mean amplitude of the NIRS signal for different time intervals such as in the first analysis step, we were also interested in the shape of the NIRS signal change elicited by different swallowing tasks. Comparably to the standard analysis of fMRI data, we used a general linear model approach. Therefore, we modeled the hemodynamic response and compared the observed NIRS signal change (observed hemodynamic response) with a mathematical model of the hemodynamic response.[38] Hence, the functional timeline of the NIRS signal was regressed to a hemodynamic response function (HRF) that mimics the actual hemodynamic response.[39] The hemodynamic response was decomposed into its components evoked by the swallowing tasks. Based on previous NIRS studies, which investigated the hemodynamic response during swallowing, we chose channels over the IFG (1, 4, 27, 31) for this analysis.[14–16] The NIRS signal was decomposed separately for these NIRS channels using the canonical HRF. The HRF was defined as the difference of two Gamma functions (alpha 1 = 6, alpha 2 = 16, beta 1 and 2 = 1, and $c = 1/16$, with 32 time bins[40]). The HRF was interpolated to the natural acquisition rate of NIRS data 10 Hz yielding a total of 300 time points (s 0 to 30 after task onset, see Fig. 1). The HRF was convolved with a square function with a 30-s duration.[41] The resulting beta coefficients are the estimates resulting from the regression analysis that have been standardized so that the variances of dependent and independent variables are 1. A high positive beta coefficient means that the observed hemodynamic response (NIRS time course) closely follows the idealized time course of the mathematical model of the hemodynamic response. If the beta coefficient is near 0, there is little to no relationship between the observed and the modeled HRF. A negative beta coefficient means that the course of the observed and the modeled hemodynamic response are inversely related. The beta coefficients per participant and condition were analyzed in a 2×2 analysis of variance (ANOVA) design with the within-subject factors task (water versus saliva swallowing task) and channel (left versus right IFG).

3 Results

The FDR analysis revealed that the strongest signal change in oxy- and deoxy-Hb could be observed over channels 1, 4, 27, and 31 in both swallowing tasks. These channel locations corresponded to the bilateral IFG (channels 1 and 4 to the left IFG, channels 27 and 31 to the right IFG[14,16]). No other channels showed significant activation changes. Table 1 summarizes the results of the FDR analysis for the different time intervals. At the beginning of the water swallowing task (s 0 to 10), oxy-Hb significantly increased over the right IFG (channel 31). At the end of the water swallowing task (s 10 to 15) and directly after water swallowing (s 15 to 20), increases in oxy-Hb were most pronounced over the bilateral IFG. In the saliva swallowing task, oxy-Hb decreased initially over the right IFG (channel 27). During saliva swallowing (s 10 to 15), the strongest increase in oxy-Hb was observed over the left IFG (channel 4). After saliva swallowing (s 15 to 25), relative increases in oxy-Hb were highest bilaterally (Table 1).

Table 1 Results of the FDR analysis.

		Ch 1	Ch 4	Ch 27	Ch 31
Oxy-Hb water swallowing	0 to 5 s				↑
	5 to 10 s				↑
	10 to 15 s		↑	↑	↑
	15 to 20 s		↑	↑	↑
	20 to 25 s				
Deoxy-Hb water swallowing	0 to 5 s			↑	
	5 to 10 s				
	10 to 15 s				
	15 to 20 s				
	20 to 25 s		↓	↓	
Oxy-Hb saliva swallowing	0 to 5 s			↓	
	5 to 10 s				
	10 to 15 s		↑		
	15 to 20 s		↑		↑
	20 to 25 s				↑
Deoxy-Hb saliva swallowing	0 to 5 s				
	5 to 10 s				
	10 to 15 s	↓			
	15 to 20 s	↓			
	20 to 25 s	↓	↓		

Note that only significant results of channels 1 and 4 (left IFG) and 27 and 31 (right IFG) are reported since all other channels did not show significant signal changes. ↑ significant increase; ↓ significant decrease in the NIRS signal change.

