Modulation of Swallowing Behaviour by Olfactory and Gustatory Stimulation

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Doctor of Philosophy

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Preface

This PhD thesis is presented according to the referencing style recommended by the American Psychological Association Publication Manual (6th ed.). Spelling adheres to the format recommended by the Oxford Dictionary, accessed at http://oxforddictionaries.com.

The swallowing neurophysiology research programme was undertaken at the University of Canterbury Swallowing Rehabilitation Research Laboratory, located at the Van der Veer Institute for Parkinson's and Brain Research, Christchurch, between January 2008 and April 2010. The programme was supervised by Dr Maggie-Lee Huckabee, of the Department of Communication Disorders, University of Canterbury, and Professor Richard Jones, of the Department of Medical Physic and Bioengineering, Christchurch Hospital, and Department of Communication Disorders, University of Canterbury.

Preliminary results of this research programme have been presented at the following national and international conferences:

1. The 17th Annual Dysphagia Research Society meeting in New Orleans, USA, 5-7 March 2009.

2. The 3rd Annual Biomouth Symposium at Sir John Walsh Research Institute, Faculty of Dentistry, University of Otago, Dunedin, New Zealand, 10-11 June 2009.

3. Canterbury Health Research Poster Expo at NZi3 Building, Creyke Road, University of Canterbury, Christchurch, New Zealand, 24 June 2009.

4. The Department of Communication Disorders Postgraduate Research Conference at the Coppertop, University of Canterbury, Christchurch, New Zealand, 12 November 2009.

5. The 4th Biomouth symposium at the Van der Veer Institute, 40 Stewart Street, Christchurch, New Zealand, 8-9 June 2010.

6. The 8th Asia Pacific Conference on Speech, Language, and Hearing at the Central Lecture Theatre, University of Canterbury, Christchurch, New Zealand, 11-14 January 2011.

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Abstract

Swallowing impairment or dysphagia can be a consequence of several neurological and anatomical disorders such as stroke, Parkinson's diseases, and head and neck cancer. Management of patients with dysphagia often involves diet modification, sensory stimulation, and exercise programme with the primary goal being safe swallowing to maintain nutrition.

The aim of this project was to evaluate the effects of lemon odour and tastant on swallowing behaviour in healthy young adults. Specifically, the neural excitability and biomechanical characteristics of swallowing were measured in two studies. Neural excitability was evaluated by measuring motor-evoked potentials (MEPs) from the submental muscles which were evoked by transcranial magnetic stimulation (TMS) of the motor cortex. Biomechanical characteristics were evaluated through measures of submental muscle contraction, pressure changes in the oral cavity and pharynx, and the dynamics of the upper oesophageal sphincter (UES).

Two groups of volunteers (16 in each group) participated in two separate studies. In the MEP study, 25% and 100% concentrations of lemon concentrate were presented separately as olfactory and gustatory stimuli. The four stimuli were randomly presented in four separate sessions. The olfactory stimulus was nebulized and presented via nasal cannula. Filter paper strips impregnated with the lemon concentrate placed on the tongue served as the gustatory stimulus. Tap water was used as control. TMS-evoked MEPs were measured at baseline, during control condition, during stimulation, immediately poststimulation, and at 30-, 60-, and 90-min poststimulation. Experiments were repeated using the combination of odour and tastant concentration that most significantly influenced the MEP.

The biomechanical study used (a) surface electromyography (sEMG) to record contraction of the submental muscles, (b) lingual array with pressure transducers to record glossopalatal pressures, and (c) pharyngeal manometry to record pressures in the pharynx and the UES. Similar methods of presenting the stimuli were used to randomly present the 25% and 100% concentrations of lemon odour and tastant. All data were recorded concurrently during stimulation. The concentration of odour and tastant that produced the largest submental sEMG

amplitude was selected for presentation of combined stimulation. Data were then recorded during combined stimulation and at 30-, 60-, and 90-min poststimulation.

Results from the MEP study showed increased MEP amplitude at 30-, 60-, and 90-min poststimulation during swallowing compared to baseline, but only for the combined stimulation. Poststimulation results from the biomechanical study showed decreased middle glossopalatal pressure at 30 min and decreased anterior and middle glossopalatal contact duration at 60 min. No poststimulation changes were found in sEMG and pharyngeal manometry measures. During combined odour and tastant stimulation, there were increased pressure and contact duration at the anterior glossopalatal contact and decreased hypopharyngeal pressure. Generally, these changes correspond to increased efficiency of swallowing.

In conclusion, these are the first studies to have measured the effects of flavour on neural excitability and biomechanics of swallowing and the first to have shown changes in MEP and several biomechanical characteristics of swallowing following flavour stimulation. These changes were present poststimulation, suggesting mechanisms of neural plasticity that may underlie potential value in the rehabilitation of patients with dysphagia.

Acknowledgement

My heartfelt gratitude to my first supervisor, Dr Maggie-Lee Huckabee, for giving me the opportunity to pursue my PhD under her supervision. The same goes to Professor Richard Jones for taking me as his student. Both of them have given me invaluable guidance and assistance during the course of my study, which I will forever treasure. I would not have been able to complete this work without their continuing encouragement and support.

This project was hugely dependent on my research participants, whom I would like to sincerely express my gratitude for their invaluable time spent in the lab. I wish more people were like them, who selflessly volunteered to participate in research. I hope their efforts were not in vain, as this research may potentially benefit patients.

Many people have contributed in some ways along the course of my study. Sebastian Doeltgen patiently taught me the techniques to record MEPs, which constituted a major part of this project. He still responds to my emails whenever I need assistance with anything, for which I am most grateful. As interraters, Aamir Al-Toubi, Amy Collings, and Li Pyn Leow generously spent their precious time extracting the data. Associate Professor Peter Smith shared his statistics knowledge for data analyses in the first study. Daniel Myall was always there to help with computer glitches and also some aspects of data analyses. To the wonderful people in the swallowing lab group—in Christchurch, Boston, and Auckland—thank you for sharing your knowledge and continually supporting me in my study, specifically to Phoebe Macrae who was always willing to lend a helping hand whenever I interrupted her work to ask questions or request something. To the people at the Department of Communication Disorders and the Van der Veer Institute, fellow students, friends around Canterbury, and others who I may have left out, thank you for everything.

Last but not least, I am very grateful for the continuing support of my family, particularly my husband, Johari, for whom I will forever be indebted. To my children, Mikhael and Misha, I am so sorry for neglecting both of you when I was

consumed with my work; I hope one day you would understand my passion to further my studies in this area.

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Abbreviations

ANOVA	Analysis of variance
BOLD	Blood-oxygenation level-dependent
CI	Confidence interval
CN	Cranial nerve
CPG	Central pattern generator
DTI	Diffusion tensor imaging
EGG	Electroglottography
EMG	Electromyography
FEESST	Flexible endoscopic evaluation of swallowing with sensory testing
fMRI	Functional magnetic resonance imaging
ICC	Intraclass correlation coefficient
IOPI	Iowa Oral Pressure Instrument
ISI	Interswallow interval
ISLN	Internal branch of superior laryngeal nerve
LP	Laryngopharynx
LTP	Long-term potentiation
MEG	Magnetoencephalography
MEP	Motor-evoked potential
NA	Nucleus ambiguus
NME	Neuromuscular exercise
NTS	Nucleus tractus solitarius
OERP	Olfactory event-related potential
PET	Positron emission topography
pMEP	Pharyngeal motor-evoked potential
PPW	Posterior pharyngeal wall

PROM	Passive range of motion
rCBF	Regional cerebral blood flow
RF	Reticular formation
SD	Standard deviation
sEMG	Surface electromyography
SMA	Supplementary motor area
SPECT	Single photon emission computed tomography
SPSS	Statistical Package for Social Sciences
TMS	Transcranial magnetic stimulation
TTS	Thermal-tactile stimulation
UES	Upper oesophageal sphincter
VAS	Visual analogue scale

Chapter 1

Introduction

Swallowing is an innate physiological function which is important for human survival as it is the main route for nourishment (Miller, 2002; Thach, 2001). Swallowing impairment, or dysphagia, is a leading cause of malnutrition and aspiration pneumonia (Langmore et al., 1998; Massey & Shaker, 2003), which, if left untreated, can be fatal. Therefore, ensuring safe and efficient swallowing is vital in maintaining optimal bodily function.

Swallowing can be described in four stages (Daniels & Huckabee, 2008): (a) preoral, (b) oral, (c) pharyngeal, and (d) oesophageal stages. The preoral stage is experienced before ingestion where the "interaction of preoral motor, cognitive, psychosocial, and somataesthetic elements" occur (Leopold & Kagel, 1997, p. 202). These factors can modify the swallowing behaviour by cortical involvement, which adapts the swallowing gesture for food intake. The oral stage is a volitional phase where swallowing can be consciously controlled. The oesophageal stage is a reflex phase where peristalses of the oesophageal muscles transport the bolus into the stomach. Unlike the oral and oesophageal phases which can be regarded as either purely volitional or reflexive, respectively, the pharyngeal phase is considered to contain elements of both. Although the onset of pharyngeal swallowing is considered reflexive (Miller, 2002), this can be modulated by changing the reflexive component towards a more volitional control, for example by the 3-s prep (see Section 2.4.1.1).

The neural control of swallowing is divided into three components (Miller, 1982): (a) the afferent system, (b) the central pattern generator (CPG) in the brainstem, and (c) higher brain centres which modulate the swallowing response. The key components of the CPG for swallowing are in the brainstem (Miller, 1999). Despite the role of the CPG to initiate the patterned motor response of swallowing, it can be "modulated by peripheral sensory input and descending cortical and subcortical pathways" (Miller, 1999, p. 109). This modulation could include olfactory and gustatory components of food under preparation for swallowing.

There have been many studies evaluating gustatory effects on swallowing biomechanics (Chee, Arshad, Singh, Mistry, & Hamdy, 2005; Ding, Logemann, Larson, & Rademaker, 2003; Hamdy et al., 2003; Kaatzke-McDonald, Post, & Davis, 1996; Leow, Huckabee, Sharma, & Tooley, 2007; Logemann et al., 1995; Miyaoka et al., 2006; Palmer, McCulloch, Jaffe, & Neel, 2005; Pelletier & Lawless, 2003; Sciortino, Liss, Case, Gerritsen, & Katz, 2003) but few on olfactory effects (Ebihara et al., 2006; Munakata et al., 2008). Studies which evaluate the underlying neural effects of olfactory and gustatory stimulation are even scarcer with a single report documenting effects of olfactory input on the cortical area activation (Ebihara et al., 2006) and another report on the effects of gustatory input on neural transmission (Mistry, Rothwell, Thompson, & Hamdy, 2006). How olfaction and gustation affect swallowing are important clinical questions given the approach of utilizing sensory modulation of taste and smell for rehabilitation of patients with dysphagia.

Studies on animal models showed activation in the nucleus tractus solitarius (NTS), nucleus ambiguus (NA), and pontine swallowing neurons when the sensory nerves for swallowing were stimulated (Amirali, Tsai, Schrader, Weisz, & Sanders, 2001; Jean & Car, 1979; Jean, Car, & Roman, 1975). Other researchers who evaluated sensory stimulation on swallowing biomechanics proposed increased activation of the brainstem swallowing control, or the CPG, as the mechanism that modulate swallowing behaviour. For this project, it was hypothesized that swallowing can be modulated following odour and tastant stimulation as previous research documented changes in swallowing biomechanics when sour taste was presented (Section 2.3.4.2). Changes in the swallowing neural substrates are suspected to follow olfactory and gustatory stimulation as increased regional cerebral blood flow to the orbitofrontal cortex and the insula has been reported following presentation of the odour of black pepper oil to patients with swallowing impairment for 30 days (Ebihara et al., 2006). These cortical areas are important in the regulation of swallowing (see Section 2.1.2.3).

This research programme was carried out to answer the question: Can smell and taste affect swallowing? Two aspects of swallowing were evaluated: (a) its neural transmission from motor cortex to the submental muscles and (b) swallowing biomechanics, specifically, contraction of the submental muscles, pressure changes

in the oral cavity and pharynx, and the dynamics of the upper oesophageal sphincter (UES).

To investigate how sensory stimulation can affect swallowing, suitable stimuli needed to first be determined. Two separate studies were carried out to select a stimulus, and then determine two concentrations for use in subsequent studies (Chapter 3). The motor-evoked potential (MEP) study (Chapter 4), followed by the biomechanical study (Chapter 5) was then performed on two separate groups of volunteers. A supplementary study to support data from the biomechanical study was also conducted to strengthen the findings.

Results from both studies are discussed and integrated into the existing knowledge of swallowing neural control (Chapter 6). The findings suggest that simultaneously presenting smell and taste—that is, flavour—can affect swallowing, and the effects are still present after stimuli are removed. The presence of a poststimulation effect may benefit patients undergoing rehabilitation for swallowing impairment.

Chapter 2

Literature Review

2.1   Swallowing

Swallowing is a complex neurophysiological task accomplished by 26 pairs of muscles, six cranial nerves, and many brain regions (Donner, Bosma, & Robertson, 1985; Hamdy, Mikulis et al., 1999; Martin, Goodyear, Gati, & Menon, 2001; Mosier, Liu, Maldjian, Shah, & Modi, 1999; Toogood et al., 2005). Besides being the main route for nutrition and hydration, swallowing is also important in a person's emotional well-being and quality of life (Morgan & Ward, 2001), as eating is frequently part of a social event.

Normal swallowing function has been described by multiple authors who have divided swallowing into two stages (Jean, 1984a, 2001), three stages (Miller, 1999; Mosier & Bereznaya, 2001), four stages (Khosh & Krespi, 1997; Logemann, 1983; Shaker, 2006), five stages (Avery-Smith, 2004; Leopold & Kagel, 1997), or six stages (Huckabee & Pelletier, 1999). For ease of explanation, the functional anatomy and physiology of normal swallowing will be described in four stages: the preoral, oral, pharyngeal, and oesophageal stages (Daniels & Huckabee, 2008).

2.1.1   Functional Anatomy and Physiology in Normal Swallowing

Parameters in the preoral phase include physiological effects that occur when one anticipates food and first smells or sees the food (Leopold & Kagel, 1997). The peripheral sensory inputs of vision and olfaction are integrated and processed in the orbitofrontal cortex (Rolls, 1998). The anticipation of food can initiate physiological processes that support swallowing (Emond & Weingarten, 1995; Maeda et al., 2004); for example, the salivary reflex in the submandibular gland is stimulated when odour stimulus is presented (Lee & Linden, 1992).

The oral phase of swallowing is characterized by a number of biomechanical processes, including labial closure, lingual control, glossopalatal closure, and buccinator press. When a bolus first enters the oral cavity, the tongue is grooved in the midline to accept the bolus. Once food is in the mouth, the labial seal is maintained to prevent anterior spillage (Logemann, 1983). The bolus is held in the mouth between the tongue and anterior palate, and the lateral part of tongue against the alveolus. The velum during this stage is pulled downward and seals the oral cavity by making contact with the elevated back of tongue. With the bolus now on the tongue, the tongue elevates in the midline to transfer the bolus laterally between the posterior teeth for mastication. At this point, the buccal musculature holds the bolus within the oral cavity laterally and glossopalatal closure prevents premature spillage into the pharynx posteriorly (Huckabee & Pelletier, 1999; Logemann, 1983). Solid food can then be masticated to reduce its particle size (Prinz & Lucas, 1995). This is achieved with rotary lateral jaw and tongue movement until a cohesive bolus is formed. Sensory information from the bolus, such as its texture, volume, temperature, and chemical composition, plays a role in mastication by continually sending feedback to the central pattern generator for mastication (Lund, 1991). The act of chewing also releases the aroma from food, which is brought towards the olfactory receptors in the oropharynx by airflow via respiration (Heath, 2002).

The onset of swallowing signifies the end of oral phase and the start of pharyngeal phase. The pharyngeal swallow is an all-or-none reflex (Miller, 2002). At the end of the oral phase there will be a drop of the tongue base and a push from the tongue blade to propel the bolus into the pharynx. With these simultaneous tongue movements, the deep muscle receptors at the base of the tongue will be activated and, paired with superficial sensory and cortical input, will elicit the swallowing reflex, signifying the start of the pharyngeal phase of swallowing. Cortical inputs may arise from the limbic system, frontal lobe, basal ganglia, and other areas associated with feeding (Daniels & Huckabee, 2008; Leopold & Kagel, 1997). Swallowing can only be elicited if the graded potentials from these inputs reach a threshold to elicit an action potential in the NTS. The NTS will use this sensory information to generate a motor plan, which will be transferred to the NA and other motor neurons nearby. Thus, the muscles involved in swallowing will be activated (see Section 2.1.2.2).

The onset of the pharyngeal phase has been extensively studied radiographically; however, different methods have been used to define this onset. Ekberg and Olsson (1997) affirmed that pharyngeal swallowing starts when the hyoid bone moves "distinctively anteriorly" (p. 156). Most other authors agreed that hyoid displacement signify the beginning of pharyngeal phase, but the exact moment in time when this phase begins can be verified by monitoring bolus movement. For example, Leonard and McKenzie (2006) considered that pharyngeal swallowing was initiated before the bolus passed the valleculae, but Pouderoux, Logemann, and Kahrilas (1996) reported that 94% of swallows from their healthy participants occurred after the bolus overflowed from the valleculae and reached pyriform sinus. However, studies on healthy older adults by Stephen, Taves, Smith, and Martin (2005) brought the authors to conclude that swallowing was triggered by many factors, bolus position at the onset of pharyngeal swallowing being one of them, and this position can vary considerably within an individual.

Other methods which do not involve radiation have also been used to study the onset of swallowing. Pouderoux et al. (1996) examined the onset of swallowing with submental electromyography (EMG) and electroglottography (EGG). Concurrent videofluoroscopy was used to record swallowing. They found that the onset of submental EMG and EGG was nearly synchronous with the onset of laryngeal movement seen on the videofluoroscopy. Pouderoux et al. suggested that any of those methods could be used to indicate the onset of pharyngeal swallowing. Other researchers have used the EGG (Kaatzke-McDonald et al., 1996) and EMG (Crary, Carnaby Mann, & Groher, 2007) to determine the approximate start of hyolaryngeal excursion. Other methods that have been used were direct viewing (Kaatzke-McDonald et al., 1996) and palpation at the thyroid notch (Murry, 1999).

The pharyngeal phase of swallowing consists of a number of biomechanical activities which occur simultaneously (Logemann, 1983). They include: (a) hyolaryngeal excursion which deflects the epiglottis, (b) velopharyngeal closure, (c) base of tongue to posterior pharyngeal wall approximation, (d) pharyngeal peristalsis and shortening, (e) elevation and closure of larynx to protect the airway, and (f) relaxation of the UES. The schematic diagram showing these structures is shown in Figure 1.
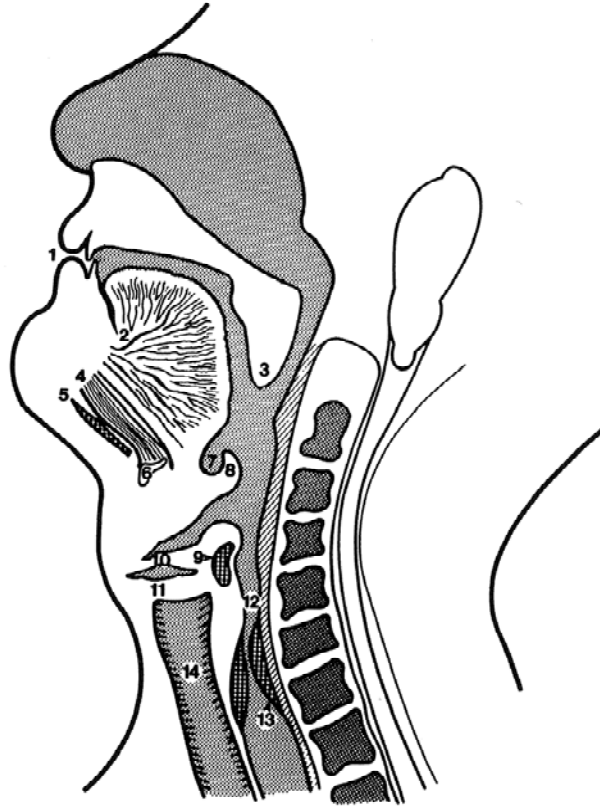
Figure 1. A diagram showing the anatomical structures involved in swallowing. 1, lips; 2, tongue; 3, velum; 4, geniohyoid muscle; 5, mylohyoid muscle; 6, hyoid bone; 7, valleculae; 8, epiglottis; 9, arytenoid cartilage; 10, false vocal folds; 11, true vocal folds; 12, pyriform sinuses; 13, cricopharyngeus muscle; 14, trachea. (From Perlman, Lu, & Jones, 2003, p. 157).

In healthy adults, hyolaryngeal excursion is in the superior and anterior direction, accomplished primarily by contraction of the suprahyoid and strap muscles. During anterior hyoid movement, the epiglottis is deflected to cover the laryngeal vestibule (Perlman, VanDaele, & Otterbacher, 1995) and traction force will be applied to pull open the cricopharyngeus muscle (that is, the UES, Cook et al., 1989). Ishida, Palmer, and Hiimae (2002) found that anterior hyoid movement was more consistent compared to superior movement, which prompted the authors to speculate that anterior hyoid movement is crucial in pharyngeal phase of swallowing, specifically for UES opening.

During pharyngeal phase of swallowing, velopharyngeal closure is achieved by elevation and retraction of the velum. The velopharyngeal port is completely closed to prevent bolus from entering the nasal cavity (Logemann, 1983). However, Huckabee and Pelletier (1999) asserted that nasal regurgitation is more often "related

to dyscoordination of pharyngeal stripping rather than velopharyngeal closure directly" (p. 36).

The base of tongue and posterior pharyngeal wall must approximate to provide the initial positive pressure to push the bolus through the pharyngeal lumen. This is contiguous from the "drop and push" event of the base of tongue to elicit the swallowing reflex. It also assists with epiglottis deflection (Khosh & Krespi, 1997). Pharyngeal peristalsis via contraction of the pharyngeal constrictors is utilized to clear small boluses from the pharynx (Kahrilas, 1993). During contraction of the pharyngeal constrictors, the pharyngeal cavity is shortened and the UES is brought superiorly to accept the approaching bolus.

The airway is protected during swallowing by epiglottic deflection which is mainly achieved by anterior hyolaryngeal excursion. The superior and anterior displacement of larynx will keep the larynx under the base of tongue away from the ingested material (Shaker, 2006). Further laryngeal protection to prevent penetration and aspiration is also in place. Protection mechanisms include: (a) true vocal folds closure via arytenoids approximation, (b) ventricular folds closure, (c) posterior hooding of the arytenoids over the folds when the arytenoids rock forward, and (d) compression of the quadrangular membrane (Daniels & Huckabee, 2008).

The UES is made up of fibres from the inferior pharyngeal constrictors (the thyropharyngeal and cricopharyngeal muscles) and the oesophageal circular muscles (Donner et al., 1985; Sivarao & Goyal, 2000). It is closed at rest to prevent (a) regurgitated materials from stomach and oesophagus entering the pharynx and (b) aspiration of air into the oesophagus (Donner et al., 1985). Closure of the UES depends on three factors: (a) contraction of the cricopharyngeus muscle, (b) passive force from the elastic property of the tissue, and (c) compression from structures surrounding the sphincter (Miller, Bieger, & Conklin, 2003).

The UES must open to allow the bolus to pass into the oesophagus. Three mechanisms are involved: (a) relaxation of the sphincteric muscles, (b) anterior hyolaryngeal excursion, and (c) traction force of laryngeal suspension. Additionally, pressures from the bolus and contracting pharyngeal musculature can distend the sphincter (Cook et al., 1989; Miller et al., 2003). The contraction of the inferior

pharyngeal constrictor plays a role in UES opening as it facilitates bolus transfer through the lower pharynx. Once the bolus is in the oesophagus, it is carried towards the stomach via oesophageal peristalsis (Donner et al., 1985).

2.1.2   Neural Control in Normal Swallowing

The pharynx is a shared pathway for swallowing, speech, and respiration (Donner et al., 1985). Due to this anatomical complexity, complex neural control mechanisms are required to integrate swallowing with respiration. Only one activity can occur at a time, thus, respiration ceases during swallowing (Butler, Postma, & Fischer, 2004). This is referred to as swallowing apnoea, or the cessation of respiration during swallowing, which is vital to protect the airway (Klahn & Perlman, 1999). Most swallowing occurs during midexpiration (Hiss, Treole, & Stuart, 2001; Klahn & Perlman, 1999).

The neural substrates controlling swallowing are divided into three components (Miller, 1982): (a) the afferent system, comprised of the trigeminal, glossopharyngeal, and vagus cranial nerves; (b) the brainstem swallowing centre, constituting a central pattern generator; and (c) higher brain centres which modulate the swallowing response. The schematic representation of these components is shown in Figure 2.

2.1.2.1   The Afferent System in Swallowing

Sensory input is important for safe swallowing as it modulates the central pattern generator to alter peripheral muscle output to accommodate the bolus to be swallowed (Bieger, 2001). In addition to the sensory involvement during the preoral stage (vision and smell, see Section 2.3.4), sensory modulation comes from the bolus itself via its taste, consistency, texture, viscosity, volume, and temperature. This sensory information is conveyed to the higher brain centres for processing via the trigeminal, facial, glossopharyngeal, and vagus cranial nerves. Taste is also processed when it first reaches the NTS (Rolls, 1989). Proprioception (movement of the bolus and its spatial orientation) is also important sensory information which is conveyed primarily by the trigeminal nerve innervating the mucosa in the oral cavity.
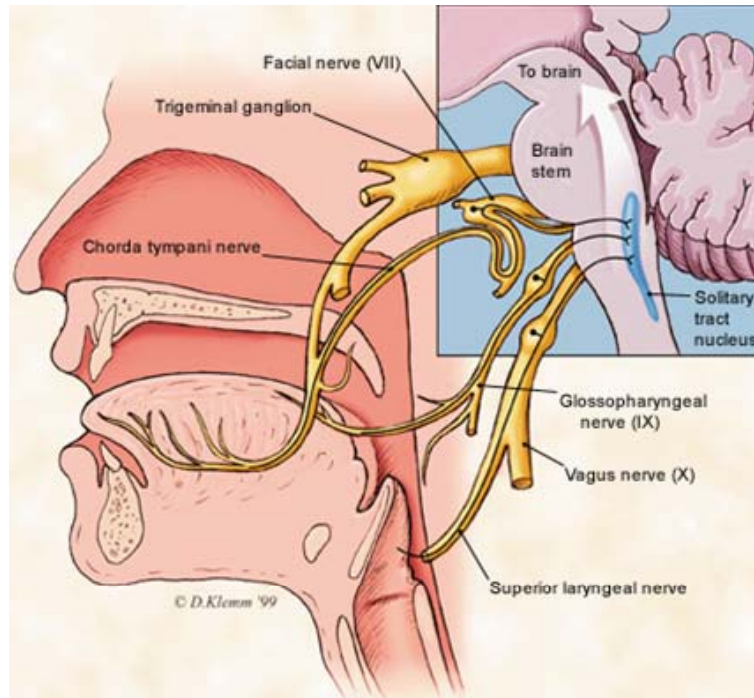
Figure 2. Schematic representation of neural control in swallowing. (Illustration by Dave Klemm, Georgetown University School of Medicine. Used with permission. Downloaded from http://www.aafp.org/afp/20000115/427_f3.jpg).

Jafari, Prince, Kim, and Paydarfar (2003) evaluated the impact of anaesthetizing the internal branch of superior laryngeal nerve (ISLN) on swallowing. The ISLN carries afferent fibres from the larynx and laryngeal surface of epiglottis (Sanders & Mu, 1998). Jafari et al. reported increased incidence of penetration and aspiration, with all of their healthy participants reporting the sensation of globus and having to swallow with effort. Similar results were reported by others following administration of superior laryngeal nerve block (Sulica, Hembree, & Blitzer, 2002). Administration of topical anaesthesia can also cause swallowing impairment (Chee et al., 2005; Fraser et al., 2003), but to a lesser degree to that of total nerve block. The differences in the degree of swallowing impairment following block or topical anaesthesia may suggest that the mechanoreceptors are not fully anaesthetized when topical anaesthetic is applied onto the mucosa compared to block anaesthesia (Jafari et al., 2003).

