The Influence of Volition on Breathing–Swallowing Coordination in Healthy Adults

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This research was designed to clarify the role of cortical modulation in the coordination of respiration and swallowing. Time-locked recordings of submental surface electromyography, nasal airflow, and thyroid acoustics were used to evaluate nonnutritive breathing–swallowing coordination (BSC) and swallowing apnea duration (SAD) of 20 healthy adults during 3 conditions. These conditions represented a continuum of volitional through nonvolitional swallowing control on the basis of a decreasing level of cortical activation: voluntarily initiated swallows during wakefulness, nonvolitional awake swallows, and reflexively initiated swallows during sleep. Differing proportions of swallows at the cusps between inspiration and expiration were found between the volitional and nonvolitional conditions, irrespective of the level of arousal. SAD was unaltered by condition. In conclusion, BSC is influenced by degree of volition but not by level of arousal. This implies that cortical influence on BSC is limited to conditions in which swallowing is voluntarily initiated and indirectly implicates the recruitment of the supplementary motor or insular cortices. SAD remained stable across conditions and may therefore be considered relatively impervious to suprabulbar influence.

Keywords: breathing–swallowing coordination, adult, arousal, sleep, volitional motor control

Typically, adult humans exhale before and after swallowing, with an obligatory but brief cessation of respiration during swallowing, referred to as swallowing apnea (Clark, 1920; His, Treole, & Stuart, 2001; Klahn & Perlman, 1999; Martin-Harris et al., 2005; Perlman, Ettema, & Barkmeier, 2000). The precise neural substrates involved in this pattern of breathing–swallowing coordination (BSC) and the duration of swallowing apnea (SAD) are unclear despite these phenomena receiving substantial attention in the literature, BSC may be the result of a complex interaction of multiple subcortical neural networks influenced by descending cortical input. Brainstem contribution to mammalian BSC is well documented (Feroah et al., 2002; Larson, Yajima, & Ko, 1994; Saito, Ezure, & Tanaka, 2002). In addition, preliminary evidence supports a suprabulbar influence on BSC in both animals (Aleksandrova, Aleksandrova, & Bagaev, 2000) and humans (Hadjikoutsis, Pickersgill, Dawson, & Wiles, 2000; Kelly, Huckabee, & Friend, 2006; Nishino & Hiraga, 1991). Furthermore, despite being fundamentally controlled by brainstem central pattern generators (CPGs) (Miller, 1999), both respiration (Davenport & Reep, 1995) and swallowing (Kern, Jaradeh, Arndorfer, & Shaker, 2001) are independently amenable to cortical influence. Therefore, it is likely that BSC, albeit largely brainstem mediated, is influenced by descending cortical input.

Investigating potential suprabulbar influences is difficult for many reasons, including the limitations of current neural imaging techniques, the sharing of the neural substrates of respiration and swallowing, and the ethical and practical limitations of invasive research on humans. However, one way to investigate the presence of suprabulbar influence, particularly the cerebral cortex, on BSC is to compare BSC under volitional and reflexive swallowing conditions, a paradigm originally suggested by Kern et al. (2001) to determine the role of cortical efferent control over swallowing.

Although the volitional versus nonvolitional paradigm is appealing, creating conditions under which truly reflexive swallows can be elicited is challenging. In prior research where “reflexive,” “spontaneous,” or “subconscious” swallowing conditions were evaluated, liquid boluses were administered (e.g., Nishino, Yonzawa, & Honda, 1985) and/or participants were awake (e.g., Shaker et al., 1992). Both of these situations are problematic when trying to elucidate suprabulbar contributions to BSC owing to the potential impact of bolus ingestion (Preiksaitis, Mayrand, Robins, & Diamant, 1992) and cortical influences associated with heightened arousal.
The impact of bolus ingestion is an important consideration given that the cortex is thought to be involved in sensory processing during liquid swallowing (Hiraoka, 2004). When comparing saliva and liquid swallows, an electroencephalogram study demonstrated that “both the cortical process associated with sensory information of pharyngeal swallowing and the cortical preparatory process of pharyngeal swallowing depend on the type of swallowing task” (Hiraoka, 2004, p. 155). Thus, the inclusion of nutritive swallowing should be avoided if efferent cortical control is to be elucidated. Furthermore, when participants are awake, the influence of potential anticipation or oral preparation (and therefore cortical activation) cannot be entirely eliminated. The mere fact that participants are awake inherently implies some degree of cortical activation and especially so when there is no apparent attempt to distract participants from thinking about their swallowing (e.g., Shaker et al., 1992). In order to demonstrate truly valid spontaneous, reflexive, nonvolitional swallowing, research participants should not be awake.

