Influence of attention and bolus volume on brain organization during swallowing

Iva Jestrović* James L. Coyle† Subashan Perera‡ Ervin Sejdić

Abstract

It has been shown that swallowing involves certain attentional and cognitive resources which, when disrupted can influence swallowing function with in dysphagic patient. However, there are still open questions regarding the influence of attention and cognitive demands on brain activity during swallowing. In order to understand how brain regions responsible for attention influence brain activity during swallowing, we compared brain organization during no-distraction swallowing and swallowing with distraction. Fifteen healthy male adults participated in the data collection process. Participants performed ten 1 ml, ten 5 ml, and ten 10 ml water swallows under both no-distraction conditions and during distraction while EEG signals were recorded. After standard pre-processing of the EEG signals, brain networks were formed using the time-frequency based synchrony measure. The brain networks formed were then compared between the two sets of conditions. Results showed that there are differences in the *Delta*, *Theta*, *Alpha*, *Beta*, and *Gamma* frequency bands between no-distraction swallowing and swallowing with distraction. Differences in the *Delta* and *Theta* frequency bands can be attributed to changes in subliminal processes, while changes in the *Alpha* and *Beta* frequency bands are directly associated with the various levels of attention and cognitive demands during swallowing process, and changes in the Gamma frequency band are due to changes in motor activity. Furthermore, we showed that variations in bolus volume influenced the swallowing brain networks in the *Delta*, *Theta*, *Alpha*, *Beta*, and *Gamma* frequency bands. Changes in the *Delta*, *Theta*, and *Alpha* frequency bands are due to sensory perturbations evoked by the various bolus volumes.

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Changes in the Beta frequency band are due to reallocation of cognitive demands, while changes in the *Gamma* frequency band are due to changes in motor activity produced by variations in bolus volume. These findings could potentially lead to the development of better understanding of the nature of dysphagia and various rehabilitation strategies for patients with neurogenic dysphagia who have altered attention or impaired cognitive functions.

Keywords: EEG, graph theory, brain network, dysphagia, swallowing, attention.

1 Introduction

Deglutition (i.e., swallowing) is an essential neuromuscular event which provides the transportation of food and liquids from the oral cavity to the stomach. The process of swallowing has been artificially subdivided into phases to enable description of the numerous and overlapping biomechanical events that occur within the one- to two second duration of a typical liquid swallow that does not involve oral preparation of solid food in prior to transport to the pharynx and esophagus (Ertekin et al., 2003; Stevenson and Allaire, 1991). This process can be divided into four distinctive phases (i.e., oral preparatory, oral transit, pharyngeal, and esophageal), all of which overlap somewhat in their sequence of occurrence. The first phase of swallowing activity consists of primarily voluntary actions, while the remaining stages are characterized by primarily involuntary actions (Dodds, 1989). Swallowing under conditions requiring volitional augmentation of oral activity, posture, or other swallowing maneuvers alter the intensity of voluntary recruitment and are hypothesized to result in changes on cognitive demands during the different stages of the swallowing process (Brodsky et al., 2012a).

Dysphagia (swallowing disorders) is caused by either disruption of the swallowing mechanism itself, or by disease and brain lesions introduced by conditions such as stroke, which disrupt sensorimotor function through damage to central neural structures without focally altering the peripheral aerodigestive mechanism (Cichero and Murdoch, 2006). There are a number of causes of dysphagia, but the most common in adults are neurological conditions such as stroke (Gottlieb et al., 1996), physical traumatic brain injuries (Lazarus and Logemann, 1987), cerebral palsy (Rogers et al., 1994), and Parkinson's or other neurodegenerative diseases (Murray, 1999). Dysphagia often leads to the development of other adverse medical conditions, such as dehydration (Smithard et al., 1996), malnutrition (Foley et al., 2009), failure of the immune system (Curran and Groher, 1990), respiratory infection (Marik and Kaplan, 2003), and in general, a decreased quality of life (McHorney et al., 2000).