Deoxy-Hb initially increased over the right IFG when swallowing water (s 0 to 5, channel 27). After the water swallowing task (s 20 to 25), deoxy-Hb decreased significantly in this condition. In the saliva swallowing task, deoxy-Hb decreased already during the task (s 10 to 15) as well as after the task (s 15 to 25), especially over the left IFG (channels 1 and 4).

The time course of the NIRS signal changes during the swallowing tasks is shown in Fig. 1. Figure 2 shows the topographical distribution of the NIRS signal changes during water and saliva swallowing. As one can see in Fig. 2, the strongest NIRS signal changes (increase in oxy-Hb and decreases in deoxy-Hb) were observed over the bilateral IFG (channels 1, 4, 27, and 31) for both, saliva and water swallowing, as also revealed statistically by the FDR analysis. The time course of oxy-Hb differed between saliva and water swallowing especially during the first 5 s, whereas the time course of deoxy-Hb differed between both swallowing tasks during the whole task period (Figs. 1 and 2).

The beta coefficients for oxy-Hb were analyzed in a 2×2 ANOVA design with the within-subject factors task (water versus saliva swallowing task) and channel (ch 4 versus ch 31). For the analysis of oxy-Hb, we only chose channels 4 (left IFG) and 31 (right IFG) since FDR analysis indicated that the oxy-Hb signal changes were strongest for these two channels. The main-effect task was significant [$F(1,15) = 4.5$, $p < 0.05$, $\eta^2 = 0.23$]. Post hoc tests revealed that the beta coefficients for oxy-Hb were higher during the saliva ($M = 0.23$; SE $= 0.05$) than during the water swallowing task ($M = 0.15$; SE $= 0.03$). This means a stronger event-related response for oxy-Hb during saliva than during water swallowing.

Statistical analysis of the beta coefficients for deoxy-Hb also consisted of a 2×2 ANOVA design with the within-subject factors task (water versus saliva swallowing task) and channel (ch 1 versus ch 27). For the analysis of deoxy-Hb, we chose channels 1 and 27 since FDR analysis indicated that the deoxy-Hb signal changes were strongest in these two channels. No significant effects were found.

Figure 3 shows the beta coefficients for oxy-Hb separately for channels 1, 4, 27, and 31.

4 Discussion

In this study, we investigated the hemodynamic response assessed with NIRS during swallowing of water and saliva. Overall, both tasks led to the strongest NIRS signal change over the bilateral IFG. Besides this overlap in activation, some differences in the topographical distribution and time course of the NIRS signal between these two tasks were observed.

In general, both swallowing tasks led to the strongest NIRS signal changes over the bilateral IFG as revealed by the FDR analysis. This is in line with prior NIRS studies that investigated NIRS signal changes during either a water swallowing task[14,16] or saliva swallowing.[15] The IFG including Broca's area is associated with sensations of the mouth and pharynx.[42] It is involved in motor speech production but also in the control of nonspeech or orofacial sensorimotor behaviors.[5,13] Relative concentration changes in the NIRS signal over this brain region might be also caused by neuronal activation in deeper brain areas, such as the insula. The insula receives afferent inputs from many different brain regions, which are active during swallowing, and is therefore strongly involved in the swallowing process.[5,13,18,42,43] NIRS can only assess changes in hemodynamic responses a few centimeters (0.5 to 3 cm) from the

