ABSTRACT

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If using a sweetened citrus tastant (i.e., a chemical that stimulates the taste buds and produces a sense of taste) to coat a pill could make swallowing pills easier, this could have a considerable positive impact on the ability to swallow pills in healthy adults and on those with identified swallowing difficulties who need to take a variety of oral medications. In this study, it was predicted that pills would be cleared from the pharynx more quickly and efficiently if a pill was coated with a tastant. Thus, the following study examined the effect of a pleasant citrus tastant on pill swallowing in healthy individuals (7 male; 17 female) aged 19–49 years (M = 27.83 years). Durational measures of swallowing were obtained from real-time ultrasound images of the oropharyngeal swallow. It was hypothesized that swallow durations would be shortest for citrus-coated tablets, followed by water swallows and then plain pills. Although results from statistical analyses did not support a quicker oropharyngeal swallow for one stimulus over another, rationale for lack of significant findings, such as a ceiling effect for healthy pill swallowing, are provided.

THE EFFECT OF A CITRUS TASTANT ON PILL SWALLOWING

By

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Dedication

To those I have helped and will help, through passion, compassion, and creativity.

To Birds, who always told me to follow my bliss.

To Ian, my husband and best friend, who is a constant source of inspiration and encouragement and who I love beyond all words.

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Introduction

The purpose of swallowing food and liquid is more than just to assuage hunger and satisfy the need to rid the mouth of excess secretions. Swallowing consistently takes place in social interactions as people gather around the table and discuss the day's events. Joyous occasions, such as weddings and birthdays, would be mundane and bland without opportunities to swallow, and sad occasions would lose their sense of comfort. We swallow to live but most people also live to swallow as chefs spend years in culinary institutes to make what is nutritious also full of flavor. What we place in our mouths is not only about survival but it is also about taste and activating our tongue's taste receptors in positive ways so that we would want to continue to consume the same substances. The act of swallowing is critical to remaining in good health, especially as people age and find themselves having to take more and more pills. These compact transporters of nutrients and carefully manufactured chemicals are most often unflavored and can be large. As a result, swallowing tablets can be a challenge, albeit an often necessary one. For that reason, the following study is intended to determine if adding a tastant (i.e., a chemical that stimulates the taste buds and produces a sense of taste) to a pill can facilitate swallowing ability or make swallowing easier.

Introduction to Swallowing

The act of swallowing in healthy individuals is commonly taken for granted. Humans place food in their mouths, chew, and swallow without much thought regarding the underlying processes and movements that are responsible for the physical act of

swallowing. However, there are 25 pairs of muscles in the mouth, pharynx (throat), larynx (voice box), and esophagus actively involved in the four-stage process of swallowing (Kendall, 2008).

The *preparatory stage*, the only stage of swallowing in which action is almost completely voluntary, occurs exclusively in the oral cavity. It is in this stage that food is tasted and either accepted by the individual for ingestion, thus initiating the entire process of the swallow, or rejected as a noxious substance and expectorated. The bolus, a mass of food particles, is positioned and moved by the tongue between each row of teeth for mastication (responsible muscles: temporalis, masseter, and medial and lateral pterygoid). It is mixed with saliva to dilute the bolus to a consistency adequate for swallowing and to lubricate the bolus to ease transfer from the mouth to the esophagus. The buccinator muscle within the cheeks prevents residue from accumulating within the buccal cavity, a space between the gums and the cheek. Anterior bolus loss, or spillage of the bolus from the front of the mouth, is inhibited by the sphincteric action of the orbicularis oris muscle surrounding the lips, while premature bolus spillage into the pharynx is prevented through elevation of the posterior portion of the tongue against the soft palate (Ardran 1951; Groher, 1997; Kendall, 2008; Logemann, 1998).

During the *oral stage*, the bolus is propelled from the oral cavity to the pharynx. To initiate motion and propulsion, the surface of the tongue contacts the alveolar ridge immediately behind the teeth. As the soft palate elevates through contraction of the levator palati muscle, the posterior tongue depresses through action of the hyoglossus and styloglossus muscles, thereby forming an opening to the pharynx. As the surface of the tongue applies pressure to the alveolar ridge and anterior portion of the hard palate

immediately behind it in a series of rapid motions, the bolus makes its way toward the back of the oral cavity on the dorsum (i.e., back) of the tongue. In the meantime, the soft palate contacts the posterior pharyngeal wall to close off the nasopharynx (nasal passageway) from bolus penetration; additional protection of the nasopharynx is provided by constriction of the side walls of the nasopharynx. The hyoid bone, located above the laryngeal structures, begins to elevate and move forward as the mylohyoid and geniohyoid muscles at the base of the tongue contract to start the pharyngeal swallow.

The *pharyngeal stage* involves passage of the bolus through the pharynx and into the esophagus. The mandibular muscles, which include the medial and lateral pterygoid, masseter, and temporalis muscles stabilize the tongue base as the bolus is moved in a posterior direction by the tongue's piston-like actions (Kendall, 2008; Logemann 1998). The pharynx elevates through contraction of the palatopharyngeus muscles and the pharyngeal walls stiffen, beginning a descending stripping wave. The pressure produced by actions of the tongue and pharyngeal walls in a closed cavity moves the bolus back while the suprahyoid muscles pull the hyoid and the attached larynx (hyolaryngeal complex) in an anterior and superior direction. The hypopharyngeal chamber expands which causes a decrease in pressure in the pharyngoesophageal segment, making it possible—in concert with the tongue's piston-like action against the superior and middle pharyngeal constrictor muscles—for the bolus to make its way through the pharynx and into the upper esophagus (Groher, 1997). As the hyoid and larynx elevate, the thyrohyoid muscles contract, the intrinsic laryngeal muscles aid to partially close the vocal folds, and the epiglottis lowers over the laryngeal opening to help prevent aspiration (i.e., entrance of foreign particles into the airway below the level of the vocal folds). Breathing is

stopped for a centisecond. At the entrance of the esophagus, the upper esophageal sphincter, which is normally closed through contraction of the cricopharyngeus muscle, relaxes and opens. Hyolaryngeal elevation aids in creating a traction force to open the upper esophageal sphincter at the entrance to the esophagus (Logemann, 1998). The bolus can now enter the esophagus. The force of pharyngeal contractions will move the bolus from the level of the glottic opening once the bolus is in the pharyngoesophageal segment (Kendall, 2008). The velum, hyoid, and epiglottis will return to their original resting state and the larynx will open for respiratory duties once again.

In the *esophageal stage*, the bolus moves through the esophagus and reaches the stomach through a peristaltic wave ranging in speed and intensity; smooth and striated muscles of the esophagus contract in a coordinated fashion (Kendall, 2008, Logemann, 1998). Contraction of the smooth muscles is controlled by motor nuclei in the brainstem and contraction of the striated muscles is controlled by the autonomic nervous system. At the bottom of the esophagus, the lower esophageal sphincter, which is normally contracted, is relaxed during swallowing so that the bolus can be transferred into the stomach. Secondary and tertiary esophageal peristalsis may occur when primary peristalsis fails to get the bolus completely down the esophagus. Secondary peristalsis occurs when receptors sense distension of the esophageal lumen. Only the smooth muscles of the esophagus are active in tertiary peristalsis (Kendall, 2008).

Taste

Taste receptors, which are composed of modified epithelial cells that regenerate every 7–10 days, are responsible for the ability to taste a substance (Cowart, 1988).

Although they are found primarily in the papillae, or taste buds, of the tongue, they are also present throughout the oral cavity on the soft and hard palate, pharynx, larynx, epiglottis, and upper esophagus. It is uncertain if taste receptors in these latter locations possess the same perception qualities as those on the tongue, although they have been found to perceive nonsaline chemicals (Bradley, 2000; Pritchard, 1991).

Within each taste receptor is a taste cell. When a tastant combines with saliva, this novel mixture enters through the receptor's taste pore to produce taste perception. Although specified regions of the tongue perceive taste qualities with more intensity than other areas of the tongue, all areas of the tongue can perceive all taste qualities (Collings, 1974; Pelletier, 2007). Thus, the notion that sensation for sweet is found at the anterior portion of the tongue, salty at the antero-lateral sides of the tongue, sour at the mid-lateral sides of the tongue, and bitter at the posterior portion of the tongue is simply a myth. Umami, a fifth taste receptor that perceives flavor elicited from glutamate as found in meat, milk, and fish, was discovered in 2000 (de Araujo, Kringelbach, Rolls, & Hobden, 2003).

A total of four types of papillae are innervated by different cranial nerves to allow for the perception of taste: fungiform, foliate, circumvillate, and filiform. *Fungiform papillae* comprise approximately 24% of all lingual taste buds in their location along the anterior portion of the tongue (Pelletier, 2007). While 25% of fungiform papillae are innervated by the chorda tympani, a branch of the facial nerve (CN VII), the other 75% is innervated by the trigeminal nerve (CN V). Found on the mid-posterior portion of the tongue, *foliate papillae* comprise approximately 28% of the tongue's total taste buds. Innervation is derived from both the glossopharyngeal nerve (CN IX) as well as the

chorda tympani branch of the facial nerve (CN VII). *Circumvillate papillae* can be found in a V-shaped formation on the dorsal posterior portion of the tongue. Although there are typically 8–12 of these papillae on the tongue, they house they greatest number of taste buds—approximately 48%—and are innervated exclusively by the glossopharyngeal nerve (CN IX). *Filiform papillae* are the most plentiful of all papillae; however, these structures located along the dorsal portion of the tongue are the only papillae that do not contain taste buds; they are responsible for lingual tactile perception (Pelletier, 2007). With regards to nonlingual taste receptors, the small collection that is found on the soft palate is innervated by the greater petrosal branch of the facial nerve (CN VII). Although not consistently found on the velum, fungiform papillae in this location have been found to perceive salt.

Although there appears to be little change in the number of taste receptors from birth to middle age, the number of circumvillate and foliate papillae has been demonstrated to decrease in the elderly (Cowart, 1981). In addition, salivary flow reduction, development of thicker saliva, degeneration of papillae, and loss of keratinized cells which provide protection to tissues of the oral cavity can be attributed to changes in gustatory sensation (Cowart, 1981).

Taste Development

Limited evidence has been found regarding taste preferences in the fetus (DeSnoo, 1937; Liley, 1972), which has been shown to develop specialized taste cells between the 7th and 8th weeks of gestation and mature taste buds between the 13th and 15th weeks (Bradley, 1967). The fetus is consistently exposed to a changing environment

as fetal receptors make contact with ingested amniotic fluid. In addition, taste receptors may be stimulated by secretions within the fetal salivary system (Weiffenbach, Daniel, & Cowart, 1980).