Although once believed to be mediated purely reflexively at the brainstem level and executed peripherally without higher level neural input, multiple and bilateral hemispheric regions have been shown to be activated before, during and after swallowing (Hamdy et al., 1997), (Michou and Hamdy, 2009), (Ertekin et al., 2003), (Stevenson and Allaire, 1991). Specifically, large swallowing neural networks involving bilateral primary motor and sensory cortices, supplemental and premotor cortices, Heschls gyri, cingulate gyri, Brocas area and the insula, and superior temporal gyri have been identified using functional magnetic resonance imaging(Mosier et al., 1999). And likewise, activation of numerous other anterior frontal and temporal cortical and subcortical structures have been observed during swallowing in healthy individuals (Hamdy et al., 1999).

Many of the cerebral areas activated during swallowing are responsible for several cognitive functions and are active during the processing of language; some, when damaged, have been strongly implicated in impaired cognitive processes such as attention (Corbetta and Shulman, 2002). Hence interest in an interaction between cognition, language, and swallowing has increased and increased speculation that central neurogenic dysphagia may have a cognitive component, has risen in the past decade. During typical swallowing clinical testing using videofluoroscopy or fiberoptic imaging, patients are instructed to swallow after receiving a verbal command from an examiner. Several studies have identified significant differences between swallows prompted by a verbal instruction compared to spontaneous swallows in healthy and dysphagic patients (Daniels et al., 2007), (Matsuo and Palmer, 2008) (Nagy et al., 2013), (Nonaka et al., 2009). Similarly, the effect of attention on swallowing function has also been implicated, with significantly altered reaction times and timing of swallow physiologic events observed in healthy and dysphagic participants when challenged by a divided attention task (Brodsky et al., 2012b), (Brodsky et al., 2012a).

Cerebral reorganization after brain damage has received much attention as it relates to the effects of rehabilitative efforts after stroke and brain injury. It has been shown that successful dysphagia rehabilitation is correlated with brain reorganization following cerebral injury and during the natural course of other specific neurological disorders (Hamdy et al., 2000). Whereas in the past dysphagia has been treated mainly using a bottom-up method of restoring peripheral function to improve swallow function, plasticity of swallowing related to reorganization of damaged central as a construct, a more top-down process, is currently receiving much attention (Doeltgen and Huckabee, 2012), (Robbins, 2011). However most current methods of observing brain function during swallowing and swallowing rehabilitation rely on bulky, sophisticated and impractical instrumentation that, like language and attentional interference, introduce unnatural variables to the swallowing task. Thus, it is essential to ascertain patterns of brain activity during swallowing using more practical and meaningful methods, to provide a better understanding of neurogenic swallowing difficulties in order to generate more research into top-down rehabilitation strategies using swallowing network research that preserves natural swallowing conditions.

One way of analyzing brain activity during swallowing is to use electroencephalography (EEG) (Jestrović et al., 2014), (Jestrović et al., 2015a). This portable, affordable and non-invasive technique enables the participant to swallow naturally without any imposed postural or other conditions. Unlike functional magnetic resonance imaging or near-infrared spectroscopy, EEG is characterized by a very good temporal resolution, which enables analysis of both longer and shorter duration swallowing events. Furthermore, EEG enables simultaneous analysis of the relationships and interactions between different brain regions using statistical methods such as the graph theory approach. We have previously shown that the graph theory approach applied to EEG signals during swallowing can provide important insight into swallowing neurology (Jestrović et al., 2015b). Moreover, EEG examines the underlying transit of neural information among brain regions, rather than just observing the product of that activation (i.e. areas that are ultimately activated).

Therefore, it is germane to the investigation of neurogenic dysphagia and the effects of behavioral treatment of dysphagia, in which patients must perform volitional augmentation of oropharyngeal activities, to investigate the effects of external distraction on brain activity during swallowing, using more practical and less invasive methods. In this study, we hypothesize that the brain network is different between no-distraction swallowing and swallowing with distraction. Characterizing the brain networks during swallowing with distraction could potentially explain the reason for higher risk of aspiration within some groups of dysphagic patients (Barrett and Burkholder, 2006), (Mattingley et al., 1994) and potentially lead to the development of better rehabilitation strategies for dysphagia patients who also have altered attention or impaired cognitive function resulting from neurological disorders.

2 Methodology

2.1 Data acquisition from participants

Data was collected from 15 healthy male subjects, aged from 18 to 35. The number of 15 subject is considered as a sample of convenience. All participants provided informed consent, and also age, height, and weight. The protocol was approved by the Institutional Review Board at the University of Pittsburgh.