2.1.2.2   Brainstem Control in Swallowing

Much of what we know about brainstem control of swallowing has been learned from studies in animal models. Following stimulation of the superior

laryngeal nerve in sheep, neuronal activities in the NTS, NA (Jean & Car, 1979), and pontine swallowing neuron (Jean et al., 1975) were triggered, with different latencies. Jean et al. (1975) further stimulated the thalamic nucleus antidromically, which produced activity in the pons, but not in the medulla, suggesting that information from the medulla was sent to the thalamus via the pons. Amirali et al. (2001) mapped the brainstem swallowing circuitry in rats by stimulating the recurrent laryngeal nerve to evoke swallowing. They measured the amount of neural cells labelled with Fos protein (a metabolic marker which induces protein expression when neurons fire action potentials) indicating that neural activation was present in those cells. They further confirmed the involvement of the NTS, the NA, and the reticular formation (RF) during swallowing. Amirali at el. proposed that the site of the CPG for swallowing is the NTS, NA, RF, and the ventral part of RF. This is supported by studies from previous researchers who found absence of a swallow when there are lesions in these areas (Doty, Richmond, & Storey, 1967).

The CPG for swallowing consists of two main groups of neurons (Jean, 2001): (a) the dorsal swallowing group containing the generator or programming neurons and (b) the ventral swallowing group, also known as the switching neurons. There is also a third component—organizing interneurons—which can be excitatory or inhibitory depending on the sensory feedback (Jean, 1984a). Excitatory effects are generally influenced by inputs from the periphery and inhibitory effects are triggered through the central connections (Jean, 1984b). The dorsal swallowing group, with the NTS as a central component, and adjacent RF, accepts sensory information relevant to swallowing and uses the information to generate a motor plan for swallowing. The motor plan is then conveyed to the ventral swallowing group via the interneurons (Jean, 1984a). The ventral swallowing group includes the NA and RF surrounding it. Motor output for swallowing is executed through this ventral group (Altschuler, 2001; Jean, Amri, & Calas, 1983).

The basic motor plan for sequencing swallowing can be performed without afferent feedback (Broussard & Altschuler, 2000; Jean, 1984b; Miller, 1972b). However, this motor programme is primitive and may not be suitable for safe bolus swallowing. Afferent input is crucial for a safe and efficient bolus transfer. Sensory information from pharynx and larynx is continually conveyed to the NTS via the cranial nerves (Ootani, Umezaki, Shin, & Murata, 1995). The NTS is the primary

sensory nucleus that receives information directly from the facial, glossopharyngeal, and vagus nerves and indirectly from the trigeminal nerve (Love & Webb, 2001; Miller, 1972a, 1999). The NA is the primary motor nucleus for swallowing which contains nuclei for the glossopharyngeal, vagus, and spinal accessory nerves. The NA and reticular area immediately ventral to the NTS also convey information to the trigeminal, facial, and hypoglossal motoneurons (Cunningham & Sawchenko, 2000; Jean et al., 1983). This information is important to modulate the muscles involved in swallowing to ensure safe bolus transport. Additionally, information from the NTS is also conveyed to the pontine neurones, and then towards the cortex via the thalamus (Jean et al., 1975) for processing of oropharyngeal sensation. Later experiments have shown that information from the NTS is sent to the pons via the NA (Amri, Car, & Jean, 1984) and direct projections exist from NTS to the trigeminal and hypoglossal motor neurons (Amri, Car, & Roman, 1990).

2.1.2.3   Cortical Control in Swallowing

The CPG for swallowing in the brainstem can be modulated by inputs from the periphery and the cortex (Dziewas et al., 2003; Miller, 1999). This modulation may include olfactory (smell) and gustatory (taste) components of food that are under preparation for swallowing as well as its flavour, which is the combined perception of smell and taste. Several studies have revealed a cortical role in initiating and regulating swallowing function (Hamdy, Aziz, Rothwell, Hobson et al., 1997; Martin & Sessle, 1993; Miller, 1992, 1999). The cortex receives inputs from afferent nerves, integrates these inputs with information stored in other cortical areas (such as the limbic system), and then sends that input to the CPG to modify motor output that is optimal for the bolus that a person is preparing to swallow (Lund & Kolta, 2006). Odour information is conveyed directly to the cortex; therefore, it will be processed before being transmitted to the medulla. In contrast, taste information is processed in the NTS when it is first sent there by the afferent fibres of facial, glossopharyngeal, and vagus cranial nerves (Rolls, 1989).

Fibres from the lateral precentral gyrus (motor strip) are known to project to the NTS and the NA (Larson, 1985). These projections play a role in swallowing, particularly during the voluntary, preparatory stage. Moreover, it has been reported that fibres from the frontal part of the cortex, including the motor cortex, terminate in

the pontine and medullary reticular formation (Kuypers, 1958), which may influence the muscles innervated by motoneurons from these areas. As there are direct connections from the cortex to the medulla, information from the cortex may influence medullary motoneurons in coordinating muscle movements during swallowing.

Earlier studies on animals have indicated that swallowing can be triggered when the fronto-orbital cortex is stimulated (Jean & Car, 1979). However, only those neurons associated with the oral and pharyngeal stages were activated, prompting the authors to suggest that cortical contribution can only influence swallowing during these stages. Recent animal studies have suggested cortical involvement during the pharyngeal phase of swallowing (Thexton, Crompton, & German, 2007). Thexton et al. documented that decerebrate animals had "substantial or complete filling of the vallecular space with liquid … to elicit a pharyngeal swallow" (p. 593) compared to swallows which started before liquid reaches the vallecular space in intact animals. The authors suggested that the threshold for a swallowing reflex is increased in decerebrate animals, implying that cortex has an influence in pharyngeal swallowing. However, this may also indicate that there was not enough sensory stimulation to the NTS and its surrounding reticular formation to trigger a pharyngeal swallowing (Miller, 1999), that is, the cortex may not have any influences on the initiation of pharyngeal swallowing.

Previous reports postulated that cortical involvement in swallowing is predominantly associated with the volitional stage of swallowing (Satow et al., 2004; Sumi, 1969). Other evidence that the cortex, but not the motor cortex, is involved in swallowing is the absence of the second component of the Bereitschaftpotential (a premotor potential) during swallowing, which may indicate that neural activities for swallowing from the supplementary motor area are conveyed directly to the brainstem, thus bypassing the motor strip (Huckabee, Deecke, Cannito, Gould, & Mayr, 2003).

Several studies have investigated the cortical areas that were activated during swallowing. Hamdy, Mikulis, et al. (1999) used a blood-oxygenation level-dependent (BOLD) technique as measured by functional magnetic resonance imaging (fMRI) to examine which cortical areas were activated during volitional swallowing in

10 healthy volunteers. They found that the areas consistently activated during swallowing were the anterorostral cingulate cortex, caudolateral sensorimotor cortex, anterior insula, frontal opercular cortex, superior premotor cortex, anteromedial temporal cortex, anterolateral somatosensory cortex, and precuneus, with the anterior cingulate, premotor, opercular, and sensorimotor cortices having the strongest activations. These activations were bilateral but there was hemispheric asymmetry in most participants, particularly in the insula, operculum, and premotor cortices. The finding of lateralization corresponds to a previous study utilizing transcranial magnetic stimulation (TMS) to map the representation of swallowing musculature on the cortex (Hamdy et al., 1996). Hamdy, Mikulis, et al. (1999) also reported early activation of the premotor area, which they hypothesized to play a role in preparation for the upcoming swallowing event. As fMRI has relatively poor temporal resolution, they were not able to report how much earlier the area was activated.

Zald and Pardo (1999) utilized regional cerebral blood flow (rCBF) scanning with positron emission tomography (PET) to compare brain areas activated during swallowing with those activated during tongue movement in eight healthy volunteers. Zald and Pardo reported that the regions critical to the control of swallowing were the inferior precentral gyri bilaterally, the right anterior insula, and the left cerebellum; these regions were differently activated compared to tongue movement. As the volunteers were asked to move their tongue from side-to-side for the tongue movement, the differences seen in this study may be true as the tongue movement is noticeably different from the normal tongue movement during swallowing. Other areas activated during swallowing were the putamen, thalamus, and part of the right temporal lobe. The authors pointed out that dysphagia can manifest as a symptom by multiple lesions in the brain due to the distributed nature of areas involved in swallowing. Hamdy, Rothwell, et al. (1999) also used PET imaging to study cortical areas activated during swallowing. They identified increased rCBF in several brain areas in eight healthy male volunteers. Areas included the bilateral caudolateral sensorimotor cortex, right anterior insula, right orbitofrontal and temporopolar cortex, left mesial premotor cortex, left temporopolar cortex and amygdala, left superiomedial cerebellum, and dorsal brainstem.

Studies of cortical control in swallowing using fMRI and PET imaging have identified numerous cortical regions that are activated during swallowing. None has

shown how information from these areas is transferred to the periphery to modulate swallowing. In the future, other forms of investigation may be able to demonstrate how cortical brain areas influence the brainstem to modulate swallowing. As of present, diffusion tensor imaging (DTI) tractography (Gong et al., 2009) and MEPs triggered by TMS can demonstrate neural connections and the pathway from motor cortex to target muscles, respectively, but not the functional use of the pathway. More information regarding MEPs is discussed in Chapter 4.

From the literature, it is apparent that many brain areas are involved in swallowing; damage to any of these parts has the potential to produce dysphagia. This may indicate that cortical input is necessary to ensure safe and efficient swallowing. However, how cortical input modulates swallowing at the brainstem level and influences the periphery directly (via corticobulbar pathways) is not known. Most studies have evaluated swallowing as a single event—albeit with different phases representing different aspects of swallowing—which may obscure the exact brain areas involved for specific features of swallowing. Information regarding the various cortical areas involved during the different stages of swallowing is likely to improve our understanding of dysphagia, which can be manipulated in therapy and may subsequently improve treatment of dysphagia.

2.2   Swallowing Impairment

Swallowing impairment or dysphagia is often a major consequence of a cerebrovascular accident or stroke (Smithard et al., 1997; Spieker, 2000). With the advance of medical technologies, more stroke victims are surviving and the number of elderly individuals is increasing. Consequently, there will be potentially more patients with dysphagia as aging may predispose patients to medical conditions that may impair swallowing function (Nicosia et al., 2000). The effects of age on swallowing are discussed in Section 2.3.1.

The incidence of dysphagia following stroke has been widely investigated, but results differ, ranging from 40 to 80%, depending on the method used to identify swallowing impairment (Martino et al., 2005). A higher incidence is reported when dysphagia is evaluated with instrumentation, followed by clinical testing, as opposed to the lowest incidence based on clinical screening. Teasell, Foley, Fisher, and

Finestone (2002) reported that greater than 55% of patients with medullary stroke had dysphagia at the onset of their stroke. Patients with dysphagia stayed longer at hospital and had prolonged and incomplete recovery compared to patients without dysphagia. Twenty-five percent of patients with dysphagia developed aspiration pneumonia, and Teasell, Foley, Fisher et al. (2002) considered that aspiration "appeared to be an early complication of stroke and dietary modifications did not prevent its development" (p. 115). In another study, a higher incidence of aspiration pneumonia was recorded in patients with medullary and cerebellar strokes, compared to patients with pontine stroke (Teasell, Foley, Doherty, & Finestone, 2002).

2.3   Factors that Can Affect Swallowing Function

Many factors can influence swallowing: (a) individual differences, such as age, sex, anatomical variables, emotional state, and general well being; (b) food/bolus factors; for example, the size and temperature of the foodstuff; and (c) environmental factors. Only factors considered important to the current research design are elaborated here. Where appropriate, the discussions were further divided into healthy versus patient population or immediate versus late effects.

2.3.1   Age

Several studies have shown an age effect on normal swallowing function. In older participants, compared to their younger counterparts, there is an increased duration of (a) oropharyngeal swallowing (Robbins, Hamilton, Lof, & Kempster, 1992), (b) velopharyngeal closure (Rademaker, Pauloski, Colangelo, & Logemann, 1998), (c) pharyngeal contraction (Perlman, Schultz, & VanDaele, 1993; van Herwaarden et al., 2003), and (c) cricopharyngeal opening (Logemann, Pauloski, Rademaker, & Kahrilas, 2002; Rademaker et al., 1998). Other reported changes in the elderly compared to the young were increased pharyngeal pressures (Bardan, Kern, Arndorfer, Hofmann, & Shaker, 2006), increased pharyngeal transit time (Rademaker et al., 1998), longer pharyngeal delay (Logemann et al., 2000), decreased hyoid movement (Logemann et al., 2000), and later start of submental muscles activation (Ding et al., 2003). However, Rademaker et al. (1998) found no differences in oral transit time in females from the age of 20 to 89 years despite the

differences observed in pharyngeal transit time, velopharyngeal closure, and UES opening. There was, however, an interaction between oral transit time and bolus volume, that is, the elderly had longer oral transit time when a larger bolus was given compared to a smaller bolus. The effects of bolus volume are discussed in Section 2.3.3. In another study on age and sex differences, the onset of swallowing apnoea was earlier in older male adults compared with younger male adults, but no differences were observed in the female group (Hiss, Strauss, Treole, Stuart, & Boutilier, 2004). The effects of sex are discussed in Section 2.3.2.

Normal aging is known to affect swallowing function, perhaps partly because there is an increase in sensory threshold as shown by Aviv (1997). He used air pulse stimulation to elicit the laryngeal adductor reflex to assess laryngopharyngeal sensory threshold in healthy subjects from different age groups. He reported that there was a "progressive increase in sensory discrimination threshold with each decade of life" (p. 75S), with the threshold for those in the 61-87 age group being significantly different from their younger counterparts. Aviv stressed the importance of sensory deficit as a possible contributor to motor impairment and dysphagia, as well as aspiration. Contrary to Aviv (1997), Fucile et al. (1998) reported that aging itself does not lead to swallowing impairment, at least in an elderly population using a series of behavioural tests. The disagreement between Aviv and Fucile et al. may be due to the use of different measurements to assess impairment. Although Fucile et al. concluded that aging was not a cause for dysphagia, the loss of teeth may be associated with dysphagia, as their feeding performance depended on denture wearing. About 70% of denture wearers avoided hard food. Additionally, Fucile at el. reported a trend towards poorer performance on oral praxis skill in participants more than 70 years although this was not significant. No direct examination of the sensory system of swallowing was included; hence, the conclusion that aging does not influence swallowing may be debated. Furthermore, the finding that denture wear has an implication on feeding performance may indicate that sensory attributes play a role in swallowing as wearing a denture would decrease the area of mucosa exposed to the oral cavity.

2.3.2   Sex

Effects of Sex in Healthy Population

Several studies evaluated differences between males and females on swallowing. Robbins et al. (1992) reported a longer duration in UES opening in females when compared to males. They reasoned that the diameter of the UES in females is smaller, which required longer opening for a bolus to pass compared to males. In a study conducted by Sciortino et al. (2003), participants were given a mechanical, cold, and/or sour stimulation to the anterior faucial pillars. They found that female participants had a longer duration of submental muscles activity compared to males. They did not suggest that the effect was due to the stimulation and, indeed, agreed with Robbins et al.'s explanation that the submental muscles have to contract longer to sustain the UES opening. From these studies, it can be concluded that gender effect is mainly due to anatomical differences, rather than an interaction between gender and sensory stimulation.

The water swallow test (Hughes & Wiles, 1996) was also used to evaluate gender differences for swallowing measures. This test requires the subject to drink "as quickly as is comfortably possible" (p. 110). Reportedly, females demonstrated a lower volume per swallow, decreased swallowing velocity, and decreased interswallow interval compared to males (Alves, Cassiani Rde, Santos, & Dantas, 2007). Similar to Robbins et al. (1992) and Sciortino et al. (2003), Alves et al. (2007) attributed their findings to the anatomical differences between males and females, and concurred with findings from other studies which reported longer UES duration in females than in males to compensate for these differences. Additionally, they found no influences of height, body mass index (< 40 kg/m^2), or age (< 77 years) across gender. The authors asserted that anatomical differences accounted for the differences observed between males and females but they did not elaborate why height, in particular, was not a significant factor. One possible explanation is the unequal sample size (there were 36 males and 75 females) with skewed distribution of body mass index where data were not normally distributed.

Guinard, Zoumas-Morse, and Walchak (1998) evaluated parotid saliva flow when participants were given different sensory attributes, including taste (sweet, umami, and bitter), mouthfeel (astringency and viscosity), and texture (bolus

adhesiveness and bolus cohesiveness). The taste and mouthfeel sensory attributes represent chemical and trigeminal stimulation while the textured (solid) food—which required mastication—represents mechanical stimulation. Results indicated that mechanical stimulation produced higher saliva flow rate compared to chemical stimulation. Increased salivary flow was recorded in all conditions compared to water. The flow rate increment in males was greater than in females with all stimuli. The authors suggested that males produced a greater increase in salivary flow due to anatomical differences, as the larger gland in males would produce more saliva. Unfortunately, the authors did not measure mastication (duration or strength) or the hedonic factors of participants towards the stimulation, which may influence the findings.

Effects of Sex in Patients with Dysphagia

Two studies have evaluated sex differences with regard to dysphagia outcome. Mann et al. (1999) assessed 128 patients (82 males) with acute first stroke using bedside clinical assessment and videofluorography where different examiners performed the two examinations separately. The examiners were blinded to the findings of the other examination. Interestingly, being a male greater than 70 years of age and presenting with delayed oral transit and penetration seen videofluoroscopically, was found to be a predictor for the combined outcome of "swallowing impairment, chest infection, or aspiration at 6 months poststroke" (p. 746). Unfortunately, no further comments on sex were made as this was not a study specifically designed to evaluate sex differences with regards to dysphagia. In another study on taste disorders in poststroke patients, Heckmann et al. (2005) evaluated 102 patients (57 males) with acute first stroke. They reported more impaired taste function in males compared to females and concluded that males are more susceptible to taste dysfunction and are less able to compensate for gustatory loss. This was in line with findings that men experienced more severe decline in taste perception with aging (Mojet, Christ-Hazelhof, & Heidema, 2001) compared to women. However, no literature has speculated as to why males behave differently from females in this aspect. As taste stimulation could potentially be used in managing patients with dysphagia, taste loss should be put into consideration when prescribing treatment, particularly for patients where the gustatory cortex is involved in the stroke.

2.3.3   Bolus Volume and Consistency

Effects of Bolus Volume and Consistency in Healthy Population

Increases in bolus volume have been shown to affect swallowing, both in healthy controls and dysphagic patients. In normal participants, it has been shown that as the bolus volume increased, there was a decreased oral transit time (Rademaker et al., 1998), decreased pharyngeal transit time (Rademaker et al., 1998), increased hyoid elevation (Logemann et al., 2000), and increased duration of: (a) the cricopharyngeal opening (Logemann et al., 2000; Rademaker et al., 1998), (b) oropharyngeal closure (Rademaker et al., 1998), and (c) swallowing apnoea (Butler et al., 2004). Also reported were an earlier onset of swallowing apnoea (Hiss et al., 2004) and earlier base of tongue and posterior pharyngeal wall movements (Logemann et al., 2000) when a larger bolus was used compared to a smaller bolus. These studies used liquid boluses, except for Hiss et al. (2004) who also included thick liquid and pureed consistencies in their study. They reported later onset of swallowing apnoea with increased bolus viscosity.

The biomechanical measures affected by bolus volume are similar in most studies. For example, a shorter time is recorded for oral and pharyngeal transit time when a larger bolus was swallowed compared to a smaller bolus (Logemann et al., 1995; Rademaker et al., 1998). Owing to the larger bolus, its head is positioned more posteriorly in the oral cavity before swallowing compared to a smaller bolus (Tracy et al., 1989), thus less time is needed for it to traverse the pharyngeal lumen. Similarly, a larger bolus needs more time to travel through the UES than a smaller bolus, hence the increased duration of UES opening when larger bolus was swallowed compared to a smaller bolus.

Effects of Bolus Volume and Consistency in Patients with Dysphagia

In patients with dysphagia, increased bolus volume has been reported to increase the number of swallows, increase oral residue, decrease pharyngeal swallowing delay, increase contact time between back of tongue and posterior pharyngeal wall, increase duration of airway closure, decrease pharyngeal transit time and increase penetration/aspiration score (Abou-Elsaad, 2003; Bisch, Logemann, Rademaker, Kahrilas, & Lazarus, 1994; Logemann et al., 1995).

Moreover, Pelletier and Lawless (2003) reported less aspiration and penetration with smaller boluses using teaspoon feeding compared with cup feeding.

The effect of bolus volume would depend on the pathophysiology experienced by the patient. If a patient has a sensory deficit, a larger and sour bolus would be more appropriate as it would maximize the sensory input for a better timing of pharyngeal swallowing. Indeed, Logemann et al. (1995) reported that increased bolus volume reduced the pharyngeal swallowing delay in patients with dysphagia. In contrast, a patient with oromotor deficit would require a small bolus for easier manipulation to avoid increased oral residue or premature spillage into the pharynx. The same study by Logemann et al. showed that patients had increased oral residue when larger bolus was used compared to a smaller bolus. Nevertheless, the volume of a bolus is just one aspect of its characteristics; other attributes, such as the consistency and texture, must also be considered when diet modification is prescribed for a patient (Abou-Elsaad, 2003).

2.3.4   Sensory Input

Sensory deficits, particularly in the laryngopharyngeal area, are often associated with penetration and aspiration in patients with dysphagia (Ludlow, 2004). Penetration and aspiration, both commonly diagnosed radiographically or endoscopically, are instances where food or liquid is seen at the airway entrance above the vocal folds or when it enters the airway, respectively (Logemann, 2003).

Aviv et al. (1996) investigated laryngopharynx (LP) sensory abnormalities in poststroke patients presenting with dysphagia using an air puff delivered to the anterior wall of the pyriform sinus. Sensory threshold determination was performed for each patient by presenting the air puffs in ascending and descending order. The mean of the lowest detected pressure was used as the patient's sensory threshold. To ensure that patients were responding to the air puff and not to the clicking sound, a placebo condition was also incorporated into the procedures. Aviv et al. reported moderate to severe LP sensory deficits in patients with dysphagia consistent with expectations for the site of lesion. The sensory deficits were ipsilateral when the lesion was in the brainstem, and contralateral when the lesion was above the brainstem level. The authors found no correlation between severity of gag

impairment and severity of LP sensory deficits. Although gag impairment is easier to evaluate than LP sensory deficits, the finding that no correlation exists between these two measurements would suggest that quantitative sensory evaluation is needed in managing patients with dysphagia.

Aviv (1997) further highlighted the importance of intact sensory modalities to avoid aspiration. He reported a progressive increase in sensory discrimination thresholds in the elderly compared to the young (elaborated in Section 2.3.1). Aviv stressed the importance of sensory deficits as possible contributors to motor impairment and dysphagia, as well as aspiration. Setzen, Cohen, Mattucci, Perlman, and Ditkoff (2001) strengthened this observation with their study on aspiration risk using flexible endoscopic evaluation of swallowing with sensory testing (FEESST), similar to the equipment used in previous studies (Aviv, 1997; Aviv et al., 1996). Setzen et al. reported that in patients with dysphagia, those with sensory deficits were more likely to aspirate compared to patients without sensory abnormalities. In another study of sensory deficits and prevalence of aspiration, Setzen et al. (2003) found that 15% of patients aspirated when they had a sensory deficit without motor impairment. However, if the sensory deficit was accompanied by a motor problem, 100% of the patients aspirated. In this study, sensory testing was done with FEESST, and motor function was evaluated using endoscopy while the participants made a forceful "eee" sound. If the lateral pharyngeal walls contracted towards the midline during phonation, motor function was considered normal. The importance of intact sensation in swallowing is further strengthened by findings from Sulica, Hembree, and Blitzer (2002) who reported higher incidence of premature spillage, pharyngeal residual, and laryngeal penetration in healthy subjects following bilateral superior laryngeal nerve block.

A magnetoencephalography (MEG) study on diminished sensory input to the oropharynx showed decreased activation in the primary sensory and motor cortex, suggesting cortical involvement in interpreting sensory input to modulate swallowing (Teismann et al., 2007). As sensory input has been shown to have effects on swallowing, sensory stimulation is considered a useful approach in managing patients with dysphagia (Hägg & Larsson, 2004; Hamdy, 2003; Hamdy, Rothwell, Aziz, Singh, & Thompson, 1998; Power et al., 2004; Theurer, Bihari, Barr, & Martin, 2005). Hence, olfactory and gustatory stimuli—both types of sensory

stimulation—could be a useful adjunct in dysphagia management. The anatomy and physiology of olfaction and gustation are described in Sections 2.5.1 and 2.5.2, respectively. In this section, the effects of olfaction and gustation on swallowing are explored further.

2.3.4.1   Olfactory Stimuli

Immediate Effects Following Olfactory Stimulation

The effects of olfaction on swallowing have not been extensively studied. Mameli and Melis (1993) and Mameli et al. (1995) performed experiments on rabbits to evaluate the influence of olfaction on activity of the hypoglossal nerve and muscles of the tongue (genioglossus, styloglossus, hyoglossus, and superior longitudinal muscles). The authors found that there were excitatory or inhibitory effects on the hypoglossal nerve fibres, dependent on the stimulus intensity used. Olfactory effects on the muscle fibres were generally excitatory, seen as an increase in the spontaneous firing rate of the motor unit. This finding strongly suggests that the use of olfaction may aid in increasing muscle contraction. Additionally, the anterior belly of digastric muscle, which is involved in mouth opening, was examined to evaluate the effects of olfaction on the trigeminal nerve; however, no changes in its electrical activity were recorded, indicating that olfactory stimulus did not affect this cranial nerve. In another study which evaluated the effect of trigeminal stimulation on olfactory event-related potentials (OERPs) from the somatosensory cortex, Bensafi, Frasnelli, Reden, and Hummel (2007) concluded that trigeminal stimulation has a role in the perceptual odour recognition in humans. The authors reported higher OERPs when odour was presented with trigeminal stimulation compared to the odour presented without trigeminal stimulation. However, it is not known how this integration is processed. Previously, Mameli and colleagues documented no effect of olfaction on the trigeminal nerve in rabbits, unlike Bensafi et al. who reported its role in odour recognition in humans. Other attributes of odour related to humans, for example, the hedonics factor, may play a role in odour perception, which may not be measurable in rabbits. Hence, the pleasantness and tolerability ratings of a stimulus should be taken into account in selecting a stimulus for swallowing study.

Two studies have evaluated the effects of smell on the contraction of submental muscles during swallowing in healthy adults. When nebulized orange or eucalyptus oil was presented via nasal cannula, Abu-Hijleh, Huckabee, and Jones (2006) identified a small increase in the peak EMG amplitude of submental muscles compared to presentation of a neutral mist. However, no differences were seen in the EMG duration or measures of breathing-swallowing coordination. Schuermann (2008) used the more complex odours of hot buttered popcorn and cinnamon bun and reported no differences in submental muscle contraction compared to swallowing performed without olfactory input. There was also no effect of odour on breathing-swallowing coordination. Thus, the author concluded that for the complex stimuli under evaluation, there was no effect of olfaction on swallowing, or that such effects were not achieved or not seen due to limitations in the methodology of the study. The limitations mentioned by the author included the stimuli, which may be differently perceived by participants, and the method of delivery, which used nasal cannula inserted into the nares. This method of stimuli delivery may not be natural and some participants may find it uncomfortable. Nevertheless, noneffective stimulation, as reported by Schuermann, may not indicate that the stimulus has no effect on swallowing as no other outcomes of swallowing were evaluated. Other physiologic features of swallowing not evaluated may have been overlooked. Swallowing is a complex behaviour and many other factors may influence its execution. As Abu-Hijleh et al. used a less complex odour than Schuermann and there was one positive result seen in the former study, at least some effect of olfaction on swallowing could not be refuted.