There are more data detailing a significant role for taste preferences in the regulation of food intake in the newborn. Infants' diets consist primarily of formula or milk. However, infants emerge from the womb with more sophisticated preferences and taste detection ability than may be expected. Infant facial expression has provided information that infants are able to differentiate sour and bitter from each other and from salt, and are able to discriminate sweet as opposed to non-sweet tastes (Rosenstein & Oster, 1988; Steiner, 1973, 1979; Steiner, Glaser, Hawilo, & Berridge, 2001). In particular, a small (n = 12) study carried out by Rosenstein & Oster (1988) found that 2-hour-old newborns with no previous experience with tastants responded to sucrose with facial relaxation and sucking. Infants reacted to sour, bitter, and salty solutions by, for example, similarly wrinkling their noses and lowering and raising their brows in the upper- and mid-facial regions. However, reactions differed in the lower-facial region with infants displaying lip pursing in response to sour solutions and mouth gaping in response to bitter solutions. Differentiating facial expressions in the lower-facial region were absent for salty solutions.

As is employed in the discrimination of visual stimuli, infant sucking patterns have been used reliably to provide evidence of taste preference. Crook (1978) found that infants' sucking patterns were reliably lengthened when provided .4 M (molar solution) of sucrose and shortened when given .1 M, .3 M, or .6 M sodium chloride during a pause in sucking. Newborns between 1 and 3 days old have been found to exert increased

sucking pressure in the anterior portion of the tongue in response to increases in the sweetness of a solution, seen as facilitating ingestion; disruption of sucking and increases in posterior tongue pressure have been found to occur in response to quinine hydrochloride and sodium hydrochloride solutions (Nowlis, 1977; Nowlis & Kessen, 1976). Additional studies have reported differing levels of heart rate and respiration (Crook & Lipsitt, 1976), and lateral tongue movements (Weiffenbach, 1977) for different tastes.

A combination of genetic and environmental influences is considered responsible for newborns' preference for sweet substances and aversion to bitter and sour substances (Bartoshuk, 1990; Birch, 1999; Cowart, 1981). At a rudimentary level, parents provide infants with genes. As a result, they pass on genetic predispositions that promote the ingestion of substances containing nutrients required for growth and survival (Birch, 1999). In turn, taste aversions may be the result of years of genetic adaptation, thereby explaining infants' aversion to bitter tastes; poisons are typically bitter (Cowart, 1981; Rosenstein & Oster, 1988). Preference for specific tastes is also the result of an infant's exposure to the taste. For example, Crystal and Bernstein (1995, 1998) found that infants whose mothers experienced moderate-to-severe vomiting during pregnancy show preference for the taste of salt. In addition, children will only eat those foods to which they are exposed by their caretakers. This, for example, explains infants' growing preference for salty foods between 3 and 6 months since this is the period of time in which most infants are weaned from sweet formula and are exposed to salty foods (Harris & Booth, 1987; Schwartz, Issanchou, & Nicklaus, 2009).

Sour Preference

Sour stimuli produce secretion of the largest amount of saliva of all taste stimuli (i.e., sour, sweet, bitter, salty, umami). The amount of saliva produced affects ability to perceive sour taste in adults since perception is largely related to salivary flow rates in addition to salivary pH. Sourness is a reflection of a substance's acidity, or pH. When a sour taste, which is elicited by weak acids and is associated with the presence of hydrogen, is introduced to the taste receptors, salivation increases in response. As a result, the bicarbonate concentrations, which serve as a buffer for the perception of sour by influencing the availability of hydrogen, increase with salivary pH in an attempt to bring the pH to a homeostatic level. Therefore, the intensity of sour perception is diminished due to the increases in salivary pH (Spielman, 1990). Those with higher salivary flow rates have been found to possess higher sour-taste thresholds than those with low salivary flow rates (Norris, Noble, & Pangborn, 1984). Thus, adults who possess high salivary flow rates and pH will consistently rate sour stimuli as more intense than those with lower salivary flow rates and pH (Norris et al., 1984). Despite the depth of information found regarding adults' perception of sour taste, data regarding the mechanics of sour perception in infants and children are less clear-cut.

Research suggests that preference for sour solutions intensifies beyond early infancy. Whereas older infants (aged 2–24 months) have demonstrated decreased ingestion of sweet solutions when citric acid is added (Vazquez, Pearson, & Beauchamp, 1982), 23% of 15- to 20-month-old infants (Blossfeld et al., 2007) and 35% of 5- to 9-year-old children (Liem & Mennella, 2003) have been found to show preference for extremely sour fruit juice. Some research has suggested that the sour preferences

demonstrated by young children are related to a growing desire to seek thrills and explore the world in addition to a willingness to try unfamiliar foods (Liem & Mennella, 2003; Liem et al., 2004; Urbick, 2000). In addition, a moderately-sized study conducted via questionnaire consisting of 50 children suggested that the more citric acid within a sucrose solution that 8- to 11-year-old boys reported to prefer was related to a greater amount of fruit they reported to consume (Liem, Bogers, Dagnelie, & de Graaf, 2006). This finding suggests that acceptance of sour taste could be related to children's acceptance of fruit.

Research with young adults has provided the bulk of information regarding how taste preferences change with age. Although taste preferences typically vary by individual depending on concentration of stimulant, in general, adults regard sour tastes as negative, along with strongly salty and bitter tastes, while considering sweet and mildly salty tastes as pleasant (Moskowitz, Kumaraiah, Sharma, Jacobs, & Sharma, 1976). While increasing concentrations of sweet may enhance the pleasantness of a substance, at no point does increasing concentration of sour or bitter stimuli heighten rating of pleasantness (Moskowitz et al., 1976).

Few studies have been conducted regarding taste preferences in older adults. However, there is research to support that an age-related decline in preference for sweet substances, especially in females, exists. Enns, Van Itallie, and Grinker (1979) revealed that, when sweetness preference is assessed via hedonic scaling and paired comparison techniques using standard solutions of sucrose (.056–1 M), older adults' (M = 71.1 years) sweet preferences are relatively similar to those of children (M = 10.6 years) and young adults (M = 18.7 years). However, the older female adults reported liking the stronger

sucrose solutions less than the other groups evaluated. Similarly, Laird and Breen (1939) found that, when rating five gradations of juice sweetness, older female adults preferred pineapple juice that was less sweetened, in comparison to the preferences of any other group investigated (i.e., participants aged 18–40 years and 50–68 years).

Olfaction

Although taste is primarily discussed when referring to sensory experiences exhibited while eating, olfaction, or the sensation of smelling, must be elicited in combination with taste to produce flavor. Perceptions derived from taste (gustation), smell (olfaction), and chemical chemesthesis (chemical irritation) combine within the oral cavity to produce a sense of flavor (Bartoshuk, 1990). Olfactory receptors are located at the top of the nasal cavity, under the eyes. When the sensation of a food with a strong smell, such as onions, is inhaled via the nostrils, tactile receptors along the inside of the nose are stimulated to the point that it is possible to directly sense the pungent odor's path to the olfactory receptors. However, when eating less volatile foods, odors make their way from the mouth to the nasal cavity where the olfactory receptors pick them up. Localization cues to specific receptors are absent for food odors when eating. Therefore, the entire experience of eating is localized to the mouth which receives the tangible, tactile input (Bartoshuk, 1990).

The foods people ingest are driven by olfaction after a holistic connection is made cognitively between the smell of a food and what happens when it is tasted and, subsequently, consumed. It is only after the olfactory characteristics of a food are processed that taste cues, in addition to textural cues, are factored into the sensory

experience used to identify a food (Bartoshuk, 1990). Most vitamins within foods are present in small amounts and are not perceived at either the olfactory or taste levels. However, when vitamins are present in concentrated tablet form, olfaction and taste can combine to produce a flavor that may not be considered pleasant to swallow.

Swallowing Pills and Medications

It can be assumed that most healthy individuals pay little-to-no attention to the actions involved when swallowing, nor are they actively aware of the physical actions that make the process possible. Swallowing is an innate action performed in the healthy, normally-developing fetus as early as the 12th week of gestation and is present at birth (Humphrey, 1970). Swallowing, although partially under volitional control in the preparatory and oral stages, is not under volitional control in the pharyngeal and esophageal stages. Therefore, perhaps the only instances in which some of the small but essential actions involved in swallowing are actively perceived are when a piece of food or liquid enters the trachea and the person must cough to expectorate the particle to avoid blocking the airway, and when a person has to swallow a pill. In the preparatory stage of swallowing, a person grinds a bolus to a certain consistency and size so that it can be easily swallowed (Kendall, 2008; Logemann, 2008). On the other hand, pill swallowing requires a person to swallow whole a substance of a set texture (typically solid) and set size without the luxury of being able to chew it to a comfortable consistency. To obviate choking, a person must ensure that the tablet is in a comfortable position in the mouth (i.e., in the back of the mouth where a bolus is typically positioned right before the swallow reflex occurs), using water or other lubricants (e.g., applesauce) to force the pill

down. Because very few people go through life without being prescribed medication or taking vitamins, being able to successfully swallow tablets is a critical life skill.

Medications are prescribed for individuals in order to cure illness, help them feel better or allow their bodies to function better. However, if medication regimens are not adhered to because of problems with swallowing tablets, an individual may face a higher incidence of morbidity and mortality—especially if one possesses a swallowing disorder, or dysphagia (Carnaby-Mann & Crary, 2005). Even in healthy individuals, problems swallowing tablets are quite commonly reported. A questionnaire conducted by general practitioners in Norway found that 1 out of 3 women and 1 out of 6 men have issues swallowing tablets (Andersen, Zweidorff, Hjelde, & Rødland, 1995). Moreover, a national survey conducted in 2000 indicated that 40% of adults have problems swallowing pills, prompting 14% to delay taking a dose of their medication and 8% to completely skip taking a dose (DeRoche, Macclaren, & Sonies, 2000). Size of a pill has been determined as the most important inhibiting factor—as opposed to shape, coating, or surface area—in clearing a pill through to the esophagus. Not surprisingly, large-sized pills have been determined as more difficult and less comfortable to swallow than smaller ones (Channer & Vijee, 1986; Overgaard, Hojsted, Hansen, Moller-Sonnergaard, & Christrup, 2001).