EEG signals were recorded with an array of 64 EEG electrodes. Electrodes were positioned using the actiCAP active electrodes (BrainProducts, Germany) EEG cap, which was positioned according to the 10-20 international electrode system (Jasper, 1958). The EEG signals were amplified using the actiCHamp amplifier (BrainProducts, Germany). The P3 electrode was chosen as the reference electrode. Impedance of all electrodes was below 15 kΩ. Data was recorded at a sampling rate of 10 kHz and saved using PyCorder acquisition software. In order to identify the presence of occurrence of swallowing events, we concurrently recorded swallowing vibrations with a dual-axis accelerometer positioned on the anterior part of the participant's neck. The capabilities of the dual-axis accelerometer system in the detection of swallowing events were described in detail in our previous studies (Jestrović et al., 2013).

After setting up all devices (Figure 1) participants were asked to consume ten individual 1 ml water boluses, ten 5 ml water swallows, and ten 10 ml water swallows. Then, participants were asked to repeat the same sequence while they watching a video to occupy their attention and present cognitive demands.

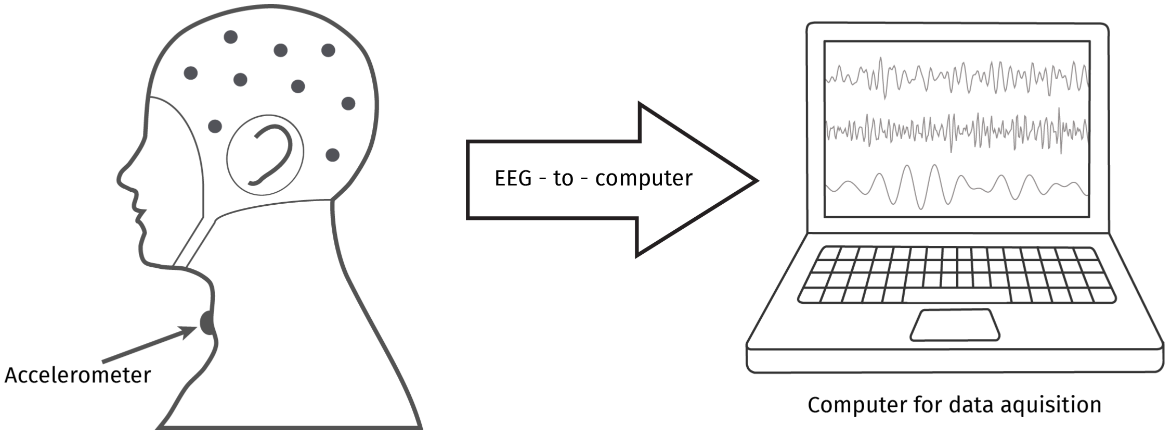

Figure 1: The experimental procedure used in this study.

2.2 Pre-processing steps

EEGlab MATLAB toolbox (Delorme and Makeig, 2004) was used for pre-processing of EEG signals. First, all signals were downsampled to 256 Hz. Next, we filtered signals from 0.1 Hz to 100 Hz using an elliptical infinite impulse response (IIR) band-pass filter. The same type of filter was also used for removing the noise from the power supply, with cut-off frequencies at 58 Hz and 62 Hz. Next, EEG signals were segmented based on the onset and offset of separate swallows as determined by accelerometer signals. In the last step, we removed artifacts from the EEG signals using the Independent Component Analysis (ICA) algorithm (Hyvärinen and Oja, 2000).

2.3 Network constructions

The pre-processed signals were filtered into the commonly used frequency bands of interest: *Delta* ($< 4Hz$), *Theta* ($4-7Hz$), *Alpha* ($8-15Hz$), *Beta* ($16-31Hz$), and *Gamma* ($> 32Hz$). Connectivity networks were constructed with time-frequency based phase synchrony measures proposed by Aviyente et al. (2011) applied to the filtered signals.