Late Effects Following Olfactory Stimulation

Ebihara, Ebihara, Maruyama, et al. (2006) recruited 105 elderly and physically disabled patients, mainly due to stroke, with stable physical symptoms and cognitive presentation for the preceding 3 months. Prior to intervention, an odour identification test was carried out; all groups showed low scores in this test but they did not differ from each other. Each group of patients inhaled volatile black pepper oil, lavender oil, or distilled water for 1 min immediately before each meal for 30 days. Swallowing was assessed by recording the number of swallows via submental EMG and visual observation of laryngeal movement, as well as the latency of swallowing reflex from the time a 1-ml bolus was injected into the

pharynx through a nasal catheter. The participants were not aware of the bolus injection. At the end of the study, patients who inhaled black pepper oil showed an increase in the number of swallows and a reduction in the latency of the swallowing reflex compared to presentation of lavender oil or distilled water. Additionally, the authors evaluated cortical changes in 10 participants who have had history of aspiration pneumonia and were in the black pepper oil group. Pre- and post-intervention scans of single photon emission computed tomography (SPECT) were taken. They reported an increase in rCBF in the insula and orbitofrontal cortices 30 days later compared to baseline measures. These brain areas are known to receive information from olfactory cortex (Carlson, 2001; Kettenmann, Hummel, Stefan, & Kobal, 1997). The fact that these areas can be modulated by simply exposing patients to olfactory stimulus may indicate the value of olfaction in rehabilitation of patients with swallowing impairment. Furthermore, the authors reported an increase in the number of swallows and a reduction in the latency of the swallowing reflex, which corresponds to improved swallowing performance. However, no other swallowing measures were included, which could improve our understanding of the effect of olfaction on swallowing.

In another study utilizing similar black pepper oil stimulation, Munakata et al. (2008) reported increased oral intake in eight paediatric patients (age 19-97 months) on tube feeding when black pepper oil was used for 3 months. Findings from Ebihara, Ebihara, Maruyama, et al. (2006) and Munakata et al. (2008) support the use of smell in the rehabilitation of patients with swallowing problems.

No other literature was found regarding the effects of olfaction on swallowing function. The effects of olfactory input on swallowing neural function in healthy volunteers have not yet been investigated, although Ebihara, Ebihara, Maruyama, et al. (2006) have reported increased rCBF in the insula and orbitofrontal cortices in elderly poststroke patients.

2.3.4.2   Gustatory Stimuli

Gustatory stimulation has been shown to affect swallowing although some discrepancies exist in the literature regarding the changes in swallowing outcome

following the stimulation protocol. However, these discrepancies may be explained by the different methodologies used in the studies.

Immediate Effects Following Gustatory Stimulation

Ding et al. (2003) evaluated the effects of taste on EMG of several swallowing muscles in 40 healthy participants. Participants were given 5 ml of liquid tastants (sweet, salty, sour, and water as control) which they held in the mouth for 10 s until the command to swallow was given. Holding the bolus in the mouth and using a 5-ml bolus may introduce confounding factors to this research as there will be more sensory stimulation due to the increased volume and time that the bolus was in contact with oral mucosa compared with when dry swallowing was used. Ding et al. found that activation of the submental and infrahyoid muscles started earlier when sweet and sour tastes were used, and higher EMG levels were recorded during contraction when salty taste was used, compared to the control condition. Taste fibres, which are contained in the facial, glossopharyngeal, and vagus cranial nerves, are known to synapse in the NTS. Taste is processed in the NTS before it is transmitted to the higher centres via the thalamus (Rolls, 1998). Although not evaluated, Ding et al. proposed that more neurons were activated in the NTS when these stimuli were presented, thus sending more signals to the NA, which then "activate[d] cranial motor nuclei … at a faster speed or a higher intensity" (p. 984). To further investigate the effects of sensory stimulation on the excitability of neurons in the NTS, a study on this topic is highly warranted.

In contrast to Ding et al., who reported improved swallowing performance when sour taste was used, Sciortino et al. (2003) did not find any changes in swallowing biomechanics following sour stimulation. Different methodologies were used in the studies; therefore, the contrasting results were not surprising. Sciortino et al. added a sour taste component in their study which evaluated the effects of anterior faucial pillar stimulation on swallowing biomechanics in 13 healthy participants. EMG of the submental muscles was recorded, from which some biomechanical aspects were calculated. Swallowing response time was calculated from the time of bolus infusion to the onset of swallow-specific EMG. Although no effects were seen when only sour stimulation was presented, the authors reported a significant decrease in swallowing response time when all three stimuli (cold, mechanical, and taste)

were combined compared to no stimulation. However, the effect was short-lived and it was not seen in subsequent swallows. These results were similar to Kaatzke-McDonald et al.'s study (1996) which also evaluated cold, taste, and mechanical stimulation to the anterior faucial pillars. Additionally, Kaatzke-McDonald et al. reported significant differences when cold stimulation was compared to feigned stimulation (where laryngeal mirror was brought towards the faucial pillars but no contact was made). Sciortino et al. proposed three possible mechanisms for the effects seen in their study: (a) the stimuli changed the receptors characteristics, thus lowering the threshold; (b) there was an increase in "oral awareness" (p. 22), which then excited the cortex to modify swallowing; and (c) the swallowing response threshold was unchanged but the summation of sensory stimuli led to the changes seen in the EMG recordings. Results reported in this study could be challenged as the methods of applying the tactile thermal stimulation to the anterior faucial pillars were questionable; the authors counted aloud from 1 to 10 to indicate a 10-s time frame instead of relying on a digital timer. Furthermore, the number of strokes given in the 10-s window was not reported or may not be standardized among all participants; the number of strokes applied to the faucial pillars was specified in Kaatzke-McDonald et al.'s study.

Palmer et al. (2005) inserted intramuscular electrodes into the geniohyoid, mylohyoid, and anterior belly of digastric muscles of healthy adults and compared the effects of swallowing a 3-ml water bolus with a 3-ml sour bolus (lemon solution). They reported stronger muscle contraction with the sour bolus when compared to water bolus. Contraction of the three muscles was also more closely approximated when sour bolus was presented compared to water bolus. With the positive effects seen on swallowing, they proposed that the taste stimulus, or other "strongly flavoured bolus" (p. 216) could be used in helping to manage patients with dysphagia. However, Palmer et al. did not report participants' perception of the stimuli, which may have an effect on the findings. Other studies have shown that a strongly flavoured stimulus may not improve swallowing (Chee et al., 2005; Hamdy et al., 2003). Though results were contradictory, these studies (Palmer et al. versus Chee at al. and Hamdy et al.) cannot be directly compared as Palmer et al. evaluated muscle activity following the intervention and Chee et al. and Hamdy et al. measured

volitional swallowing activity via the water swallow test (discussed in the succeeding paragraphs).

Chee et al. (2005) hypothesised that taste (glucose, citrus, and saline) would increase swallowing speed during a water swallow test (Hughes & Wiles, 1996). However, the stimuli, which were cooled to 4°C, were reported to decrease the volume of ingested bolus per second and increased interswallow interval (ISI) in 22 normal adults. Similar effects were reported when 20 participants were given oral anaesthesia (to decrease oral sensation). Most of the participants rated the tastants as intense. The authors proposed that the "heightened sensory input" (p. 398) increased the participants' alertness as a protective mechanism towards noxious stimuli, thus the decreased rate of ingested bolus.

Hamdy et al. (2003) evaluated the effects of thermal (cold) and chemical (citrus) stimulation on swallowing in 65 healthy participants and in 22 patients following stroke using the water swallow test (Hughes & Wiles, 1996). Participants were asked to drink as quickly and as comfortably as possible a 50-ml solution and the number of swallows, volume ingested, and the time taken to complete the tasks were noted. The healthy participants were divided into younger (< 60 years old) and older age groups. The poststroke patients were divided into patients with dysphagia and patients without dysphagia (assessed by clinical assessment). Results showed that the ISI was reduced in the young subjects when cold citrus solution was used compared to water at room temperature. No changes in the ISI were detected in the elderly. The same cold citrus solution reduced swallowing speed and swallowing capacity in both groups of healthy participants compared to water at room temperature. Both patient groups showed reduced swallowing speed and swallowing capacity when cold citrus solution was used compared to water at room temperature. These results were similar to Chee et al.'s who also used cold taste stimulation. Hamdy et al. suggested that the "heightened sensory input may have generated a mildly noxious stimulus … causing the subject to attend more carefully to the task or through a conscious unpleasant perception of the bolus" (p. 75). The findings from Chee et al.'s and Hamdy et al.'s studies support the role for sensory stimulation in the management of patients with dysphagia, whereby slowing the transit time and reducing the size of a bolus may benefit patients who need more time to attend to the bolus and minimize aspiration.

Miyaoka et al. (2006) examined the effects of taste (sweet, sour, salty, bitter, and umami) on swallowing in 10 healthy adults. Using a psychometric method, they evaluated the subjective difficulty of swallowing each taste stimulus. On a five stage rating scale, participants were to report how easy or hard it was to swallow a stimulus compared to a standard stimulus. Their participants rated sweet food as easier to swallow, and bitter and sour foods as more difficult to swallow compared to the standard stimulus. In addition, the authors measured EMG activity in the suprahyoid muscles to evaluate the effects of taste on the biomechanics of swallowing. They reported three distinct bursts that correspond to mouth opening, bolus transfer to posterior oral cavity and pharynx, and laryngeal elevation. They measured the duration of the oral phase as the time from the second burst of suprahyoid activity on the EMG to peak of activity at the third burst. The authors reported no differences in the duration of the oral phase or the amplitude of peak muscle activity when sweet, sour, salty, bitter, and umami taste qualities were used, compared to distilled water. Similarly, no effects were seen when higher concentration of each tastant was used compared to the lower concentration stimuli. Results from Miyaoka et al.'s study did not show any differences in motor aspect of swallowing, but perceptual aspects (as rated by the participants) were modulated by the stimulation. The authors measured only the EMG activity of suprahyoid muscles as the outcome measurement for the motor aspect; therefore, one may not discount other motor changes following taste stimulation which may be present but were not measured in this study.

Leow et al. (2007) investigated the effects of sweet, sour, salty, and bitter tastes on submental muscle contraction in 25 healthy adult females. The participants were asked to chew and then swallow samples of gelatine cubes which were mixed with the tastants. Leow et al. reported that the sour tastant was prepared (chewed) in a shorter time compared to bitter and salty tastants. Moreover, the duration of submental EMG was decreased with sweet and sour stimuli compared to bitter stimulus. The sour taste provided the greatest amplitude of muscle EMG compared to other tastes. Leow et al. also reported no differences in the timing of swallowing apnoea within the respiratory cycle across all stimuli, with apnoeas predominantly occurring during midexpiration. Although this study incorporated chewing as a method, the swallowing manoeuvre after the chewing showed that it can be

modulated by taste. As the act of chewing will lengthen the time the stimulus is in the oral cavity, this may increase the time oral mucosa was exposed to the stimulation—similar to holding the bolus in the mouth prior to swallowing as was adopted in Ding et al.'s (2003) study. Likewise, Ding et al.'s finding of increased EMG amplitude is duplicated in Leow et al.'s study.

Logemann et al. (1995) used a sour bolus in an experiment to examine its effect on swallowing in 27 patients with neurogenic dysphagia. The patients were divided into two groups based on the aetiology of their dysphagia. The first group consisted of patients with dysphagia due to stroke (19 patients) and the second group consisted of patients with dysphagia due to other neurological problems (eight patients). The unequal number of patients in each group may bias the results reported in this study. Using videofluorography, the authors recorded swallowing when boluses of liquid barium and barium mixed with lemon juice were swallowed. The authors reported shorter swallowing onset time in all patients when lemon juice was added. Specifically for patients with dysphagia due to stroke, Logemann et al. reported a shortened oral transit and pharyngeal transit time, shortened pharyngeal delay time, and increased efficiency of oropharyngeal swallowing as a result of sour bolus presentation. The patients with dysphagia due to other neurological problems had late onset of tongue base to posterior pharyngeal wall (PPW) movement and shortened duration of tongue base contact to the PPW. These results support the use of sour taste in managing patients with dysphagia, particularly when the dysphagia was due to stroke.

Pelletier and Lawless (2003) examined the effects of citric acid and citric acid-sucrose mixtures on 11 patients with dysphagia. They found that the patients demonstrated less aspiration and penetration (confirmed endoscopically) when 5 ml of citric acid was given compared to deionized water. The citric acid-sucrose mixture resulted in a trend towards fewer incidents of aspiration and penetration but the effects were not significantly different to administration of water. Pelletier and Lawless also reported an increase in the frequency of spontaneous swallowing after the initial swallow which they presumed to be due to continuing stimulation of the taste receptors from excess boluses. They suggested that there was greater sensory input to the NTS by the continuing stimulation and increased salivation, which then lowered the swallowing threshold. Pelletier and Lawless have demonstrated that

citric acid has beneficial effect on swallowing but when it was mixed with sucrose, this effect is decreased. This would suggest that sour taste on its own can modulate swallowing; however, boluses of 5 ml were given, where the effect of volume may play a role. Nevertheless, this study supports the use of sour taste in managing patients with dysphagia.

Ebihara et al. (2005) investigated the effects of capsaicin troche on swallowing in 64 elderly participants (mean age 82 years) "with stable physical status" (p. 825). They measured the latency of the swallowing reflex and the sensitivity of the cough reflex. After 4 weeks of capsaicin troche supplementation before every meal, the experimental group showed a shorter swallowing latency time and improvement in cough reflex sensitivity compared to the group given placebo troche. The authors proposed that capsaicin improved swallowing by increasing the release of substance P, which is involved in nociception. With increasing substance P level, the sensory system is consequently more reactive towards any mechanical, thermal, or chemical changes, thus improving swallowing and cough reflexes.

Late Effects Following Gustatory Stimulation

A study in animal models has indicated the usefulness of gustatory stimulation in increasing the efficiency of swallowing. In one study utilizing anaesthetized rats with ligation of the major salivary ducts, Kajii et al. (2002) found that sour taste decreased the latency of the first swallow and increased the number of swallows compared to distilled water. The swallows were recorded at three time points: (a) during stimulation, (b) at 10 s poststimulation, and (c) at 30 s poststimulation. They claimed that the swallows were achieved by chemically (as opposed to mechanically) inducing the swallowing reflex in the pharynx and larynx, primarily via the superior laryngeal nerve, and assisted by pharyngeal branch of the glossopharyngeal nerve. The authors justified this claim with observation that no swallowing reflex was observed when the same procedures were repeated with saline. After the stimulus was turned off, some successive swallows continued, indicating that excitation of the neural substrates was prolonged. Prolonged excitation of neural substrates can lead to the development of long-term potentiation (LTP), which has been implicated as the mechanism involved in neural plasticity (Cooke & Bliss, 2006). The effect was greater when a higher concentration acid was

used, which they proposed was associated with substance P release from the sensory nerves. Substance P is a neurotransmitter mainly involved in nociception and it is released when a sensory nerve is stimulated (Ganong, 2002). More substance P is released when a higher concentration stimulus is presented compared to a lower concentration stimulus. Although the sensory stimulation has been discontinued, some residue of the stimulus may continue to excite the sensory receptors, thus prolonging the effect seen in Kajii et al's study. The concentration of substance P is maintained until it is degraded or binds to its receptors (Ganong, 2002). Once LTP is induced following the initial stimulation, it can last for a longer duration, probably up to 2-4 days (Aslam, Kubota, Wells, & Shouval, 2009; Le Ray & Cattaert, 1999). Other researchers evaluating long-term changes in swallowing function have also suggested the involvement of LTP in brain plasticity (Doeltgen, Dalrymple-Alford, Ridding, & Huckabee, 2010; Fraser et al., 2002). It is intriguing that sensory stimuli could still have an effect after the stimulus was removed and probably indicated that the presence of substance P made the system more reactive towards the progress of LTP.

In summary, most studies have reported changes in swallowing, either excitatory or inhibitory, when gustatory stimuli were used. The proposed mechanism resulting in these changes is the influence of sensory stimulation on the NTS, which subsequently affects the swallowing motor system. Most participants in Logemann et al.'s study (1995) reported that the sour bolus was not a pleasant taste, thus the authors suggested future researchers look at determining the optimal concentration of sour tasting material to improve swallowing but yet have an acceptable taste.

2.3.4.3 Visual Stimuli

The effects of visual stimulation on swallowing behaviour have only been minimally investigated. Only one report was identified which postulated that swallowing would improve with increased visual input to the cortex. Maeda et al. (2004) recruited seven healthy young adults (mean age 27 years) and measured swallowing during dry and 3-ml bolus swallows, while coloured pictures of a drink or an unrelated object (a pair of scissors) were shown. They found increased peak EMG amplitude and decreased latency of the start of contraction of the suprahyoid muscles during bolus swallowing when a drink-related visual stimulus was presented

compared to the unrelated object. The observation strengthened their hypothesis that visual input can influence swallowing.

2.3.4.4 Multimodal Sensory Stimulation

Sensory representation in the orbitofrontal cortex can be unimodal or multimodal (Rolls, 1989). Unimodal representation indicates that the cortex can only be stimulated when one modality of sensory input is presented, compared to multimodal representation where more than one type of sensory inputs can stimulate the cortex. The representation of taste, odour, and visual stimuli in the caudolateral orbitofrontal taste areas are unimodal and account for 47%, 12%, and 10% of the neurons, respectively. The convergence of taste with odour, taste with vision, and odour with vision are 10%, 17%, and 4% of the neurons, respectively. In addition, neurons in the ventral posteromedial nucleus of the thalamus, which is known to convey taste information, are also responsive to tactile stimuli (Rolls, 1989). As many types of sensory representation are present in the cortex, activation of these areas would be enhanced when more types of stimulation are included. Therefore, it could be hypothesized that swallowing will be more affected if several types of stimuli are combined.

2.3.4.5 Decreased Sensory Stimulation

The reverse of increased sensory input is decreased sensitivity of the sensory system, which can be achieved by anaesthesia. Studies have demonstrated that the use of analgesics have a negative impact on swallowing (Ali, Laundl, Wallace, DeCarle, & Cook, 1996; Fraser et al., 2003; Fujiki et al., 2001; Jafari et al., 2003; Sulica et al., 2002). Anaesthesia can also impair oral spatial sensitivity (Engelen, van der Bilt, & Bosman, 2004) and decrease stereognostic (shape and texture recognition) ability (Dahan, Lelong, Celant, & Leysen, 2000). Although inhibition is not generally a focus on rehabilitation, these studies support the manipulation of sensory input to facilitate swallowing.

To summarize, sensory input is important for the regulation of swallowing. Increasing the frequency of stimulation, or the type of differing sensory modalities, is known to increase facilitation of swallowing. However, not all cases of swallowing

impairment need swallowing to be faster for it to be safer or more efficient, as the slowing of swallowing has been shown to decrease patient's risk of aspiration (Hamdy et al., 2003). Thus, the inclusion of sensory stimulation may benefit patients with dysphagia, whether to increase the swallowing efficiency or to slow swallowing to give time for patients to manoeuvre the bolus safely.

2.3.5 Medical Conditions

Medical conditions that can give rise to swallowing problems can be grouped into: (a) neurologic disorders, (b) structural problems, (c) psychiatric disorders, and (d) iatrogenic causes (adapted from Palmer, Drennan, & Baba, 2000). Neurogenic dysphagia results from many conditions, including stroke, traumatic brain injury, neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease, and multiple sclerosis, and iatrogenic causes, such as after a tumour resection in the neck region. Some patients will not complain of being dysphagic, particularly if his/her condition is due to a gradual decline in neurological function (Buchholz & Robbins, 2003). Buchholz and Robbins further elaborated that failure to recognise dysphagia could happen if any one or more of these three factors were present: (a) compensation which has been linked with neuroplasticity, (b) a reduction in the laryngeal cough reflex, or (c) a cognitive impairment. Generally, patients in a state of delirium or impaired alertness have increased risk of aspiration because of reduced or absent awareness of food in their mouth (Langmore, Skarupski, Park, & Fries, 2002). Even if the sensory aspects of the glossopharyngeal and vagus nerves are intact, these patients would still have a problem recognizing the presence of food in the mouth due to "oral or gustatory agnosia" (Perlman, Lu, & Jones, 2003, p. 158).

Structural problems affecting swallowing can be congenital or due to a medical condition. Examples of congenital anatomic abnormalities are cleft lip and palate, velopharyngeal incompetence, and laryngeal clefts (McCulloch, Jaffe, & Hoffman, 2003). Medical conditions that can give rise to dysphagia are postintubation oedema, laryngeal web, pharyngeal masses, and diverticulae (Buchholz & Robbins, 2003).

Psychogenic swallowing disorders are conditions in which all possible physical diagnoses have been excluded, the most common disorder is globus pharyngeus or globus hystericus (McCulloch et al., 2003). Globus is a sensation of a lump in the throat and it is associated with psychological problems. More younger women than men were reported to have dysphagia in Ekberg and Wahlgren's (1985) study, such that the authors suggested that women are more prone to psychogenic swallowing disorders.

Iatrogenic causes that can lead to dysphagia can be grouped into three causes: (a) surgical resection, (b) radiation fibrosis, and (c) medications (discussed in Section 2.3.6). Besides the obvious anatomical effect of surgical resection and radiation fibrosis on swallowing, another symptom attributed from these causes is xerostomia, a dry mouth condition due to lack of saliva. Xerostomia can also result from systemic diseases and salivary gland hypofunction (McCulloch et al., 2003; Thie, Kato, Bader, Montplaisir, & Lavigne, 2002). When salivary flow is reduced, there is a prolonged oral preparation time (Perlman et al., 2003) but with no change in bolus transit time (Logemann et al., 2001).

2.3.6   Medications

The use of medications can have both positive and adverse effects in managing patients with dysphagia. For example, Levodopa used in patients with Parkinson's disease was found by Fonda, Schwarz, and Clinnick (1995) to be beneficial because it reduced tremor in the muscles associated with swallowing. However, a meta-analysis of seven studies which evaluated the effects of Levodopa on swallowing in patients with Parkinson's diseases showed no association between Levodopa and swallowing improvement (Menezes & Melo, 2009). It has also been noted that medications that can impair cognitive function may also impair the voluntary stage in swallowing, specifically the oral stage (Feinberg, 1997).

One of the common side effects of medications that could negatively influence swallowing is xerostomia, or abnormal dryness of the mouth due to decreased salivary production. In a review of medications used to treat age-related diseases, Gallagher and Naidoo (2009) found that "swallowing difficulties", gastrointestinal effects, taste disturbance, and xerostomia were mentioned as possible

side effects in 5%, 65%, 12%, and 25%, respectively, of the medications under evaluation. They also evaluated 10 patients with oropharyngeal dysphagia, and reported that 6 (60%) had xerostomia, all of whom took three to nine medications that noted xerostomia as a side effect.

Other adverse effects of medications that can potentially affect swallowing are muscle wasting associated with long-term steroid use, muscle dysfunction associated with hypo- or hyper-thyroid problems, tardive dyskinesia in the orofacial and lingual muscles following antipsychotic medications, decreased appetite, taste alteration, nausea, abdominal discomfort, pharyngeal ulceration, anorexia, drug-induced confusion, stomatitis, and superinfection (Feinberg, 1997). Additionally, in a study on a nursing home population, Langmore et al. (2002) reported that one of the predictors for pneumonia is increased number of medications taken by a patient.

In summary, many factors can influence swallowing function and how patients respond to treatment. What is important to note is that dysphagia is not a disease; it is a presentation of an underlying problem, which sometimes could be overlooked. Therefore, every patient's concern should be taken into account in identifying the best approach to address the problem. Treatment should be based on the individual's presenting pathophysiology symptoms, with the end result of achieving adequate oral diet for nutrition.

2.4 Management of Swallowing Impairment

As detailed earlier in this chapter, dysphagia can be a consequence of several anatomical and physiological deficits and involves the psychological well being of the patient. Therefore, the best management of this disorder is a multidisciplinary approach in which professionals from different backgrounds work together for the benefit of the patient (Massey & Shaker, 2003). The compensatory approach to dysphagia is usually introduced first at the early stage of patient's management (Logemann, 2003). However, as compensatory techniques do not induce long-term improvements in swallowing function, rehabilitation techniques have been developed to manage patients with dysphagia, as these techniques can lead to long-term improvements in swallowing. Nevertheless, compensatory techniques still play an

important role in maintaining oral intake, as the benefits of rehabilitative techniques may be minimal or, at least, not apparent during the early phase of treatment.

2.4.1 Compensatory Approach

The compensatory approach to dysphagia provides immediate adaptation to swallowing biomechanics. Ideally, the success of this approach should be confirmed instrumentally before it is prescribed to the patient (Daniels & Huckabee, 2008; DePippo, Holas, Reding, Mandel, & Lesser, 1994). The benefits may be seen as improved bolus containment and flow compared to when no compensatory technique is used. Improved bolus containment and flow may result in reducing the amount of pooling and residue, respectively. The targeted end result is elimination of aspiration, which can decrease the risk of aspiration pneumonia in the patient. Examples of this approach are sensory enhancement, volitional control of oral transfer, postural changes during feeding, bolus modification, and breath-holding techniques (Daniels & Huckabee, 2008).

2.4.1.1 Sensory Enhancement and Volitional Control of Oral Transfer

Adequate sensory input from the oral cavity and pharynx is critical for elicitation of swallowing (Ertekin, Kiylioglu, Tarlaci, Keskin, & Aydogdu, 2000; Yahagi, Okuda-Akabane, Fukami, Matsumoto, & Kitada, 2008). Patients with swallowing impairment, particularly due to neurological problems, may have sensory deficit in the oral cavity and pharynx and present with the pathophysiologic feature of delayed pharyngeal swallow. Sensory enhancement is a compensatory technique to facilitate timely onset of swallowing. The enhancement may be presented prior to swallowing by increasing sensory input in the preoral and oral stages of swallowing. For example, presenting visually appealing food (Maeda et al., 2004) which smells pleasant (Abu-Hijleh et al., 2006) may enhance sensory input in the preoral stage. A strong flavour, for example sour, and cold food (Hamdy et al., 2003) may add multimodal sensory modalities that could potentially increase the sensory input to trigger swallowing.

Thermal-tactile stimulation (TTS) is a therapy which involves multimodal sensory modalities. TTS is a compensatory technique in managing patients with

dysphagia in which a probe is moved against the anterior faucial pillar from base to midline prior to swallowing. Sciortino et al. (2003) reported that TTS on its own was not effective in facilitating swallowing compared to when it was combined with sour stimulation. This finding strengthens the hypothesis that multimodal sensory stimulation can increase swallowing efficiency. However, the use of a sour bolus alone has been shown to improve the onset of oral swallowing, reduce pharyngeal delay, reduce oral and pharyngeal transit times, and decrease frequency of aspiration in poststroke patients compared to when no sour bolus is given (Logemann et al., 1995).

Carbonation of water is a compensatory method used in dysphagia management that is reported to have mixed results. Miura, Morita, Koizumi, and Shingai (2009) reported that submental EMG changes when carbonated fluid was used were similar to the effect seen with citric acid. Presumably, these effects were different compared to a control condition. However, Ding et al. (2003) found no differences when carbonated water was compared to distilled water. The dissimilarity may be explained by the different methods used in both studies; the 5-ml bolus in Ding et al.'s study may not be as effective as the 60-ml continuous drinking in Miura et al.'s study as less carbon dioxide bubbles were likely present in a small bolus compared to a larger bolus (Miura et al., 2009).

Volitional control of oral transfer can be achieved by following the 3-s prep in which patients are asked to hold the bolus in the oral cavity for 3 s before attempting to swallow. This technique may benefit patients with delayed pharyngeal swallowing as volitionally controlling the bolus prior to swallowing can modify the reflexive component of swallowing to be under increased volitional control (Huckabee & Pelletier, 1999).

2.4.1.2   Postural Changes during Feeding

Repositioning one's posture during feeding can be used to change pharyngeal dimension and redirect bolus flow (Daniels & Huckabee, 2008). As this technique relies upon the patient's cooperation, patients with cognitive impairment may not be suitable candidates for this approach. Examples of compensatory techniques involving postural changes are chin tuck and head turn.