Prior researchers have argued that BSC is dependent on level of arousal (Kelly et al., 2006; Nishino & Hiraga, 1991). However, owing to methodological issues, these studies do not provide conclusive evidence that reduced level of arousal, and therefore cortical activity, influences BSC. For example, Nishino and Hiraga studied patients who were still under general anesthesia postoperatively. Although the cortical and diencephalic input on the respiratory CPG is minimized by anesthesia (Neubauer, Melton, & Edelman, 1990), the effects of anesthesia may not be limited to suprabulbar structures. Thus, it is plausible that the global suppression of brain activity, potentially including brainstem structures, induced by the anesthetic was, at least in part, responsible for the atypical BSC observed by Nishino and Hiraga (1991). For this reason BSC during natural sleep was compared with wakefulness in a recent pilot study (Kelly et al., 2006). During sleep the proportion of swallows preceded by expiration but followed by inspiration was higher and that of swallows preceded and followed by expiration was lower than during wakefulness. Although this pilot study reported decreased variability in BSC during heightened arousal and subsequently heightened cortical activation, the role of the cortex remains speculative given that a bolus was introduced in one condition (wakefulness) and not the other.

The present study provides a much more stringent comparison of BSC between volitional and nonvolitional swallowing conditions than previously adopted (Kelly et al., 2006). Sleep, particularly non-REM sleep, may provide the ultimate condition of relative cortical quiescence relative to wake given the reduction in global cerebral blood flow (see review by Hobson & Pace-Schott, 2002) and, therefore, a condition in which voluntary input executed by the cortex into BSC is eliminated. Further comparison between two nonvolitional swallowing conditions, sleep and spontaneous wake, will identify whether heightened arousal alone is sufficient to alter BSC. Thus, the overall comparison of swallowing during sleep with spontaneous and volitional swallowing during wakefulness provides a continuum of cortical activation on which cortical contributions can emerge. Similarly, the comparison of SAD across the same conditions will also elucidate cortical contribution to SAD.

Method

Participants

Twenty participants were recruited by advertisement following approval by the Canterbury Regional Health Ethics Committee: 5 healthy young men (mean age 28.2 ± 6.1 years), 5 healthy young women (mean age 27.8 ± 5.7 years), 5 healthy older men (mean age 69.6 ± 3.8 years), and 5 healthy older women (mean age 71.6 ± 3.7 years). None of the participants had a medical history of myocardial infarction, breathing disorder, swallowing difficulties, severe head or neck injury, head or neck surgery, sleep disorder, neurological disorder, gastroesophageal reflux disease, paralysis of the diaphragm, chronic fatigue syndrome, or psychiatric disorder (e.g., anxiety, depression). Potential participants who were taking medication that affected their sleep or level of alertness or attention were also excluded.

Participant Tasks

BSC was monitored under three conditions along a continuum of volitional through nonvolitional swallowing.

Volitional wake swallows. A total of 15 volitional saliva swallows on command were performed by each participant. To ensure that body position was comparable to that in the sleep condition, participants were asked to perform 5 swallows in each of three horizontal body positions (in random order): supine, prone, and on either right or left side (chosen according to the side the participant felt he or she would most likely sleep).