2.4 Network measures

We used the Brain Connectivity Toolbox (BCT) (Rubinov and Sporns, 2010) running in MATLAB to calculate each of the following network measures:

- The *clustering coefficient* describes the ratio between the number of existing edges between the nearest neighbor of the node and the maximum number of possible edges (Stam and Reijneveld, 2007). In the case of the weighted network, the clustering coefficient is calculated as:

  $$C_i = \frac{1}{S_i(D_i-1)} \sum_{j,k} \frac{w_{ij}+w_{ik}}{2} a_{ij}a_{ik}a_{jk}, \tag{1}$$

  Where the parameter $S_i(D_i-1)$ normalizes the clustering coefficient to be in the range $0 < C_i^W < 1$. a_{ij}, a_{ik}, and a_{jk} all have a value of one in a case of connection between two nodes. The mean clustering coefficient is defined as:

  $$C = \frac{1}{N} \sum_{j=1}^{N} C_j. \tag{2}$$

- The *characteristic path length* is the average shortest path length that connects every pair of nodes. (Strogatz, 2001; Achard and Bullmore, 2007). The characteristic path length contains information about connection strength between node i and node j (Rubinov and Sporns, 2010), and is defined as as:

  $$L_i = \frac{1}{N(N-1)} \sum_{i,j \in N, i \neq j} d_{i,j}, \tag{3}$$

  Furthermore, the mean characteristic path length is equal to:

  $$L = \frac{1}{N} \sum_{i \in N} L_i. \tag{4}$$

- The *small-worldness* describes the optimal organization in the network that would provide the most efficient communication between nodes (Bassett and Bullmore, 2006). The small-world network should satisfy two conditions:

  $$\gamma = \frac{C}{C_{random}} \gg 1, \tag{5}$$

  where γ is the normalized clustering coefficient, and

  $$\lambda = \frac{L}{L_{random}} \approx 1, \tag{6}$$

  where λ is the normalized characteristic path length. C_{random} is the mean clustering coefficient of the random network, and L_{random} is mean characteristic path length of the random network. C_{random} and L_{random} are calculated as the average mean clustering coefficient and average mean characteristic path length from from the 100 random networks generated using the Markov-chain algorithm (Sporns and Zwi, 2004; Maslov and Sneppen, 2002). Finally, we can say that a network has small-world properties if its ratio:

  $$S = \frac{C/C_{random}}{L/L_{random}} \tag{7}$$

  is higher than one ($S > 1$).

2.5 Data analysis

To examine differences in swallowing brain networks based on volume (1/5/10 ml) and task (neutral/distraction), we fit a series of linear mixed models with each network characteristic as the dependent variable (i.e. volume, task and volume by task interaction) as fixed effects of interest, and a participant random effect to account for multiple measurements from the same participant. We appropriately constructed means contrasts to make pairwise comparisons between different volumes for a given task, and between different tasks for a given volume. Next, to examine whether participant age was associated with network characteristics, we fit another set of linear mixed models stratified by task and volume. We used each network characteristic as the dependent variable, and we used age as the fixed-effect independent variable, and a participant random effect to account for multiple trials of the same participant. We used SAS® version 9.3 (SAS Institute, Inc., Cary, North Carolina) for all statistical analysis.

3 Results

We analyzed 900 swallows of various volumes in the no-distraction condition and during the distraction. Results of the network measures are presented with the mean values (± standard deviation) of the network measure on the vertical axis, and the frequency bands on the horizontal axis. Results are presented in colored bars that are paired based on bolus volume (blue = 1mL, red = 5mL, green = 10mL) and experimental conditions (left bar = no-distraction condition, right bar = distraction condition). Black dots on the plots represent statistically significant differences between no-distraction condition swallowing and swallowing with distraction within the frequency bands of interest.

3.1 Distraction effects on brain networks

Figure 2 summarizes the mean value of the clustering coefficient for various bolus volumes consumed during the two different states. No-distraction swallowing of all bolus sizes (1 ml, 5 ml, and 10 ml) exhibited a higher clustering coefficient than swallowing with distraction in the *Theta*, *Alpha*, and *Beta* frequency bands ($p < 0.03$). Also, 10 ml no-distraction swallowing had a higher clustering coefficient than 10 ml swallowing with distraction in the *Gamma* frequency band ($p < 0.01$).

Figure 3 summarizes the mean value for characteristic path length for various bolus volumes consumed during the two different states. The no-distraction swallowing showed significantly higher characteristic path length than did swallowing with distraction during 5 ml swallowing within the *Delta*, *Theta*, and *Beta* frequency bands ($p < 0.02$). Also, the no-distraction swallowing showed higher characteristic path length than did swallowing with distraction during 10 ml swallowing within all frequency bands of interest.