Chin tuck is a postural change in which the patient is asked to bring his or her chin down towards the neck before food is transferred to the posterior oral cavity. The new position shortens the pharynx with consequent decrease in the pressure and duration of pharyngeal contraction (Bulow, Olsson, & Ekberg, 1999). In contrast, no manometric changes were reported by Castell, Castell, Schultz, and Georgeson (1993) during chin tuck. During a chin tuck manoeuvre, the posterior part of tongue is moved towards the posterior pharyngeal wall (Welch, Logemann, Rademaker, & Kahrilas, 1993), this pose puts the epiglottis in a more protective position to protect the larynx and may increase the pharyngeal pressure (Davies, 1999). Lingual swallowing pressure was also reported to increase during chin tuck compared to neutral position (Hori et al., 2011). Studies on patient population have shown that chin tuck improved swallowing and decreased the frequency of aspiration compared to control swallowing (Bulow, Olsson, & Ekberg, 2001; Ertekin, Keskin et al., 2001).

Head rotation to one side redirects bolus to the opposite side in the pharynx (Ohmae, Ogura, Karaho, Kitahara, & Inouye, 1998). Therefore, in patients with swallowing problem due to weakness on one side of the pharynx, head rotation to the weaker side redirects bolus into the pharynx with normal contractile function. During head rotation, the hypopharyngeal wall on the opposite side is stretched with consequent dilation of the pharyngeal cavity (Tsukamoto, 2000). Other biomechanical changes seen during head rotation are increased pharyngeal pressures at the level of valleculae and pyriform sinus corresponding to the rotation side, increased duration from peak pharyngeal pressure to the end of UES opening, and decreased UES resting pressure at the opposite side of head rotation (Ohmae et al., 1998). Increased pharyngeal pressure at the rotation side will ensure that misdirected bolus (if present) can be cleared from the pharynx. Changes in the dynamics of the UES associated with head rotation may facilitate bolus transfer towards the oesophagus. In patients with unilateral oropharyngeal dysphagia, head rotation has been shown to improve swallowing (Ertekin, Keskin et al., 2001) and decrease aspiration (Logemann & Kahrilas, 1990) compared to when no manoeuvre was involved.

2.4.1.3   Bolus Modification and Breath-Holding Techniques

Bolus modification is a technique in which liquid is thickened or solids are pureed to suit patient's swallowing physiologic abnormalities (Molseed, 1999). The beneficial effect of using bolus modification as a compensatory technique has to be evaluated with an appropriate instrument before recommending it to the patient (DePippo et al., 1994). Diet modification should only be prescribed when other compensatory techniques are not feasible (Logemann, 2003) as removing certain type of food—such as thin liquids—can be difficult for the patient (Logemann, 1999) and decrease in food intake may lead to dehydration (Molseed, 1999).

As diet modification has to match a patient's ability to swallow safely, correct diagnosis is vital. For example, a patient with oral stage dysphagia characterized by poor tongue control resulting in premature spillage and pooling in the valleculae may have difficulty taking liquid as the liquid can trickle into the valleculae prior to swallowing and cause aspiration. A thickened liquid and smaller bolus per swallow may mediate this problem (Abou-Elsaad, 2003). In contrast, a patient with oral transit phase dysphagia characterized by delayed pharyngeal swallow resulting in preswallow pooling in the valleculae may need more sensory input from the oral cavity to trigger a timely swallow. Thus, a larger bolus volume with additional sensory attribute such as sour taste may help improve the elicitation of swallowing (Logemann, 2003).

Breath-holding techniques are designed to protect the airway. The supraglottic and super-supraglottic swallows are two techniques which involve taking a deep breath, swallow during the breath-holding, followed by coughing before resuming respiration. The super-supraglottic swallow includes bearing down (as in trying to lift heavy thing, or swallow hard) during the swallow (Boden, Hallgren, & Witt Hedstrom, 2006; Logemann, 1983). These techniques can prevent aspiration (and penetration for super-supraglottic swallow as it closes the laryngeal inlet) before and during the swallow.

In conclusion, compensatory techniques—which are designed to redirect bolus flow to eliminate or reduce the symptoms of dysphagia—may be useful during swallowing but they do not necessarily change the physiology of swallowing

(Logemann, 1999) to retain a long-term effect on function. Rehabilitative techniques can be prescribed to change swallowing neural substrates for long-term effect.

2.4.2   Rehabilitative Approach

Dysphagia rehabilitation is defined as any strategies or "interventions that when provided over the course of time are thought to result in permanent changes in the substrates underlying … swallowing mechanisms" (Huckabee & Pelletier, 1999, p. 4). Neuronal changes in the unaffected cortical areas, or plasticity, particularly in patients with unilateral stroke, have been reported in patients with resolution of dysphagia (Barritt & Smithard, 2009). The main aim of rehabilitative treatment is to restore function, preferably to near normal, which may be achieved by interventions in the form of special training routines (Bass & Morrell, 1992). The choice of intervention is based on the physiologic abnormalities and the resulting presenting symptoms (for review, see Daniels & Huckabee, 2008, pp. 252-254). Therefore, dysphagia needs to be diagnosed correctly before attempting to manage the patient as different diagnoses require different treatment protocols (Bartolome & Neumann, 1993; Huckabee & Pelletier, 1999). A treatment prescribed to a patient that does not appropriately address the patient's physiologic abnormality could potentially be hazardous as it can exacerbate the symptoms, thus increasing the risk of aspiration (Garcia, Hakel, & Lazarus, 2004).

Several rehabilitative techniques designed to manage dysphagia are oral motor exercises and neuromuscular exercises, as in effortful swallowing, Mendelsohn manoeuvre, and head-lift exercises (Daniels & Huckabee, 2008). Although not generally considered a rehabilitative technique, sensory stimulation, which may have long-term effect on swallowing, is included in this discussion.

2.4.2.1   Oral Motor Exercises

The anatomical structure primarily involved in oral motor exercises for swallowing is the tongue. The Iowa Oral Pressure Instrument (IOPI) has been used in studies evaluating lingual pressures during isometric task and during swallowing.

Oral Motor Exercises in Healthy Population

Robbins, Levine, Wood, Roecker, and Luschei (1995) and Nicosia et al. (2000) reported similar lingual pressure during normal swallowing in elder and young cohorts, but lingual pressure during a maximal isometric task was decreased in the elders compared to the younger group. Additionally, Nicosia et al. also reported that elders needed more time to achieve the maximal pressure. The authors of these studies concluded that there was a decline in muscle strength in the elderly when compared to younger individuals. Swallowing pressure was similar in both groups because normal swallowing function uses submaximal pressure; the pressure reserve is utilized in a stressed situation (Robbins et al., 1995).

Another study was conducted to evaluate the effects of lingual exercise on muscle strength (Robbins et al., 2005). Ten healthy elderly participants (age 70-89 years) completed an 8-week progressive lingual resistance exercise programme. At the end of the study, all participants exhibited increased isometric and swallowing pressures, and increased lingual volume by 5.1% when scanned with magnetic resonance imaging. Another tongue exercise experiment on 31 young participants (age 20-29 years) compared the effects of two types of tongue exercises (using tongue depressor or IOPI) with no tongue exercise for 1 month (Lazarus, Logemann, Huang, & Rademaker, 2003). Posttreatment, the authors reported increases in tongue strength for both types of exercise compared to no treatment. However, no differences were noted between the exercise using tongue depressor and IOPI. Thus, it may be possible to achieve the same outcome using the relatively cheaper tongue depressor compared to IOPI.

Oral Motor Exercises in Patients with Dysphagia

Subsequent to their encouraging findings on healthy volunteers, Robbins et al. (2007) conducted an 8-week isometric lingual exercise programme using IOPI in six acute ($\leq$ 3 months) and four chronic poststroke patients. At baseline, all patients presented with aspiration, penetration, or oropharyngeal residue, confirmed videofluoroscopically. All 10 patients were analysed as a group. Compared to baseline, the maximum isometric pressure and swallowing pressure were increased, and the penetration-aspiration scale was decreased, indicating increased swallowing safety after the exercise programme. Although lingual exercises are commonly used

in clinical practice for dysphagia management, data on its effectiveness are scarce. Nonetheless, Robbins et al. has shown that oral motor exercises can positively influence swallowing, be it in health or in dysphagic condition.

2.4.2.2   Neuromuscular Exercises

Neuromuscular exercises (NMEs) are prescribed to overcome weakness, fatigue, and disrupted muscle tone (Clark, 2003). There are three categories of NME outlined by Clark: active exercise, passive exercise, and physical agent modalities. Active exercises are exercise strategies designed to improve swallowing function. One example of active exercise is strength training with the aims to increase strength (by increasing the amount of force a muscle can produce), endurance (the amount of force that can be sustained over time), and power (the speed at which force is produced). An important aspect in active exercise is the specificity of training (Kleim & Jones, 2008), that is, the appropriate NME is prescribed based on the diagnoses of neuromuscular impairments. Passive exercises are exercises that are performed by clinicians; for example, when patients could not move their limbs, the clinician would exercised the limb for them using an exercise technique called passive range of motion (PROM). Although PROM is frequently used in limb musculature, it may have a very limited therapeutic advantage in swallowing rehabilitation. Physical modalities used as NME are heat, cold, vibration, electricity, sound, and electromagnetic waves, all of which can influence the muscles directly. For instance, neuromuscular electrical stimulation has been successfully used to manage patients with dysphagia (Fraser et al., 2002). In this document, however, physical modalities are grouped under Sensory Stimulation (Section 2.4.2.3) together with other sensory stimulation, particularly smell and taste, which is not included in the review article by Clark (2003).

Safer swallowing may be achieved by prolonging UES relaxation or increasing the amount of pressure to push the bolus through pharyngeal lumen, for example, by performing Mendelsohn manoeuvre or effortful swallowing, respectively. These swallowing techniques are muscle strengthening exercises, which include manipulation of musculature involved in swallowing (Logemann, 1998, 2003; Murry, 1999). Considerable research evaluating the effects of neuromuscular exercises on swallowing has been reported (Boden et al., 2006; Bulow et al., 1999,

2001; Bulow, Olsson, & Ekberg, 2002; Ding, Larson, Logemann, & Rademaker, 2002; Doeltgen et al., 2007; Gallas, Marie, Leroi, & Verin, 2009; Garcia et al., 2004; Hind, Nicosia, Roecker, Carnes, & Robbins, 2001; Hiss & Huckabee, 2005; Huckabee, Butler, Barclay, & Jit, 2005; Huckabee & Steele, 2006; Kahrilas, Logemann, Krugler, & Flanagan, 1991; Neumann, Bartolome, Buchholz, & Prosiegel, 1995; Steele & Huckabee, 2007; Witte, Huckabee, Doeltgen, Gumbley, & Robb, 2008; Yoshida, Groher, Crary, Mann, & Akagawa, 2007) but as the focus of this project is not on neuromuscular exercises, this research will be only briefly summarised in this document.

Neuromuscular Exercises in Healthy Population

An exercise technique that is prescribed in the treatment of dysphagia to assist in UES opening is the Mendelsohn manoeuvre. The Mendelsohn manoeuvre is described as a "voluntary prolongation of laryngeal excursion at the midpoint of the swallow" (Kahrilas et al., 1991, p. G450). Using videomanometry, Boden at al. (2006) evaluated changes in the pharyngeal lumen and UES during swallowing when Mendelsohn manoeuvre was performed. They studied 10 healthy participants who were first taught the manoeuvre before data collection. Compared to control swallows, the authors reported differences at the level of inferior pharyngeal constrictor, that is, increased pharyngeal pressure and prolonged duration of pharyngeal contraction, and prolonged bolus transit time. The maximal UES contraction (the second peak of M wave) was decreased and the duration of UES opening was not prolonged compared to control swallowing. These results did not support the role of Mendelsohn manoeuvre, which is to prolong the opening of UES. The neuromuscular exercise may not have an effect in healthy participants as the swallowing muscles were in optimal condition.

Another exercise technique that can be prescribed to patients with dysphagia is effortful swallowing. Reduced maximal hyoid movement and reduced laryngeal elevation were reported by Bulow et al. (1999) when participants in their study completed effortful swallowing compared to normal swallowing. At the initiation of the effortful swallowing, the hyoid was in a higher position compared to normal swallowing, which also elevated the larynx. Thus, the relative maximal hyoid movement and laryngeal elevation were reduced during effortful swallowing

compared to normal swallowing. Bulow et al. speculated that increased tension in the muscles during effortful swallowing caused muscle shortening, thus the initial lifting of hyoid bone. Daniels and Huckabee (2008) offered an alternative explanation to the reduced laryngeal elevation seen in Bulow et al. study. During effortful swallowing, all swallowing muscles are recruited to enforce swallowing with effort. As the muscles that pull the hyoid posteriorly (posterior belly of digastric, stylohyoid, and middle pharyngeal constrictor) are larger than the muscles that pull it anteriorly (anterior belly of digastric, mylohyoid, and geniohyoid), the cumulative effect is seen as a reduction in maximal hyoid movement.

Hind, Nicosia, Roecker, Carnes, and Robbins (2001) compared the effects of effortful and normal swallowing in 20 healthy participants (age 45-93 years) when they ingested 3-ml boli. Durations of hyoid maximum anterior excursion, laryngeal vestibule closure, and UES opening were longer and lingual pressure was higher during effortful swallowing compared to regular swallowing. The authors suggested that effortful swallowing may be a technique to include volitional component in airway closure, as the larynx was closed for a longer duration, which may decrease the frequency of aspiration.

Another neuromuscular exercise that may be beneficial in the treatment of dysphagia is head-lift exercises, which were described by Shaker et al. (1997, p. G1518) as

> … three repetitive 1-min sustained head raisings in the supine position, interrupted by a 1-min rest period. These … exercises were followed by 30 consecutive repetitions of head raisings in the supine position, interrupted by a 1-min rest period. … For both sustained and repetitive head raising, volunteers were instructed to raise their heads high enough to be able to observe their toes without raising their shoulders off the ground.

Head-lift exercises in healthy elderly participants produced larger diameter of UES opening, increased anterior hyolaryngeal excursion (Easterling, Grande, Kern, Sears, & Shaker, 2005), and decreased hypopharyngeal intrabolus pressure (signifying decreased pharyngeal outflow resistance) compared to baseline (Shaker et al., 1997). A lot of complaints associated with the exercises were reported by the participants, for example neck pain, such that only 50% and 70% of the participants completed the exercises and reached the goals for isometric and isokinetic exercises,

respectively. Thus, the authors proposed that "a more structured and progressive program is needed to attain the … exercise goals" (Easterling et al., 2005, p. 137).

As head-lift was deemed difficult to carry out, Yoshida, Groher, Crary, Mann, and Akagawa (2007) tested another exercise which they thought could give similar results, at least in increasing the contraction of submental muscles, which is also part of the pharyngolaryngeal system that is involved in UES opening (Cook et al., 1989; Kahrilas et al., 1991). However, the alternative exercise chosen by Yoshida et al. may not be an equal comparison to head-lift as different set of muscles may be involved during its execution. The authors examined isometric and isotonic tasks for both head-lift and tongue press exercises and compared how these tasks affected the surface EMG (sEMG) of submental muscles. They reported no therapeutic advantage (in sEMG measurement) of head-lift compared to tongue press exercises; in fact, isotonic tongue press exercise produced higher sEMG readings than isotonic head-lift exercise. Therefore, the authors proposed the use of tongue press exercise, which is less strenuous, especially in patients who find head-lift difficult to master. Unlike head-lift which has been documented to have an effect on UES opening (Shaker et al., 1997), tongue press exercise may not be effective in this regard. Unfortunately, the authors did not include measures of UES in this study. However, Yoshida et al. did not discount the therapeutic benefit of head-lift exercises in dysphagia management, as their study evaluated 10 isometric head-lifts and 10 s isotonic head-lifts compared to the head-lift exercises recommended by Shaker (as above, 1997).

Neuromuscular Exercises in Patients with Dysphagia

Lazarus, Logemann, and Gibbons (1993) evaluated the effects of exercises (supraglottic, super-supraglotic, and Mendelsohn) on some swallowing measures in a nonoral postsurgical oral cancer patient with dysphagia. The swallowing exercises were performed during bolus swallowing and compared with swallowing without the exercises. Lazarus et al. reported no aspiration and decreased pharyngeal residue when Mendelsohn manoeuvre was performed compared with swallowing without performing the exercise. However, the location of the residue was not stated. Compared to the other two exercise techniques, Mendelsohn manoeuvre was the best exercise for the patient to accomplish safe swallowing. Thus, it was chosen as the exercise to be utilised by this patient. Postintervention videofluoroscopy three

months later showed he was swallowing safely when Mendelsohn manoeuvre was performed. It was documented that the patient had to use this technique every time he ate; otherwise, he would aspirate. Although no other data were recorded to evaluate neural changes that may occur following the intervention, the fact that he can eat orally when the Mendelsohn manoeuvre was used would suggest that this technique is beneficial to him. Unfortunately, no other long-term data was obtained from this patient as he had a recurrent cancer and passed away two years later.

Neumann, Bartolome, Buchholz, and Prosiegel (1995) evaluated patients' progress from tube feeding to oral diet when direct and indirect swallowing therapy were administered. Direct swallowing therapy consisted of compensatory strategies (such as postural adjustment and head rotation) and swallowing techniques (for example, supraglottic swallowing and Mendelsohn manoeuvre), while indirect swallowing therapy included methods that were utilised to enhance the sensory aspects of swallowing which can indirectly affect swallowing or taught patients the skills needed to perform direct therapy. The latter was divided into three categories: (a) stimulation, for example, faucial pillars stimulation with cold laryngeal mirror prior to swallowing; (b) assisted exercises, such as lingual exercises where the patient was requested to push against a wooden spatula held by the therapist; and (c) independent exercises, for example, the skill to elevate larynx is taught to patients, which is useful in Mendelsohn manoeuvre. Indirect swallowing therapy attempts to "stimulate the swallowing reflex and restore voluntary orofacial, lingual, and laryngeal motor activity" (p. 2). Fifty-eight patients (age 22-84 years) seen over 5 years for treatment of dysphagia were retrospectively studied. Based on clinical and radiographic assessments, the swallowing therapist prescribed indirect therapy alone to 29 patients, both direct and indirect methods to 28 patients, and direct therapy alone to one patient. As the number of patients in each category of treatment was not comparable, the efficacy of each treatment in improving swallowing cannot be concluded. Nevertheless, the authors reported 67% and 14% of the patients were exclusively oral feeding and tube feeding, respectively, at the end of the study. This shows that swallowing therapy, which also comprises of neuromuscular exercises, is beneficial for patients to resume oral diet.

The effects of effortful swallowing (along with other swallowing techniques) in patients with dysphagia were evaluated by Bulow et al. (2001). The participants

were five patients who had severe pharyngeal dysphagia with misdirected swallowing and three patients who had moderate pharyngeal dysphagia with delayed swallowing initiation. The number of participants used in this study was small and they have different types of dysphagia, which may be affected differently with the swallowing technique. The authors reported that effortful swallowing did not reduce the number of misdirected swallows but the depth of contrast penetration is significantly reduced in this group of patients. Four of the eight patients were reported to have difficulties performing the effortful swallowing, which may bias the results reported in this study.

Shaker et al. (2002) evaluated swallowing performance in 11 patients with dysphagia following head-lift exercises. They reported larger diameter of UES opening, increased anterior hyolaryngeal excursion, and decreased postswallow pyriform sinus residue compared to baseline measures. Postdeglutitive aspiration was also eliminated in all patients; however, predeglutitive aspiration was still present. This phenomenon is consistent with the aim of head-lift exercises, which is to assist in the opening of UES; thus, any aspiration prior to swallowing may not be eliminated by this technique.

2.4.2.3 Sensory Stimulation

Sensory stimulation is used in the management of patients with dysphagia as a compensatory technique (Ebihara et al., 2005; Hamdy et al., 2003; Logemann et al., 1995; Pelletier & Lawless, 2003; Rosenbek, Roecker, Wood, & Robbins, 1996). However, there is evidence that cortical plasticity is apparent if stimulation is given up to 30 days (Ebihara et al., 2006). What is not currently known is how long the effects of the initial sensory stimulation can last. Not many research projects have evaluated the long-term effect of sensory stimulation; Mistry et al. (2006) recorded pharyngeal motor-evoked potentials (pMEPs) in nine healthy volunteers up to 60 min poststimulation following the presentation of sweet (glucose), bitter (quinine), or neutral (water) tastes. The stimuli were refrigerated at 4°C. Using visual analogue scale (VAS), participants were asked to rate the pleasantness/unpleasantness of each solution. The volunteers rated water as neutral and glucose as pleasant; quinine was rated as unpleasant. Mistry et al. reported reduced pMEPs 30 min poststimulation following sweet and bitter tastes, which they attributed to a behavioural consequence

of the strong flavour used. However, as the stimuli were presented cold, there is another factor to consider, that is, reduced temperature, which may confound the results.

Vision, olfactory stimuli, and other environmental factors that could heighten a person's perception of food acceptability may influence swallowing at the early stage, with a goal of producing safer swallowing and an increase in food intake. Olfaction has been reported as a rehabilitation modality in studies of patients with swallowing impairment where positive results were seen (Ebihara et al., 2006; Munakata et al., 2008). Ebihara et al. (2006), who used black pepper oil for 30 days in elderly patients, reported improvement in swallowing biomechanics and increased rCBF in the insula and orbitofrontal cortices (discussed in Section 2.3.4.1). Similarly, Munakata et al. (2008) reported increased food intake when black pepper oil was presented to children with tube feeding. These studies verified the use of olfactory stimulation in managing patients with dysphagia.

Fraser et al. (2002) evaluated the effects of pharyngeal stimulation on corticobulbar excitability in healthy adults and patients with dysphagia due to stroke. They reported increased corticobulbar excitability when the pharynx was stimulated at 5 Hz using 75% maximum tolerated intensity for 10 min. The effect lasted for 90 min poststimulation. In the patient group, increased corticobulbar excitability was associated with improvement in swallowing measures and reduction in the frequency of aspiration. Using fMRI, the authors found that the main effects were seen in the sensorimotor cortex, particularly in the unaffected hemisphere. The authors concluded that "sensory-induced changes in corticobulbar excitability … may … promote recovery of function after brain injury" (p. 837).

In conclusion, many treatment approaches, including sensory stimulation, have significant rehabilitative potential which, based on definition, would bring about lasting effects in swallowing function. Limited data are available on the long-term effects of sensory stimulation, particularly of smell and taste, which deserve further investigation. This is an important task to undertake as sour taste has been reported to have beneficial effect in swallowing but its long-term effect as a rehabilitative tool is not known.

2.5 Chemical Senses

There are four types of chemical senses (Shepherd, 1994): (a) common chemical, (b) internal chemoreceptors, (c) smell, and (d) taste. The common chemical senses, smell, and taste, are external sensory modalities. Internal chemoreceptors are responsible for monitoring chemical changes inside the body, such as the carotid body in the internal carotid artery which detects changes in oxygen levels and glucose receptors in the brain which monitor blood glucose levels. The common chemical senses are composed of free nerve endings in the mucous membrane of the eyes, nose, and the gastrointestinal tract. These neural cells are sensitive to chemical irritants, both in vapour and liquid form. Information from these sites is mainly carried by the trigeminal nerve, hence the term trigeminal stimulation. The common chemical senses and internal receptors are not the main focus of this project and are, therefore, not discussed further.

2.5.1 Olfaction

Olfaction is one of the five senses in humans. It is a primitive and important sense for survival, particularly in animals, as odours can be detected from great distances via air flow. Carlson (2001) noted that odours are able to "evoke memories, often vague ones that seem to have occurred in the distant past" (p. 236). It is difficult to describe an odour, as the olfactory system "appears to be specialized for identifying things, not for analyzing particular qualities" (p. 236). Sniffing increases odour detection because less than 10% of the air that we breathe reaches the olfactory epithelium (Carlson, 2001).

Olfaction is the only sensory system in the body that is transmitted directly to the cortex, unlike other sensory modalities that travel through the thalamus, which is the relay centre for sensory information (Levine, 2000). Olfactory receptors are embedded in the nasal cavity. Odours are picked up by these receptors, which, unlike other sensory receptors, are actually neurons (Coren, Ward, & Enns, 2004; Levine, 2000). The unmyelinated axons of the olfactory nerve (CN I) project across the cribiform plate to the olfactory bulb (Noback, Strominger, Demarest, & Ruggiero, 2005; Steward, 2000), which is situated in the anterior cranial fossa subjacent to the frontal cortex. In the olfactory bulb, these axons synapse with dendrites of mitral and

tufted cells in the olfactory glomeruli. The axons of these cells then travel through the olfactory tract (Steward, 2000).

Axons from the olfactory tract project directly to the amygdala and to two regions of the limbic cortex—the entorhinal and pyriform cortices—which are the primary olfactory cortices (Carlson, 2001; Cerf-Ducastel & Murphy, 2003; Coren et al., 2004). The amygdala sends olfactory information to the hypothalamus, the entorhinal cortex sends it to the hippocampus, and the pyriform cortex sends it to the hypothalamus and the orbitofrontal cortex, via the dorsomedial nucleus of the thalamus (Carlson, 2001). The olfactory pathway in the medial thalamus is important in "learning behaviours based on olfactory cues" (Levine, 2000, p. 469). In the orbitofrontal cortex, information about taste and olfaction are combined to give the sense of flavour (Carlson, 2001). Imaging studies have also identified activation in the insula and cerebellum following olfactory stimulation (Cerf-Ducastel & Murphy, 2003; Kettenmann et al., 1997).

Following cortical processing, odour information is sent back to the olfactory bulb as feedback afferent input (Wilson, Kadohisa, & Fletcher, 2006), but the actual process of how this happens is not yet known. However, studies in rats have shown that olfactory information from the olfactory bulb, insula, and mediofrontal cortex travels to the NTS (Neafsey, Hurley-Gius, & Arvanitis, 1986; Terreberry & Neafsey, 1983). Figure 3 shows the schematic representation of the olfactory system.

The sensitivity of olfaction decreases with age (Boyce & Shone, 2006; Kremer, Bult, Mojet, & Kroeze, 2007; Ship, 1999), partly because the olfactory epithelium is gradually replaced with nonolfactory epithelium, which lacks olfactory receptors, as a person ages (Hadley, Orlandi, & Fong, 2004). Adults more than 65 years of age are considered as elderly (Chavez & Ship, 2000); therefore, the age limit should be considered in studies utilizing odour stimulus.

Mixed results have been found on differences between how males and females perceive smell. Superior perception has generally been found in females compared to males (Doty, Applebaum, Zusho, & Settle, 1985; Kobal et al., 2000; Kobal et al., 2001) but no sex differences were found by Hummel, Konnerth, Rosenheim, and Kobal (2001). As there are disagreements in studies, sex needs to be

considered in studies that have odour as a stimulus. Using equal number of males and females may control the effect of sex.
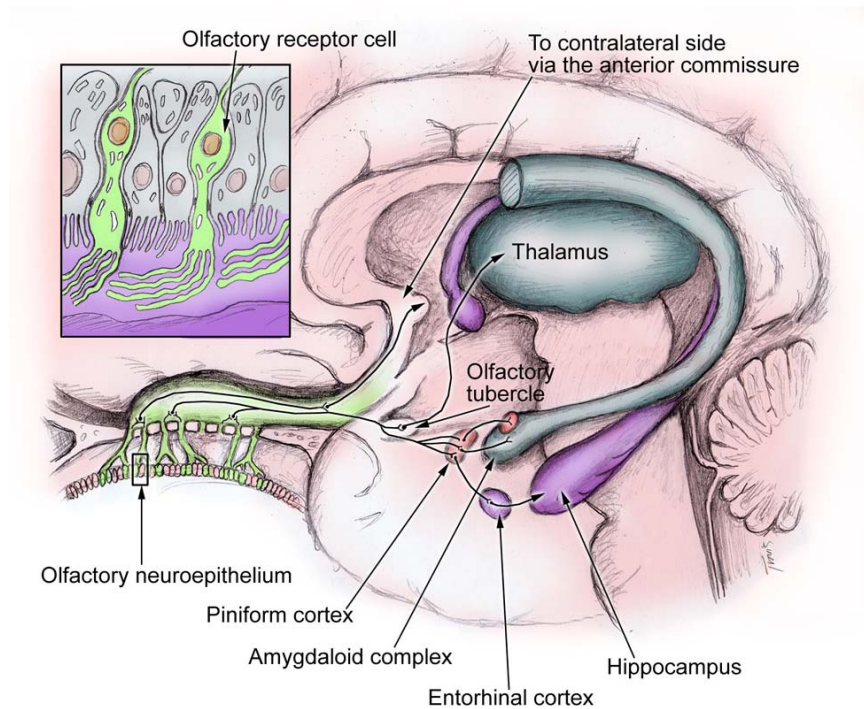
Figure 3. Schematic representation of the olfactory system.
(Image reprinted with permission from eMedicine.com, 2010. Available at:
http://emedicine.medscape.com/article/835585-overview).