In an attempt to make pills more conducive to swallowing, health practitioners often advise patients to alter solid doses through crushing or opening up capsules and mixing them in such substances as applesauce or pudding. Instead of swallowing pills with water, juice is sometimes used. Within healthcare settings, nurse practitioners often feel pressured to deliver medication to patients in a timely manner. However, this task

becomes a challenge when delivering medication to those who are either bereft of the mental capacity to consent to medication administration, expectorate their medication, or simply refuse to take pills (Stubbs, Haw, & Dickens, 2008). When working with such patients, surreptitious administration is not uncommon, especially if alternate modes of medicine administration (i.e., transdermal, parental/injectable, buccal, rectal, intranasal, or sublingual) are unavailable. However, pharmaceutical manufacturers are typically purposeful in how they develop and market medication; pills are placed in a form that allows for proper absorption in the gastrointestinal tract in the correct anatomic area (e.g., esophagus, stomach, intestine) and ensures that the medication releases active agents at the correct rate (Stubbs et al., 2008). Not only does alteration of certain medication doses decrease medication efficacy and cause it to be unpalatable, but alteration of medication doses can also quickly increase a medication's toxicity, reduce chemical stability of a medication (e.g., as in amlodipine, isosorbide, mononitrate, dinitrate, atorvastatin, topiramate, cabergoline, pergolide), produce physiochemical drug-drug interactions, or—in the case of steroids, hormones, and cytotoxins—even cause harm to the administrator handling the medication from exposure (Griffith & Tengnah, 2007; Stubbs et al., 2008; Wright et al., 2006). Further, crushing of tablets can cause cross-contamination with other medications when mortar and pestles or pill crushers are not cleaned out, and some of the tablet can be lost in the crushing device, inhibiting the patient from receiving the full dose. In addition, if medication is added to a food substance, it is highly possible that the patient will receive a smaller dose of the medication if the patient does not consume the entire food portion (Stubbs et al., 2008). Data reported from the UK Patient Safety Agency between 2005 and 2006 indicated that modified-release opiate tablets and

cytotoxics were the medications most commonly altered in medication-related incidents (Stubbs et al., 2008). A review conducted by Stubbs et al. (2008) found that, out of 266 instances of dosing modification, 4.5% were of medications that pharmaceutical manufacturers specifically indicated should not be crushed or opened. Those medications most frequently altered were those targeting the central nervous system (55.6%), followed by cardiovascular (22.6%), endocrine (10.9%), musculoskeletal (3.4%), gastrointestinal (3.4%), and respiratory (0.4%) system medications, as well as antibacterial medications (3.8%). Problems with the organ systems these medications target are frequently cited as causes of dysphagia.

Another method of easing pill swallowing is to split tablets where they are scored and take each half separately. A study investigating patients' rationales for subdividing tablets indicates that, of the 30% of medications (275 prescriptions) divided upon the initiative of patients themselves, 13% were split to make pills easier to swallow (Rodenhuis, De Smet, & Barends, 2004). Medications that can be broken without compromising drug safety or effectiveness are commonly scored. However, a small research study conducted in the Netherlands via patient questionnaire of 140 medications has indicated that not all scored tablets are easy to break, and many break unevenly (Rodenhuis, De Smet, & Barends, 2003). These complaints were reported for 15% and 28% of prescriptions, respectively. At times, these issues result in loss of a portion of a tablet and, consequently, the medication's potency if a medication's therapeutic range is narrow. Although pill splitters provide a mechanical means of breaking a tablet and ease any difficulty experienced from breaking a tablet by hand, they have not been found to accurately split pills into equal halves (Van Santen, Barends, & Frijlink, 2002). Negative

experiences with pill administration could give rise to poor compliance with medication regimen.

Medication acceptance is a common issue, especially with adolescents and children. Negative attitude toward wanting to swallow pills has been found to play a role in medication non-acceptance (Hansen, Tulinius, & Hansen, 2008); however, reports from healthcare practitioners and parents have indicated that poor medication acceptance can primarily be attributed to problems with swallowing pills due to size and taste aversion (Hansen, Tulinius, & Hansen, 2008; Jahnsen & Thorn, 1987). Many pills are oral administration only and, although no data exist detailing if children are less resistant to medication in liquid suspension, there is less medication available in liquid form than in tablet form. In addition, as a child grows, it becomes more difficult to provide necessary doses in liquid suspension (Polaha, Dalton, & Lancaster, 2008). Therefore, learning how to tolerate swallowing pills is largely unavoidable.

A large (n = 304) study requiring parents of children and adolescents aged 0–26 years to complete a mailed survey found that, although medication refusal is more common in adolescents who are chronically ill and required to swallow more pills than those who are healthier, those ill adolescents evidence better pill swallowing abilities than those adolescents who are healthier and swallow fewer pills (Polaha, Dalton, & Lancaster, 2008). Perhaps as a result of necessity and increased practice, there is some evidence that individuals' difficulties swallowing tablets diminish with age (Andersen, Zweidorff, Hjelde, & Rødland, 1995).

Antibiotics such as clarithromycin or sparfloxacin, medications containing alkaloids, such as quinine or berberine, and the antipyretic acetaminophen are bitter in

taste (Suzuki et al., 2003). To mask the unpleasant taste, medications have been chemically modified, coated with polymers, microencapsulated, or placed in capsules. However, in order to prepare medications that require a large amount of active substance in one dose, the pills must often be manufactured in bulky, large forms which, as discussed, pose another pill swallowing complication (Suzuki et al., 2003). Because it is critical that older adults ingest medications without difficulty, in addition to pill size, pill taste must be taken into account when considering type of medication prescribed and compliance with a successful medication regimen.

Effects of Temperature and Tastants on Swallowing

Many attempts have been made to change the characteristics of a bolus in order to improve swallowing function in patients with dysphagia. In particular, introducing a cold bolus to the swallow system has been found to aid in triggering the pharyngeal swallow (Bisch, Logemann, Rademaker, Kahrilas, & Lazarus, 1994; Miyoka et al., 2006). Furthermore, increasing the size of a bolus has been found to extend the duration of upper esophageal sphincter opening and protective airway closure as well as contribute to posterior movement of the tongue base and pharyngeal wall contraction (Bisch et al., 1994; Hiss, Strauss, Treole, & Stuart, 2004). Taste, which is a powerful sensory stimulus, has also been used to facilitate swallowing. Specifically, ingesting a sour bolus has been demonstrated to reduce swallow onset time, oral transit time, pharyngeal transit time, and increase the efficiency of the oropharyngeal swallow in individuals with dysphagia, in addition to contributing to reduced levels of aspiration (Logemann et al., 1995; Sciortino, Liss, Case, Gerritsen, & Katz, 2003).

Given that sensory loss is a significant factor in the manifestation of dysphagia—especially in individuals post-stroke—it would seem logical to increase sensory input to compensate for the deficiency. Sour is one of the strongest tastes an individual can experience. Sensed primarily by receptors on the sides of the tongue as well as a large number of additional oral receptors, the sensation of sour taste travels to the nucleus tractus solitarius of the brain's medulla via the facial nerve, the chorda tympani, and the otic ganglion. Once in the nucleus tractus solitarius, second-order relay neurons contact neurons in the pons which contact the lateral hypothalamus, amygdala, and thalamus, which contain fibers that have connections to the sensory cortex. Strongly-flavored sour taste increases receptor response, thus increasing stimulation to the nervous system and cortical swallowing centers and sending a clear and robust signal that a swallow is imminent (Logemann et al., 1995). As a result of this taste stimulation, the threshold required to trigger a pharyngeal swallow is effectively lowered making the swallow more efficient.

The seminal study in support of the use of sour bolus in swallowing was conducted by Logemann et al. (1995). Nineteen individuals who had suffered a stroke (M = 64 years) and 8 individuals who had experienced other neurogenic etiologies such as closed head injury, multiple sclerosis, AIDS, brain tumor, and anoxia (M = 38.5 years) were included. Each participant experienced a delayed onset in the oral stage of swallowing and/or a delay in triggering of the pharyngeal stage. Participants were asked to swallow 3 boluses each of 1mL and 3mL liquid barium and then 3 boluses each of 1mL and 3mL 50% Real Lemon Juice with 50% liquid barium while undergoing videofluoroscopy. Both groups of participants demonstrated a significant improvement in

onset of oral swallow when given the sour bolus. Improvements in reduced oral transit time and pharyngeal transit time, and improved oropharyngeal swallow efficiency were also seen, all of which facilitate a safer swallow and reduce the risk of aspiration. Those participants who had experienced stroke demonstrated significantly reduced pharyngeal swallow delay time, while those participants who had other neurogenic deficits demonstrated significantly reduced aspiration. Although participants uniformly reported the sour bolus as not pleasant, they found it to be tolerable. Pelletier (2007) explained that citric acid inherent in the use of lemon was responsible for producing the sensation of sour in this study's participants. The high dose of citric acid may have stimulated chemesthesis. This sensation has been demonstrated in other stimulants—such as carbonation (Bulow, 2003)—to reduce penetration, aspiration, and oral transit times, as well as decrease retention of a bolus. Logemann et al. (1995) explained that the sour bolus could contribute to increased salivation which, in turn, increases bolus volume. Research supports that increased bolus volume to 5mL reduces oral transit time and pharyngeal delay time, thus supporting its use for patients with dysphagia (Bisch et al. 1994).

Pelletier and Dhanaraj (2006) conducted a study in which 10 healthy individuals (M = 25.5 years) were delivered a total of 11 taste stimuli, including citric acid monohydrate and barium sulfate-citric acid. In a randomized order, participants were given each 10mL stimulus in both moderate and high concentrations. Participants rinsed their mouths with water between trials to ensure that previous tastes were not perceived. Peak amplitude and duration of each swallow were analyzed and participants were asked to rate each sample for palatability. Peak lingual pressures for the moderate

concentrations of citric acid monohydrate and barium sulfate-citric acid were significantly higher than water, despite the fact that the high barium sulfate-citric acid stimuli were rated the least palatable of all of the stimuli. This finding is important in support of citric acid stimuli since the amount of lingual pressure generated when the tongue presses against the hard palate is important to propel the bolus to the back of the oral cavity and elicit a safe swallow. Although healthy older individuals are typically able to create enough lingual pressure when swallowing, those who are less healthy may have decreased pressure reserve and may not generate enough lingual pressure, thereby placing them at higher risk for aspiration (Robbins, Levine, Wood, Roecker, & Luschei, 1995). Thus, added citrus tastants could make swallowing safer and more efficient.

Despite evidence supporting decreased oral transit time with sour stimuli there is evidence that suggests that its unpalatable taste actually increases oral transit time. Hamdy, Jilani, Price, Parker, Hall, and Power (2003) conducted a study which included 65 healthy adult participants (M = 45 years) and 22 participants who had experienced acute stroke (M = 67 years). Participants took part in a water swallow test which required them to quickly but comfortably drink 50mL of water while hyolaryngeal elevations (i.e., swallows) were counted. Mean interstimulus interval was calculated (i.e., time to complete the task/number of swallows during the task) as well as mean swallowing volume velocity (i.e., volume drunk/time taken) and mean swallowing volume capacity (i.e., volume drunk/number of swallows). In a single-blinded, randomized manner, the water was presented at either room temperature (21°C), at a cold temperature (4°C), at room temperature with 5mL (10%) citrus lemon juice added, or at a cold temperature with 5mL citrus lemon juice added. Between trials, participants were asked to drink

25mL of room temperature water to rinse the mouth of any residual stimulus. In contrast to previous studies, it was found that the combination of cold and citrus water *slowed* the speed of swallows as well as *reduced* swallowing capacity in both healthy and acute stroke participants. The interstimulus interval was unaffected in all participants, except in the healthy <60-year-old participants when they had received the cold citrus stimulus; the interstimulus interval decreased. It was reasoned that the heightened sensory input produced by the sour stimulus may have been considered noxious, thereby causing participants to alter their swallowing behavior (i.e., swallow more slowly) by paying close attention to the task of swallowing. Moreover, a protective mechanism that decreases bolus volume and alters swallowing behavior in order to reduce the chance of aspiration of a noxious stimulus may have taken place.