Figure 4 summarizes the mean value for the small-world parameter for various bolus volumes consumed during the two different states. Swallowing with distraction for the all bolus volumes (1 ml, 5 ml, and 10 ml) showed a higher small-world parameter than did no-distraction swallowing in the *Beta* frequency band ($p < 0.03$). In the *Delta* frequency band, 5 ml swallowing with distraction had a higher small-world parameter than did 5 ml no-distraction swallowing ($p < 0.01$). Also, in the *Alpha* frequency band 10 ml swallowing with distraction had a higher small-world parameter than did the 10 ml no-distraction swallowing ($p < 0.01$).

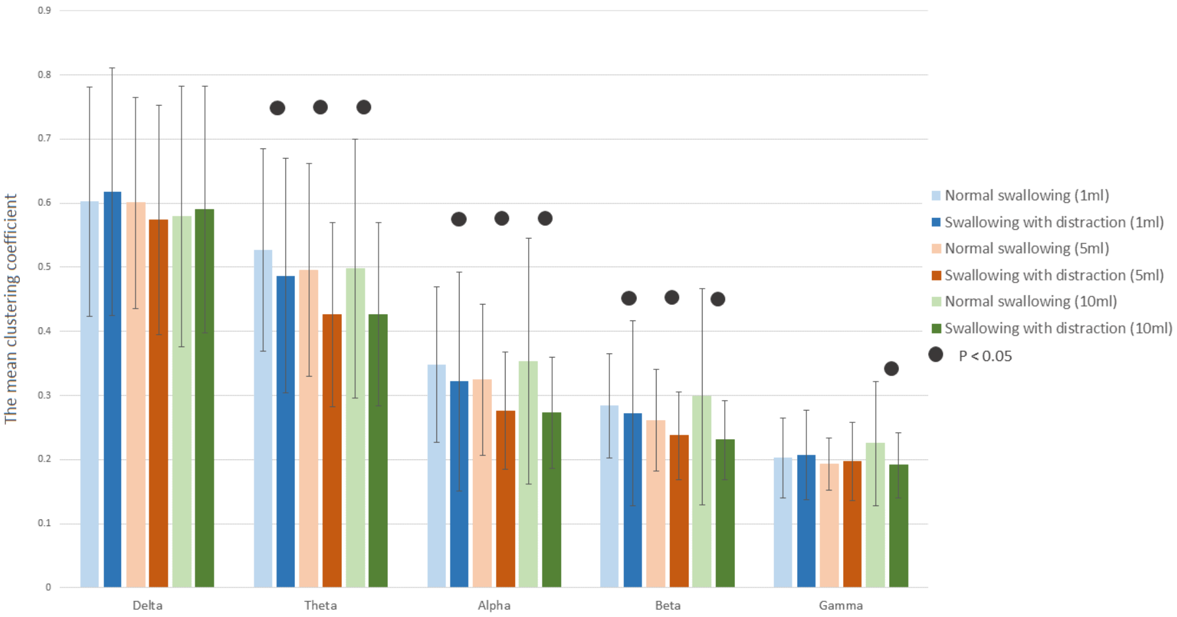

Figure 2: The value of mean clustering coefficient, C, for different bolus volumes and for different frequency bands. The black dots show whether there is significant statistical difference between no-distraction swallowing and swallowing with distraction.

3.2 Volume effects on brain networks

In the *Beta* frequency band during no-distraction swallowing, 1 ml swallowing showed a higher clustering coefficient than did the 5 ml swallowing ($p = 0.04$). During swallowing with distraction, 1 ml swallowing showed a higher clustering coefficient than did the 5 ml swallowing within all frequency bands of interest ($p < 0.05$). Also, during swallowing with distraction, 1 ml swallowing showed a higher characteristic path length than did 5 ml swallowing within the *Delta*, *Theta*, and *Alpha* frequency bands ($p < 0.05$).