Spontaneous wake swallows. Participants performed 20 saliva swallows as they engaged in a handheld computer or brainteaser game while assuming the supine position on a comfortable bed. Because the participants were aware that they were taking part in research on swallowing, the distraction task was used to ensure that spontaneous (naïve) swallows were performed. In addition, to ensure minimal attentional focus on swallowing, this distraction condition was performed prior to the highly volitional swallowing task (described above).

Reflexive sleep swallows. These swallows were performed overnight while participants slept in whatever position they felt most comfortable. The number of sleep swallows varied between participants.

Equipment

BSC and SAD were derived using simultaneous time-locked recordings of three physiological measures (Kelly, Huckabee, Jones, & Frampton, in press). These data were captured by an integrated hardware–software system (Kay Elemetrics Swallowing Workstation; Lincoln Park, NJ) and sampled at 250 Hz.

Submental surface electromyography (SEMG). SEMG measured the muscle activity associated with contraction of the floor of mouth muscles during swallowing. The skin was cleaned using alcohol, and men were required to shave prior to commencement of data collection. Electrolyte gel was applied to 2 cm silver chloride electrodes (Thought Technology Triode; Montreal, Quebec, Canada). The active electrodes were positioned over the collective submental muscle group in midline and between the thyroid cartilage and the mental protuberance of the mandible (Huckabee & Pelletier, 1999). The electrodes remained in situ for
the entire protocol. The submental SEMG signal was amplified, band-pass filtered (50–220 Hz), rectified, and digitized.

Laryngeal microphone. Thyroid acoustics were used to confirm swallowing onset and to rule out submental SEMG artifact. The laryngeal microphone was positioned lateral to the thyroid and taped in position with standard surgical tape. The microphone was a modified omnidirectional condenser microphone with a frequency response of 50–12500 Hz., which was connected to a preamplifier (Mini-Mic Preamp MP13; Rolls Corporation, Salt Lake City, UT).

Nasal cannula. Nasal airflow, using an adult-size nasal cannula, was recorded to determine SAD and the respiratory-phase cycle preceding and following each swallow. Nasal prongs were situated at the entrance to each nostril, affixed to the cheek using surgical tape and secured firmly around the head.

Mercury switch position monitor. In order to determine body position, a position monitor was secured to a soft elasticized band fitted around the chest (Kelly et al., in press). The distinction between four body positions could be made as a result of associated changes in the output voltage: side-lying (left = 1.02 V, right = 0.69 V), upright (1.55 V), supine (0.35 V), and prone (1.33 V). The position monitor was connected to a custom-made sensor box, and the output was fed into the auxiliary channel of the swallowing workstation.

Electroencephalography (EEG). Sleep status was retrospectively confirmed using four-channel EEG (Curcio, Ferrara, Pergianni, Fratello, & De Gennaro, 2004). Eight 9-mm bipolar tin EEG electrodes were secured on the scalp (according to the international 10–20 EEG positioning system): two on the forehead (FP1 and FP2), two over the occipital lobe (O1 and O2), two at central-right position (C4), and two at central-left (C3). The two electrodes at each of the central sites (C3 and C4) were positioned in a rostral–caudal fashion to one another. The EEG montage was bipolar longitudinal (FP1–C3, C3–O1 and FP2–C4, C4–O2). The eight EEG electrodes were connected to Thought Technology EEG Flex/Pro sensors, which were in turn connected to the appropriate channels of the Thought Technology Procomp Infiniti EEG sensor box. Each EEG channel was sampled at 250 Hz and data stored on an external hard drive. The EEG data were viewed using a band-pass (Butterworth) IIR filter with a bandwidth of 0.5–40 Hz. Initiation of data acquisition of the EEG signals and the swallowing workstation was synchronized manually.

Data Analysis

All swallows (represented by simultaneous bursts of thyroid acoustics and SEMG activity in the absence of nasal airflow) were assigned to one of four respiratory-phase categories based on the phase of respiration preceding and following the swallowing apnea (SA): inspiration–SA–inspiration (II), inspiration–SA–expiration (IE), expiration–SA–expiration (EE), and expiration–SA–inspiration (EI). SAD was measured manually for all swallows using the computer cursor.