2.5.2   Gustation

Unlike olfaction, which relies on a single cranial nerve, gustatory stimuli are detected via several cranial nerves that innervate taste buds in the oral cavity, pharynx, and larynx. Taste sensation from the anterior two-thirds of the tongue is carried by the facial nerve, whilst the glossopharyngeal nerve carries taste fibres from the posterior third of the tongue. Meanwhile, the taste buds in the pharynx, larynx, and on the epiglottis are innervated by the vagus nerve.

Gustatory information travels via the facial (CN VII, chorda tympani and greater superficial petrosal branches), glossopharyngeal (CN IX, lingual branch), and vagus (CN X, superior laryngeal branch) cranial nerves into the rostral part of the NTS in the medulla (Rolls, 1998). CN VII synapses on the most rostral part of the

NTS, CN X synapses just rostral to the obex (the most caudal part of the NTS), and CN IX synapses in between CN VII and CN X in the NTS (Miller, 1999).

From the NTS, this information then travels to the ventral posteromedial thalamus, before projecting to the primary gustatory cortex in the frontal operculum and rostral insula (Carlson, 2001; O'Doherty, Rolls, Francis, Bowtell, & McGlone, 2001; Ogawa et al., 2005; Rolls, 1989, 1998). From the primary gustatory cortex, neurons project to the secondary gustatory area in the caudolateral orbitofrontal cortex (Carlson, 2001; Rolls, 1989), which is situated anteriorly from the primary taste region. There are also neural taste projections to the limbic system (particularly hypothalamus) and the amygdala (Carlson, 2001; Coren et al., 2004; Levine, 2000; O'Doherty et al., 2001). Small et al. (1999) evaluated the cortical gustatory areas using PET scan; they reported an asymmetrical representation of taste, greater in the right hemisphere, within the insula, parietal and frontal opercula, and caudolateral orbitofrontal cortex.

No literature was found regarding the pathway of gustatory input from the higher centres back to CPG in the medulla to modulate swallowing function in humans. However, a study on cats reported an ipsilateral descending pathway from the orbitofrontal cortex and insula via the pyramidal tract, which is then bilaterally distributed to the NTS (Willett, Gwyn, Rutherford, & Leslie, 1986).

Finger and Morita (1985) examined the gustatory system of catfish and proposed the same distinction of neural pathway in mammals, and probably humans. They reported that the facial and vagal taste fibres terminate in separate regions in the brain and serve a different function. The taste fibres from the facial nerve have connections with the trigeminal nuclei, whereas the vagal taste fibres is connected to the NA and is directly involved in initiating swallowing. Based on these findings, the authors highlighted vagal function in protecting the airway, which corresponds to its role in initiating a swallow. Figure 4 shows the schematic representation of the gustatory system in humans.
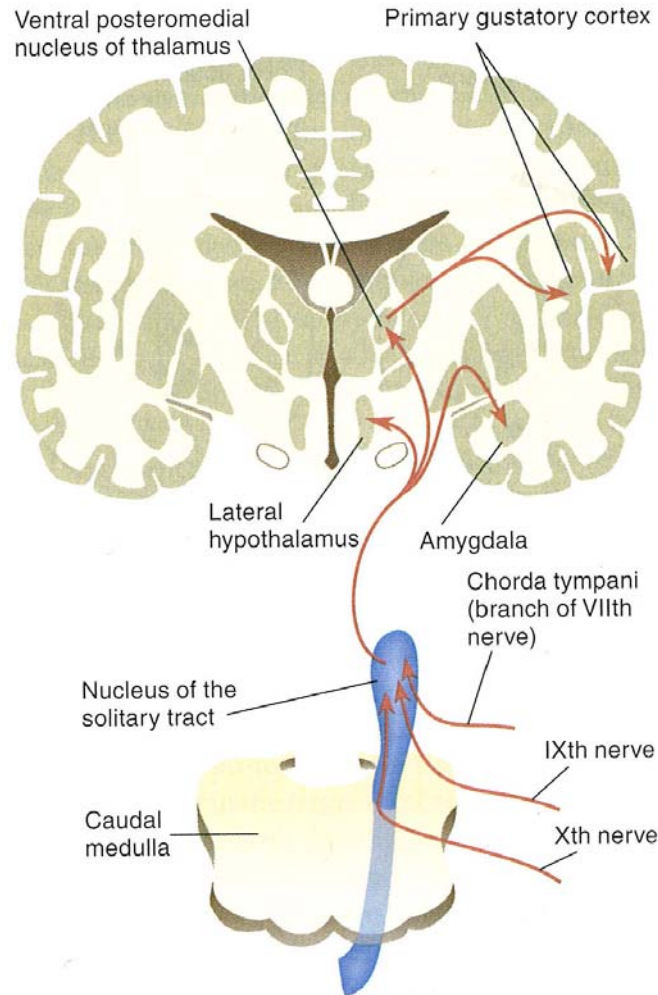
Figure 4. Schematic representation of the gustatory system. VIIth nerve, facial nerve; IXth, glossopharyngeal nerve; Xth, vagus nerve. (From Carlson, 2001, p. 234).

Taste is one of the stimulants for saliva production (Pedersen, Bardow, Jensen, & Nauntofte, 2002). Xerostomia—a condition where there is decreased salivary flow—can affect gustation as saliva lubricates the taste buds to facilitate taste transduction. Decreased salivary flow has also been shown to affect swallowing (see Section 2.3.5).

Besides having a role as a chemical receptor for taste in foods, studies have shown that the peripheral taste receptors are also important in nutritional balance as they can respond to the nutritional needs of an individual (Gilbertson, 1998). It appears that the activity of sodium channels in the taste receptors is similarly regulated by hormones as the sodium channels in the kidney, which is responsible for salt and water balance in our body. For example, when a person is in a salt-deprived

state, changes in the properties of the taste receptors would drive him/her to consume food high in salt content (Levine, 2000).

Decreased taste sensitivity has been associated with aging but it is generally accepted that this is mainly due to the loss of smell (Boyce & Shone, 2006; Bromley & Doty, 2010; Steward, 2000), particularly the retronasal smell (Pelletier, 2007). This is due to the fact that the sense of taste is more resilient compared to smell as it is conveyed by three cranial nerves compared to smell which is conveyed by one cranial nerve. However, the decline in taste is quality-specific, that is, not across all taste modalities. Using a taste sensitivity test with sip and spit method, Kremer et al. (2007) found that the elderly (mean age 71 years) have decreased sensitivity to salty and sour tastes, but the taste of sweet and bitter were not reduced. This may strengthen the basis that sweet and bitter tastes are two important tastes for survival—one to assure adequate nutrition and the other to avoid poisoned food. No study of sex differences on taste perception was found.

2.5.3   The Importance of Olfaction and Gustation in the Modulation of Swallowing

Taste stimulation, particularly sour, has been shown to improve swallowing (Ding et al., 2003; Leow et al., 2007; Logemann et al., 1995; Pelletier & Lawless, 2003), worsen it (Chee et al., 2005), or have no effect on swallowing (Hamdy et al., 2003). These differences could be due to the methodological disparities among the studies. Limited studies on olfactory stimulation also indicate the beneficial effect of smell in the rehabilitation of patients with swallowing impairment (Ebihara et al., 2006; Munakata et al., 2008). However, how these effects are integrated into the modulation of swallowing is not entirely known. Most authors proposed that taste stimulation increased activation in the NTS, which subsequently increase the contraction of muscles involved in swallowing. No studies on the long-term effect of sour stimulation on swallowing have been conducted. This is an important research area to update the current knowledge regarding sensory stimulation in rehabilitation of patients with dysphagia.

Although the olfactory and gustatory systems are separate entities, both senses must be stimulated for flavour detection (Bear, Connors, & Paradiso, 2007).

Information from both senses is processed independently and integrated at the higher centres, mainly in the orbitofrontal cortex, anterior cingulate cortex, and insula (Grabenhorst, Rolls, & Bilderbeck, 2008; Small et al., 2004). Babaei et al. (2010) have shown that more cortical areas are activated when flavoured liquid is presented compared to water. Thus, presenting more than one modality of sensory stimulation—for example, combined odour and tastant—may be of greater benefit in the rehabilitation of dysphagia compared to presenting one type of sensory stimulation.

2.6   Limitations in Knowledge and Aims of Project

Studies that have investigated the effects of sour taste on swallowing have been contradictory. Some reported improved swallowing function (Ding et al., 2003; Leow et al., 2007; Logemann et al., 1995; Pelletier & Lawless, 2003), while others stated that swallowing worsens following the stimulation (Chee et al., 2005). There is also a study which reported no effect with sour taste stimulation (Hamdy et al., 2003). These differences could be due to the methodological disparities among the studies (discussed in Section 2.3.4.2).

The aim of this research programme was to examine the effects of (a) olfaction, (b) gustation, and (c) combined olfactory and gustatory stimulation on aspects of swallowing neural substrates and swallowing biomechanics. Specifically, this programme aimed to evaluate changes in the (a) neural excitability of motor pathway which controls the submental muscles and (b) swallowing biomechanics including electrical activity in the submental muscles, tongue-to-palate pressures, pharyngeal pressures, and the dynamics of the UES. Ultimately, this project would answer the question of whether stimulation of these sensory fields has any effects on swallowing function in healthy participants. Outcomes from this study may guide the development of sensory-based rehabilitation approaches for individuals with swallowing impairment.

2.7   Research Hypotheses

The following hypotheses were formulated based on the stimuli (odour, tastant, or combined stimulation) and outcome measurements (MEP, sEMG, lingual

pressure, and pharyngeal manometry). They were expanded to include the effects of low and high concentrations and the effects of time (during- and post-stimulation). Hypotheses 1-3 are on the effects of sensory stimulation on the MEPs measured at the submental muscles. Hypotheses 4-15 concern the effects of sensory stimulation on the biomechanics of swallowing.

2.7.1   Hypothesis 1

Hypothesis 1 addresses the effects of olfactory stimulation on the excitability of neural transmission from the motor cortex to the submental muscles.

Background and Key Question

There are limited studies on the effects of olfaction on swallowing. Ebihara et al. (2006) reported shortened latency of swallowing onset in a group of patients 1 min following the first inhalation of black pepper oil and 30 days later compared to other groups exposed to lavender oil or neutral (distilled water) odour. The experimental procedures were carried out before each mealtime where patients were exposed to the smell for 1 min immediately before the meal. Using similar methods, Munakata et al. (2008) documented increased oral intake in paediatric patients on tube feeding when black pepper oil was used for 3 months. Findings from Ebihara et al. (2006) and Munakata et al. (2008) provide initial support for the use of smell in managing patients with swallowing problems. This study aims to answer the question: What are the effects of presenting olfactory stimulation on the neural excitability of swallowing?

Hypothesis 1

Olfactory stimulation increases the excitability of neural transmission associated with swallowing. That is, the MEPs measured at the submental muscles have a shorter latency and greater amplitude in the presence of an olfactory stimulus compared to no stimulation. This increased excitability is retained, at least temporarily, for up to 90 min poststimulation. A higher concentration odour produces greater effects than a low concentration odour.

Rationale

There will likely be an effect on neural transmission as Ebihara et al. (2006) and Munakata et al. (2008) both report changes in swallowing biomechanics following olfactory stimulation (see also Section 2.3.4.1). Ebihara et al. (2006) reported increased rCBF measured with SPECT in the right medial orbitofrontal cortex (anterior cingulate cortex) and left insula following inhalation of black pepper oil. This would suggest that olfactory information is conveyed to these areas. Daniels and Foundas (1997) suggested that the insula has connections to the primary and supplementary motor cortices, thalamus, and the NTS. Increased signals to the NTS will increase NA activation; therefore, there will be an increase in muscle activation, which is seen as the shorter latency and greater amplitude of the MEPs compared to when no stimulation was presented. The higher concentration stimulus would produce greater MEP amplitude than a lower concentration stimulus as increased molecular concentration may excite more receptors, thus increasing neural excitation. The effects may last up to 90 min or more poststimulation as some of the odour molecules will be present after the stimulation is switched off. Furthermore, studies in animal models have suggested the mechanism of LTP, which plays a role in neural plasticity, is present in the sensory-motor network after removal of stimulus (Le Ray & Cattaert, 1999). Clinical studies on humans have also shown that the effects of sensory stimulation may present up to 30 min (Mistry et al., 2006), 60 min (Fraser et al., 2002; Fraser et al., 2003), or 90 min (Fraser et al., 2002) after removal of stimuli.

Significance

If proven effective, results from this study will improve clinicians' understanding on the use of olfactory stimulus in rehabilitation of patients with dysphagia and might guide management decisions. Olfactory stimulus can be presented without active participation of the patient; therefore, it may be particularly useful in patients with cognitive impairment who have swallowing problems.

Proposed Study

This hypothesis will be investigated by way of a TMS-triggered MEP study of the submental muscles. Submental MEPs will be recorded following low and high concentrations of odour stimulation in two separate sessions (Chapter 4). In each session, submental MEPs will be recorded at baseline, during control condition,

during low or high odour stimulation, immediately poststimulation, and at 30-, 60-, and 90-min poststimulation.

2.7.2   Hypothesis 2

Hypothesis 2 investigates the effects of gustatory stimulation on the excitability of neural transmission from the motor cortex to the submental muscles.

Background and Key Question

Several studies have evaluated the effects of sour taste on the biomechanics of swallowing, but none have evaluated its neural effects. Furthermore, findings from these studies were contradictory. Therefore, this study aims to answer the question: What effect does sour taste have on the excitability of neural transmission for swallowing?

Hypothesis 2

Gustatory stimulation increases the excitability of neural transmission associated with swallowing. That is, during presentation of a gustatory stimulus, MEPs have a shorter latency and greater amplitude compared with saliva swallows in which there is no additional gustatory stimulus. This increased excitability is retained, at least temporarily, for up to 90 min poststimulation after removal of the stimulus. A higher concentration tastant produces greater effects than a low concentration tastant.

Rationale

Improved swallowing biomechanics following gustatory stimulation were consistent in most studies (Section 2.3.4.2). Hamdy et al. (1997) documented shorter latency and increased amplitude in the mylohyoid muscles following trigeminal and vagus nerves stimulation. They explained that the brainstem motoneuron is activated by the stimulation; therefore, when an action potential induced by the TMS reaches the neuron, the neuron is near its threshold level, and thus it will fire earlier, giving the shorter latency. The neurons involved in swallowing will also be near its threshold level when gustatory stimulus is added, thus there will be a shorter MEP latency. Higher amplitude will be seen because input from afferent fibres will all

converge on the NTS, and more motoneurons will be activated. The effects will last for at least up to 90 min poststimulation as some of the tastant molecules will be present in the taste buds after the stimulus is removed. Additionally, studies in animal models have suggested the mechanism of LTP is recruited, which plays a role in neural plasticity (as above, Le Ray & Cattaert, 1999). Also, studies on humans have showed effects were still apparent at 30-, 60-, and 90-min poststimulation (as above).

Significance

Improved understanding of the use of gustatory stimulus in rehabilitation of patients with dysphagia might guide management decisions. An inexpensive gustatory stimulus may be purchased from the local market and minimized the additional financial burden on families of patients who may not be able to provide for themselves.

Proposed Study

A TMS-triggered MEP study of the submental muscles will be conducted. Submental MEPs will be recorded following low and high concentrations of tastant stimulation in two separate sessions (Chapter 4). In each session, submental MEPs will be recorded at baseline, during control condition, during low or high tastant stimulation, immediately poststimulation, and at 30-, 60-, and 90-min poststimulation.

2.7.3   Hypothesis 3

Hypothesis 3 focuses on the effects of combined olfactory and gustatory stimulation (flavour) on the excitability of neural transmission from the motor cortex to the submental muscles.

Background and Key Question

No studies have evaluated the effects of flavour on the neural control of swallowing. Thus, this study aims to answer the question: How is the neural excitability associated with swallowing affected by combined smell and taste stimulation?

Hypothesis 3

When both olfactory and gustatory stimuli are presented simultaneously, there is an increase in the excitability of neural transmission compared to no stimulus presentation or to the independent presentation of olfaction or gustation. The MEPs have a shorter latency and greater amplitude compared with baseline or either stimulus given independently, and the effect is present for up to 90 min poststimulation.

Rationale

Improved swallowing biomechanics seen in studies utilizing either one of the stimuli (Sections 2.3.4.1 and 2.3.4.2) would suggest that when the two stimuli are combined, the combined effect may be greater. Rolls (2005) demonstrated that there was a "neural substrate for the convergence of taste and olfactory stimuli to produce flavour" (p. 53) in the lateral anterior part of the orbitofrontal cortex, which was not activated by either stimulus alone. Therefore, combined olfactory and gustatory stimulation may contribute to increased excitability of neural transmission as the convergence of flavour processing on the neural systems would increase excitation (Rolls, 1998; Small, Jones-Gotman, Zatorre, Petrides, & Evans, 1997). The combined sensory effects will be maintained for at least up to 90 min poststimulation as there will be some odour and tastant molecules present on the sensory receptors after the stimuli were removed. Additionally, the mechanism of LTP, as above, plays a role in the poststimulation effects. Studies on humans have also showed that effects were still present at 30-, 60-, and 90-min poststimulation (as above).

Significance

Improved understanding of the use of flavour in rehabilitation of patients with dysphagia might guide management decisions. Fu et al. (2004) proposed that the integration of sensory information such as olfaction and gustation could "modulate mechanisms involved in food selection and emotional reactions" (p. 1040) towards food intake. Therefore, these stimuli may be used in patients with dementia who have difficulty swallowing, as this can increase the sensory input into NTS, which will increase the rate of firing in neurons associated with swallowing, and then translate that into better swallowing performance.

Proposed Study

A TMS-triggered MEP study of the submental muscles will be conducted (Chapter 4). Submental MEPs will be recorded at baseline, during control condition, during combined odour and tastant stimulation, immediately poststimulation, and at 30-, 60-, and 90-min poststimulation.

2.7.4   Hypotheses 4-6

Hypotheses 4-6 address the effects of olfactory and gustatory stimulation on the sEMG of the submental muscles.

Background and Key Question

Anterior and superior hyolaryngeal excursions, which are important events to open the UES for bolus transfer into the oesophagus, are assisted by contraction of the submental muscles. Contraction of this group of muscles can be used to identify swallowing by measuring electrical activity using EMG (Crary et al., 2007; Pouderoux et al., 1996). If the MEP amplitudes of the submental muscles are increased up to 90 min poststimulation following odour and/or tastant presentation (Hypotheses 1-3), the next question is: What effect does the same stimulation have on the contraction of the submental muscles?

Hypothesis 4

Olfactory stimulation increases contraction of the submental muscles. The amplitude of the submental sEMG is greater when lemon odour is presented compared to no odour presentation. The duration of the muscle contraction is longer following odour presentation compared to baseline. The increase in amplitude and duration is larger when high concentration odour is presented compared to the presentation of low concentration odour.

Hypothesis 5

Gustatory stimulation increases contraction of the submental muscles. There is an increase in the amplitude of the submental sEMG when lemon tastant is presented compared to no tastant presentation. The duration of the submental contraction is longer than the baseline. The increase in amplitude and duration is

larger when high concentration tastant is presented compared to the presentation of low concentration tastant.

Hypothesis 6

Combined olfactory and gustatory stimulation affects the submental muscle contraction more than the independent presentation of either odour or tastant, or when compared to baseline. The amplitude of the submental sEMG is greater when odour and tastant are presented simultaneously compared to baseline. The amplitude is larger when compared to the odour or tastant presented independently. The duration of submental contraction is longer during combined stimulation compared to the independent presentation of either odour or tastant, or when compared to baseline. The effects of combined odour and tastant stimulation are evident even after the stimuli have been removed for at least up to 90 min poststimulation.

Rationale

The effects of odour on the submental EMG have been evaluated, but the stimuli used were not lemon odour. Abu-Hijleh et al. (2006) reported increased sEMG amplitude with presentation of the odour of orange oil, but no changes in sEMG duration were reported. In contrast, Schuermann (2008) found no differences in the sEMG when the odours of hot buttered popcorn and cinnamon bun were compared to no odour presentation. As the stimulus used in Abu-Hijleh's study (orange oil odour) was more closely related to lemon odour, the hypothesis that lemon odour increases the amplitude of the submental sEMG seems plausible.

Sour taste has been shown to increase the amplitude of submental contraction compared to water or other taste stimuli (Leow et al., 2007; Palmer et al., 2005). However, the increase in the duration of the submental contraction compared to control conditions did not reach significant level in both studies. Several durational measures were reported to increase following effortful swallowing compared to normal swallowing (Hind et al., 2001; Hiss & Huckabee, 2005). Effortful swallow is a swallow which is performed with force. Thus, the increased sEMG amplitude following sensory stimulation may also increase the duration of muscle contraction.

The effects of odour and tastant stimulation will be present poststimulation due to the mechanisms of LTP which plays a role in neural plasticity (Cooke & Bliss,

2006; Le Ray & Cattaert, 1999; see Section 4.7.2). Also, studies on humans have showed effects were still apparent at 30-, 60-, and 90-min poststimulation (as above). These rationales also support subsequent hypotheses below.

Significance

If proven effective, results from this study will help clinicians to determine if odour and tastant are useful in the rehabilitation of patients with dysphagia, specifically in patients with decreased hyolaryngeal excursion. Sensory stimulation has the potential to decrease aspiration by reducing postswallow residues as improved hyolaryngeal excursion will open the UES longer and permit bolus transfer into the oesophagus.

Proposed Study

The amplitude and duration of contraction of the submental muscles will be recorded via sEMG following odour and tastant stimulation (Chapter 5). SEMG will be recorded at baseline, during control condition, during stimulation, and at 30-, 60-, and 90-min poststimulation.

2.7.5   Hypotheses 7-9

Hypotheses 7-9 investigate the effects of olfactory and gustatory stimulation on the lingual pressure.

Background and Key Question

Studies have evaluated lingual swallowing pressures (Ball, Idel, Cotton, & Perry, 2006; Hind, Nicosia, Gangnon, & Robbins, 2005; Nicosia et al., 2000; Pelletier & Dhanaraj, 2006; Steele & Huckabee, 2007) but the effect of odour stimulation on lingual swallowing pressure is not known. Pelletier and Dhanaraj (2006) showed that sour taste increased lingual swallowing pressure. However, they used chilled 10-ml citric acid boli as the stimuli, for which bolus volume or temperature, or both, may have contributed to the increased pressure.

Hypothesis 7

Olfactory stimulation affects the lingual swallowing pressure. Lingual swallowing pressure amplitude is higher when lemon odour is presented compared to

no odour presentation. The tongue-to-palate contact duration is longer following odour presentation compared to no odour presentation. The increase in pressure amplitude and contact duration is greater when high concentration odour is presented compared to the presentation of low concentration odour.

Hypothesis 8

Gustatory stimulation affects the lingual swallowing pressure. Lingual swallowing pressure amplitude is higher when lemon tastant is presented compared to no tastant. The tongue-to-palate contact duration is longer following tastant presentation compared to no tastant presentation. The increase in pressure amplitude and contact duration is greater when high concentration tastant is presented compared to the presentation of low concentration tastant.

Hypothesis 9

Combined olfactory and gustatory stimulation affects the lingual swallowing pressure more than the independent presentation of either odour or tastant, or when compared to baseline. The amplitude of the lingual pressure is greater when odour and tastant are presented simultaneously compared to baseline. The amplitude is greater when compared to the odour or tastant presented independently. The duration of the tongue-to-palate contact is longer during combined stimulation compared to the independent presentation of either odour or tastant, or when compared to baseline. The effects of combined odour and tastant stimulation are present for at least up to 90 min poststimulation.

Rationale

Pelletier and Dhanaraj (2006) examined the effects of taste on lingual swallowing pressure. They found that citric acid elicited higher lingual swallowing pressure compared to water (peak mean anterior lingual pressures for acid and water are 210 mmHg and 150 mmHg, respectively). The authors used large 10-ml boli in the study and it is possible that retronasal odours may have also contributed to, or been totally responsible for the higher lingual pressures seen in that study.

Lee and Linden (1991, 1992) nebulized freshly squeezed lemon juice for 1 min to investigate the salivary reflex of parotid and submandibular glands. They concluded that the effect seen in their study was due to the acid, not the odour, as a

similar response was seen when odourless citric acid was used instead of the lemon juice. However, the authors' conclusion does not discount the possibility of olfactory effect in both cases.

Abu-Hijleh et al. (2006) reported increased sEMG amplitude with presentation of the odour of orange oil. Another study reported that an increase in lingual pressure is accompanied by increases in sEMG amplitude in the submental muscles (Brady, Klos, & Johnson, 2000). Therefore, it could be speculated that the increase in sEMG recorded in Abu-Hijleh et al. study may represent not only increased submental muscle contraction as was found by the authors, but also increased lingual pressure, which was not measured in the study. Furthermore, Palmer et al. (2008) reported a strong relationship between tongue-to-palate pressure generation and the contraction of floor-of-mouth muscles; the stronger the muscles of floor-of-mouth contract, the greater glossopalatal pressure is generated.

Significance

If this hypothesis is supported, patients with dysphagia due to reduced lingual control might benefit from the use of odour and tastant in rehabilitation. Sensory stimulation has the potential to decrease the incidence of aspiration by decreasing premature spillage due to patient's inability to contain the bolus in the oral cavity during oral phase of swallowing, provided that the volume given per swallow is small enough for the patient to manage.

Proposed Study

A lingual manometry study using the lingual array supplied by Kay® Digital Swallowing Workstation (Kay Elemetrics Corporation, New Jersey, USA) will be conducted to evaluate the amplitude and duration of tongue-to-palate contact (Chapter 5). Measurements will be recorded at baseline, during control condition, during stimulation, and at 30-, 60-, and 90-min poststimulation.

2.7.6   Hypotheses 10-12

Hypotheses 10-12 are on the effects of olfactory and gustatory stimulation on the pharyngeal pressure and the dynamics of the UES.

Background and Key Question

Several studies have looked at pharyngeal pressure following behavioural interventions (Ali et al., 1996; Boden et al., 2006; Bulow et al., 2002; Dantas et al., 1990; Shaker et al., 1994; Steele & Huckabee, 2007) but no study has evaluated the immediate effects of odour or taste on pharyngeal pressure during swallowing. Moreover, no poststimulation data exists to document the effects of flavour stimulation on the biomechanics of swallowing over a long time course.

Hypothesis 10

Pressures in the pharynx and UES are positively affected by olfactory stimulation. There is an increase in the pharyngeal pressure amplitude following lemon odour presentation compared to no odour presentation. There is an increase in the duration of the pressure generation in the pharynx following odour presentation compared to no odour presentation. The high concentration odour produces a greater increase in the amplitude and duration of pharyngeal pressure compared to the low concentration odour. The relaxation pressure in the UES is more negative when lemon odour is presented compared to no odour presentation. The duration of the UES opening is longer following odour presentation compared to baseline. The high concentration odour produces more negative relaxation pressure and longer duration of UES opening than the low concentration odour.

Hypothesis 11

Pressures in the pharynx and UES are positively affected by gustatory stimulation. Pharyngeal pressure amplitude increases following lemon tastant presentation compared to no tastant presentation. The duration of pressure generation is longer during tastant presentation compared to baseline. The high concentration tastant produces a greater increase in the amplitude and duration of pharyngeal pressure compared to the low concentration tastant. The relaxation pressure in the UES is more negative when lemon tastant is presented compared to no tastant presentation. The duration of the UES opening is longer following tastant presentation compared to baseline. The high concentration tastant produces more negative relaxation pressure and longer duration of UES opening than the low concentration tastant.