There is also research which both supports and questions use of sour bolus in swallowing. Palmer, McCulloch, Jaffe, and Neel (2005) conducted a small study in which bipolar hooked-wire electrodes were inserted into the mylohyoid, anterior belly of the digastric, and geniohyoid muscles of 8 healthy participants (age range = 21–37 years). Participants were asked to hold either 3mL water or 3mL lemon solution (50% water and 50% ReaLemon) in their mouths and—when directed—to swallow five trials of each presented in random order. Electromyography (EMG) was conducted to examine onset of EMG activity for each muscle, offset of EMG activity for each muscle, and EMG at the time of the swallow command. Strength of muscle activation was estimated. A significant effect was found for tighter approximation of muscle activation across the onsets of the three muscles with use of the sour bolus. In support of the use of sour bolus, the study found that more than half (4 out of 7) of the participants experienced quicker swallow

onset times and all participants experienced closely-timed activation of all three muscles when a sour bolus was provided. It was rationalized that the engagement of increased taste receptors caused these robust responses. Yet, the fact that almost half (3 out of 7) of the participants demonstrated longer swallow onset times raises questions regarding the use of a sour bolus. Additionally, a trend for increased duration of muscle activity with sour bolus was observed; however, there was no significant effect to strongly support use of sour bolus.

In all of the above studies, it is important to consider the methodological differences which may account for some of the varied results in swallow timing. For example, participants in Logemann et al. (1995) and Palmer et al. (2005) were asked to swallow small 1mL and/or 3mL boluses, whereas participants in Hamdy et al. (2003) were requested to quickly and comfortably swallow a 50mL bolus while being timed. In the latter study, which focused on sequential swallows, participants kept liquid in their mouths during swallows, which may have caused hesitation in swallowing and, as a result, increased oral transit times due to the unpleasant bolus taste. Although the oral stage was greatly slowed, once the pharyngeal swallow was enacted, a strong swallow could be expected. In addition, not all studies included individuals with medical conditions. Given that other swallowing treatments, such as chin tuck, have been shown to reduce or eliminate aspiration in persons with dysphagia and have no significant effect on swallowing performance in healthy individuals (Bulow, 2001), results from Pelletier and Dhanaraj (2006) and Palmer et al. (2005) with healthy participants may not completely generalize to ill individuals.

Sour stimuli are not palatable to many individuals. Therefore, research has been conducted investigating means of providing individuals with sour stimuli that are more palatable than very sour substances but possess the same effectiveness. However, sweetness has been found to suppress sourness in healthy individuals as evidenced by Pelletier, Lawless, and Horne (2004). In their first experiment, 19 healthy older participants (M = 72.2 years) and 21 healthy younger participants (M = 22.6 years) tasted and rated the intensity of sucrose sweetness and sourness in 9 liquid samples. Each sample consisted of deionized water, sucrose, citric acid, or a combination of citric acid monohydrate and sucrose. Their second experiment consisted of 33 healthy older participants (M = 74.2 years) and 39 younger participants (M = 21.7 years) who tasted and rated 6 samples in the same manner as in the first experiment. The significant difference between the two experiments was that the second used aspartame instead of sucrose since it is shown to add less viscosity and volume to liquid barium while still sweetening it, making such a solution (if found to be effective) preferable for videofluoroscopic studies (Pelletier, Lawless, & Horne, 2004). However, regardless of the type of sweetener used (i.e., sucrose or aspartame), the effects of sour were suppressed similarly in both young and older participants. This occurred even when the temperature of a sweet-sour stimulus was reduced, as discovered in an extension of the second experiment. Thus, it is possible that coating a pill with a sweetened sour tastant may not significantly affect swallowing ability. However, this is unknown given that there are no previous studies that have been conducted on sour tastants and pill swallowing.

In general, several modes of sour stimuli application have been conducted. One mode of application is to add a sour stimulus to a bolus in order to stimulate oral and pharyngeal taste receptors. This has specifically been shown to shorten swallow onset time, oral transit time, pharyngeal transit time, and pharyngeal delay as well as reduce aspiration as seen on videofluoroscopic swallow studies (Logemann et al., 1995). Another mode of application entails applying the sour stimulus to a specific oropharyngeal area (e.g., anterior faucial pillars) with a lemon glycerin swab or lemon-flavored probe. This has specifically been shown to enact a quicker swallow response using surface electromyography which demonstrated earlier activation of infrahyoid and submental muscles (Ding, Logemann, Larson, & Rademaker, 2003; Sciortino et al., 2003).

Although there are studies that point to increased oral transit time in swallowing with a sour bolus, there are several more studies that support its ability to decrease oropharyngeal swallow speed and improve swallow efficiency. There is a dearth of studies on this topic that have been conducted with larger sample sizes and participants who are as uniform as possible in their diagnosis and site(s) of lesion. And finally, there are few studies regarding the ability to swallow pills and—perhaps most significant to the present study—no known studies investigating the effect of sweetened citrus tastants and pill swallowing.

Rationale and Objectives

The purpose of the present study is to determine if a tablet coated with a pleasant citrus-flavored tastant will improve ease of swallowing pills in healthy adults. There is a

paucity of scientific data on the effect of tastants on pill swallowing in the adult population. Difficulty swallowing pills is, however, a common complaint among adults. If using a sweetened citrus tastant to coat a pill could make swallowing pills easier, this could have a considerable positive impact on the ability to swallow pills in healthy adults, older individuals, and on those with identified swallowing difficulties who need to take a variety of oral medications. It was anticipated that swallowing would be more efficient and comfortable if a pill would be cleared from the pharynx more quickly and with greater ease. The following questions will therefore be addressed in the present investigation:

- Will time for oropharyngeal swallow be shortest for citrus-coated tablets, followed by water swallows and then plain pills?
- Will duration of hyoid movement required to complete an oropharyngeal swallow differ between a large pill coated with citrus tastant and an uncoated large pill?
- Will the time to complete a pill swallow be affected by the participant's attitude toward the tastant?

Methods

Participants

A total of 24 healthy adults (7 male; 17 female) between the ages of 19 and 49 years (M = 27.83 years; SD = 9.28), who were determined bereft of significant issues swallowing pills or known swallowing disorders were selected for this study. Participants were actively recruited via mass email (Appendix A) to undergraduate students in an introductory hearing and speech sciences class receiving class credit for participation, and to University of Maryland graduate students in the speech-language pathology and audiology programs, who received neither academic credit nor monetary compensation for participation. Participants were not excluded from the study on the basis of gender, race, ethnic origin, or sexual preference.

Prior to acceptance in the study, positive responses to any one or more of the following six screening questions, either provided via email correspondence or phone consult, were used to determine exclusion from study participation:

(1) Have you ever had an allergic reaction to calcium?

(2) Do you have or have you ever had hypercalcemia (high amounts of calcium in the blood)?

(3) Have you ever had kidney stones?

(4) Are you taking any medications that may be contraindicated with increased calcium intake (gallium nitrate (Ganite), cellulose sodium phosphate (Calcibind), etidronate (Didronel) phenytoin (Dilantin) or a tetracycline antibiotic to treat an infection (such as doxycycline, minocycline, Vibramycin))?

(5) Have you ever had a problem swallowing (dysphagia)?

(6) Are you allergic to any of the following: glycerin, sorbitol, xanthan gum, neotame, sodium citrate, citric acid, potassium sorbate, sodium benzoate, propylene glycol, N & A flavors,

cellulose, croscarmellose, titanium dioxide, vegetable magnesium stearate, FD&C Yellow No 5 Lake, FD&C Blue No 1 Lake?

Those participants selected were requested to defer taking a calcium supplement on those days in which they were scheduled to take part in the study. In addition, participants were instructed not to have a high-fiber meal (e.g., bran, whole-grain cereal or bread, fresh fruits), ingest high amounts of alcohol, or drink more than 8 cups of coffee on each day they took part in the study because there is possibility for fiber, alcohol, and caffeine to affect calcium metabolism. High amounts of fiber have been found to result in reduced urinary calcium excretion, although reduced calcium absorption occurs (Shah et al., 2009), whereas alcohol (De Kalbfleisch, Lindeman, Ginn, & Smith, 1963; Wolf et al., 2000) and possibly caffeine (Barger-Lux & Heaney, 1995) result in increased calcium excretion and reduced calcium absorption.

Procedures

Preliminary Data Collection

All trials took place in the ultrasound laboratory located in 0147 Lefrak Hall, Department of Hearing and Speech Sciences, University of Maryland, College Park. The institutional review board of the University of Maryland, College Park approved the protocol before commencement of the study. Individual informed consent was obtained from all participants before they took part in the study.

Prior to participation in the actual pill swallowing study, on the first day of experimental measures, participants answered a short written series of screening

questions (Appendix B) that pertained to pill swallowing ability and habits, and calcium intake. Six of the 16 questions had been presented to individuals when initially screened on the phone or via email for study participation. Once again, any one positive response to one or more of the initial phone/email screening questions (Appendix B, items 1, 3, 4, 5, 7, or 16) would have indicated elimination from the study. For each of the two sessions, if one positive response was provided for either item 2 ("Have you taken any calcium supplements today?") or item 6 ("Have you had a high-fiber meal today, ingested high amounts of alcohol, or more than 8 cups of coffee today?") a participant would be asked to return on an alternate day for the session. No participants were eliminated or asked to return on an alternate day for a session on the basis of their responses.

A brief oral-motor examination was performed assessing the strength and movement of the tongue and lips to rule out oral and perioral structural or functional abnormalities, all of which are essential to normal swallowing function. The tongue is one of the major organs involved in preparing an ingested substance for swallowing; in a healthy individual, its strength creates sufficient negative pressure against the alveolar ridge to thrust a substance to the posterior oral cavity through to the pharynx, and its wide range of motion allows for manipulation of the substance in preparation for swallowing. Therefore, any signs of tongue weakness or decreased range of motion could indicate swallowing difficulties. Ability to maintain symmetry when moving lips is an indication of lip strength important for both building negative pressure for swallowing in addition to retaining substances to be swallowed within the oral cavity. Vocal quality was assessed to ascertain if there was a possibility that airway protection when swallowing could be compromised. It was not deemed necessary to conduct a full oral-motor examination

since targeted participants were healthy and any general difficulties swallowing would be ascertained from questionnaires. Individuals were asked to round and retract their lips, extend, elevate, depress, and lateralize their tongue, say "ah," and push their tongue tip against an individually wrapped, disposable tongue depressor. Inability to conduct any of the above tasks with full range of motion, aperture, or strength would lead to elimination from the study; however, no participants were eliminated based on their results on this exam.