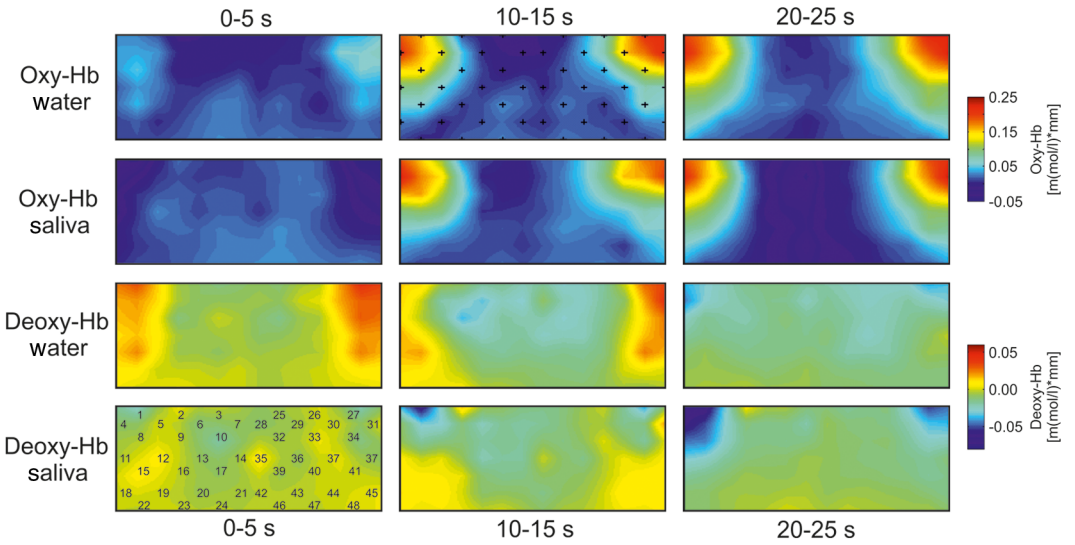

Fig. 2 Grand average topographic maps of oxy- (upper two panels) and deoxy-Hb (lower two panels) during the water and saliva swallowing task, averaged across different time intervals (s 0 to 5 left panel, s 10 to 15 middle panel, and s 20 to 25 right panel). In the upper middle map, the 48 NIRS channel locations are additionally marked with crosses and in the lower left map the 48 NIRS channel locations are marked with the corresponding channel numbers.

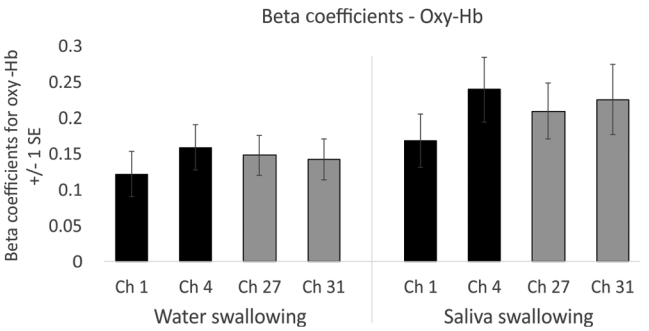

Fig. 3 Beta coefficients for oxy-Hb for the water (left) and saliva (right) swallowing tasks, presented separately for channels over the left (channels 1 and 4, black bars) and right (channels 27 and 31, gray bars) IFG, which showed the strongest signal changes during the tasks compared to all other NIRS channels. There was an overall significant stronger event-related response for oxy-Hb during saliva than during water swallowing.

surface of the head.[14,42] Nevertheless, activation changes in deeper brain structures such as the insula might also influence relative concentration changes in oxy- and deoxy-Hb assessed over the IFG using NIRS.[44,45] Summing up, both swallowing tasks activated the IFG in a comparable way.

When swallowing water, oxy-Hb strongly increased over the right IFG directly after task onset. In contrast, when swallowing saliva, oxy-Hb decreased over the right IFG during the first 5 s after task onset. Afterward, oxy-Hb increased in a comparable manner than during water swallowing. Probably, this delayed increase in oxy-Hb during swallowing saliva might be a sign of differences in task demands. Swallowing saliva might have been more effortful with lower sensory stimulation in the oropharynx than swallowing water, which might also explain the stronger event-related responses for oxy-Hb during saliva than during water swallowing.[4,30,31] Humbert et al. also found that swallowing saliva elicited a stronger blood oxygenation level dependent response assessed with fMRI in regions important for swallowing than swallowing water. The authors argue that swallowing saliva is more difficult to produce after repeated, sequential dry swallows where saliva is gradually diminished, involving more lingual pressure generation.[4,46] This increased effort during swallowing saliva might lead to stronger neuronal activation over the IFG and consequently to a higher consumption of oxy-Hb at the beginning of the swallowing task as found in this study. This resulted in an initial decrease in oxy-Hb over the IFG during saliva swallowing. Such an initial decrease in oxy-Hb caused by neuronal activation is generally described as "initial dip."[47,48]