Hypothesis 12

Combined olfactory and gustatory stimulation positively affects the pharyngeal and UES pressures more than the independent presentation of either odour or tastant, or when compared to baseline. The amplitude of the pharyngeal pressure is greater when combined odour and tastant are presented compared to baseline. The amplitude is larger when compared to the odour or tastant presented independently. There is longer duration of the pressure generation when combined stimulation is compared to the independent presentation of either odour or tastant, or compared to baseline. The relaxation pressure in the UES is more negative when combined odour and tastant are presented compared to baseline or when compared to the odour or tastant presented independently. The duration of the UES opening is longer during combined stimulation compared to the independent presentation of either odour or tastant, or when compared to baseline. The effects of combined odour and tastant stimulation are still present after the stimuli are removed, for at least up to 90 min poststimulation.

Rationale

Abu-Hijleh et al. (2006) identified an increase in the peak sEMG amplitude of submental muscles compared to neutral smell when the odour of orange oil was used. Increased sEMG activity during tongue-to-palate emphasis while swallowing with effort has been shown to increase contact pressure in the upper pharynx (Huckabee & Steele, 2006). Thus, the increased sEMG amplitude seen in Abu-Hijleh et al. study could also indicate an increased pressure in the pharynx, which was not measured in the study.

Palmer et al. (2005) compared the effects of swallowing a 3-ml water bolus with a 3-ml sour bolus (lemon solution). They reported stronger muscles contraction (geniohyoid, mylohyoid, and anterior belly of digastric muscles) with the sour bolus compared to water. These are the muscles involved in the upward and forward movement of the hyolaryngeal complex, which, at the same time would shorten the pharyngeal lumen, ultimately increasing its luminal pressure. Interestingly, a weak negative correlation was reported between the peak amplitude of submental sEMG and midpharyngeal pressure (Huckabee et al., 2005), which indicated that "the more submental [sEMG] measures increased, the less pharyngeal pressures increased"

(Huckabee & Steele, 2006, p. 1068). Similarly, when volunteers were asked to do effortful swallowing with tongue-to-palate emphasis, both submental sEMG and pressure in the upper pharynx were increased (Huckabee & Steele, 2006). Studies which compared the effects of effortful and normal swallowing on pharyngeal manometry showed that with effortful swallowing, there was an increase in the peak pressure and duration of contact pressure in the pharynx, although not all differences are significant (Witte et al., 2008). Therefore, it could be speculated that increased pressure in the pharynx will be concomitant with an increased duration.

Traction force during the upward and forward movement of the hyolaryngeal complex helps to open the UES (Cook et al., 1989). When there was an increase in traction force, which may be due to the increased contraction of the submental muscles, the opening of the UES will be larger, thus more negative relaxation pressure will be recorded. Similarly, as the duration of submental contraction was speculated to increase following sensory stimulation, the prolonged muscle contraction will also prolong the opening of the UES.

Significance

Patients with dysphagia due to symptoms related to weak pharyngeal pressure would benefit from treatment utilizing odour and tastant stimulation if this hypothesis is supported. Sensory stimulation can decrease the incidence of aspiration by strengthening pharyngeal contraction, thus decreasing postswallow residues. Postswallow residue is harmful because it can be inhaled when patient starts to breathe at the end of a swallow.

Proposed Study

Pharyngeal manometry study using a solid-state pharyngeal manometer connected to the Kay® Digital Swallowing Workstation will be conducted to evaluate the amplitude and duration of pharyngeal contact pressure and the dynamics of the UES (Chapter 5). Measurements will be recorded at baseline, during control condition, during stimulation, and at 30-, 60-, and 90-min poststimulation.

2.7.7   Hypotheses 13-15

Hypotheses 13-15 concern the differences between the experimental and control conditions during simultaneous presentation of odour and tastant.

Background and Key Question

The aim of the main biomechanical study was to evaluate if the same stimulus presentation as in the MEP study can change biomechanics of swallowing, without the concern for control stimulation. Thus, the supplementary study was designed to evaluate the differences between control condition and during stimulation when both odour and tastant are presented.

Hypothesis 13

The presentation of combined lemon odour and tastant affects submental contraction more compared to water. The amplitude of the submental sEMG is greater when lemon odour and tastant are presented simultaneously compared to water. The duration of the submental contraction is longer during lemon stimulation compared to water.

Hypothesis 14

The presentation of combined lemon odour and tastant affects lingual swallowing pressure more compared to water. The amplitude of the lingual pressure is greater when combined lemon odour and tastant are presented compared to water. The duration of the tongue-to-palate contact is longer during lemon stimulation compared to water.

Hypothesis 15

The presentation of combined lemon odour and tastant affects pressures in the pharynx and UES more compared to water. The amplitude of the pharyngeal pressure is greater when combined lemon odour and tastant are presented compared to water. There is longer duration of the pressure generation when lemon stimulation is compared to water. The relaxation pressure in the UES is more negative when combined lemon odour and tastant are presented compared to water. The duration of the UES opening is longer during lemon stimulation compared to water.

Rationale

The independent presentation of odour and tastant have been shown to affect swallowing biomechanics compared to no stimulation or when a neutral stimulus was used (Abu-Hijleh et al., 2006; Leow et al., 2007; Palmer et al., 2005). Therefore, it was hypothesized that the presentation of combined lemon odour and tastant would have a greater effect on the biomechanics of swallowing compared to the control condition which uses water as a stimulus.

Significance

Results from this study will strengthen findings from the main biomechanical study.

Proposed Study

The supplementary study where combined odour and tastant stimulation is presented using water or lemon as the stimulus will be carried out. The differences between both conditions will be evaluated (Chapter 5).

Chapter 3

Determination of Odour and Tastant Concentrations for Swallowing Studies

3.1   Background

The effects of sour taste on swallowing have been investigated in healthy participants and in patients with dysphagia but the results have been contradictory (Chee et al., 2005; Ding et al., 2003; Hamdy et al., 2003; Leow et al., 2007; Logemann et al., 1995; Miyaoka et al., 2006; Palmer et al., 2005; Pelletier & Lawless, 2003; Sciortino et al., 2003). Differences in research methodologies, particularly in the choice of stimuli, could account for some discrepancies. Some studies did not clearly specify what stimuli were used, some used stimuli which may not be available commercially thus limiting transfer of research to clinic practice, and some used freshly squeezed lemon juice which may not be reproducible and therefore, difficult to control for concentration. Therefore, choosing an appropriate stimulus which is widely available and can be prepared by clinicians for use in therapy is an important step before studies of sensory stimuli effects on swallowing can be carried out.

Miyaoka et al. (2006) evaluated the effects of five basic tastes (sweet, sour, salty, bitter, and umami) on swallowing in 10 healthy volunteers. Each tastant was added to a thickening agent dissolved in distilled water to derive two different concentrations: one low, and the other high. Their participants rated the subjective difficulty of swallowing and suprahyoid EMG was recorded to assess the duration of oral, oropharyngeal, and pharyngeal phases in three sessions. Results showed that sour and bitter tasting foods were subjectively more difficult to swallow compared to sweet food. No differences in duration of swallowing were recorded between the high and low concentrations of each taste across all sessions. Peak EMG activity showed a decreasing trend when higher concentration tastants were used compared to the lower concentration stimuli. However, this trend was present in the first and

second sessions only, with no differences detected in the third session. The authors reported "no consistent tendency throughout the three sessions" (p. 45) in the EMG amplitude and concluded that stimulus concentration has no effect on swallowing measures. Although this study provides valuable information about the influence of concentration, further research would be required to ascertain if the lack of significant effects extend to a wider variety of concentrations and other biomechanical parameters of swallowing.

Chee et al. (2005) and Mistry et al. (2006) reported decreased swallowing efficiency when taste was included in their study and proposed that the decline in swallowing efficiency was due to the participants' perception of the stimulus as being noxious. Chee et al. evaluated the effects of taste (10% citrus acid, 10% glucose, 0.9% saline, and 0.5 mM quinine) and topical anaesthesia (0-, 10-, 20-, and 40-mg Lidocaine) on swallowing efficiency using the water swallow test (Hughes & Wiles, 1996). A VAS where participants rated the pleasantness and intensity of a given tastant was also included in the study. Participants rated all taste solutions as intense; however, pleasantness ratings were mixed. Most participants rated sweet as pleasant (96%), quinine and saline were unpleasant (79% and 91%, respectively), and citrus solution as either pleasant, unpleasant, or both (24%, 33%, and 43%, respectively). No explanation of the mixed results of pleasantness of citrus was offered by the authors. Chee at al. reported that sweet, sour, and salty solutions reduced swallowing speed, and quinine and saline increased ISI compared to water. The authors also reported that 40 mg Lidocaine reduced swallowing speed and increased ISI compared to water. As the results for taste and anaesthesia were similar, Chee et al. proposed that their stimuli, which was rated as intense, "heightened [the] sensory input … [and] altered behaviour … by causing the subject to attend more carefully to the task" (p. 398). Another explanation to the results seen in Chee et al.'s study is that the stimuli may also activate free nerve endings of the trigeminal nerve, which are responsive to chemical irritation in the mouth and nasal cavity (Coren et al., 2004). This may be possible as the stimuli used were rated as intense by the subjects. However, perception is a very subjective measure and its influence on the nervous system may not correlate with stimulation at the periphery (receptor level). A potential confound in this study was the use of stimuli presented at 4°C, which has been shown in some studies to influence swallowing (Bisch et al.,

1994; Hamdy et al., 2003; Kaatzke-McDonald et al., 1996; Miura et al., 2009; Miyaoka et al., 2006). Therefore, it is unclear if changes are due strictly to the gustatory input or are influenced by temperature.

Mistry et al. (2006) examined the effects of pleasant and aversive taste stimulation (10% glucose and 0.5 mM quinine hydrochloride solutions, respectively) on neural excitability, specifically the pharyngeal MEP. An 11-point VAS was also used to rate the pleasantness of glucose and quinine. The VAS ranged from the rating of extremely pleasant (+5) to extremely unpleasant (-5) with neutral (0) in the middle; the participants rated glucose as pleasant (mean score 2.1, SD 0.4) and quinine as unpleasant (mean score -3.6, SD 0.6) compared to water as control (mean score -0.1, SD 0.3). The high VAS scores for glucose and quinine compared to water may indicate that the participants perceived the stimuli as more intense. The authors reported decreased pharyngeal MEPs 30 min poststimulation following both glucose and quinine stimulation, which they proposed was due to inhibitory effects in the NTS consequent to the strong flavour used. As only one concentration of each stimulus was used, the effect of using a milder concentration that may be perceived differently by the subjects could not be compared with these results. Results from the Chee et al. (2005) and Mistry et al. (2006) studies indicate that a strong stimulus could be perceived as noxious and may impair swallowing function. Thus, it is important to select a stimulus that is not adversely perceived by participants and therefore may positively change swallowing function.

Small, Zatorre, and Jones-Gotman (2001) evaluated taste perception in 28 patients with unilateral resection of the right anteromedial temporal lobe, including the amygdala, based on confirmation by PET scans. The amygdala is part of the limbic system which plays a role in emotion and learning. Imaging studies have shown topographically separate amygdala activation when both pleasant and aversive tastes were presented (O'Doherty et al., 2001), which Small et al. (2001) argued could be related to the intensity and palatability of the stimuli. The higher the intensity, the more unpleasant and less palatable the stimulus would be. The study by Small et al. was an excellent study of taste perception with careful control of methodological confounds. All patients involved had at least four-fifth of the amygdala removed. Furthermore, the stimuli were brought to room temperature before being presented to the participants. This method eliminated the effect of

temperature which may consequently affect taste perception. To evaluate the differences in perception between patients and the control group, Small et al. presented five concentrations of each taste stimulus (sweet, sour, bitter, and salty) for the participants to rate. They reported that their patients showed deficits in the perception of taste intensity compared to the control group. The authors concluded that taste perception is a form of emotional learning and unlike olfaction, which is important in identifying food, taste perception is "an affective judgement about whether to accept or reject the food" (p. 430). Other studies have also reported the importance of taste as a protective mechanism from ingesting poisonous food. For example, Zald, Hagen, and Pardo (2002) reported increased rCBF in the amygdala when an aversive taste (bitter) was presented compared to water. However, Zald et al. did not find increased rCBF in the amygdala following pleasant (sweet) stimulation compared to water. This discrepancy may be explained by the known role of amygdala, that is, in emotion and learning, as Zald et al. reported that their subjects failed to identify the quinine by name compared to sucrose. Failure to identify this stimulus may render quinine as a novel stimulation and comparing it with a known stimulation (sucrose) may account for differences in neural representation. Another methodological aspect that may influence the results was the fact that only participants with "normal hedonic ratings" (p. 1069) were included. Those who rated the pleasantness and intensity of sucrose > 5 were excluded form analyses. This may have biased the data.

Only 10% of the odour that we breathe in is picked up by the odour receptors (Carlson, 2001), in contrast to the taste receptors which can pick up most of the tastant molecules (Gilbertson, 1998) as they are dissolved in saliva which bathes the taste buds. As less odour molecules may be detected by its receptors compared to tastant, selecting the most appropriate stimulus is primarily based on the best odour stimulus perceived and tolerated by the volunteers. Other factors associated with the stimulus, such as its concentration, may also influence how swallowing is affected.

3.2   Aims of Studies

The purpose of the following preliminary experimental study was to find a suitable lemon stimulus out of three sources (Pilot Study 1: Stimuli selection). The

choice was made based on its pleasantness, tolerability, and the participants' ability to identify it as "lemon". After selection of an appropriate stimulus, two concentrations were chosen as the stimuli for subsequent studies in the evaluation of the effects of olfaction and gustation on swallowing function (Pilot Study 2: Concentration selection).

3.3   Methods

3.3.1   Study Design

This two-step randomized prospective study was designed to select the most appropriate lemon stimulus (Pilot Study 1) and then select two suitable concentrations (Pilot Study 2). Three sources of lemon odour were tested in Pilot Study 1: water-based, alcohol-based, and oil-based stimuli. The selected stimulus was then used in the next stage (Pilot Study 2) to determine two appropriate concentrations for subsequent swallowing studies.

3.3.2   Participants

Seven healthy adult volunteers (5 female; age range 27-51, mean 37.4 years) were recruited for both studies. The volunteers reported no health conditions that affected their smell and taste functions on the day the experiment was carried out.

3.3.3   Instrumentation

A nebulizer cup was filled with approximately 6 ml of the experimental lemon solution. A DeVilbiss PulmoMate® compressor/nebulizer (Model 4650I, Sunrise Medical, Somerset, Pennsylvania, USA) was used to present the olfactory stimuli via nasal cannula (Airlife™ Adult Cushion Nasal Cannula with 2.1-m Crush Resistance Supply Tube, Cardinal Health, McGaw Park, Illinois, USA) which was inserted into both nares.

3.3.4   Stimuli

Three lemon stimuli were used: (a) water-based reconstituted lemon concentrate (Country Gold lemon juice, Steric Trading Pty Ltd, Villawood, NSW, Australia); (b) alcohol-based lemon odour (Hansells natural lemon essence, Old Fashioned Foods Limited, Auckland, New Zealand); and (c) oil-based lemon odour (Boyajian pure lemon oil, Boyajian Incorporated, Massachusetts, USA). All stimuli are commercially-available and were purchased in the local food markets. The solution direct from the bottle was used as the 100% stimulus. Water was added to lower the concentration of the stimuli. The concentrations tested were 0% (plain tap water), 20%, 40%, 60%, 80%, and 100% (undiluted form).

As temperature has been reported to affect swallowing (Miyaoka et al., 2006), all procedures were performed at room temperature. The stimuli were exposed to room temperature at least one hour prior to the procedures. Moreover, the room temperature was monitored and kept in the range of 18-22ºC by cooling or heating the room.

3.3.5   Pilot Study 1: Stimulus Selection

3.3.5.1   Procedures

The volunteers were asked to not ingest any food one hour prior to the procedures to ensure that the receptors, particularly on the tongue, were not contaminated with food residuals (Miura et al., 2009). Volunteers were seated comfortably in a chair. The nasal cannula was inserted into both nares and fixed to the nebulizer cup, which was connected to the nebulizer. Repositioning of the tubing was done if there was reported discomfort. The volunteers were asked to breathe normally. Water was first nebulized to give the volunteers the feeling of nebulized air entering their nostrils. The volunteers were reminded to remember this feeling because they would be asked to rate the lemon odours that will be presented to them later based on the water mist as the solution with the lowest intensity. When they were comfortable with the nebulized air, 100% lemon odour from one of the sources was presented (randomized across the three sources) and the participants were again reminded to remember the intensity, this time as having the highest intensity. Then,

the 0%, 20%, 40%, 60%, 80%, and 100% preparations of the odour stimuli from the same source were randomly presented. There was at least 1 min break between each stimulus presentation, and the participants were encouraged to sip water during these breaks. The same procedures were repeated with the other two lemon sources in randomized order.

Three 100 mm VASs were presented to the volunteers to acquire ratings of the intensity, pleasantness, and tolerability of the stimulus. The three VASs were completed following each stimulus presentation. Participants were informed that the left side of each scale was equivalent to the stimulus having the least intensity, being the least pleasant, and least tolerable, respectively, whereas the right side of the scale represented the other end of the spectrum. Similar information was written on the VAS as "Not perceived", "Unpleasant", and "Intolerable", on the left side of the scale, and "Strongly perceived", "Pleasant", and "Tolerable", on the right side of the scale, respectively (Appendix A). Following each stimulus presentation, participants were requested to mark on the VAS where they perceived that particular stimulus to be best represented on the scale. Additionally, they were also asked to report if they produced a cough associated with presentation of the stimulus.

3.3.5.2   Data Analyses

The markings on the VASs were measured with a ruler and documented in a spreadsheet. Data were tabulated and the means were graphed accordingly. Out of the seven participants, six completed the VASs for water-based stimulation and four for alcohol- and oil-based stimulation. Due to the unequal sample size, three separate nonparametric Friedman's ANOVAs (Dawson & Trapp, 2001) were used for all analyses followed by posthoc Wilcoxon signed-rank tests. Additionally, results were interpreted based on descriptive statistics.

3.3.5.3   Results

Water was used as the diluting agent in all solutions. The water-based lemon concentrate mixed best (that is, no separation of the liquids was observed). Not surprisingly, the oil-based lemon stimuli did not mix well with water and the container had to be shaken to ensure proper mix, especially right before the nebulizer

was switched on. The alcohol-based lemon essence appeared to mix adequately with less separation than the oil-based stimuli but not as thoroughly as water-based stimuli requiring the container to be shaken before each procedure to ensure proper mix.

The water-based odour stimuli at 100% concentration stimulated the cough reflex in one volunteer. The volunteer reported that the coughing was due to increased salivation which she had not managed to clear efficiently. No other coughing was observed.

Intensity

Nonparametric Friedman's ANOVAs for water- and oil-based odour perception of intensity were not significant; $\chi^2(5) = 8.21$, $p = .15$ and $\chi^2(5) = 9.46$, $p = .09$, respectively. Friedman's ANOVAs for alcohol-based odour perception was significant; $\chi^2(5) = 16.29$, $p = .01$. However, posthoc Wilcoxon signed-rank test revealed no differences between perception of intensity for alcohol-based stimuli at 0% and each of the other concentrations ($p = .07$, $p = .07$, $p = .14$, $p = .07$, and $p = .07$ for comparisons between 0% and 20%, 40%, 60%, 80%, and 100%, respectively).

As the concentrations did not yield statistically significant differences in VAS scores, descriptive statistics were employed. Base purely on mean VAS scores, perception of the intensity of the water-based stimuli increased when the concentration was increased (Figure 5), indicating that the participants correctly rated the intensity of the different stimuli. The perception of the alcohol-based lemon odour was questionable, as the higher concentration (60%) was perceived as having less intensity of lemon to that of the lower concentrations (20% and 40%, see Figure 5). The oil-based stimuli were perceived as having a high intensity at the low concentration of 20%, as well as the 40%, 60%, 80%, and 100% (Figure 5), that is, the participants could not discriminate the differences between low and high intensity of the oil-based stimuli.
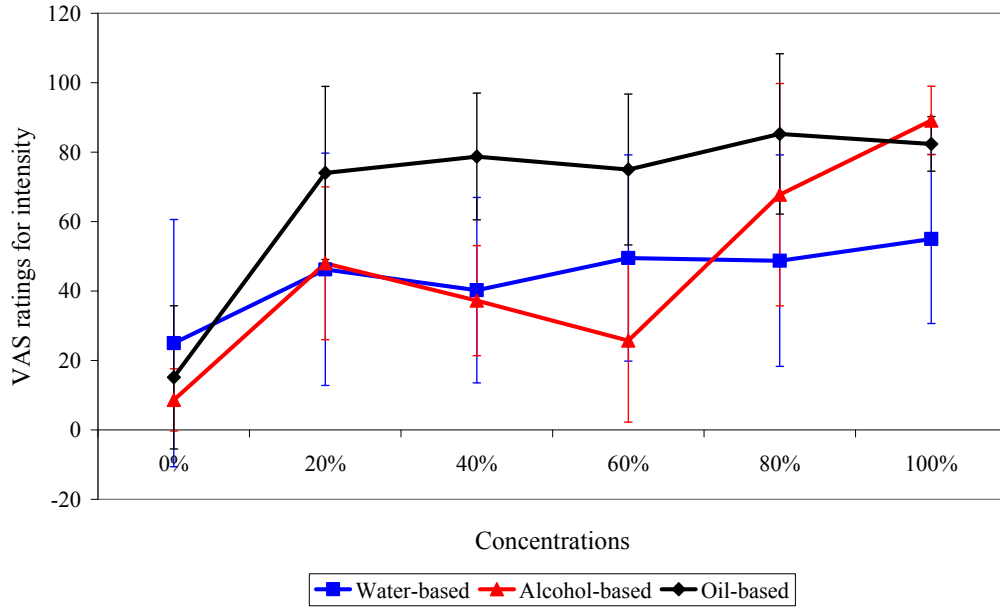
Figure 5. Mean VAS ratings (error bar as SD) for intensity at each concentration for each stimulus.

Pleasantness

Nonparametric Friedman's ANOVA for pleasantness was significant for water-based stimuli; $\chi^2(5) = 12.73$, $p = .03$. Posthoc Wilcoxon signed-rank test revealed differences in pleasantness for water-based stimuli between 0% and 20%, 0% and 80%, and 0% and 100% ($p = .03$, $p < .05$, and $p = .04$, respectively; see Figure 6). Friedman's ANOVAs for pleasantness were not significant for alcohol- and oil-based stimuli; $\chi^2(5) = 10.25$, $p = .07$ and $\chi^2(5) = 6.08$, $p = .30$, respectively.

Base purely on mean VAS scores for the ratings of pleasantness, the water-based stimuli showed a general decrease in pleasantness when concentration was increased, except for the slightly higher ratings for 40% (70.3) and 60% (71.5) compared to 20% (59.8). However, the 100% concentration was not deemed too unpleasant, with mean rating of 55.0 (Figure 6). The pleasantness ratings for both alcohol- and oil-based lemon solutions did not show the same pattern of decline as the water-based solutions. In fact, the alcohol-based solutions were rated as similarly pleasant up to the concentration of 60%; the 80% and 100% concentrations were rated as less pleasant than the lower concentrations stimuli. The oil-based stimuli were generally rated as less pleasant than the water- or alcohol-based stimuli.
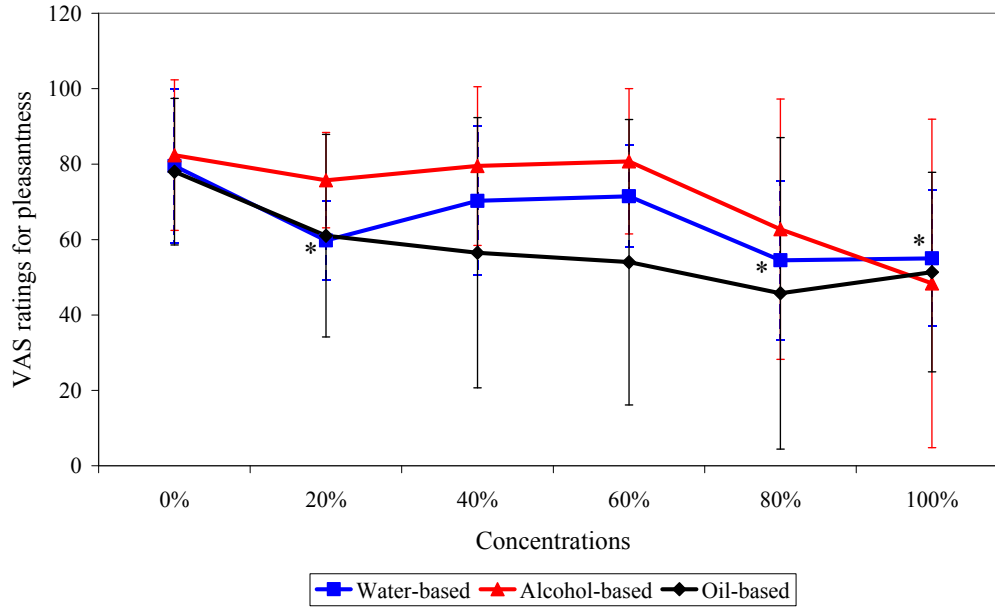
Figure 6. Mean VAS ratings (error bar as SD) for pleasantness at each concentration for each stimulus. *$p < .05$ compared to pleasantness rating at 0% for water-based stimuli.

Tolerability

Nonparametric Friedman's ANOVAs for tolerability were not significant for water- and alcohol-based stimuli; $\chi^2(5) = 9.48$, $p = .09$ and $\chi^2(5) = 10.99$, $p = .52$, respectively. Friedman's ANOVAs for tolerability was significant for oil-based stimuli; $\chi^2(5) = 11.20$, $p < .05$. However, posthoc Wilcoxon signed-rank test revealed no differences between 0% and each of the other concentrations (20%, 40%, 60%, 80%, and 100%).

Base purely on mean VAS scores, all stimuli were generally well tolerated. The 80% oil-based lemon odour was rated as the least tolerable stimulus, followed by 100% alcohol-based, and 100% oil-based odour (52.5, 56.5, and 65.6, respectively; see Figure 7). All other tolerability ratings were rated more than 70.0. The water-based lemon concentrate was the best tolerated solution in its undiluted form compared to the alcohol- and oil-based stimuli (83.8 for water-based versus 56.5 and 65.6 for alcohol- and oil-based, respectively).
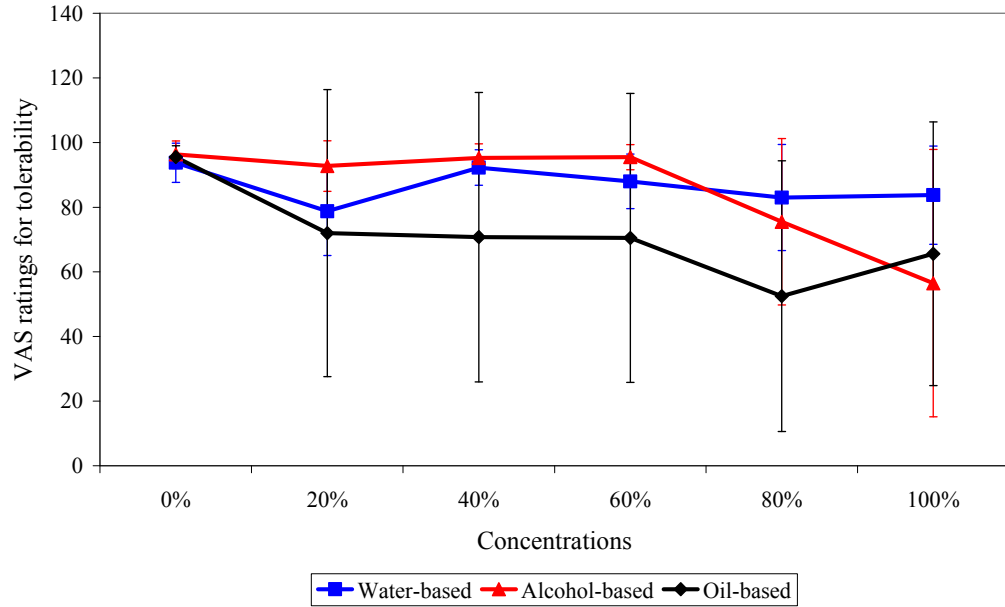
Figure 7. Mean VAS ratings (error bar as SD) for tolerability at each concentration for each stimulus.