The 1 ml swallowing with distraction showed a higher clustering coefficient than did the 10 ml swallowing with distraction within all frequency bands of interest, while the 1 ml no-distraction swallowing had a lower clustering coefficient than did the 10 ml no-distraction swallowing ($p < 0.05$). The 1 ml no-distraction swallowing showed a lower characteristic path length than did 10 ml no-distraction swallowing within the *Beta* and *Gamma* frequency bands ($p < 0.01$). The 1 ml swallowing with distraction showed a higher characteristic path length than did 10 ml no-distraction swallowing within the *Theta* and *Alpha* frequency bands ($p < 0.01$). Furthermore, in the *Gamma* frequency band during the no-distraction swallowing and the swallowing with distraction, the 1 ml

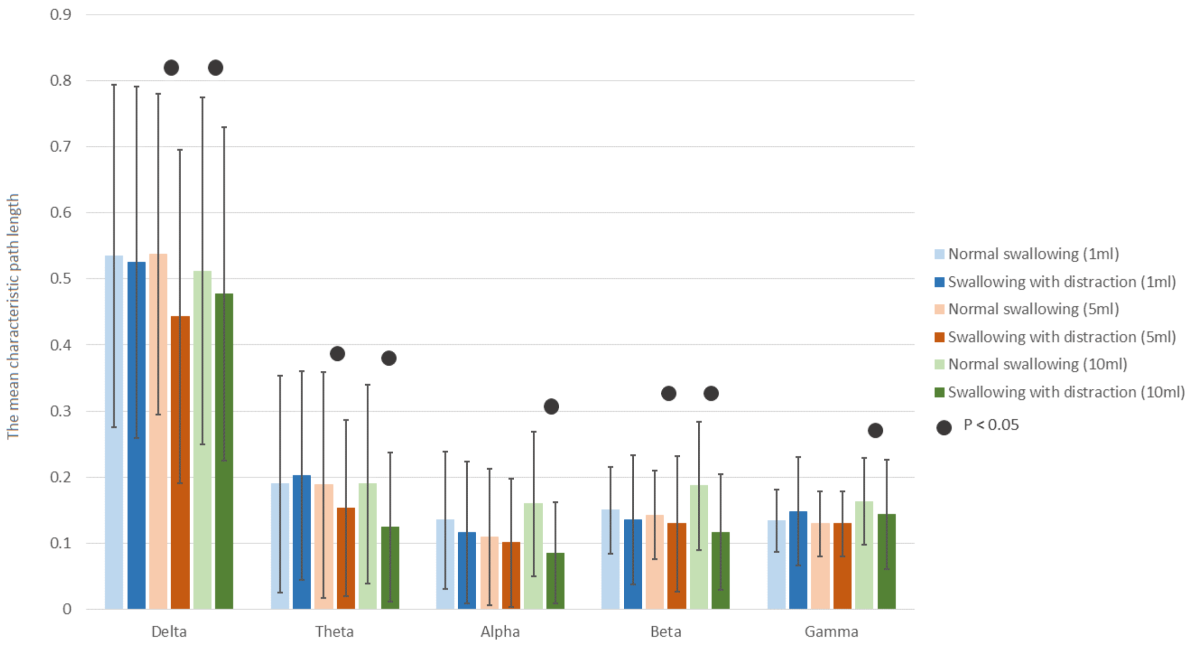

Figure 3: The value of mean characteristic path length, L, for different bolus volumes and for different frequency bands. The black dots show whether there is significant statistical difference between no-distraction swallowing and swallowing with distraction.

swallowing showed a higher small-world parameter than did the 5 ml swallowing ($p < 0.01$). Also, 1 ml swallowing with distraction had a lower small-world parameter than did 10 ml swallowing with distraction in the *Theta* frequency band ($p = 0.02$).

During no-distraction swallowing, 5 ml swallowing had a lower clustering coefficient and characteristic path length than did 10 ml swallowing within the *Alpha*, *Beta*, and *Gamma* frequency bands ($p < 0.05$). Also, during no-distraction swallowing 5 ml swallowing had a lower small world parameter than did the 10 ml swallowing within the *Theta* and *Gamma* frequency bands ($p < 0.01$).

3.3 Age effects on brain network

Lastly, we investigated age dependence on the swallowing characteristics during both no-distraction swallowing and swallowing with distraction. Results did not depend on the subject's age in any of the frequency bands of interest for both swallowing conditions.