Deoxy-Hb also increased during water swallowing especially over the right IFG directly after task onset. After water swallowing, deoxy-Hb decreased bilaterally. This is in line with prior NIRS studies that also investigated the NIRS response during a water swallowing task.[14,16] For the saliva swallowing task, we observed a steady decrease in deoxy-Hb after task onset especially over the left IFG. A stronger decrease in deoxy-Hb in the saliva swallowing condition compared to water swallowing might be also explained by the stronger sensorimotor demands in the saliva compared to the water swallowing task, which lead to stronger neuronal activation during swallowing saliva.[4,21]

During water swallowing, the NIRS signal change was strongest over the right IFG, whereas during saliva swallowing the signal change was most pronounced over the left IFG. These differences in the topographical distribution are in line with findings of prior fMRI studies. In a meta-analysis, Sörös et al. also found comparable lateralization effects. They report an inherent right hemispheric dominance for water swallowing. The different properties of saliva and water might explain differences in sensorimotor processing and motor responses required to swallow these distinct fluids and consequently, at least in part, differences in lateralization. Water is generally more voluminous and colder than saliva. Water also might evoke gustatory sensations leading to a stronger right hemispheric activation.[18] In an fMRI study, Martin et al. found a strong left lateralized activation during saliva swallowing. The authors also report

on a strong left lateralized activation during voluntary tongue movements.[32] Probably, during saliva swallowing stronger tongue movements were involved than during water swallowing leading to the stronger activation pattern over the left hemisphere during saliva than during water swallowing. Our finding of different lateralization of IFG activation for water and saliva swallowing suggests that lateralization of swallow-related brain activity depends on the specific behavioral context of the swallowing act.

In line with prior NIRS studies, we found a prolonged time course of the NIRS signal change during both swallowing tasks. For instance, oxy-Hb reached its maximum at the end of the swallowing task (s 15 after task onset, see Fig. 1). Prior NIRS studies also report on a prolonged time course of the hemodynamic response for swallowing tasks that exceeds the active task period.[14–16,29,49]

When comparing the time course of oxy- and deoxy-Hb during both swallowing tasks, we found that oxy- and deoxy-Hb changed in the opposite direction during saliva swallowing but not during water swallowing (see Figs. 1 and 2). According to the mechanism of neurovascular coupling, neuronal activation is coupled with increases in rCBF, which in turn is accompanied by increases in cerebral blood volume via volumetric expansion in vessels already perfused or by increasing the portion of vessels actually perfused. An increase in rCBF typically goes along with increases in oxy-Hb.[21–23] Changes in oxy-Hb are sensitive indicators of changes in rCBF. In contrast, the direction of changes in deoxy-Hb is determined by the degree of changes in venous blood oxygenation and volume.[22] This indicates that although it is theoretically assumed that increases in oxy-Hb go along with decreases in deoxy-Hb,[21,50] oxy- and deoxy-Hb measure partly different physiological processes. Empirical studies also show that oxy- and deoxy-Hb often change in the same direction.[14–16,22,51] Hence, oxy- and deoxy-Hb are somehow related, but that does not mean that both signals always show relative concentration changes in opposite directions.[22] In this study, we found that oxy- and deoxy-Hb changed in the opposite direction during saliva swallowing (Figs. 1 and 2). During water swallowing, oxy- and deoxy-Hb increased, although oxy-Hb showed a later peak activation than deoxy-Hb (Fig. 1). Hence, our present results support the fact that oxy- and deoxy-Hb measure partly different physiological processes and therefore are not necessarily inversely related.