In addition, to ensure that participants had no swallowing disorders, they were asked to fill out a published and widely-used questionnaire ("Speech-Language Pathology Swallowing Questionnaire," Appendix C; Sonies et al., 1987) that pertains to swallowing ability. Possible responses were rated on a scale of 1 to 4, where "1" = *normal, none, never*, "2" = *mild, a little, occasionally*, "3" = *moderate, a fair bit, often*, and "4" = *severe, lots, usually-always*. Exclusion from the study was based on swallowing difficulty typical in a population with dysphagia, per one response of "3" or "4" on items 5–8, 19, or 25 ("Do you have difficulty swallowing liquids?"; "Do you have difficulty swallowing purees, soft, or sticky food?"; Do you have difficulty swallowing solids?"; "Have you eliminated any foods from your diet because of difficulty swallowing?"; "Does food or pills ever stick in your throat?"; "Do you have pain when swallowing?") or three or more responses of "3" or "4" to the remaining questions with the exception of the following items which would not indicate a swallowing difficulty: items 3 ("Do you notice drooling at night"), 11 ("Are you a fast eater?"), 12 ("Are you a slow eater?"), 14 ("Do you experience discomfort with hot or cold temperatures?"), 15 ("Do you experience discomfort with spicy food?"), and 20 ("Do you experience

heartburn/indigestion?"). It was reasoned that drooling at night could be indicative of sleeping with one's mouth open or allergies, eating either fast or slow could be related to eating schedules or habit, temperature and spice discomfort could be related to lowered thresholds/increased sensitivity to taste stimuli or cultural factors, and heartburn/indigestion could be related to gastrointestinal issues or complications with the esophageal stage of swallowing, which was not within the scrutiny of this study. None of the participants had to be eliminated from the study based on their responses to this questionnaire.

Active Data Collection

Upon successful completion of the questionnaires and oral-motor screening examination conducted during the first session only, each participant was provided the following directions in order to obtain baseline information concerning an individual's oropharyngeal swallowing speed when ingesting water alone, and to train participants regarding how to swallow the pills:

> *You will be asked to swallow three 30cc medicine cups of water. First, tilt your head back to move the water to the back of your mouth. When you are ready to swallow, quickly tilt your chin toward your chest and swallow hard. Each time, a small ultrasound transducer coated with a tiny bit of water soluble gel will be placed under your chin so we can record the movements of your tongue and hyoid bone as you swallow. We will also record the time it takes to complete a swallow. There is no discomfort, risk, or danger in this procedure. Please wait for me to say "swallow" before you swallow.*

All participants viewed their ultrasound swallow study in real-time to familiarize them to the procedure. Immediate playback allowed the investigator to determine that the data gathered were clear and measurable.

In this controlled, within-subject study, each participant was slated to swallow a total of 6 calcium tablets, either with tastant ("Pill Glide," orange cream-flavor) added or without tastant (plain). The following directions were given:

> *You will be asked to swallow three calcium tablets with 30cc water. Do not chew the tablets. A small ultrasound transducer coated with a tiny bit of water soluble gel will be placed under your chin so we can record the movements of your tongue, hyoid bone, and pill as you swallow and the time it takes to complete a swallow. There is no discomfort, risk or, danger in this procedure. Please hold the pill and water in your mouth until you are asked to swallow. If you are unable to swallow the tablet, you may spit it out or you may request additional water if needed. In addition to rinsing your mouth with 30cc water between trials, you will be given at least a minute between swallows.*

Calcium tablets (CVS calcium oyster shell, 500mg; ingredients: cellulose [plant origin], cellulose coating, croscarmellose, titanium dioxide color, vegetable magnesium stearate, FD&C Yellow No. 5 Lake, FD&C Blue No. 1 Lake) were chosen based on their large size (oblong shape with dimensions [length x width x height] of 2.0mm x 0.7mm x 0.5mm) and availability without tastant. Calcium is essential for bone growth, neurotransmitter secretion, muscle contraction, digestion, and blood coagulation. Recommended minimum daily intake for adolescents and adults is 1200–1500 mg/day (Marcus, 1996) with no guidance or limitations given regarding maximum daily intake (Theobald, 2005). Thus, even though the dose (1500 mg) exceeded the lower end (1200

mg) of the recommended minimum daily intake, the human body is known to absorb only enough calcium to fulfill dietary requirements; typically 20%–30% of intake is absorbed in the gastrointestinal tract. Any calcium determined by the body to be in excess is excreted through the urine and feces (Marcus, 1996; Theobald, 2005).

Large pills were chosen for this research based on the data suggesting that they are more difficult and less comfortable to swallow than small pills (Channer & Vijee, 1986; Overgaard et al., 2001). Thus, it was considered that if a citrus-coated tastant could make swallowing large pills easier, it would have positive impact on pill swallowing with healthy adults, older individuals, and those with swallowing difficulties. Pills would be swallowed more rapidly and efficiently and cleared from the throat without difficulty, thus having a positive impact on health and safety during swallowing.

To obtain a subjective measure from participants regarding attitude toward pill size and ease of swallowing, in the first session, the investigator asked the following question before beginning the first pill trial, while showing an individual the tablet: “Do you think this pill will be easy to swallow?”

As per directions provided to participants, each tablet was administered with 30cc water at room temperature. If more water was needed, the investigator recorded the amount needed to swallow the pill. If participants were still unable to swallow the pill despite additional water, it was determined that they would be excluded.

The study was divided into two separate sessions spread out over a series of two days (3 tablets in session 1; 3 tablets in session 2). The first session was determined to take approximately 30–45 minutes; the second session, 15–20 minutes. To control for order effects of tastant versus no tastant, participants’ dosage order was counterbalanced

using all possible combinations of pill order with the following exception: no participant could receive three of the same type of pill in one session. Thus, it was possible that some participants would receive two dosages of a tablet with tastant or two dosages of a plain tablet in a given session. However, no participant received three tastant-coated tablets or three plain tablets in a session. Tablets with added tastant were coated completely (sprayed 2 times) with the tastant immediately before administration. The investigator's back was turned from participants at all times during pill preparation. In each instance, the pill was lightly shaken in its medicine cup to fully coat the tablet with tastant and/or to initially blind participants to type of pill they were receiving. Participants were not informed regarding the tastant prior to the study. Furthermore, presence of the tastant was not discussed in either study session.

A colorless orange cream-flavored tastant ("Pill Glide"; ingredients: purified water, glycerin, sorbitol, xanthan gum, neotame, sodium citrate, citric acid) was chosen to coat tablets based on the literature which supports the effects of citrus bolus in reducing swallow onset time, transit time of a bolus across the surface of the tongue, transit time of the bolus down the throat, and increasing the efficiency of the swallow in individuals who have suffered a stroke in addition to contributing to reduced levels of aspiration (Logemann et al., 1995; Sciortino, Liss, Case, Gerritsen, & Katz, 2003).

To obviate changes occurring in the composition of the calcium pills from acidity levels present in orange or lemon juice, an organic substance could not be directly applied to the surface of the pills. Although "Pill Glide" protects the integrity of the tablet, the tastant's ingredients, including glycerin, produces a slippery surface when applied to the pills, which study participants may or may not have noticed. Non-flavored

"Pill Glide" was unavailable at the time of this study to coat the plain pills so that the plain tablets and the tablets with tastant would possess the same exact surface texture. Therefore, a confounding factor may have been introduced.

Measurements

The duration of the oropharyngeal swallow was determined by a frame-by-frame analysis conducted via a small, portable real-time ultrasound machine (GE Healthcare Logiq Book, 2004, Wauwatosa, WI). From ultrasound, the investigators obtained black and white moving digitized images of the tongue as the pill moved over the surface of the tongue into the pharynx during swallowing. As soon as a pill was placed in the mouth and prior to the swallow, the ultrasound timer was started and durational information, in seconds and number of image frames, appeared on the image for measurement of total oropharyngeal swallow duration. Total duration of the oropharyngeal swallow was recorded in real-time and measured with frame-by-frame analysis of ultrasound images as the time elapsed from the first frame in which the hyoid bone moved superiorly and anteriorly from its resting position to the frame in which the hyoid returned to its original position. Extra swallowing gestures (i.e., extra movement of the hyoid bone, excess tongue movement) and false starts were recorded; however, they were omitted from overall swallowing measurements. For all stimuli, the number of false starts observed was variable both between individuals and within a participant's trials. Per trial, only the one completed oropharyngeal swallow that pertained to the variable being looked at (i.e., baseline swallow with water only; swallow water along with the pill) was measured. A

total of 9 swallows were measured per participant: 3 with water only, 3 with plain tablets, and 3 with citrus-coated tablets.

Real-time ultrasound provides a cost-effective, dynamic, noninvasive, safe (no radiation), and efficient method by which the oropharyngeal swallow can be assessed. Ultrasound can specifically image the soft tissue structures of the oral cavity whose movement is essential to enactment of the swallow. It works by reflecting sound waves off interfaces between different tissues or materials. The air interface at the surface of the tongue allows for an efficient reflection of sound, thereby providing clear images of the lingual musculature both at rest and in motion. Contrast material does not need to be provided to distinguish internal features of the oral cavity from a bolus and there are no known bioeffects regarding this procedure which is used routinely to image the fetus (Brown & Sonies, 1997; Miller & Sonies, 2008; Sonies, Chi-Fishman, & Miller, 2003; Sonies, Parent, Marrish, & Baum, 1988; Watkin & Miller, 1997).

For all trials, the participant was seated comfortably in a relaxed, upright position. A small, 1-inch in tip length ultrasound transducer (GE Healthcare 8C-RS, Wauwatosa, WI) which provides soundwave frequencies between 4MHz and 10MHz, was placed submentally (underneath the chin) midline on the skin covering the floor of mouth muscles, angling the ultrasound beam upwards approximately 90° from a horizontal plane in relationship to the transducer to produce a sagittal view of both the tongue (i.e., genioglossus, geniohyoid, and mylohyoid muscles) and oral cavity, and then backwards approximately 10° from midline sagittal to visualize the upper surface of the tongue and shadow of the hyoid bone, as depicted in Sonies, Chi-Fishman, and Miller (2003). Each time, a small amount of ultrasound water soluble transmission gel (“LiquaSonic”) was

used to maintain adhesion between the skin and the surface of the transducer during imaging. The investigator stood to the right side of each participant, anchoring the transducer underneath the participant's chin. The investigator's focus remained on transducer positioning throughout ultrasound recording in order to ensure that the ultrasound image angle did not shift secondary to the participant's head movement. To ensure that the ultrasound transducer was placed correctly and consistently, the investigator held the transducer so that its notch faced away from the participant and was always midline and positioned straight. The resulting mid-sagittal ultrasound image displayed the hyoid on the right and the tongue tip on the left in each moving image.

Duration of each oropharyngeal swallow was calculated in milliseconds based on image frame numbers provided by the ultrasound machine. To obtain this measurement, 1000ms was divided by the number of frames per second recorded by the machine for a given scan recording (i.e., 44). This resulting number (i.e., 22.73) was multiplied by the beginning frame number (when the hyoid began to move upward in position) subtracted from the end frame number (when the hyoid returned to its original position). Although calculations were based on frames given their heightened accuracy as compared to seconds, data are reported in milliseconds, which is a more intuitive measure. Images were captured on-line and stored on recordable compact discs for later analysis.