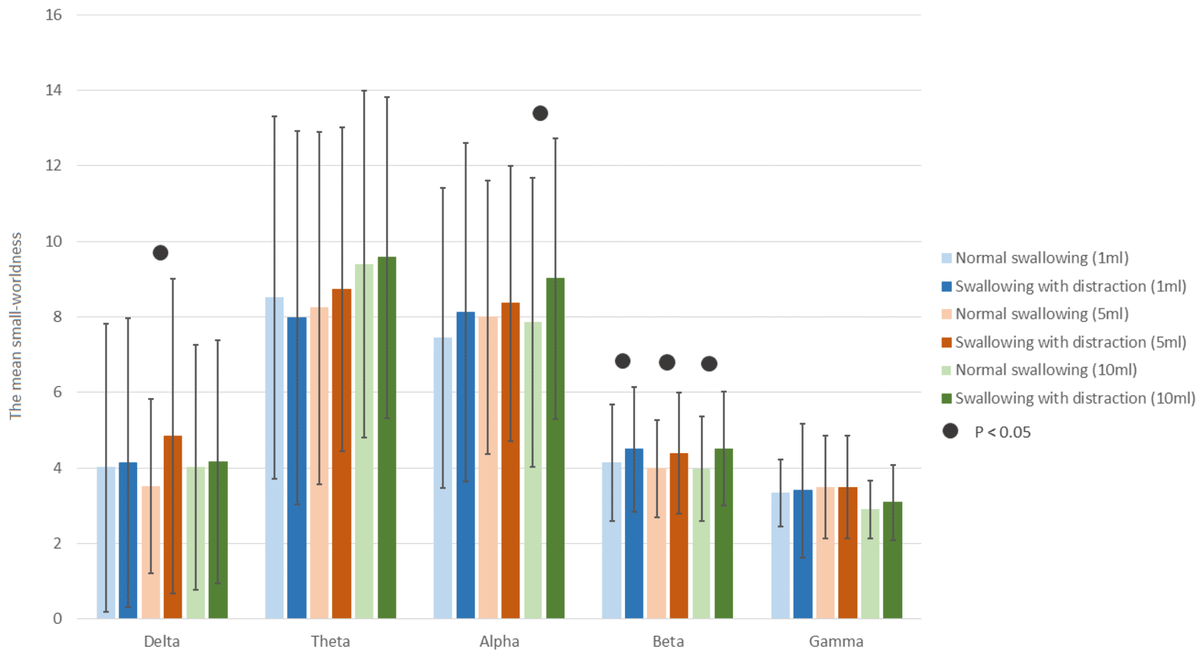

Figure 4: The value of mean small-worldness, S, for different bolus volumes and for different frequency bands. The black dots show whether there is significant statistical difference between no-distraction swallowing and swallowing with distraction.

4 Discussion

Our hypothesis, that the brain network is different for no-distraction swallowing compared with the brain network constructed during swallowing with distraction, was supported by our results. The significant statistical differences between no-distraction swallowing and swallowing with distraction are described for each frequency band of interest:

- *Delta* and *Theta*: Our results showed differences in the *Delta* and *Theta* frequency bands between no-distraction swallowing and swallowing with distraction for the clustering coefficient and characteristic path length. Changes in the lower EEG frequencies (i.e. *Delta* and *Theta*) have been previously reported as important in the process of selective attention to both auditory and visual stimuli (Lakatos et al., 2008). Also, one EEG study combined with fMRI confirmed that sensory cortices such as the auditory and visual cortices are associated with the activation of the *Delta* and *Theta* EEG frequency bands (Jann et al., 2010). This means that changes in the *Delta* and *Theta* frequency bands (i.e, higher clustering coefficient, higher characteristic path length, and lower small-worldness for no-distraction swallowing in comparison with swallowing with distraction) can be attributed to the changes in the sensory cortices produced by auditory and visual stimulation during swallowing with distraction task. Furthermore, our results also showed changes in the *Delta* and *Theta* frequency bands between the swallowing of various bolus volumes. Previous studies have shown that the *Delta* and *Theta* frequency bands are activated during sensory stimulation (Yagyu et al., 1998). The swallowing process involves different types of the sensory stimulation such as smell, taste, and touch in the oral areas, all of which have been shown to lead to subsequent alterations in swallowing motor activation patterns Bastian and Riggs (1999). The various bolus volumes used in this study differently affected sensory receptors responsible for touch, kinesthesia, and proprioception in the oral cavity. Therefore, changes in the *Delta* and *Theta* frequency bands between swallowing of the various bolus volumes may be attributable to the effects of altered afferent activity entering the swallowing brain networks caused by variations in bolus volume.