The timing of the onset of swallow-related SEMG activity was identified for all sleep swallows. The onset was defined as the time at which the SEMG tracing first increased above 3 μV immediately preceding the swallow-related SEMG peak. The sleep status in the 20 s prior to the SEMG onset was determined according to conventional sleep staging (Rechtschaffen & Kales, 1968). In this way, any movement artifact on the EEG signal generated by the swallow was excluded for sleep staging. Given that there is reactivation of various prefrontal areas during REM sleep (see review by Muzur, Pace-Schott, & Hobson, 2002), only those swallows preceded by non-REM EEG activity were used for further analysis.

Inter- and Intrarater and Statistical Analyses

The 20-s EEG epochs preceding the sleep swallows of 4 participants, one from each age and gender group, selected at random (approximately 20% of epochs), were rescoring by the primary rater and an expert in interpretation of EEG (Grant J. Carroll). Similarly, the swallows of another 4 participants, one from each age and gender group, selected at random (approximately 20% of all swallows), were reanalyzed in terms of respiratory-phase categorization (BSC) and SAD values by the primary rater and an independent rater. These two measures and the EEG epoch scores were then submitted separately to intraclass correlation testing to assess intra- and interrater reliability for each measure.

Repeated measures analysis of variance (ANOVA) was used to determine the condition effect on the proportional distribution of swallows in the four respiratory-phase categories (BSC). Respiratory-phase category and condition were entered as within-subject effects, and age and gender as between-subjects factors. Similarly, separate repeated measures ANOVAs were performed on SAD values. Condition was entered as a within-subject effect, and age and gender as between-subjects factors. The sphericity assumption for all repeated measures ANOVAs was tested using Mauchly’s test (Mauchly, 1940), and the Greenhouse–Geisser assumption for all repeated measures ANOVAs was tested using Mauchly’s test (Mauchly, 1940), and the Greenhouse–Geisser corrections were applied accordingly. Significant main or interaction effects were further explored using Fisher’s least significant difference (LSD) tests.

Results

A total of 1,047 swallows (300 volitional, 400 spontaneous, and 347 sleep swallows) were recorded and analyzed. Intraclass correlation coefficients demonstrated satisfactory inter- and intrarater reliability for sleep staging ($r = .821$ and $r = .889$, respectively), swallow categorization ($r = .988$ and $r = .996$, respectively), and SAD ($r = .967$ and $r = .951$, respectively).

BSC

Repeated measures ANOVA revealed a respiratory-phase category effect, $F(1.40, 22.5) = 64.1, p < .001$. LSD calculations revealed that the proportional distribution of EE swallows was higher ($M = 58.6\%$) than any other respiratory-phase category ($II = 2.6\%, IE = 15.9\%,$ and $EI = 22.9\%$), as depicted in Figure 1.

The repeated measures ANOVA also revealed an interaction between respiratory-phase category and condition, $F(3.39, 54.2) = 3.02, p = .032$. LSD testing revealed that volitional and nonvolitional swallowing conditions differed in terms of the proportional distribution of swallows in the four respiratory-phase categories (see Figure 2). Specifically, there was a greater proportion of IE swallows in the volitional than in the spontaneous wake condition. There was also a smaller proportion of EI swallows in the volitional condition compared with spontaneous wake and sleep conditions. But there were no differences between spontaneous wake...
and sleep conditions. There were no age or gender effects or interactions of any combination thereof.

SAD

Repeated measures ANOVA on SAD showed no condition effect, $F(2, 32) = 2.30, p = .112$, or interaction of condition and age or condition and gender. The overall mean for volitional swallows was 944.2 ms ($SE \pm 59.5$ ms), for spontaneous wake swallows was 802.3 ms ($SE \pm 52.4$ ms), and for sleep swallows was 934.4 ms ($SE \pm 68.8$ ms).