Each swallow trial was coded numerically on the ultrasound image and in a log book based on whether the pill was plain or coated with a tastant. Plain pills were coded with a 1, 2, or 3 and pills with tastant were coded with a 4, 5, or 6 at the end of the participant's identification number. Baseline swallows of water only were coded a, b, or

c. Coding provided the basis for grouping the data for later analysis without revealing the actual identity of each participant.

Post-Measures

At completion of the second appointment, participants were asked the following two questions to gauge their individual experience with the pills:

1) Did you find the pill difficult to swallow?
2) Did you find that the tastant made the pill easier to swallow?

Inter-rater and Intra-rater Reliability

To ensure that oropharyngeal swallow measurements and time calculations for swallows via ultrasound were consistently and accurately obtained, the investigator became fully familiarized with the ultrasound machine used throughout the duration of the study. Familiarization included methods for initiating and stopping recording, methods for saving each trial (including naming files) for later review, bracing the ultrasound transducer for a clear sagittal view, regardless of participants' movements, calculating swallowing time by using frame-by-frame measurements on the ultrasound machine, and knowing when measurements should begin and end based on hyoid movement.

A preliminary training procedure/pilot was completed under the supervision of the experienced advisor to ensure the investigator's good judgment when looking for markers delineating the beginning and end of hyoid movement indicating the oropharyngeal swallow. Swallows for 2 individuals (18 trials) were recorded on ultrasound for all

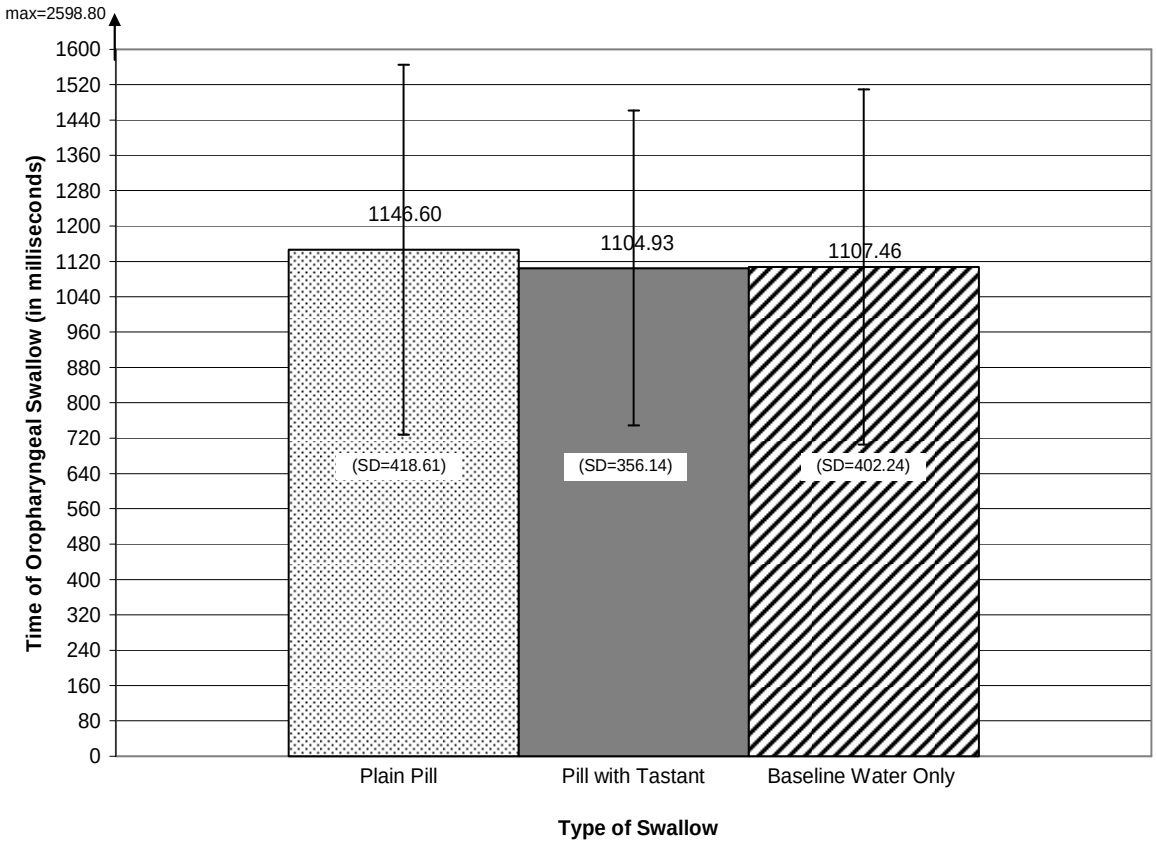
stimuli (i.e., water only, plain pills, pills with tastant) and analyzed. Close agreement between the experienced advisor and investigator for 17 out of 18 trials (94%) denoted successful training for ultrasound swallowing analysis.

Following completion of data collection, oropharyngeal swallowing time for 15% of total trials (32 trials) was calculated to determine both inter- and intra-rater reliability. The same swallows were rated independently by both the investigator and the experienced advisor, who were both blind to swallowing conditions when conducting measurements. Identifying information (code numbers printed on the upper left-hand corner of the real-time image) for type of swallow was hidden from view until after calculations were made. In each instance, calculations were compared to the investigator's previously recorded calculations determined 2–3 weeks prior. Pearson's product moment correlation revealed .90 reliability both between raters (inter-rater) and the investigator's ratings (intra-rater).

Results

The mean time for oropharyngeal swallow was calculated in milliseconds for each participant over the three swallowing trials for each condition (i.e., baseline water, plain pill, pill with tastant). Figure 1 shows results for all three types of swallows. Tables 1, 2, and 3 show individual data results in milliseconds for all trials.

Figure 1. Average Oropharyngeal Swallow Time



Note: Error bars indicate standard deviation (SD)

Table 1. Oropharyngeal Swallow Duration for Plain Pills

	PLAIN PILL									
	1			2			3			
ID #	Start	End	Swallow Time (ms)	Start	End	Swallow Time (ms)	Start	End	Swallow Time (ms)	Duration of Mean Oropharyngeal Swallow (ms)
F260231	122	185	1431.99	104	156	1181.96	220	288	1545.64	1386.53
F220331	295	341	1045.58	154	198	1000.12	370	406	818.28	954.66
F210436	284	359	1704.75	264	354	2045.70	270	309	886.47	1545.64
M320536	93	124	704.63	52	119	1522.91	81	143	1409.26	1212.27
F230638	158	192	772.82	213	247	772.82	251	324	1659.29	1068.31
M350738	127	200	1659.29	108	180	1636.56	125	177	1181.96	1492.60
F490838	100	256	3545.88	127	254	2886.71	115	175	1363.80	2598.80
F270938	90	171	1841.13	99	160	1386.53	205	244	886.47	1371.38
F401038	95	154	1341.07	145	191	1045.58	108	144	818.28	1068.31
F4611314	115	156	931.93	87	134	1068.31	160	206	1045.58	1015.27
F4912314	160	210	1136.50	125	168	977.39	127	168	931.93	1015.27
M2113314	83	124	931.93	208	257	1113.77	198	242	1000.12	1015.27
F1914322	198	238	909.20	359	420	1386.53	160	196	818.28	1038.00
M2415322	98	136	863.74	134	176	954.66	101	151	1136.50	984.97
M2116324	148	187	886.47	125	164	886.47	118	177	1341.07	1038.00
F2417324	106	148	954.66	110	143	750.09	154	190	818.28	841.01
M2318324	124	221	2204.81	153	215	1409.26	133	220	1977.51	1863.86
F2819324	112	170	1318.34	157	204	1068.31	158	196	863.74	1083.46
F2320325	178	210	727.36	192	231	886.47	216	249	750.09	787.97
F2021329	193	224	704.63	163	195	727.36	159	185	590.98	674.32
M1922329	176	202	590.98	161	193	727.36	142	169	613.71	644.02
F2523329	129	169	909.20	149	181	727.36	184	216	727.36	787.97
F222445	140	168	636.44	158	198	909.20	140	208	1545.64	1030.43
F292545	103	137	772.82	323	370	1068.31	127	178	1159.23	1000.12
						Mean Oropharyngeal Swallow Time for PLAIN PILL				**1146.60**

Table 2. Oropharyngeal Swallow Duration for Pills with Tastant Added

	PILL WITH TASTANT									
	4			5			6			
ID #	Start	End	Swallow Time (ms)	Start	End	Swallow Time (ms)	Start	End	Swallow Time (ms)	Duration of Mean Oropharyngeal Swallow (ms)
F260231	230	275	1022.85	244	295	1159.23	97	144	1068.31	1083.46
F220331	206	287	1841.13	104	151	1068.31	130	162	727.36	1212.27
F210436	215	296	1841.13	153	268	2613.95	275	316	931.93	1795.67
M320536	112	158	1045.58	79	119	909.20	72	133	1386.53	1113.77
F230638	155	187	727.36	206	255	1113.77	316	370	1227.42	1022.85
M350738	144	244	2273.00	139	195	1272.88	212	305	2113.89	1886.59
F490838	121	235	2591.22	160	219	1341.07	153	195	954.66	1628.98
F270938	194	257	1431.99	130	165	795.55	156	194	863.74	1030.43
F401038	84	140	1272.88	146	180	772.82	67	124	1295.61	1113.77
F4611314	210	242	727.36	131	171	909.20	128	173	1022.85	886.47
F4912314	103	183	1818.40	113	161	1091.04	128	178	1136.50	1348.65
M2113314	207	251	1000.12	204	241	841.01	153	192	886.47	909.20
F1914322	162	199	841.01	139	180	931.93	141	171	681.90	818.28
M2415322	117	154	841.01	102	145	977.39	119	155	818.28	878.89
M2116324	142	180	863.74	137	174	841.01	141	172	704.63	803.13
F2417324	120	161	931.93	179	220	931.93	111	147	818.28	894.05
M2318324	124	198	1682.02	138	221	1886.59	149	242	2113.89	1894.17
F2819324	121	152	704.63	118	164	1045.58	141	181	909.20	886.47
F2320325	363	390	613.71	171	204	750.09	140	177	841.01	734.94
F2021329	163	185	500.06	149	183	772.82	144	180	818.28	697.05
M1922329	82	130	1091.04	142	173	704.63	149	176	613.71	803.13
F2523329	176	203	613.71	145	210	1477.45	353	391	863.74	984.97
F222445	107	142	795.55	115	161	1045.58	213	254	931.93	924.35
F292545	148	196	1091.04	147	199	1181.96	96	150	1227.42	1166.81
						Mean Oropharyngeal Swallow Time for PILL WITH TASTANT				**1104.93**