4.1 *Conclusion and Future Directions*

Here, we showed that NIRS is an appropriate method to investigate the topographical distribution as well as the time course of the hemodynamic response during distinct swallowing tasks. Using NIRS, we replicated prior fMRI findings concerning cortical correlates of swallowing water and saliva. Furthermore, the higher temporal resolution of NIRS compared to fMRI allowed a more fine-tuned analysis of the time course of the hemodynamic response during swallowing. Accordingly, we detected differences in the time course of the NIRS signal between the two swallowing tasks. Furthermore, NIRS assesses changes in oxy- and deoxy-Hb, whereas fMRI only assesses changes in deoxy-Hb.[21] Our results show that both signals differ between the saliva and water swallowing task in a specific manner. Hence, evaluation of the hemodynamic response during swallowing might be more accurate when using relative concentration changes of both oxy- and deoxy-Hb, rather than either species alone.[52]

Since NIRS is a relative robust, cheap, user-friendly, and portable technique that enables mobile and easy assessment of the hemodynamic response in patient populations, our results indicate that NIRS might be an adequate future diagnostic and assessment tool for patients with dysphagia.[15,16,53,54] With NIRS, we were able to reveal differences in brain activation patterns underlying diverse swallowing tasks. Furthermore, real-time feedback about the level of activation in swallowing-related brain areas using NIRS might be used as future treatment of swallowing disorders.[14,16]

Disclosures

The authors declare that they have no competing interests and no conflicts of interest.

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References

1. C. Ertekin, "Voluntary versus spontaneous swallowing in man," *Dysphagia* **26**(2), 183–192 (2011).
2. S. Hamdy et al., "Organization and reorganization of human swallowing motor cortex: implications for recovery after stroke," *Clin. Sci.* **99**, 151–157 (2000).
3. I. A. Humbert and J. Robbins, "Normal swallowing and functional magnetic resonance imaging: a systematic review," *Dysphagia* **22**(3), 266–275 (2007).
4. I. A. Humbert et al., "Neurophysiology of swallowing: effects of age and bolus type," *NeuroImage* **44**(3), 982–991 (2009).
5. R. E. Martin et al., "Cerebral cortical representation of automatic and volitional swallowing in humans," *J. Neurophysiol.* **85**, 938–950 (2001).
6. G. J. J. W. Bours et al., "Bedside screening tests vs. videofluoroscopy or fibreoptic endoscopic evaluation of swallowing to detect dysphagia in patients with neurological disorders: systematic review," *J. Adv. Nurs.* **65**(3), 477–493 (2009).
7. G. R. Locke, III et al., "Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota," *Gastroenterology* **112**(5), 1448–1456 (1997).
8. G. D. Eslick and N. J. Talley, "Dysphagia: epidemiology, risk factors and impact on quality of life: a population-based study," *Aliment. Pharmacol. Ther.* **27**(10), 971–979 (2008).
9. T. Wilkins et al., "The prevalence of dysphagia in primary care patients: a HamesNet research network study," *J. Am. Board Fam. Med.* **20**(2), 144–150 (2007).
10. O. Ekberg et al., "Social and psychological burden of dysphagia: its impact on diagnosis and treatment," *Dysphagia* **17**, 139–146 (2002).
11. P. G. Mihai et al., "Brain imaging correlates of recovered swallowing after dysphagic stroke. A fMRI and DWI study," *NeuroImage Clin.* **12**, 1013–1021 (2016).
12. G. A. Malandraki, S. Johnson, and J. Robbins, "Functional MRI of swallowing. From neurophysiology to neuroplasticity," *Head Neck* **33**(Suppl. 1), S14–S20 (2011).
13. C. Ertekin and I. Aydogdu, "Neurophysiology of swallowing," *Clin. Neurophysiol.* **114**(12), 2226–2244 (2003).
14. S. E. Kober and G. Wood, "Changes in hemodynamic signals accompanying motor imagery and motor execution of swallowing: a near-infrared spectroscopy study," *NeuroImage* **93**, 1–10 (2014).
15. S. E. Kober et al., "Hemodynamic signal changes accompanying execution and imagery of swallowing in patients with dysphagia: a multiple single-case near-infrared spectroscopy study," *Front. Neurol.* **6**, 1–10 (2015).
16. S. E. Kober et al., "Voluntary modulation of hemodynamic responses in swallowing related motor areas: a near-infrared spectroscopy based neurofeedback study," *PLoS ONE* **10**(11), e0143314 (2015).