**Discussion**

The key finding of this study is that BSC differs between volitional and nonvolitional swallowing conditions but not between the two nonvolitional conditions (spontaneous wake and sleep). This indicates that BSC is altered by the degree of volitional input into swallowing but not level of arousal. This, in turn, provides strong support for the presence of descending cortical control of BSC, which needs to be confirmed via functional neuroimaging studies. In contrast, SAD remained consistent across all swallowing conditions, suggesting its relative resistance to suprabulbar influences.

One interpretation of these data is that heightened cortical activity associated with wakefulness alone was insufficient to alter BSC and that only activation of those cortical sites specifically associated with volitional swallowing can influence the brainstem modulation of BSC. Although the present study cannot identify the particular cortical site(s) involved in BSC, it is likely that those sites involved in the initiation or “planning” of volitional swallowing prior to the execution of a swallow are involved in BSC, such as supplementary motor area (SMA) (Huckabee, Deecke, Cannito, Gould, & Mayr, 2003), cingulate cortex (Watanabe, Abe, Ishikawa, Yamada, & Yamane, 2004), insular cortex, and frontal operculum (Dziiewas et al., 2003). These sites may be short listed to include those known to be involved in both swallowing and respiration, such as the insular cortex (Davenport & Reep, 1995; Kern et al., 2001) and the SMA (Colebatch et al., 1991; Huckabee et al., 2003).

It is possible that the relevant cortical sites may influence brainstem CPGs via indirect pathways as both respiration and swallowing also activate subcortical sites such as the basal ganglia (Fink et al., 1996; Mosier & Bereznaya, 2001) and thalamus (Davenport & Reep, 1995; Mosier & Bereznaya, 2001). Given that “the cortex generally acts to inhibit the diencephalic areas that facilitate respiration” (Neubauer et al., 1990, p. 443), it is possible that increased cortical activation during volitional swallowing inhibits the subcortical structures that potentially modulate swallowing and respiratory brainstem CPGs. This may subsequently influence BSC.

Cortical suppression of respiratory activity has been previously suggested. Hadjikoutis et al. (2000) hypothesized that damage to the corticobulbar tract may result in reduced suppression of inspiration, evidenced by a propensity for an increase in postswallow inspiration in patients with damage to this area. This is supported by the results of the present study, which demonstrate an increase in the incidence of one of the postswallow expiration categories (IE) and a suppression of one of the postswallow inspiration categories (EI) in the volitional swallowing condition. Thus, during volitional swallowing the cortex may directly or indirectly inhibit respiratory brainstem CPGs to increase the incidence of postswallow expiration via the pathways described above.

It is important to note that all of the “volitional” swallows in our study were prompted by an external auditory cue and, hence, were definitively volitional. In contrast, studies that elicit voluntary swallows by way of a single introductory cue risk compromising their data by way of occasional subconscious reflexive swallows. This notwithstanding, there is a definite possibility that volitional swallows elicited exogenously (i.e., reactive, as in our study) are not identical to volitional swallows elicited endogenously (i.e., self-timed). A recent study demonstrated a difference in temporal measures of swallowing between two such conditions in normal controls (Daniels, Schroeder, DeGeorge, Corey, & Rosenbek, 2007), and thus this may in turn alter BSC. If so, and if we had included volitional swallows elicited endogenously, we could well have had a different condition effect in our study. This sets the scene for an intriguing new future study.

In general, though, swallowing occurred in midexpiration (58.6%) in all three swallowing conditions. Prior research has also

![Figure 1](image1.png)

**Figure 1.** Proportional distribution (means and standard error scores) of swallows in each respiratory-phase category irrespective of condition. II = inspiration–swallowing apnea (SA)–inspiration; IE = inspiration–SA–expiration; EE = expiration–SA–expiration; EI = expiration–SA–inspiration. *$p < .05$ (determined by Fisher’s least significant difference testing).