3.3.5.4 Discussion

There were no major differences between stimuli in VAS ratings of perception except for a single difference in perception of pleasantness for water-based stimuli. Therefore, it was considered appropriate to use the stimulus that descriptively represented the best stimulus (based on the intensity, pleasantness, and tolerability).

The water-based lemon odour showed a gradual increase in the intensity ratings when the concentration was increased, compared to the alcohol- and oil-based lemon odour which showed no gradual increase in perception ratings as the concentration was increased. Moreover, the pleasantness rating for the water-based stimulus was generally decreased with increasing concentration, which indicated that participants could differentiate the low and high concentration stimuli. Furthermore, the tolerability rating for the water-based stimulus was higher compared to the alcohol- and oil-based stimuli. All of these attributes render water-based stimulus more appropriate than alcohol- or oil-based stimulus as a sensory stimulus in swallowing study.

Water constitutes approximately 60% of total body weight (Ganong, 2002), thus it could be speculated that choosing a water-based product would enhance the chemical reaction between the stimulus molecule and the smell/taste receptors. For example, odourants have to dissolve in the mucous membrane of the nasal mucosa, which is a water-based epithelium, before it can be picked up by the olfactory receptors (Bear et al., 2007). Based on the above factors and the observation that water-based solution mixed well with water, the water-based lemon concentrate was chosen as the most appropriate stimulus in this trial. Therefore, it was used as the lemon stimulus in Pilot Study 2.

3.3.6   Pilot Study 2: Concentration Selection

The water-based lemon stimulus was selected as the test stimulus based on its intensity, pleasantness, and tolerability as an odour. In addition, it mixed well with water. To select the appropriate concentrations for inclusion in subsequent studies, similar experiments were conducted to test the 0%, 20%, 40%, 60%, 80%, and 100% water-based lemon stimuli as tastants. Results from this study, as well as results for water-based solution as odourant (from Pilot Study 1), were considered to choose the suitable concentrations to be used in subsequent studies.

3.3.6.1   Procedures

The same volunteers as in Pilot Study 1 participated in this study. They were seated comfortably in a chair. Filter papers (Genuine Whatman Filter Paper No. 5, W & R Balston Ltd, Maidstone, Kent, UK) cut into 8- by 2-cm strips impregnated with tastant stimuli were used to present the gustatory stimuli. A 5-cm length of the filter paper was soaked in the stimulus and drip dried for at least 10 s. The 5-cm length was then placed on the middle of the tongue, covering approximately two-thirds of the length of the tongue from the anterior tip.

Participants were first given a filter paper impregnated with water (the 0% stimulus), followed by a 100% stimulus (the undiluted form). They were told to remember the intensity of the two stimuli, as they would have to rate the lemon tastant that would be presented to them later based on the filter paper impregnated with water as the tastant with the lowest intensity, and the 100% as having the

highest intensity. Then, the 0%, 20%, 40%, 60%, 80%, and 100% of the tastant stimuli were randomly presented. There was at least a 1-min break between each stimulus presentation and the volunteers were asked to drink few sips of water during the breaks to ensure that the previous stimulus was flushed from the taste buds. A similar 100 mm VAS (see section 3.3.5.1) as used in Pilot Study 1 was used to rate the tastants (Appendix A). After each stimulus presentation, the participants were requested to mark on the VAS where they perceived that stimulus to be best represented on the scale. Additionally, they were asked to report if there was a gag associated with the stimulus.

3.3.6.2   Data Analyses

Similar to Pilot Study 1, the markings on the VAS were measured and the values documented in a spreadsheet. Data were tabulated and the means were graphed accordingly. Three separate nonparametric Friedman's ANOVAs were again used for all analyses (for perception of intensity, pleasantness and tolerability) followed by posthoc Wilcoxon signed-rank tests. Additionally, results were interpreted descriptively.

3.3.6.3   Results

The gag reflex was not elicited in any of the volunteers for any concentrations and all stimuli were well tolerated by the participants. Nonparametric Friedman's ANOVAs for water-based taste perception was significant; $\chi^2(5) = 19.26$, $p < .01$, but the analyses for pleasantness and tolerability ratings were not significant; $\chi^2(5) = 3.05$, $p = .69$ and $\chi^2(5) = 6.97$, $p = .22$, respectively. Posthoc Wilcoxon signed-rank test revealed differences between perception of intensity for water-based taste stimuli at 0% and each of the other concentrations (20%, 40%, 60%, 80%, and 100%; at $p < .05$, $p < .05$, $p < .05$, $p < .05$, and $p = .03$, respectively; see Figure 8).
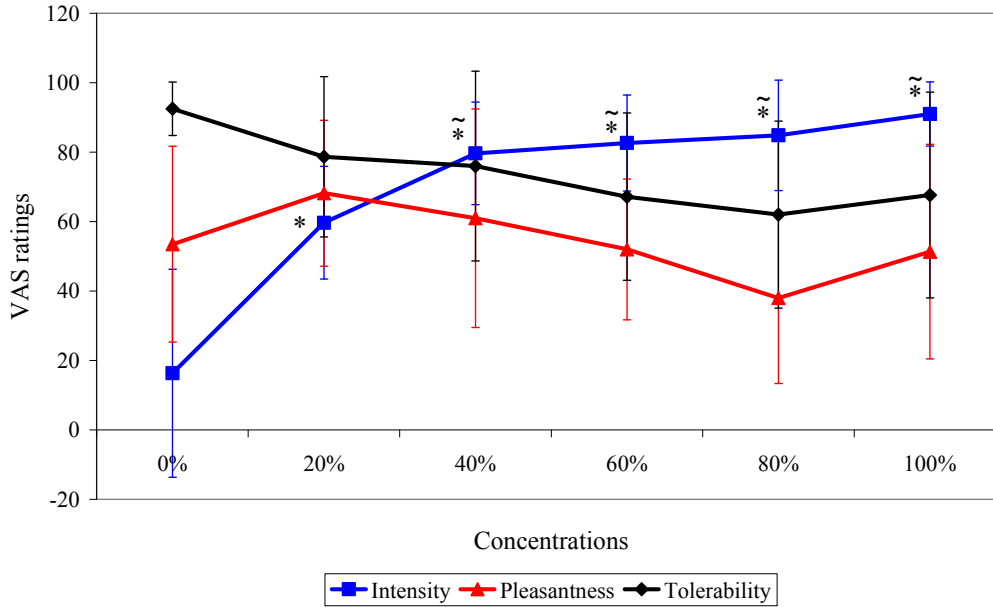
Figure 8. Mean VAS ratings (error bar as SD) of intensity, pleasantness, and tolerability for water-based tastant stimuli. *$p < .05$ compared to intensity rating at 0% and $\tilde{}p < .05$ compared to intensity rating at 20%.

From Figure 8, it is apparent that when the VAS ratings for intensity were increased, there was a general decrease of VAS ratings for pleasantness and tolerability. In addition to the significant differences between perception of intensity at 0% and the other concentrations, Wilcoxon signed-rank test for intensity ratings also showed differences between 20% and 40%, 20% and 60%, 20% and 80%, and 20% and 100% (all at $p = .03$).

3.3.6.4 Discussion

This pilot study on water-based lemon solution has shown that when the intensity of a stimulus was increased, the pleasantness and tolerability ratings decreased. Prescott, Allen, and Stephens (1984) have also reported a linear increase in the intensity ratings of a stimulus when the concentration was increased; this is similar to the findings from the water-based stimulus in this current study. However, Prescott et al. did not report the pleasantness and tolerability ratings of the different concentration stimuli. In contrast, Miyaoka et al. (2006) found no differences in the EMG activity of suprahyoid muscles when low or high concentration of tastants were given to healthy adults. However, Pelletier and Lawless (2003) found that a higher concentration stimulus has greater effect on the outcome measures of swallowing

compared to a low concentration stimulus. Therefore, to resolve this issue, two concentrations that differ from each other in the intensity level were selected to evaluate the effects of concentration on swallowing.

Higher concentration acids have been shown to evoke more swallowing reflex in rats compared to lower concentration acids (Kajii et al., 2002). Kajii et al. proposed that this was due to increased excitation in the swallowing centre during stimulation with the high concentration stimulus compared to the low concentration stimulus. They minimized the effect of increased salivation, which is known to occur when acids was used, by ligation of the salivary ducts. Thus, the different results observed were due to the differences in the stimuli concentration.

There are more odour or tastant molecules in a high concentration stimulus compared to a low concentration stimulus (Kajii et al., 2002). The molecules are picked up by its particular receptors, subsequently activating more neurons in the cortex and limbic system, which will translate into enhanced perception of the stimulus. As a high concentration stimulus has been associated with being noxious (Chee et al., 2005; Hamdy et al., 2003), the pleasantness rating is important to ensure that the chosen stimulus is not noxious. Likewise, a pleasant, low concentration stimulus must be perceived and tolerated by most participants. Additionally, the high and low concentrations must be distinguishable from each other in the intensity level to determine the effects of concentration on swallowing.

Results from Pilot Study 2 showed that the intensity ratings for the tastant solutions increased with the increase in concentration; this pattern is similar to the ratings for the intensity of odour. The intensity rating for the 20% taste solution was rated as different from the 100% concentration at $p = .03$ (VAS ratings were 59.7 and 91.0, respectively). Although the intensity rating for 20% odour was lower than the 100%, it was not rated as different from the 100% odour (46.3 and 55.0, respectively). As the intensity rating for 20% odour was rather low, it was felt necessary to increase the test concentration. For ease of measurement, the 25% concentration was selected as the low concentration stimulus. The full strength solution (100%) was chosen as the high concentration stimulus as it has the highest intensity rating for odour and taste. The pleasantness ratings for the 20% solutions were higher than 100% for both odour and tastant (59.8 vs 55.0 and 68.2 vs 51.3 for

odour and tastant, respectively). Therefore, the 100% and 25% lemon solutions were used as the high and low concentrations, respectively, in the subsequent studies.

3.4 Discussion

The sensation of taste is described as the combination of information from the olfactory and gustatory pathways (Steward, 2000). Moreover, dissimilarity in the smell and taste components has been shown to alter the perception of flavour (Kettenmann, Mueller, Wille, & Kobal, 2005). Thus, the same lemon stimulus used as tastant was used as the lemon odourant.

Flavour is the term used when there is an interaction between smell and taste (Fu et al., 2004; Small et al., 1997). Grabenhorst et al. (2008) evaluated cognitive effects on flavour perception using the same stimulus as tastant and odour. This is done by injecting a bolus of stimulus into the mouth and asking the participants to hold the bolus for 7 s before swallowing. According to the authors, this method also activates the olfactory cortex, as the act of holding the bolus in the mouth gives rise to retronasal odour stimulation. However, all orthonasal odour receptors may not be stimulated by this method, which may influence the results reported by these authors. Grabenhorst et al. reported a correlation between intensity rating and the area stimulated by BOLD signal in the orbitofrontal cortex captured with fMRI. The orbitofrontal cortex is an area known for flavour representation. On the other hand, no correlation was found for the pleasantness rating (with BOLD signals), but it was influenced by a word-based visual label. For example, a sample was rated as more pleasant when the visual label was "rich and delicious taste" compared to a visual label of "boiled vegetable water". Based on the findings from Grabenhorst et al.'s study, the intensity rating is considered as the most important rating in deciding the most appropriate concentration for use in the current studies.

The odour and tastant stimuli used in these studies may also be useful in managing patients with dysphagia. Therefore, it is important to choose a stimulus that is widely available and relatively cheap to decrease patients' financial burden in the course of their treatment.

3.5 Conclusion

The aim of this pilot study was to select, from three choices, a suitable lemon stimulus based on its intensity, pleasantness, and tolerability, as perceived by the participants. Although statistically not different, descriptively it was determined that the water-based lemon concentrate was the most appropriate stimulus to study swallowing function, compared to the oil- and alcohol-based lemon stimuli. The 25% stimulus can be perceived as lemon odour and tastant, and it is differently perceived from the 100% stimulus, particularly as taste stimuli. Thus, the two concentrations were chosen as the stimuli for subsequent studies to evaluate the effects of low and high concentrations of odour and tastant on swallowing function.

Chapter 4

The Effects of Olfaction and Gustation on Motor-Evoked Potentials of the Submental Muscle Group[1]

4.1 Background

The neural control of swallowing is divided into three components (Miller, 1982): (a) the afferent system comprised of the trigeminal, glossopharyngeal, and vagus cranial nerves; (b) the swallowing centre, or central pattern generator in the brainstem; and (c) higher brain centres which modulate the swallowing response (see Section 2.1.2). The central pattern generator for swallowing in the brainstem can be modulated by inputs from the periphery and cortex (Miller, 1999). This modulation might include olfactory and gustatory components of food that is under preparation for swallowing. Several studies have revealed a cortical role in initiating and regulating swallowing function (Hamdy, Aziz, Rothwell, Crone et al., 1997; Martin & Sessle, 1993; Miller, 1999). The cortex receives inputs from afferent nerves, integrates these inputs with information stored in other cortical areas (such as the limbic system), and then sends that input to the central pattern generator to modify motor output that is optimal for the bolus that a person is preparing to swallow (Lund & Kolta, 2006).

Hamdy et al. (2000) emphasized the need to "develop novel approaches to neuro-rehabilitation, based on objective scientific methods, and centred around an understanding of how human neuroplasticity can be manipulated" (p. 152). Cortical input has been shown to modulate swallowing. Hamdy, Aziz, Rothwell, Hobson, and Thompson (1998) believed that this input could come from both hemispheres and their excitability could be modulated by sensory input.

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[1] This study was published in *Physiology and Behavior* (Appendix B, Abdul Wahab, Jones, & Huckabee, 2010).

Fibres from the lateral precentral gyrus (motor strip) are known to project to the nucleus tractus solitarius and to the nucleus ambiguus (Larson, 1985). These projections could play a role in swallowing, specifically during the voluntary preparatory stage. Moreover, it has been reported that fibres from the frontal part of the cortex, including the motor cortex, terminate in the pons and medullary reticular formation (Kuypers, 1958), which may influence the muscles innervated by motoneurons from these areas. Thus, information from the cortex may excite or inhibit motoneurons in coordinating muscle movements during swallowing.

Prior research has shown that motoneurons can also be excited or inhibited by extrinsic sensory stimulation (Fraser et al., 2002). Electrical stimulation to the pharynx has been found to modify MEPs from pharyngeal muscles and also found to modulate subsequent swallowing function (Fraser et al., 2002). Thus, it could be speculated that other forms of sensory stimulation, such as smell and taste, could produce a similar effect and may also influence swallowing. There are many published studies which have evaluated gustatory effects on swallowing biomechanics (Chee et al., 2005; Ding et al., 2003; Hamdy et al., 2003; Kaatzke-McDonald et al., 1996; Leow et al., 2007; Logemann et al., 1995; Miyaoka et al., 2006; Palmer et al., 2005; Pelletier & Lawless, 2003; Sciortino et al., 2003) but only two studies have investigated olfactory effects on swallowing (Ebihara et al., 2006; Munakata et al., 2008). Studies which have evaluated the underlying neural effects of olfactory and gustatory stimulation are even scarcer, with a single report documenting effects of gustatory input on neural transmission during swallowing (Mistry et al., 2006) and another on the effects of olfaction on cortical areas activation during swallowing (Ebihara et al., 2006). How olfaction and gustation affect swallowing neural substrates is an important clinical question given the current approach of utilizing sensory modulation of taste and smell for rehabilitation of patients with dysphagia (Ebihara et al., 2006; Hamdy et al., 2003; Logemann et al., 1995; Munakata et al., 2008; Pelletier & Lawless, 2003).

4.2   Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) has been used to study the human nervous system since 1985 (Hallett, 2000). The main components of a TMS system

are (a) a power source, typically a capacitor; (b) a switch, usually an electronic device called a thyristor; and (c) a stimulation coil. Once the capacitor is charged, the thyristor switch will be switched on, which will then transfer the current to the coil (Epstein, 2008a; Riehl, 2008).

The TMS stimulation coil consists of a round bundle of wires. When an electric current is run through the coil, a magnetic field is generated, which enters the brain, essentially unaffected by the scalp and skull. As the electric current in the coil is only transient, it generates a changing magnetic field which, in turn, induces a circulating electric current (an eddy current) in the cortex, which can depolarize neuronal membranes (Figure 9) (Anand & Hotson, 2002; Epstein, 2008a; Kapogiannis & Wassermann, 2008). The neurons will fire when there is sufficient depolarization to trigger an action potential.
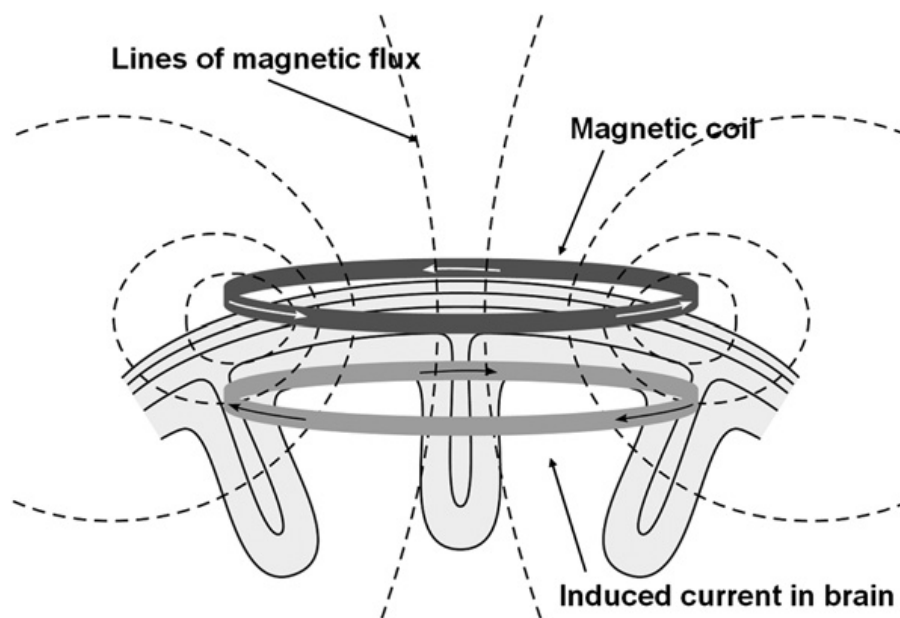
Figure 9. Induction of eddy current in the cortex. Note the opposite direction of current flow in the brain (clockwise) as compared to the current in the magnetic coil (anti-clockwise). From Hallet (2007).

The magnitude of the electric current induced in the cortex depends on several factors, among them the shape of the coil. In all types of coils, induced electric current is maximal directly under the coil and decreases with depth in the brain. Single circular coils tend to have lower spatial specificity and, hence, can stimulate large areas of cortex, including both hemispheres simultaneously. However, figure-of-eight coils are more focal and produce maximal current under the

intersection of the two round coils (Figure 10) (Anand & Hotson, 2002; Epstein, 2008b; Hallett, 2000).
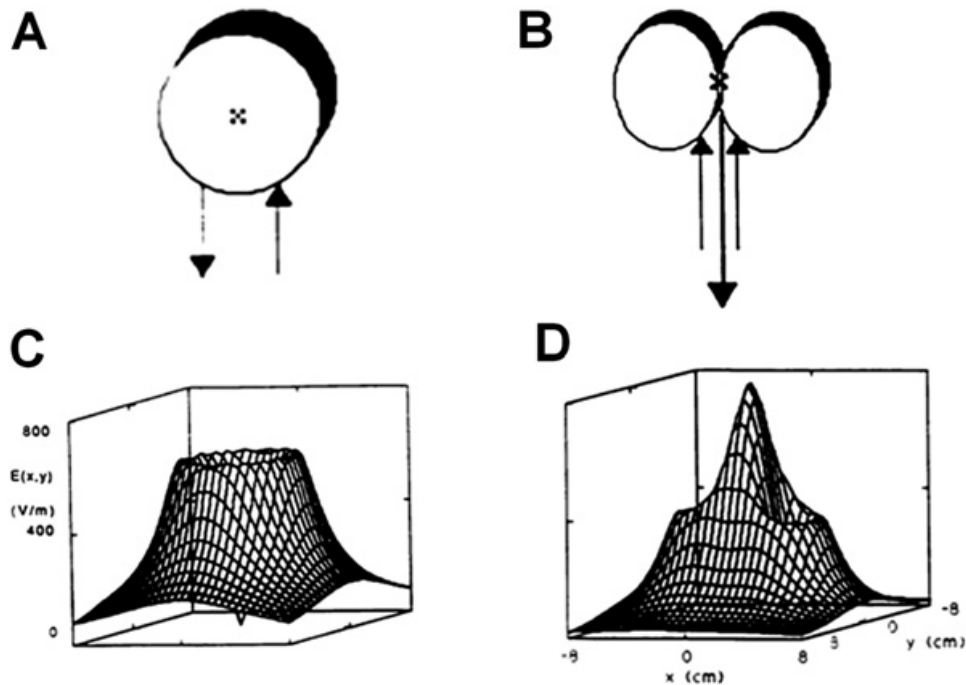
Figure 10. The shape of the stimulation coil determines the pattern of the electric field. Two stimulation coils with different shapes (A, circular coil and B, figure-of-eight coil) and their resultant electric fields (C and D, respectively). The electric field in the figure-of-eight coil is more focal compared to the circular coil. From Hallet (2007).

There are two excitatory effects following stimulation of the motor cortex. The first is an initial event which represents direct activation of the cortical neurons. These are called "direct" or D-waves. D-waves are followed by a series of other deflections—the "indirect" or I-waves—representing repeated trans-synaptic activation of the neurons (Kapogiannis & Wassermann, 2008; Lazzaro, Ziemann, & Lemon, 2008). Benecke, Meyer, Schonle, and Conrad (1988) found that MEPs produced following TMS have longer latencies compared to electrical stimulation. As I-waves are known to travel via synapses and take longer to reach the peripheral muscles compared to D-waves, Benecke et al. proposed that magnetic stimulation activates I- rather than D-waves.

When there is sufficient depolarisation to excite a neuron whose cell body lies in the motor cortex, the end result may be contraction of the muscle(s) supplied by the nerve. This can be measured from MEPs generated by the stimulated muscles. The size of the MEP depends on "the intrinsic excitability of the neurons in the

pathway and the status of its synapses" (Kapogiannis & Wassermann, 2008, p. 235). Moreover, MEP amplitude increases as TMS intensity increases. Other factors that may increase MEP amplitude are volitional contraction of the muscle (Anand & Hotson, 2002; Benecke et al., 1988) and imagining the function/use of the muscle and observing its volitional contraction (Anand & Hotson, 2002). In addition to activating the motor cortex, TMS can also produce inhibitory effects which are typically observed as a brief silent period in the motor cortex following TMS. Other ancillary effects produced by TMS are a loud auditory click with pulse delivery, somatosensory stimulation of the scalp, direct motor stimulation of scalp, face and neck muscles, and eyelid blinking.

4.3   Motor-Evoked Potential

MEPs are a measure of neural excitability from the motor cortex to target muscles (Doeltgen, Ridding, O'Beirne, Dalrymple-Alford, & Huckabee, 2009; Hamdy et al., 1996; Mistry et al., 2007) in which single-pulse TMS is used to noninvasively excite neurons in the brain. TMS depolarizes the neurons and generates an action potential. When the neurons depolarized are in the motor cortex, the action potential will produce an MEP in the muscle(s) represented by the stimulated region of the motor cortex. This evoked potential can then be recorded by EMG (Rothwell, 1997; Walsh & Pascual-Leone, 2003).

Corticobulbar contribution to muscles involved in swallowing can be evaluated by measuring the composite MEP measured from the submental muscles. Submental muscles, comprised of the anterior belly of digastric, mylohyoid, and geniohyoid muscles, are involved in superior and anterior movement of the hyolaryngeal complex, an integral biomechanical component of bolus transfer and airway protection (Kahrilas et al., 1991). Treatment approaches such as the head-lift (Shaker et al., 1997) and Mendelsohn manoeuvres (Kahrilas et al., 1991) frequently target the submental muscle group. Other researchers have also reported increased submental muscle activation when sour stimuli were presented (Ding et al., 2003; Leow et al., 2007; Palmer et al., 2005).

Using TMS to locate the topography of swallowing musculature in 20 healthy participants, Hamdy et al. (1996) reported that swallowing muscles are represented

bilaterally in the motor and premotor cortices of both hemispheres, which display interhemispheric asymmetry, independent of handedness. In patients with dysphagia, they found increased pharyngeal representation in the unaffected hemisphere with swallowing recovery. However, the number of patients studied was limited to two patients with unilateral hemispheric stroke; one presenting with dysphagia and the other with no dysphagia. In another study evaluating MEPs in paretic hand muscles, Fridman et al. (2004) reported the contribution of the dorsal premotor cortex in functional recovery following a stroke, which may be in the affected or intact hemisphere, depending on the size of lesion, either focal or extensive, respectively. These studies have shown that there is an increase in the cortical area activation following recovery of function.

In a study of pharyngeal electrical stimulation, Fraser et al. (2002) measured pharyngeal MEPs evoked by single pulse TMS before, immediately after, and at 30-, 60-, 90-, 120-, and 150-min postintervention in eight healthy subjects. The authors evaluated a range of different frequencies, intensities, and durations of electrical stimulation to determine the best stimulus to evoke the greatest MEP amplitude. They observed that stimulation at 5 Hz with 75% maximum tolerated intensity for 10-min duration produced the "largest excitatory effect on corticobulbar excitability" (p. 833) which was maximal at 60 min poststimulation. The authors also used TMS to map the topography of pharyngeal musculature representation on the cortex in three of the subjects. Fraser et al. reported that the size of the pharyngeal representation was larger at 60 min poststimulation compared to before stimulation, especially in the dominant hemisphere. Results from this study indicated that increased corticobulbar excitability is accompanied by increase in cortical area representation. Moreover, the authors also evaluated pharyngeal MEPs and swallowing function in 10 patients with dysphagia who underwent the same stimulation protocol as the healthy subjects (10 min of electrical stimulation to the pharynx at 5 Hz and 75% maximum tolerated intensity). However, the outcomes were evaluated only up to 60 min after the stimulation, in contrast to the healthy cohort where the effect was determined up to 150 min. The authors reported increased excitability in the unaffected hemisphere 60 min after the stimulation protocol. Using videofluoroscopy, they found that following electrical stimulation to the pharynx, there was an improvement in pharyngeal transit time, swallowing

response time, and aspiration score compared to prestimulation. This was in contrast to no effects seen in swallowing performance in healthy subjects and to a placebo condition of merely placing the stimulation catheter in another six patients with dysphagia. Despite no changes seen in swallowing function in the healthy subjects, Fraser et al. documented that in the healthy group, there was increased activation at the sensorimotor area (BOLD signal measured via fMRI) following electrical stimulation compared to no stimulation. This may indicate that sensory stimulation has an effect on swallowing function but it was not measurable (with the authors' outcome measures) at the periphery because the healthy subjects were swallowing at optimal level. Nevertheless, their findings that increased corticobulbar excitability is correlated with improvement in swallowing lend support to the benefits of sensory stimulation in managing patients with dysphagia.

Another study by Fraser et al. (2003) evaluated the effects of volitional water swallowing, pharyngeal stimulation, and oropharyngeal anaesthesia on the excitability of neural transmission to the pharyngeal and oesophageal musculatures. They used TMS to evoke MEPs in the pharynx and oesophagus following three conditions—volitional water swallowing, pharyngeal stimulation, and oropharyngeal anaesthesia. They reported that volitional swallowing and pharyngeal stimulation facilitated the excitability of neural transmission but the excitability after pharyngeal stimulation was greater and lasted longer—up to 60 min poststimulation—compared to the effects seen with volitional swallowing. However, Huckabee and Pelletier (1999) maintained that "the best treatment for swallowing may be swallowing" (p. 47), as sensory and motor systems are intimately integrated during swallowing; any breakdown in one of these systems will result in dysphagia. Furthermore, sensory information from the oropharynx is known to modulate the motor aspect of swallowing (Miller, 1999). Logemann (1999) also supported the use of swallowing, if it can de done safely, as an exercise to rehabilitate patients with dysphagia. Moreover, Gallas, Marie, Leroi, and Verin (2009) reported that the MEP amplitude of mylohyoid muscles was increased following 15 min of effortful swallowing exercises for 1 week in healthy volunteers. They have excluded the possibility of MEP changes over time by having two baseline measures recorded a week apart which showed stable mylohyoid MEPs during that period.