17. M. Ninaus et al., "Neurofeedback and serious games," in *Psychology, Pedagogy, and Assessment in Serious Games*, T. M. Connolly et al., Eds., pp. 82–110, IGI Global, Hershey, Pennsylvania (2014).
18. P. Sörös, Y. Inamoto, and R. E. Martin, "Functional brain imaging of swallowing: an activation likelihood estimation meta-analysis," *Hum. Brain Mapp.* **30**(8), 2426–2439 (2009).
19. N. Weiskopf, "Real-time fMRI and its application to neurofeedback," *NeuroImage* **62**(2), 682–692 (2012).
20. T. J. Huppert et al., "A temporal comparison of BOLD, ASL, and NIRS hemodynamic responses to motor stimuli in adult humans," *NeuroImage* **29**(2), 368–382 (2006).
21. A. Villringer and B. Chance, "Non-invasive optical spectroscopy and imaging of human brain function," *Trends Neurosci.* **20**(10), 435–442 (1997).
22. Y. Hoshi, N. Kobayashi, and M. Tamura, "Interpretation of near-infrared spectroscopy signals: a study with a newly developed perfused rat brain model," *J. Appl. Physiol.* **90**, 1657–1662 (2001).
23. M. Wolf et al., "Different time evolution of oxyhemoglobin and deoxyhemoglobin concentration changes in the visual and motor cortices during functional stimulation: a near-infrared spectroscopy study," *NeuroImage* **16**(3), 704–712 (2002).
24. S. Lloyd-Fox, A. Blasi, and C. E. Elwell, "Illuminating the developing brain: the past, present and future of functional near infrared spectroscopy," *Neurosci. Biobehav. Rev.* **34**(3), 269–284 (2010).
25. I. Nambu et al., "Single-trial reconstruction of finger-pinch forces from human motor-cortical activation measured by near-infrared spectroscopy (NIRS)," *NeuroImage* **47**(2), 628–637 (2009).
26. H. Kagaya et al., "Body positions and functional training to reduce aspiration in patients with dysphagia," *Jpn. Med. Assoc. J.* **54**(1), 35–38 (2011).
27. T. Matsumoto et al., "Dried-bonito aroma components enhance salivary hemodynamic responses to broth tastes detected by near-infrared spectroscopy," *J. Agric. Food Chem.* **60**(3), 805–811 (2012).
28. R. W. Mulheren, E. Kamarunas, and C. L. Ludlow, "Sour taste increases swallowing and prolongs hemodynamic responses in the cortical swallowing network," *J. Neurophysiol.* **116**(5), 2033–2042 (2016).
29. H. Sato et al., "Application of near-infrared spectroscopy to measurement of hemodynamic signals accompanying stimulated saliva secretion," *J. Biomed. Opt.* **16**(4), 047002 (2011).
30. M. K. Kern et al., "Cerebral cortical representation of reflexive and volitional swallowing in humans," *Am. J. Physiol. Gastrointest. Liver Physiol.* **280**, G354–G360 (2001).
31. K. Mosier et al., "Cortical representation of swallowing in normal adults: functional implications," *Laryngoscope* **109**(9), 1417–1423 (1999).
32. R. E. Martin et al., "Cerebral areas processing swallowing and tongue movement are overlapping but distinct: a functional magnetic resonance imaging study," *J. Neurophysiol.* **92**(4), 2428–2443 (2004).
33. R. Martin et al., "Cerebral cortical processing of swallowing in older adults," *Exp. Brain Res.* **176**(1), 12–22 (2007).
34. J. L. Lancaster et al., "Automated labeling of the human brain: a preliminary report on the development and evaluation of a forward-transform method," *Hum. Brain Mapp.* **5**(4), 238–242 (1997).