![Figure 2](image2.png)

**Figure 2.** Proportional distribution (means and standard error scores) of swallows in each respiratory-phase category for all swallowing conditions. II = inspiration–swallowing apnea (SA)–inspiration; IE = inspiration–SA–expiration; EE = expiration–SA–expiration; EI = expiration–SA–inspiration. *$p < .05$ (determined by Fisher’s least significant difference testing).
found that midexpiration is the preferred respiratory-phase category for nonbolus swallows (Hiss et al., 2001; Preiksaitis et al., 1992). This pattern may be attributed to the temporal patterns of activation of specialized brainstem neurons (Saito, Ezure, Tanaka, & Osawa, 2003). The neurons responsible for depressing expiration are either active or remain quiescent during swallowing, whereas those responsible for facilitating expiration are excited after swallowing but prior to the excitation of inspiratory-related neurons (Saito et al., 2003).

Other researchers have argued that BSC is dependent on level of arousal (Kelly et al., 2006; Nishino & Hiraga, 1991), but under a more stringent experimental design, this was not observed. This, too, may explain the conflict in terms of the age and gender effects on BSC observed in the pilot study (Kelly et al., 2006) that were found in neither the present nor prior investigations (Hiss et al., 2001).

Cortical input into SAD is unlikely, as SAD remained roughly the same for volitional and nonvolitional swallowing conditions. Research comparing SAD between similar conditions in adults also found no change (Kelly et al., 2006). These findings are supported by evidence that the duration of glottic closure is no different for nonbolus volitional, bolus volitional, and reflexive swallows elicited by bolus injection into the pharynx (Shaker et al., 1994). Furthermore, given that SAD did not alter when level of arousal increased despite the dramatic increase in cortical activity during wakefulness compared with non-REM sleep (see review by Hobson & Pace-Schott, 2002), SAD appears impervious to fluctuations in the degree of cortical activity, and therefore, primary brainstem control over SAD is implied.

Clinical Implications

The findings from our study have implications for persons who have suffered some form of cortical damage. In particular, our results suggest that adults with cortical damage, and subsequent diminished volitional control over swallowing, may exhibit aberrant patterns of BSC. Although a direct link between aberrant BSC patterns and aspiration of ingested material into the lungs is suspected but not yet confirmed (Hadjikoutis et al., 2000; Martin-Harris et al., 2005), assessing BSC at bedside may be an additional clinical noninvasive method of determining aspiration risk.

It is possible that older adults are particularly susceptible to the adverse effects of cortical damage on BSC. Cortical inhibition (Peinemann, Lehner, Conrad, & Siebner, 2001) and cognitive inhibition of information processing necessary to achieve focused attention (Milham et al., 2002) reportedly decline with age. Thus, in the event of cortical damage, older adults may be more prone to aberrant patterns of BSC during volitional swallowing than younger adults with the same lesion.

Future Research

Further investigation of the influence of cortical activity on the BSC of patients in a deep coma or patients with isolated but diffuse cortical damage would contribute to the understanding of global cortical modulation of BSC. Furthermore, investigation of the BSC of patients with discrete lesions (e.g., ischemic infarcts) in any of the areas known to be involved in swallowing and breathing, such as the SMA and insular cortex, may identify those sites involved in BSC.

Similarly, investigation of BSC via simultaneous functional MRI and EEG (Ritter & Villringer, 2006) should provide the high spatial and temporal resolution necessary to elucidate both the neural sites and the dynamics involved in cortical components of BSC (e.g., planning, execution, modulation).

Conclusion

In summary, these findings suggest that BSC is influenced by descending/efferent cortical input as evident by its modification educed by volition. More specifically, the absent effect of increased level of arousal suggests that heightened cortical activity associated with wakefulness alone is insufficient to alter BSC and that only the activation of those cortical sites specifically associated with volitional swallowing are influential. On the other hand, SAD was unaffected by condition, suggesting that SAD is most likely a relatively robust brainstem-mediated feature of the integration of breathing and swallowing.

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