Table 3. Oropharyngeal Swallow Duration for Baseline Water Swallows

BASELINE WATER SWALLOWS

	A			B			C			
ID #	Start	End	Swallow Time (ms)	Start	End	Swallow Time (ms)	Start	End	Swallow Time (ms)	Duration of Mean Oropharyngeal Swallow (ms)
F260231	210	285	1704.75	130	193	1431.99	125	182	1295.61	1477.45
F220331	78	141	1431.99	166	239	1659.29	347	436	2022.97	1704.75
F210436	35	114	1795.67	215	283	1545.64	363	424	1386.53	1575.95
M320536	28	72	1000.12	138	249	2523.03	292	443	3432.23	2318.46
F230638	43	101	1318.34	228	271	977.39	396	440	1000.12	1098.62
M350738	76	131	1250.15	230	295	1477.45	366	435	1568.37	1431.99
F490838	47	92	1022.85	220	274	1227.42	377	426	1113.77	1121.35
F270938	65	119	1227.42	236	297	1386.53	401	453	1181.96	1265.30
F401038	135	172	841.01	292	326	772.82	426	457	704.63	772.82
F4611314	102	150	1091.04	236	289	1204.69	356	398	954.66	1083.46
F4912314	100	165	1477.45	244	292	1091.04	378	421	977.39	1181.96
M2113314	75	113	863.74	231	277	1045.58	398	440	954.66	954.66
F1914322	127	173	1045.58	277	311	772.82	429	460	704.63	841.01
M2415322	90	156	1500.18	212	249	841.01	313	347	772.82	1038.00
M2116324	114	153	886.47	211	264	1204.69	369	424	1250.15	1113.77
F2417324	87	128	931.93	254	285	704.63	395	424	659.17	765.24
M2318324	48	108	1363.80	210	279	1568.37	396	454	1318.34	1416.84
F2819324	126	158	727.36	231	271	909.20	397	435	863.74	833.43
F2320325	134	168	772.82	243	273	681.90	401	433	727.36	727.36
F2021329	105	144	886.47	274	298	545.52	395	420	568.25	666.75
M1922329	106	134	636.44	178	200	500.06	315	335	454.60	530.37
F2523329	40	69	659.17	197	227	681.90	382	414	727.36	689.48
F222445	86	137	1159.23	172	221	1113.77	269	315	1045.58	1106.19
F292545	110	140	681.90	206	248	954.66	332	374	954.66	863.74
						Mean Oropharyngeal Swallow Time for BASELINE WATER ONLY				**1107.46**

Data were submitted to a 1-way repeated-measures analysis of variance (ANOVA) with the within-subject factor of type of swallow (plain pill, pill with tastant, baseline water only). No significant main effect was encountered, F (2, 23) = .19, p>.05, indicating that duration of oropharyngeal swallow did not significantly alter based on swallowing condition. At first glance (Figure 1), mean swallow time appears shortest for pills with tastant (*M* swallow time = 1104.93ms; SD = 356.14), followed by water-only swallows (*M* swallow time = 1107.46ms; SD = 402.24) and then plain pills (*M* swallow time = 1146.60ms; SD = 418.61). However, a trend cannot be substantiated. Of the 24 participants, time for oropharyngeal swallow was shortest for pill with tastant for 10 participants, followed by baseline water swallows for 11 participants, then plain pill for 3 participants. Only 3 participants' mean oropharyngeal swallowing measurements followed the progression of shortest (pill with tastant) to longest (plain pill) swallowing duration as displayed in Figure 1.

To investigate if a significant difference existed in duration of hyoid movement to complete an oropharyngeal swallow when ingesting large plain pills versus large pills with tastant, a planned comparison via paired t-test was conducted. Swallows were not shown to be significantly different, with t (23) = .73, p>.05, thereby indicating that time to swallow pills with tastant was not shorter than time to swallow plain pills.

In response to the follow-up question, "Did you find that the tastant made the pill easier to swallow," 10 participants (42%) reported that the tastant aided in pill swallowing function while 14 participants (58%) reported that the tastant did not aid in pill swallowing function. To investigate if time to complete a pill swallow was affected by the participant's attitude toward the tastant, data were submitted to a 2 (group) x 2

(condition) repeated-measures ANOVA with the within-subject factor of type of pill (plain or with tastant) and the between-subject factor of attitude toward the tastant in its ability to aid in pill swallowing. No significant main effect was found for the within-subject factor of pill type, with F (1, 22) = 1.16, p>.05, or the between-subject factor of attitude toward the tastant in its ability to aid in pill swallowing, with F (1, 22) = .29, p>.05. Furthermore, no interaction was found for the within- and between-subject factors, with F (1, 22) = 3.62, p>.05, although the p-value approached significance at .07. Duration of oropharyngeal swallow was shortest for the pill with tastant for 6 of the 10 participants who reported that the tastant aided pill swallowing. However, although some participants reported that the tastant aided in pill swallowing and slightly more than half of the participants indeed swallowed the pill with tastant in the shortest amount of time, there is no clear evidence to suggest that those participants actually benefited from the tastant.

Of the 24 individuals taking part in the study, a total of 7 participants (29%) reported having difficulty swallowing pills at some point in their lives per response to item 8 in the "Screening Questionnaire" (Appendix B). However, they did not swallow any differently than the other participants in the sample for any of the stimuli given. Large pills (tablets the size of the calcium pills) were consistently listed as difficult to swallow by all 7 participants; however 2 individuals also reported problems swallowing medium tablets (those tablets smaller than the size of the calcium pills but larger than the size of baby aspirins). Despite some participants' contentions that swallowing pills was difficult for them, only 4 participants thought that the large calcium pill would be difficult to swallow when first shown the pill. Two held fast to their initial reaction,

considering the pill difficult to swallow after taking part in the study, whereas the other 2 participants acknowledged that the pill was easier to swallow than initially believed.

A total of 17 participants (71%) reported taking at least one tablet a day (pill size not specified; range = 1–7 pills), 13 (54%) of whom reported taking two or more tablets per day (Appendix B, item 9). Thus, pill swallowing is an everyday task for most individuals in this sample which consists of people of varied ages. Those who took three or more pills per day (5 individuals) reported few-to-no difficulties associated with swallowing as per responses to the "Speech-Language Pathology Swallowing Questionnaire" (Appendix C). Only 2 participants reported that they were "fast eaters," while 1 participant reported "difficulty chewing hard food." Both eating quickly and chewing hard food rely heavily upon the preparatory stage of the swallow. Tongue movement during the preparatory stage is critical for efficiently moving the bolus between rows of teeth to allow for proper mastication and mixture of the bolus with saliva so that it can be swallowed easily. However, because chewing is not a task involved in pill swallowing—pills are swallowed whole!—adept tongue movement within this stage is essential to move the pill to the posterior portion of the tongue and to create enough pressure against the alveolar ridge for the swallow to occur.

A total of 5 participants reported that they experienced discomfort with "hot or cold temperatures" or "spicy food" to either a *moderate* or *severe* degree per responses to the "Speech-Language Pathology Swallowing Questionnaire" (Appendix C). Of those participants, 2 experienced shortest mean oropharyngeal swallowing duration with the pill with tastant and longest with water only, while the remaining 3 participants experienced the opposite: longest mean oropharyngeal swallowing duration with the pill

with tastant and shortest with water only. It is possible that those in both groups possess lower thresholds for extreme stimuli and are therefore affected more by it. Those participants in the former group may therefore desire to clear the mouth of the strong stimuli and swallow quickly while those in the latter group may find the stimuli more difficult to negotiate within the mouth due to the intensity. Therefore, it may take those participants longer to swallow the strong stimuli and shorter to swallow water, which is considered a neutral stimulus in regard to taste.

Between study sessions 1 and 2, the following patterns for shortest oropharyngeal swallowing duration were observed: pill with tastant (session 1)/pill with tastant (session 2) = 6 participants; plain pill/plain pill = 3 participants; plain pill/pill with tastant = 9 participants; pill with tastant/plain pill = 5 participants; plain pill/tie between pill with tastant and plain pill = 1 participant. A total of 9 participants experienced the shortest oropharyngeal swallowing duration for their first of three pill swallowing trials in session 1; whereas 7 participants experienced the shortest oropharyngeal swallowing duration for their first of three pill swallowing trials in session 2. No participants experienced shortest oropharyngeal swallowing duration for the first of three pill swallowing trials in both sessions 1 and 2.

Discussion

The present study aimed to address the following questions: 1.) Will time for oropharyngeal swallow be shortest for citrus-coated tablets, followed by water swallows and then plain pills? 2.) Will duration of hyoid movement required to complete an oropharyngeal swallow differ between a large pill coated with citrus tastant and an uncoated large pill? 3.) Will the time to complete a pill swallow be affected by the participant's attitude toward the tastant? In each case, results were not found to be statistically significant.

Several important explanations may be attributed to the lack of significant findings. One such explanation can be ascribed to a ceiling effect. A normal oropharyngeal swallow for water in healthy individuals aged 19–83 years is estimated to be between 1 second and 1.5 seconds (approximate range = .91–1.69 seconds) (Sonies, Stone, & Shawker, 1984). While these data are in line with the present study's findings for test swallows, there are no known normative data for healthy individuals when swallowing pills. In individuals with dysphagia, it has been researched that median time to swallow a 4.05mm tablet is 56.7 seconds, with a range of 5.2–323.0 seconds (Carnaby-Mann & Crary, 2005). This is a much wider range than for those with normal swallowing function. It is possible that a healthy person's speed in swallowing pills cannot improve significantly beyond that which is typical for swallowing water. Therefore, there would be no significant difference found in speed of swallowing between water, pills with tastant, or pills without tastant.

It can be surmised that oropharyngeal swallowing times could vary based on individual issues (e.g., organic disorder, phobia stemming from a bad experience/choking

episode). The present study recruited individuals without general swallowing difficulty, given the knowledge that if those with swallowing problems were to be actively recruited, all participants would need to have very similar issues (e.g., all participants with the same neurological insult, all participants who have experienced stroke in the same area of the brain) in order for valid results to be obtained. Some participants reported a history of difficulty swallowing large- and medium-size pills. However, it is possible that differences in oropharyngeal swallowing duration (for both water and pill swallows) are more exaggerated in disordered populations. Although positive results were not demonstrated in the current study, procedures could be applied to those with dysphagia and known pill-swallowing problems to investigate if swallowing ability is enhanced when a citrus tastant is applied to a tablet.

It is also possible that results were affected by the sweetened characteristic of the orange cream-flavored tastant. It was regarded as pleasant to both the investigator and to several study participants (e.g., “like candy”), many of whom reported that it aided in swallowing the pill (e.g., “Anything that tastes pleasant you want to swallow because it tastes good”). However, in one previous study, sweet citrus tastants in liquid form were found ineffective to enact improved swallowing function due to sweet suppression of the sour taste (Pelletier, Lawless, & Horne, 2004). The tastant used in the present study may not have produced enough chemesthesis (e.g., as is enacted by very sour lemon), which has been demonstrated in previous studies to show improvement in swallowing (Logemann et al., 1995; Pelletier, 2007; Pelletier & Dhanaraj, 2006).