35. J. T. P. Talairach, *Co-Planar Stereotaxic Atlas of the Human Brain: 3-D Dimensional Proportional System: An Approach to Cerebral Imaging*, Thieme Medical Publishers, New York (1988).
36. G. Bauernfeind et al., "Separating heart and brain: on the reduction of physiological noise from multichannel functional near-infrared spectroscopy (fNIRS) signals," *J. Neural Eng.* **11**(5), 056010 (2014).
37. A. K. Singh and I. Dan, "Exploring the false discovery rate in multichannel NIRS," *NeuroImage* **33**(2), 542–549 (2006).
38. R. B. Buxton et al., "Modeling the hemodynamic response to brain activation," *NeuroImage* **23**(Suppl. 1), S220–S233 (2004).
39. M. Uga et al., "Optimizing the general linear model for functional near-infrared spectroscopy. An adaptive hemodynamic response function approach," *Neurophotonics* **1**(1), 015004 (2014).
40. K. J. Friston et al., "Analysis of fMRI time-series revisited," *NeuroImage* **2**(1), 45–53 (1995).
41. S. E. Kober and G. Wood, "Repetition suppression in aging: a near-infrared spectroscopy study on the size-congruity effect," *NeuroImage* **157**, 196–208 (2017).
42. J. R. Augustine, "Circuitry and functional aspects of the insular lobe in primates including humans," *Brain Res. Rev.* **22**(3), 229–244 (1996).
43. S. Hamdy et al., "Cortical activation during human volitional swallowing: an event related fMRI study," *Am. J. Physiol. Gastrointest. Liver Physiol.* **277**, G219–G225 (1999).
44. N. Liu et al., "Inferring deep-brain activity from cortical activity using functional near-infrared spectroscopy," *Biomed. Opt. Express* **6**(3), 1074–1089 (2015).
45. T. Hashimoto, Y. Minagawa-Kawai, and S. Kojima, "Motion illusion activates the visual motion area of the brain. A near-infrared spectroscopy (NIRS) study," *Brain Res.* **1077**(1), 116–122 (2006).
46. I. Mansson and N. Sandberg, "Effects of surface anesthesia on deglutition in man," *Laryngoscope* **84**(3), 427–437 (1974).
47. K.-S. Hong and N. Naseer, "Reduction of delay in detecting initial dips from functional near-infrared spectroscopy signals using vector-based phase analysis," *Int. J. Neural Syst.* **26**(3), 1650012 (2016).
48. G. Jasdzewski et al., "Differences in the hemodynamic response to event-related motor and visual paradigms as measured by near-infrared spectroscopy," *NeuroImage* **20**(1), 479–488 (2003).
49. S. R. Jadcherla et al., "Esophageal reflexes modulate frontoparietal response in neonates: novel application of concurrent NIRS and provocative esophageal manometry," *Am. J. Physiol. Gastrointest. Liver Physiol.* **307**(1), G41–G49 (2014).
50. F. Scholkmann et al., "A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology," *NeuroImage* **85**(Pt. 1), 6–27 (2014).
51. Y. Hoshi and M. Tamura, "Near-infrared optical detection of sequential brain activation in the prefrontal cortex during mental tasks," *NeuroImage* **5**(4), 292–297 (1997).
52. M. M. DiStasio and J. T. Francis, "Use of frontal lobe hemodynamics as reinforcement signals to an adaptive controller," *PLoS ONE* **8**(7), e69541 (2013).
53. A. Sakudo, "Near-infrared spectroscopy for medical applications: current status and future perspectives," *Clin. Chim. Acta* **455**, 181–188 (2016).
54. H. Yang et al., "Neural and cortical analysis of swallowing and detection of motor imagery of swallow for dysphagia rehabilitation—a review," *Prog. Brain Res.* **228**, 185–219 (2016).

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