It is well known since Magendie in 1825 wrote (cited from Miller, 1982) that swallowing is subdivided into three phases; first one is the oral phase, mostly under voluntary control, second is the pharyngeal phase, a kind of “swallowing reflex”; and third is esophageal phase, involuntary and autonomic. However, oral and pharyngeal phases are firmly related to each other toward the end of oral phases. Therefore, they can be called “oropharyngeal swallowing” or “bucco-pharyngeal swallowing”. It has been recently documented that the cerebral cortex could be involved with the oropharyngeal swallowing as demonstrated by studies using neuroimaging techniques in humans. Animal studies have also shown that there is a network in the brainstem called “central pattern generator” (CPG) where swallowing could be arranged according to the needs.

In daily life, we swallow more than 1000 times; however, this number changes according to different reports. All the swallowing movements during daily life cannot be initiated or triggered by the cerebral cortex, some of them may occur without cortical influences. According to this view, swallows can be classified as two types. One of them is the “voluntary induced swallows” which are very frequent during meal times. While other times, including sleep, we are often unaware of our swallowing. These could be called “spontaneous” or “reflexive” swallows. Probably, a third type of swallowing movement may also exist during some stressful emotional conditions. Spontaneous and emotional swallows are certainly “saliva swallows” and mostly in reflexive nature. It may be speculated that there may be some neural control from limbic and/or extrapyramidal system in saliva swallows. As a matter of fact, the reflexive swallows could also describe some clinical conditions. A normal human fetus can swallow by the 12th gestational week, before the cortical and subcortical structures have developed. It has also been reported that swallowing is still possible in the human anencephalic fetus. Thexton & Crompton 1998; Jean 2001; Miller et al 2003; Peleg and Goldman 1978; Pritchard 1965. Similarly, pharyngeal phase of swallowing without oral phase may also be considered as a reflexive swallow in both human and animals. Furthermore, the activation of the pharyngeal phase of swallowing without subsequent activation of the esophageal phase is reported as a common finding in humans especially during dry swallowing or saliva swallowing throughout daily life and it is called the failed swallow. In humans, failed swallows occur 3-4% of the time during wet swallows and 29-38% of the time during dry swallows.

During voluntary induced swallowing, the cascade of the sequential muscle activation does not essentially change from mouth to esophagus. This is one of the lines for the existence of CPG in human swallowing. This
may mean that after the triggering of the oro-pharyngeal swallowing either in the oral cavity for voluntary swallow or in the pharyngeal spaces for reflexive swallow, orderly and sequentially muscle activation of more than 33 muscle pairs invariably reaches from lip through the esophagus. If we mention again, this sequential muscle activation is a function of the CPG of the swallowing. This pattern of oro-pharyngeal activation has been known since more than fifty years ago in mammals.\[1,19,20,24\]

The overall pattern of electromyographic activity during reflexive swallowing represents the response of the brainstem pattern generator, a purely peripheral sensory input, independent from any descending cerebral influence.\[20\] However, during the swallowing in intact human and in high level animal organisms, it is possible that descending cortical drives and sensory inputs from oropharynx can converge in order to provide a safe and satisfactory swallow. However, the CPG governs not only the timing of motor response of each phase of swallowing, but also controls the timing between the phases of swallowing\[16\] according to the cortical evaluation and the present condition of sensory feedback from the oropharynx. The experimental insufficiency of sensory coding would produce an uncertain evaluation of the human central nervous system. The main role of the oropharyngeal mucosal receptors is to contribute to the initiation of swallowing, but when swallowing is triggered cortically or reflexively the pattern and sequential activity of the swallow is not essentially changed. Thus, the stereotypic movements of the oro-pharyngeal swallowing are also controlled by the CPG of the brainstem like in experimental animal studies.\[3,4,29\] The interneurons at the nucleus tractus solitarius (NTS) (premotor neurons) situated at the medulla oblongata are rather motor generator neurons involved in the triggering, shaping and timing of the sequential and rhythmic swallowing pattern. NTS receives not only peripheral sensory inputs, but also cortical and subcortical descending drives. On the other hand, premotor neurons in and around NTS contain the “switching neurons” which distribute the swallowing output to the various motoneuron pools properly.\[1,29\] Before and during swallowing, the sensory inputs from the oropharynx to the somatosenry cortical areas may be expected in addition to that of the medullary swallowing network for precise information from both the bolus and the position of the oropharynx.\[10–12\] Therefore, the sensory input appears to be vital to the oro-pharyngeal swallowing. Sensory inputs from the oral cavity, especially tonsillar pillar, base of the tongue and oro-pharyngeal mucosa have been proposed to be important for the triggering of swallows.\[1,3,4,27,32–36\]

Unfortunately, neither only cerebral cortex nor oro-pharyngeal input alone have not systematically produced or inhibited human swallowing completely. Important convergence from both motor and sensory inputs on the brainstem swallowing network of CPG must be necessary for the human voluntary swallows. The initiation or triggering of swallowing is probably more complex in human and may be dependent on the type of bolus; single or consecutive swallows, voluntary or reflex induced swallowing. It has been clearly demonstrated that in human the solid foods and liquids reaches the valleculae in advance of swallowing.\[17,38\] The initiation of swallow can be expected from the posterior part of oral cavity to the hypopharynx depending on the different kind of bolus. Recently in consecutive swallow and/or drinking, pharyngeal bolus accumulation of masticated or drinking material has been identified in the valleculae of pharynx.\[10–41\] Thus, the hypopharynx may be a crucial trigger point in the elicitation of the pharyngeal swallow.\[40\]