Difference between robust results in previous studies and the present study may be a result of varied bolus consistency. In all previous studies on sour bolus, stimuli were

provided in liquid form (Hamdy et al., 2003; Logemann et al., 1995; Palmer, McCulloch, Jaffe, and Neel, 2005; Pelletier, 2007; Pelletier & Dhanaraj, 2006). However, a pill, as given in the current study, is a solid bolus that cannot alter in volume within parts of the mouth before it is swallowed. Therefore, general tongue movement to maneuver the bolus and subsequent initiation of the swallow may differ between consistencies, thereby allowing for differences in the duration of the oropharyngeal swallow.

Moreover, results may have been affected by texture changes procured when coating a tablet with manufactured "Pill Glide." Adding organic substances, such as lemon or orange juice, directly to the surface of the pills would have caused changes in pill composition and, therefore, pill texture due to high acidity levels. Although "Pill Glide" protected the integrity of the tablet, the tastant's ingredients, including glycerin, produced a slippery surface when applied to the pills. Thus, an unavoidable confounding factor was introduced to the study. Therefore, it could not be determined conclusively if the results found were the product of taste alone, especially given participants' varied impressions of the tastant. Although comments regarding the pill with tastant's texture were not directly elicited through a targeted query, reactions to the pill's slippery nature varied from neutral reports of "I didn't notice" to positive reports of "it allowed the pill to slide down easier" to a few negative reports of "it was slimy." Because non-tastant "Pill Glide" does not exist, it was not possible to rule out the confounding variable of slippery texture as either speeding up or slowing down swallows in the present study.

As with many studies within the field of speech-language pathology, a reduced number of study participants may prevent robust results from being obtained. This study was no exception. Given the small sample size of the present study, it is possible that if a

greater number of participants were included, the results may have reached, at the very least, a trend indicating that oropharyngeal swallow time for pills with tastant is shorter than that for water only and then plain pills. In addition, an increased number of trials per participant for each condition may have yielded more accurate means and/or robust data to support a tendency or trend. This is especially salient because considerable variation between oropharyngeal swallow times was seen for many participants for the same type of swallow (see Tables 1, 2, and 3).

It is important to consider the reality that not only is the literature on pill swallowing scant, but also measurements in prior studies were made using different instrumental techniques than ultrasound, such as videofluoroscopy. In ultrasound, the oropharyngeal swallow is imaged and measured by examining movement of soft tissues (e.g., outline of superior tongue surface) and shadow of a solid structure (i.e., hyoid bone). Swallow measurements begin when the hyoid shadow moves in a superior and anterior direction and end when the hyoid shadow returns to its initial resting position. Meanwhile, maximal hyoid displacement corresponds with the pill passing into the hypopharynx over the lowered epiglottis along with posterior tongue contact with the palate (Sonies, Chi-Fishman, & Miller, 2003). At no point is it possible to measure the swallow simply by looking at the pill. However, videofluoroscopy images boney structures and the surface of only those soft structures (e.g., tongue) coated with barium, making it easy to interpret. Therefore, the oropharyngeal swallow would be assessed by looking at *actual pill* movement (if infused with barium) from when it passes the ramus of the mandible and subsequently passes through the upper esophageal sphincter (Watkin & Miller, 1997). Difficulty swallowing a pill would likely indicate problems with the

inter-relationship and sequencing of innervation between the floor of mouth muscles, tongue, and hyoid. In addition to difficulties moving the pill with the tongue in an anterior-posterior direction to the tongue's posterior surface, there may be difficulty building enough lingual pressure against the alveolar ridge through agility and strength of the floor of the mouth muscles. Insufficient negative pressure to propel the pill would preclude initiation of hyoid movement for the oropharyngeal swallow. There may also be difficulties maintaining a wide enough aperture to the pharynx through elevation of the soft palate and posterior tongue depression. Although ultrasound is a fairly accurate instrument to envision the oropharyngeal swallow and, with proper midline sagittal transducer placement, can image the pill on the tongue and its movement to the posterior oral cavity, it cannot clearly show the tongue's contact with the alveolar ridge and at no point can opening to the pharynx be viewed. Proof of a successful pill swallow is in the pill's disappearance from the real-time ultrasound image. Of course, videofluoroscopy entails radiation exposure to the participant and therefore may be unethical for use in studies involving healthy individuals without swallowing problems. Videofluoroscopy can also be more costly than ultrasound to operate. However, it is possible that measurements within the present study would have an even greater level of discrimination if videofluoroscopy was the instrument of choice. Through barium coating, the tongue, the velum and their movements can be clearly imaged and the path of the pill can be traced from the mouth to the upper esophageal sphincter, or lower. Yet, alternatively, it is possible that a measure such as videofluoroscopy would have shown greater differences in the duration of the oropharyngeal swallow both between and within participants' trials—as opposed to showing more clustered means—because of the

instrument's ability to show more of the pill movement with respect to imaged anatomy. As opposed to ultrasound in which judgment of hyoid movement may be questionable if, for example, the transducer placement is not maintained midline sagittal, there are typically no unclear images in videofluoroscopy that might question pill progression through the duration of the swallow.

Given concerns regarding a limit to oropharyngeal swallowing time in healthy individuals, future research should focus on pill swallowing with individuals who have difficulty swallowing and older individuals. Many people with dysphagia and older individuals have co-occurring, multiple issues that require taking medications, making swallowing pills necessary and unavoidable. Although data from this study is not sufficiently robust to support coating a tablet with a pleasant sweetened citrus-flavored tastant to enact a shorter swallow in healthy individuals, it is possible that those with greater variability in oropharyngeal swallow time may experience a safer and easier pill-swallowing experience with a citrus-flavored tastant. It is also possible that a tastant producing heightened chemesthesis, such as very sour lemon, that minimally alters the texture of the pill while maintaining the integrity of the tablet may reveal more promising results. Nevertheless, it is hopeful that with increased focus on methods to make swallowing pills easy and safe, a problem that plagues many individuals—both young and old, and those with normal swallows and those with dysphagia—can be mitigated.

Appendices

Appendix A

Research Study!

Pill Swallowing in Healthy Adults

In order to participate, it is required that you fit the following criteria:

- Healthy adult between the ages of 18–55.
- Able to swallow food, liquid, pills without any problems, such as choking.
- Not currently taking calcium supplements.

If your answer is YES to all of the above, you may be eligible to take part in the study, contingent upon passing a short screening questionnaire and making sure that you have adequate tongue and lip movements.

This study will involve 2 visits and that takes a total of 30–45 minutes. We will see how you swallow using real-time ultrasound imaging (an easy, safe assessment!).

Study participants will not be discriminated on the basis of gender, race, ethnic origin, or sexual preference.

Appendix B

ID#_____

Screening Questionnaire—Pill Swallowing In Adults

DIRECTIONS: Circle or fill in blanks, if applicable

(1)	Have you ever had an allergic reaction to calcium?	YES NO
(2)	Have you taken any calcium supplements today?	YES NO
(3)	Do you have or have you ever had hypercalcemia (high amounts of calcium in the blood)?	YES NO
(4)	Have you ever had kidney stones?	YES NO
(5)	Are you taking any medications that may be contraindicated with increased calcium intake (gallium nitrate (Ganite), cellulose sodium phosphate (Calcibind), etidronate (Didronel) phenytoin (Dilantin) or a tetracycline antibiotic to treat an infection (such as doxycycline, minocycline, Vibramycin))?	YES NO
(6)	Have you had a high-fiber meal today (e.g., bran, whole-grain cereal or bread, fresh fruits), ingested high amounts of alcohol, or more than 8 cups of coffee today?	YES NO
(7)	Have you ever had a problem swallowing (dysphagia)?	YES NO
(8)	Have you ever had any difficulty swallowing pills?	YES NO
	• If yes, do you have difficulty swallowing large pills, medium pills, or small pills?	LARGE MEDIUM SMALL N/A
(9)	How many pills/vitamins do you take a day?	_____
(10)	Do you typically take your pill(s)/vitamin(s) with food?	YES NO
(11)	Do you ever take your pill(s)/vitamin(s) with liquid?	YES NO
(12)	Do ever feel like your pill(s)/vitamin(s) get stuck in your throat?	YES NO
(13)	Do you have any major health issues that require you to take pills?	YES NO
	• List conditions:_____	
(14)	Do you have any food allergies?	YES NO
	• List food allergies: _____	
(15)	Do you dislike the taste of oranges, lemons, or limes?	YES NO
(16)	Are you allergic to any of the following: glycerin, sorbitol, xanthan gum, neotame, sodium citrate, citric acid, potassium sorbate, sodium benzoate,propylene glycol, N & A flavors, cellulose, croscarmellose, titanium dioxide, vegetable magnesium stearate, FD&C Yellow No 5 Lake, FD&C Blue No 1 Lake?	YES NO

Appendix C

ID#_____

Speech-Language Pathology Swallowing Questionnaire

Ratings: **1—Normal, None, Never**
2—Mild, A Little, Occasionally
3—Moderate, A Fair Bit, Often
4—Severe, Lots, Usually-Always

1.	Does saliva collect in your mouth?	1	2	3	4
2	Do you notice drooling during the day?	1	2	3	4
3.	Do you notice drooling at night?	1	2	3	4
4.	Do you cough, choke, or awaken with nighttime secretions?	1	2	3	4
5.	Do you have difficulty swallowing liquids?	1	2	3	4
6.	Do you have difficulty swallowing purees, soft, or sticky food (e.g., mashed potatoes, rice, puddings)?	1	2	3	4
7.	Do you have difficulty swallowing solids (e.g., meat, raw vegetables)?	1	2	3	4
8.	Have you eliminated any foods from your diet because of difficulty swallowing?	1	2	3	4
9.	Do you have excessive saliva?	1	2	3	4
10.	Do you have dry mouth?	1	2	3	4
11.	Are you a fast eater?	1	2	3	4
12.	Are you a slow eater?	1	2	3	4
13.	Has your taste sensation (for sweet, bitter, salty, etc.) changed?	1	2	3	4
14.	Do you experience discomfort with hot or cold temperatures?	1	2	3	4
15.	Do you experience discomfort with spicy food?	1	2	3	4
16.	Do you have difficulty chewing hard food (e.g., hard candy, raw vegetables)?	1	2	3	4
17.	Does food spread all over your mouth; pocket in your cheeks?	1	2	3	4
18.	Does food or liquid ever come up through your nose?	1	2	3	4
19.	Does food or pills ever stick in your throat?	1	2	3	4
20.	Do you experience heartburn/indigestion?	1	2	3	4
21.	Does food or liquid ever back up into your mouth?	1	2	3	4
22.	Do you ever cough when you eat?	1	2	3	4
23.	Have you had episodes of choking or airway obstruction when eating?	1	2	3	4
24.	Do you experience upper respiratory problems such as pneumonia or bronchitis?	1	2	3	4
25.	Do you have pain when swallowing?	1	2	3	4

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