- *Alpha*: The *Alpha* frequency band is the most dominant EEG component for the conscious person. Studies showed that the activity of the *Alpha* frequency band is less prominent when visual stimulation is present (Klimesch, 1999). Furthermore, previous studies have reported differences in the *Alpha* waveforms between attended and unattended stimuli (Marrufo et al., 2001; Yamagishi et al., 2003). Our results are in agreement with these finding by showing significant differences between no-distraction swallowing and swallowing with distraction for the characteristic path length and the small-world parameter in the *Alpha* frequency band. Thus, we can attribute these statistical differences to the different attentional demands of the no-distraction and distraction conditions while swallowing. In addition, our results showed significant statistical differences in the *Alpha* frequency band between swallowing of various bolus volumes. Studies have shown that EEG waveforms also exhibit changes in the *Alpha* frequency band during sensory stimulation (Klemm et al., 1992; Lorig et al., 1991). Therefore, changes between swallowing of different bolus volumes can be attributed to the changes in the activation of the sensory, kinesthetic, and proprioceptive receptors and pathways introduced by the variously-sized stimuli employed.

- *Beta*: Several previous studies have suggested that the *Beta* EEG frequency band is directly related to attention during sensorimotor tasks (Murthy and Fetz, 1992, 1996; Feige et al., 2000; Sanes and Donoghue, 1993; Kristeva-Feige et al., 1993). Our results demonstrated changes in the *Beta* frequency band between no-distraction swallowing and swallowing with distraction for the small-world parameter. Swallowing is a complex process that involves activation of a number of sensory receptors, as well as muscle activity in both the head and neck. Therefore, changes in the *Beta* EEG frequency band during swallowing with the distraction could be attributed to the reallocation of cognitive sources during this task (Sanes and Donoghue, 1993; Kristeva-Feige et al., 1993).

- *Gamma*: A number of studies reported changes in the *Gamma* EEG frequency band during various motor activities and muscle recruitment (Herrmann and Mecklinger, 2001; Niedermeyer and da Silva, 2005; Kristeva-Feige et al., 2002). Brodsky et al. (2012b) showed that consumption of stimuli during distraction may alter swallowing activity. Naturally, altered swallowing neural activity may also cause changes in the muscular recruitment involved in performing the swallowing act (Milnik et al., 2013). Therefore, changes in the *Gamma* EEG frequency band during swallowing with the distraction could be attributed to motor changes introduced by compromised attention. In addition, we found significant differences in the *Gamma* frequency band between the swallowing of the various bolus volumes. Alteration of bolus volume influences the kinematics of oral and pharyngeal activity, the upper esophageal sphincter opening, and hyolaryngeal excursion during swallowing, all of which are motor events (Logemann, 2006; Perlman et al., 1993; Massey, 2006). Therefore changes in the *Gamma* frequency band can be attributed to the changes motor activity in response to manipulation of bolus volume that various bolus volumes produce.

- *Limitations of the present study:* A limitation of this study is that the order of consumed stimuli was specified (i.e., 1 ml first, 5 ml second, 10 ml third), as well as the order of conditions (i.e. no-distraction swallowing first, then swallowing with the distraction). In order to overcome this limitation, future studies could randomize the order of the various manipulations of swallowing conditions. Furthermore, future studies could also investigate the influence of distraction on the swallowing of the different stimuli (i.e. nectar-thick apple juice, or solid food).

5 Conclusion

In this study we investigated the differences between the brain networks formed during swallowing of three bolus volumes in a no-distraction condition and during distraction. Swallowing EEG signals were collected from fifteen healthy male adults aged 18 to 35. Each participant performed ten 1 ml swallows, ten 5 ml swallows, and ten 10 ml swallows in both conditions. Our results showed a difference between no-distraction swallowing and swallowing with distraction in all frequency bands of interest (i.e., *Delta*, *Theta*, *Alpha*, *Beta*, and *Gamma*). In addition, our results showed differences in the swallowing of boluses of various volumes in all frequency bands of interest.

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