Beyond the cortical/subcortical drives and sensory input from the oropharynx, the sequential swallows can be controlled mostly by the CPG generating neurons in and around NTS firing a sequential or rhythmic pattern that parallel to the sequential motor pattern of the oro-pharyngeal swallowing.\[1,29,44\] However, we do not know about detail of CPG especially in human. During oro-pharyngeal swallowing, there are two main purposes for human. One of them is that the bolus should be directed to right way by entering into the esophagus. Second main purpose is the protection of the airway against any escape of the bolus or part of it. It has been shown that apart from the CPG generator of swallowing, there are some protective reflexes for swallowing. They do not always take place in the sequential muscle activation of CPG; but, they are ready for any kind of risk of aspiration of oro-pharyngeal swallowing. It is well known that the cough reflex and gag reflex are some kind of protective reflexes. However, there are some other reflexes that could be observed during studies of oro-pharyngeal swallowing and they may be important for the security of airway and the descending direction of the bolus into the esophagus.\[40\] These kind of protective reflexes can be clearly studied by the electrophysiological methods. During pharyngeal phase of swallowing, larynx is closed by the contraction of the adductor muscles of the vocal cord. The thyroartenedoid (TA) muscle of the vocal cord is a laryngeal adductor and its contraction causes laryngeal closure during pulling up larynx and this results in very dense EMG activity of the TA muscle. In the mean time, cricopharyngeal (CP) sphincter is relaxed, opened and closed accordingly during swallow-
Therefore, the refined-protective reflexes could be searched by the needle EMG inserted into the TA and/or CP sphincter muscles. For TA muscle, there can be a protective reflex just before the closure of TA by a very dense EMG activity during water swallowing. The reflex activity just before the swallowing is a protective reflex and may prevent the escape of premature pieces of bolus from intraoral to laryngo-pharyngeal spaces. Thus CPG plus oropharyngeal protective reflexes are synergistically interacted for the safe swallowing.\cite{41}

Previously, the laryngeal closure response to afferent stimulation was studied by electrical stimulation of the internal branch of the superior laryngeal nerve (SLN) in both animals and humans. These protective reflexes were induced by the stimulation of the sensory afferents of SLN.\cite{40–46} However, the repetitive stimulation of the SLN could also produce “fictive swallowing” in experimental animals, but in human SLN stimulation could never evoke any kind of swallowing patterns.\cite{49} It has been demonstrated that when the swallow is initiated, a change in sensitivity of laryngeal afferents may have occurred because of laryngeal mechanoreceptor adaptation to continuous stimulation ongoing in the pharyngeal and laryngeal regions.\cite{50}

In conventional EMG, CP-sphincter has continuous tonic activity,\cite{23,46} but during swallowing the tonic EMG activity of CP-sphincter clearly ceases and sphincter opens with a duration of 400-600 msec for a single 3-5 ml water swallow. What is important is that when the sphincter opens two bursts of EMG activity appear just before and after the EMG pause. Second burst is called rebound burst and occurs just before the EMG-pause. Second burst can not be found in each normal subject, and there-re may be related with protective reflexes. If we make intraoral topical anesthesia, the rebound burst disappears during anesthesia, rebound burst does not change significantly. Therefore, the rebound burst of CP-sphincter and earlier burst of TA of the vocal cord should be some kind of protective reflexes and probably initiated from the intraoral receptors.\cite{45,51,52} The laryngeal and glottic closure (vocal fold) and the upper esophageal sphincter have been investigated by videofluoroscopic manometric and endoscopic methods.\cite{13–16} As mentioned, the laryngeal glottic closure was found in a close temporal relation with the onset of UES opening.\cite{45,57} However, there is some variability in this time relation\cite{45–46} which is associated with the onset and duration of the UES opening and/or glottic closure. However, in this variability in airway closure and UES opening, there is even fine tuned mechanisms between the basic activity of TA muscle and the upper esophageal CP sphincter. Celik Gokyigit et al.\cite{61} demonstrated that three kind of swallowing patterns appeared between two muscles electromyographically. In the first pattern TA muscle EMG excitation is later than the onset of upper esophageal sphincter opening more than 50 msec. This kind of swallow may cause laryngeal penetration especially in neurogenic dysphagia. In the second pattern of swallow, EMG excitation basic activity of TA muscle overlaps with the CP-EMG pause. In the third pattern; the onset of EMG closure of TA muscle is earlier than CP EMG pause more than 50 msec. Third pattern is obviously much more safe because of complete closure of the airway before the bolus reached to the upper esophageal CP sphincter. Indeed, duration of the TA basic EMG activity increases and preceedes or overlaps with CP EMG pause, with an increase of bolus volumes.\cite{61} These observations in normal human subjects are not purely reflexive movements, but the contribution of the cerebral cortex and CPG of the brainstem can not be elucidated.

We did not mention other reflex mechanisms related with respiration and deglutition in this scope of review. However, swallowing mechanism may also modulate both respiratory control and laryngeal responses to sensory stimuli following swallowing act.\cite{49,50,65}

References
29. Jean A, Dallaporta M. Electrophysiological characterization of the swallowing pattern generator in the brainstem. GI Motility Online 2006, DOI: http://dx.doi.org/10.1038/gimo9


Correspondence to: Cumhur Ertekin, MD
Cemal Gürsel Caddesi, No: 422, Yalıboyu Apt., Karsiyaka, İzmir, Turkey
Phone: +90 232 381 32 04 90
e-mail: cumhureretkin@gmail.com
Conflict of interest statement: No conflicts declared.