In a study of training effects in limb muscles, Perez, Lungholt, Nyborg, and Nielsen (2004) used TMS to obtain MEP in the leg muscle following skill, nonskill, and passive training to the tibialis anterior muscle. They documented that motor cortical excitability is increased following skill motor training, whereas no effects were seen on the excitability of the motor cortex with the other two training programmes. Furthermore, motor performance of the volunteers in the skill training group showed less error compared to the nonskill and passive training groups. Based on these findings, the authors suggested that skill training is more beneficial to gait disorders than to nonskill or passive training. With regards to swallowing, swallowing itself is a skill, where patients with dysphagia are trained to acquire this skill in the course of their swallowing rehabilitation. Thus, any sensory stimulation given to a subject who was instructed to swallow may have some kind of skilled input towards the outcome measures.

Han, Kim, and Lim (2001) evaluated MEPs from the thenar muscles (a group of muscles in the palm which control thumb movement) when the muscles were at rest or contracted at 10%, 30%, 50%, or 100% of maximal contraction. TMS was discharged with intensities ranging from 110-140% of the excitability threshold at rest. They found that the optimal MEP amplitude (the maximal MEP obtained with minimum intensity stimulus) can be recorded when the muscles were moderately contracted—30% of maximal voluntary contraction—and the TMS output is 110% of the excitability threshold at rest. Studies on MEPs of the facial musculature also found that MEPs can best be evoked when background muscle contraction is present (Cruccu, Inghilleri, Berardelli, Romaniello, & Manfredi, 1997; McMillan, Graven-Nielsen, Romaniello, & Svensson, 2001). Thus, for some muscles groups, recording MEPs during muscle contraction may produce the best recording.

MEP responses can vary between subjects (Kiers, Cros, Chiappa, & Fang, 1993); however, it has been shown that repeated MEP measurements over a two-hour period after participants either completed saliva swallowing 60 times or did nothing were unchanged from baseline (Al-Toubi, Abu-Hijleh, Huckabee, Macrae, & Doeltgen, 2010). Moreover, Gallas et al. (2009) have reported stable mylohyoid MEPs over time following TMS to the motor cortex. Therefore, in a swallowing study, any MEP changes within two hours of presenting a stimulus can be assumed to be due to the stimulation protocol.

In summary, MEP recordings, which have been shown to be stable over time, can be used to measure changes in neural excitability following an intervention. As optimal MEP can be obtained when the muscles are preactivated, MEPs are best recorded when TMS is triggered during muscle contraction. When the MEP is recorded from the submental muscles, changes in the neural substrates of swallowing can be investigated as these muscles are involved in the superior and anterior movement of the hyolaryngeal complex. Adequate movement of the hyolaryngeal complex will ensure safe bolus transfer and avoid food from entering the airway.

4.4   Aims of Study

The general aim of this study was to investigate the effects of odour and tastant on the neural substrates of swallowing. The specific objectives of this study were to evaluate the influences of: (a) low and high concentrations of odourant, (b) low and high concentrations of tastant, and (c) combined odour and tastant stimulation on the excitability of the corticobulbar pathways controlling the submental muscles in healthy participants. MEPs were measured at the submental muscles using a previously published protocol (Doeltgen et al., 2009).

4.4.1   Hypotheses

The hypotheses for this study have been elaborated in Sections 2.7.1–2.7.3. In this section, only the hypotheses are presented.

4.4.1.1   Hypothesis 1

Olfactory stimulation increases the excitability of neural transmission associated with swallowing. That is, the MEPs measured at the submental muscles have a shorter latency and greater amplitude in the presence of an olfactory stimulus compared to no stimulation. This increased excitability is retained, at least temporarily, for up to 90 min poststimulation. A higher concentration odour produces greater effects than a low concentration odour.

4.4.1.2 Hypothesis 2

Gustatory stimulation increases the excitability of neural transmission associated with swallowing. That is, during presentation of a gustatory stimulus, MEPs have a shorter latency and greater amplitude compared with saliva swallows in which there is no additional gustatory stimulus. This increased excitability is retained, at least temporarily, for up to 90 min poststimulation after removal of the stimulus. A higher concentration tastant produces greater effects than a low concentration tastant.

4.4.1.3 Hypothesis 3

When both olfactory and gustatory stimuli are presented simultaneously, there is an increase in the excitability of neural transmission compared to no stimulus presentation or to the independent presentation of olfaction or gustation. The MEPs have a shorter latency and greater amplitude compared with baseline or either stimulus given independently, and the effect is present for up to 90 min poststimulation.

4.5 Methods

4.5.1 Study Design

A repeated-measures within-subject design was used to evaluate the effects of olfaction and gustation on the neural substrates underlying swallowing. Measures of MEPs were taken during and after stimulation—up to 90 min poststimulation—and compared with baseline data. Ethical approval was obtained from the regional Health and Disability Ethics Committee (see Appendices C and D for advertisement flyer and information sheet for participants, respectively).

4.5.2 Participants

Based on a priori power analysis using data from this lab (Doeltgen et al., 2009), 16 healthy participants (8 females, age range 19-43 years, mean 25.5 years, SD 7.6) were recruited for this study. An equal number of males and females was

used as Doty, Applebaum, Zusho, and Settle (1985) reported that olfactory identification ability was better in women compared to men in participants from four different ethnics and cultures. The age range 18-60 years was chosen because Aviv (1997) and Tracy et al. (1989) reported increased laryngopharyngeal sensory threshold and decreased swallowing efficiency, respectively, in healthy adults older than 60 years of age.

The participants reported being in good health with no previous history of neurological problem or dysphagia, had been a nonsmoker for at least one year prior to the study, and were not taking medication that could affect swallowing function. Subjects were asked to not ingest caffeine, alcohol, or spicy food less than 12 hours prior to the study (Hamdy, Mikulis et al., 1999; Kaatzke-McDonald et al., 1996; Sciortino et al., 2003) to ensure that no residuals were present on the taste receptors, which might alter the taste stimuli. All participants were informed of the procedures and written consent (Appendix E) was obtained prior to the experiments. Additionally, participants were requested to complete a health questionnaire form and a TMS adult safety screen form to ensure that they were eligible to participate in this study (Appendices F and G, respectively).

4.5.3   Instrumentation

A Magstim 200 (Magstim Company Ltd, Whitland, Wales, UK) transcranial magnetic stimulator with a figure-of-eight coil was used to evoke MEPs in the submental muscles. The pulse from this equipment has approximately a 100 μs rise time and a duration of 1 ms. The novel approach to evoke MEPs by submental muscle contraction during both volitional contraction and volitional swallowing (Doeltgen et al., 2009) was used in this study. This method differed from earlier research in which the MEPs were evoked during the rest condition (Mistry et al., 2006). Contraction of the submental muscles activated the transcranial magnetic stimulator for both conditions. Muscle contraction was detected with sEMG using an amplifier (Dual Bio Amps, Model ML135, ADInstruments, Castle Hill, Australia) and a recording system (PowerLab 8/30, Model ML870, ADInstruments, Castle Hill, Australia) which were connected to a custom-built trigger system. A DeVilbiss

PulmoMate® compressor/nebulizer was used for presentation of olfactory stimuli via nasal cannulas.

4.5.4 Stimuli

Two concentrations of each olfactory and gustatory stimulus were used to evaluate their effects on the neural function associated with swallowing. Chapter 3 describes the methods used to choose the appropriate stimuli. To summarize Chapter 3, two pilot studies were completed to identify lemon stimuli at high and low concentrations that were tolerated well, readily identifiable to participants as "lemon", and subjectively reported to be substantially different in intensity. Using visual analogue scales, seven participants documented the subjective ratings of intensity, pleasantness, and tolerability after randomized presentations of stimuli of different concentrations. Ultimately, the 25% and 100% water-based lemon odour and tastant were selected from the same source (Country Gold lemon juice, Steric Trading Pty Ltd, Villawood, NSW, Australia).

4.5.4.1 Olfactory Stimulus

Low (25%) and high (100%) concentrations of lemon smell were used in this study. Using nebulized air mixed with one of the lemon concentrations, participants were exposed to the nebulized odour stimulus through a nasal cannula inserted in both nares. They were asked to breathe as usual. Nebulized tap water was used as control.

Olfactory stimuli were presented continuously for a minute, then paused for 15 s to avoid adaptation (Coren et al., 2004) as olfactory adaptation can cause decreased sensitivity to the stimulus, and an adapting stimulus can differ from the test stimulus (Cometto-Muniz & Cain, 1995). The stimulus was then presented again for another minute, and this was repeated until all MEPs were recorded (see Experimental Procedures).

4.5.4.2 Gustatory Stimulus

Filter paper (Genuine Whatman Filter Paper No. 5, W & R Balston, Maidstone, Kent, UK) cut into 8- by 2-cm strips were used to present the gustatory

stimuli. A 5-cm strip of filter paper was soaked with either of the two gustatory stimuli—low or high concentration—and drip dried for at least 10 s. The length impregnated with tastant was then placed at midline, from the tip of the tongue. The 5-cm strip covered approximately two-thirds of the length of the tongue from the anterior tip. Blanks (impregnated with tap water) were used as control. By using this method, chemical molecules of the tastant were dissolved in saliva and activated taste receptors in the taste buds on the tongue surface. Injection or ingestion of a taste substance in a fluid carrier would add the additional sensory input of bolus size and viscosity, which would confound comparisons between sensory conditions. A fresh taste stimulus was replaced after three swallows to ensure that all participants had the appropriate gustatory stimulus when MEPs were recorded. Participants were asked to swallow their saliva for 15 swallows for each concentration for MEP recordings (see Experimental Procedures).

4.5.5   Experimental Procedures

All data were recorded in an odour-free room, with the smell and taste stimuli at room temperature. There were five sessions: the first four sessions used either a low or high odour stimulus, or a low or high tastant stimulus, which were randomly presented. The fifth session was the combination of odour and tastant stimulation. The concentrations with the greatest effect on the MEP, or the higher concentration of the stimuli if no effects were seen, were combined to see if there was an added effect when the two stimuli were paired.

Participants were seated comfortably in a chair. Areas under the chin and overlying the ramus of the mandible were cleaned with alcohol gauze. Two electrodes (BRS-50-K/12 Blue Sensor, Ambu A/S, Ballerup, Denmark) for sEMG recordings were placed over the submental muscle group at midline between the posterior aspect of the mandibular spine and the superior palpable edge of the thyroid cartilage. The distance between the two electrodes was 5 mm. One reference electrode was placed over the bony aspect of the participants' jaw at the ramus of the mandible. The submental muscles were chosen for MEP recordings as these muscles are easily accessible and they play an important role in bringing the hyolaryngeal complex upward and forward during swallowing.

The electrodes were connected to the EMG amplifier and recording system. The Scope software, which is commercially available for use with the Powerlab system, was used to monitor muscle activity. Data were acquired at a rate of 10 kHz using a high-pass filter at 10 Hz and low-pass filter at 2 kHz. A sweep of 200 ms (50 ms pretrigger and 150 ms posttrigger) was recorded for each discharge of the magnetic stimulator.

To investigate task-specific changes in the MEPs, data were gathered during both volitional swallowing and volitional contraction tasks. It is known that volitional contraction of the submental muscles, as in a stifled yawn, engages the corticobulbar pathway. It is less certain that pharyngeal swallowing, being a largely brainstem-driven task, utilizes this pathway, thus comparisons between these tasks may yield valuable information regarding the neural control of swallowing.

Participants were first asked to practise the volitional swallowing and volitional contraction conditions that would trigger the TMS. For volitional swallowing, they were asked to swallow as they normally would but to minimize tongue movement. For the volitional contraction condition, the instruction was to "stifle a yawn" to attain contraction of the submental muscles. The participants were required to contract the muscles during both conditions to the approximate same amplitude, using sEMG output as a biofeedback modality to master motor performance.

After the participants mastered both conditions, the sEMG threshold to trigger the TMS was determined. With output threshold for sEMG set at "100" and TMS intensity set at "0", the participants were asked to swallow. After 10 consecutive swallows, the peak amplitudes of the sEMG were averaged. Seventy-five percent of the averaged peak amplitude was taken as the threshold for triggering the TMS. This is the threshold that will be used to trigger the TMS under both volitional contraction and volitional swallowing conditions for that session. Using the same threshold value for both experimental conditions ensured that the same level of muscle contraction was employed to activate the TMS. The above procedures were repeated at the beginning of each session as the placements of electrodes were different among sessions.

Next, the hotspot to trigger the TMS on the scalp was identified. The hotspot is the location on the scalp that produces the most robust MEP in the submental muscles when stimulated. Using the International 10-20 System for electrode placement (Dyro, 1989; Fisch, 1991), the cranial vertex C_z was located and marked on the scalp. From the vertex, the motor area for the submental muscle group was estimated. Based on previous research (Doeltgen et al., 2009), this is about 4 cm anteriorly and 8 cm laterally from the vertex. Beginning from this point, the coil was moved in increments of 5 mm around the provisional hotspot while participants were asked to contract their submental muscles and briefly sustain the contraction. TMS was set at 50% intensity of the maximal TMS output. The output threshold for sEMG was set very high so that the muscle contraction itself would not trigger the TMS during this initial procedure. The coil was held over the estimated hotspot point with an orientation of about 45º from the midline (Mistry et al., 2007). This position was chosen to ensure that the induced current from the coil was perpendicular to the estimated alignment of the central sulcus. While the participants were contracting the submental muscles, the investigator depressed the foot switch or the button on the TMS handle. The intensity was increased in 10% increments, up to a level that was tolerated by the participant, if no MEPs were detected. The procedure was repeated until the hotspot was identified. This point was marked on the scalp and the same procedures were repeated in the opposite hemisphere.

After bilateral hotspots were identified, a stimulus response curve was derived to determine TMS intensity output that was appropriate for the participant. The stimulus-response curve was collected while participants maintained tonic voluntary muscle activation. This may not be the most appropriate route for determining the stimulus-response curve as Darling, Wolf, and Butler (2006) have shown that MEP amplitude is increased when either the stimulation intensity of the TMS or the contraction level in the muscle is increased. However, as the same method was used for every participant, this would probably not have had a substantial influence on the data. The cortex may have been stimulated at a higher intensity but the same intensity was used in all sessions for the particular participant. With the coil at one hotspot in either hemisphere, the area was stimulated three times, starting with a TMS intensity that produced no MEP response (that is, no MEP is generated, at 30% intensity). The intensity was increased in 10% steps until the

MEP reached maximal amplitude; that is, it did not increase in amplitude when a higher TMS intensity was applied. Three MEPs with maximal amplitude (peak to peak) were then averaged. The TMS intensity that produced 50% of this amplitude was the intensity used for all sessions. Fifty percent of the maximal amplitude of MEP was used to allow for a decrease or increase in the MEP amplitude when stimulus was presented. These procedures were repeated in the other hemisphere to determine the dominant hemisphere, which is the hemisphere that produced a more robust MEP with the lowest TMS intensity. Subsequent trials were carried out only on the dominant hemisphere but the hotspot was identified at the start of each session.

Baseline measures for volitional contraction and volitional swallowing were then determined. The previously defined sEMG threshold was engaged. The EMG-activated triggering system was locked for a period of 10 s after each contraction/swallow to avoid accidental triggering. The investigator informed the participants to "swallow when you are ready" when the equipment was set to record. Water to moisten the oral mucosa was regularly offered between contractions/swallows. Fifteen MEPs during volitional swallowing and 15 MEPs during volitional contraction were recorded at baseline, during the control condition, during stimulus presentation, immediately poststimulation (5 min), and at 30-, 60-, and 90-min poststimulation in four separate sessions. At each session, the low odour, high odour, low tastant, or high tastant stimulation was randomly presented across participants. The swallowing and contraction conditions were counter-balanced across sessions. Water was used for all control conditions.

The 15 MEPs were evaluated individually for amplitude and latency measurements. A custom-designed analysis software was used to analyse the data. Firstly, the first positive peak (P1) and the first negative peak (N1) were determined (Figure 11). Regions of interest were defined before P1 and after N1. Peak-to-peak amplitude from P1 to N1 is automatically calculated by the software, which was then transferred to an excel datasheet—this is the amplitude measurement of the MEP. Then, the latency of each MEP was determined. This is defined as the time from the triggering of the magnetic stimulator (at 0 s, which is shown as the magnetic stimulation artefact in Figure 11) to the first significant rise of P1 from baseline

(shown as the red arrow in Figure 11). The waveforms that did not conform to the usual MEP were discarded.

The means for all measurements were subjected to further analyses. After analysis of preliminary data, the odour and tastant that maximally influenced the MEP in each participant were then presented simultaneously in another session. The higher concentration stimulus was used if no effects were seen. Data were saved on the computer for offline analyses. Confidentiality was assured by assigning a coded numerical identification for each participant.
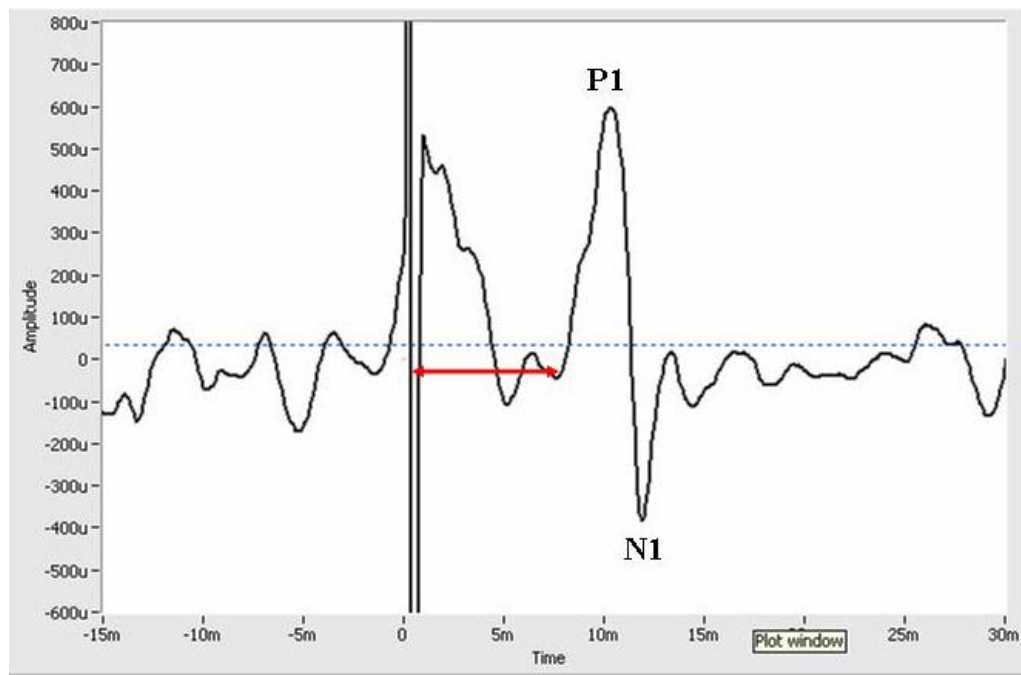
Figure 11. MEP waveform from one participant to illustrate P1, N1, and the determination of latency (the red arrow).

4.5.6   Data Analyses

MEP responses vary considerably between subjects (Ertekin, Turman et al., 2001; Kiers et al., 1993); therefore, analyses were based on percent change in amplitude or latency from baseline. Data were analysed using SPSS 17 (SPSS Inc, Somers, New York, USA).

Data were analysed separately as immediate (control condition compared to during stimulation) or late (at 5-, 30-, 60-, and 90-min poststimulation) effects. For each, repeated-measures ANOVAs were first performed to evaluate the effects of

concentration on both odour and tastant during volitional contraction and volitional swallowing. If there were no differences in the MEP amplitude or latency as a function of concentration, the data were collapsed as "odour" or "tastant" and analyses were then computed for odour, tastant, and combined stimulation. Baseline measures were included as covariates in all ANOVAs.

For both contraction and swallowing tasks, the immediate effect of stimulus was first evaluated by repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation). If there were no effects or interactions with concentration, repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by condition (control, stimulation) was conducted. When significant, posthoc t-tests were conducted to evaluate which two stimuli differed.

The effect of stimulus across time (late effect) on MEP amplitude and latency was assessed by conducting repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by time (5-, 30-, 60-, and 90-min poststimulation) for both contraction and swallowing tasks. As with previous analyses, if there were no effects or interactions with concentration, repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by time (5-, 30-, 60-, and 90-min poststimulation) was conducted. When significant, one-way ANOVAs for odour, tastant, and combined stimulation were conducted. Additionally, one sample t-tests were also conducted at 30-, 60-, and 90-min poststimulation to evaluate if there were changes from zero (= baseline). This was carried out as one of the hypotheses stated that there will be a change in MEP up to 90 min poststimulation. The hypothesis was based on previous studies that have documented a pattern of increased corticobulbar excitability following sensory intervention over time (Doeltgen, Dalrymple-Alford et al., 2010; Fraser et al., 2002; Fraser et al., 2003; Mistry et al., 2006). Bonferroni correction was not implemented as this procedure may increase the likelihood of a Type II error (Field, 2005). Other statisticians also agree that using Bonferroni correction in clinical studies with repeated measurements may not be appropriate as the data are highly correlated (Bland & Altman, 1995; Perneger, 1998). To evaluate for potential Type I error, 95% confidence interval (CI) surrounding the mean differences and effect size of each calculation were also considered.

The effect of tasks (contraction versus swallowing) was examined by comparing data from participants who had MEPs for both contraction and swallowing. For immediate effect, repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation) was conducted. If there were no effects or interactions with concentration, another repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste, combined stimulation) by condition (control, stimulation) was conducted. Similarly, for late effect, repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste) by concentration (low, high) by time (5-, 30-, 60-, and 90-min poststimulation) was conducted. If there were no effects or interactions with concentration, another repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste, combined stimulation) by time (5-, 30-, 60-, and 90-min poststimulation) was conducted.

Pretrigger EMG levels were also determined and analysed using repeated-measures ANOVAs to ensure that any changes observed in the MEPs were not due to changes in the background muscle activity. The mean EMG amplitude within the 50 ms pretrigger portion of each trial for participants with measurable MEPs during both contraction and swallowing were subjected to this analysis. For both tasks, the immediate effect of stimulus was first evaluated by repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation). If there were no effects or interactions with concentration, repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by condition (control, stimulation) was conducted. When significant, posthoc *t*-tests were conducted to evaluate which two stimuli differed. The effect of stimulus across time (late effect) on pretrigger mean EMG amplitude was assessed by conducting repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by time (0-, 5-, 30-, 60-, and 90-min poststimulation) for both contraction and swallowing tasks. As with previous analyses, if there were no effects or interactions with concentration, repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by time (0-, 5-, 30-, 60-, and 90-min poststimulation) was conducted. When significant, one-way ANOVAs for odour, tastant, and combined stimulation were conducted.

For For all analyses, $p < .05$ was taken as significant. For all repeated-measures analyses, Greenhouse-Geisser correction was reported if the assumption of sphericity was violated; that is, when Mauchly's test of sphericity was significant.

Twenty percent of the data were subjected to re-evaluation by the investigator and one other postgraduate student for intra- and inter-rater reliability tests, respectively. The postgraduate student has prior knowledge of evaluating MEP data, thus no practice session was conducted to familiarize both raters to the MEP data. The single-measures intraclass correlation coefficient (ICC) was used to analyse the data.

4.6 Results

MEPs for volitional contraction were recorded from all 16 participants but only nine participants had recordable MEPs during volitional swallowing. The ICCs for intrarater reliability for amplitude and latency measurements were .99 and .96, respectively. The ICCs for interrater reliability for amplitude and latency measurements were .76 and .58, respectively. Portney & Watkins (1993) have suggested that an ICC > .75 can be considered a good reliability and anything below this as having poor to moderate reliability. The intrarater reliability for amplitude and latency were good. The interrater reliability for MEP amplitude was also good; however, interrater reliability for latency measurement was only moderate. This may be explained by the methods used to extract the data. Using the same software for analysis, the 15 MEPs were evaluated individually for latency measurement. By definition, onset latency is the first significant rise of the P1 waveform, which could be interpreted differently by the raters. Moreover, the waveforms that did not conform to the usual MEP were discarded. There could well have been instances where the MEPs that were thought as not conforming to the usual MEP were not similar between raters.

The mean pretrigger EMG amplitudes at each time point for each condition during volitional contraction and volitional swallowing are presented in Tables 1 and 2, respectively. The repeated-measures ANOVAs of pretrigger EMG levels revealed no significant changes in any of the analyses; the F- and p-values during contraction and swallowing are presented in Table 3.

Table 1

Mean (SD) pretrigger EMG amplitudes during volitional contraction

	Mean pretrigger EMG (μV) (SD)				
	Low odour stimulation	High odour stimulation	Low tastant stimulation	High tastant stimulation	Combined stimulation
Baseline	164.78 (67.94)	167.78 (89.19)	157.39 (76.71)	150.11 (88.98)	197.79 (49.87)
Control condition	168.13 (66.17)	170.96 (78.22)	154.37 (83.37)	164.30 (87.26)	191.86 (59.23)
During stimulation	155.71 (62.35)	175.04 (105.08)	162.46 (86.58)	164.17 (85.10)	193.21 (62.21)
5 min post	153.24 (57.11)	160.74 (77.53)	150.74 (69.46)	165.24 (91.66)	188.20 (59.51)
30 min post	153.85 (63.76)	162.15 (89.40)	161.12 (82.08)	172.13 (86.65)	191.06 (56.51)
60 min post	174.72 (80.00)	158.21 (72.15)	148.80 (78.08)	166.92 (77.37)	193.47 (88.35)
90 min post	156.53 (73.51)	168.73 (96.65)	151.79 (93.67)	151.95 (77.14)	200.35 (81.59)

Table 2

Mean (SD) pretrigger EMG amplitudes during volitional swallowing

	Mean pretrigger EMG (µV) (SD)				
	Low odour stimulation	High odour stimulation	Low tastant stimulation	High tastant stimulation	Combined stimulation
Baseline	168.74 (52.78)	175.87 (89.64)	156.51 (48.22)	166.66 (94.15)	204.88 (49.19)
Control condition	171.91 (57.09)	178.61 (94.41)	157.03 (67.30)	168.94 (85.04)	199.77 (64.60)
During stimulation	172.98 (53.76)	180.58 (92.69)	155.50 (76.71)	181.71 (102.32)	193.59 (50.79)
5 min post	170.42 (65.22)	181.87 (85.32)	156.80 (63.50)	164.97 (84.80)	197.42 (45.00)
30 min post	165.74 (48.53)	171.65 (83.67)	167.57 (71.08)	171.25 (82.17)	205.53 (63.03)
60 min post	185.64 (68.07)	176.92 (85.89)	143.71 (69.13)	174.82 (88.52)	198.65 (63.16)
90 min post	174.50 (68.31)	178.26 (91.22)	163.25 (83.41)	165.97 (80.00)	215.86 (88.69)

Table 3

F- and p- values of repeated-measures ANOVAs of pretrigger EMG levels during volitional contraction and swallowing

Repeated-measures ANOVAs		Main and interaction effects	Contraction		Swallowing	
			F^a	p	F^a	p
Immediate effect	Stimulus by concentration by condition	Stimulus	0.12	.74	0.39	.55
		Concentration	0.27	.62	0.75	.41
		Condition	< 0.001	.99	0.67	.44
		Stimulus x Conc	0.02	.88	0.23	.65
		Stimulus x Condition	0.60	.46	0.67	.62
		Conc x Condition	0.75	.41	1.17	.31
		Stim x Conc x Cond	1.84	.21	0.74	.41
	Stimulus by condition	Stimulus	1.81	.20	1.32	.30
		Condition	0.01	.93	0.01	.92
		Stimulus x Condition	0.32	.73	0.42	.58
Late effect	Stimulus by concentration by time	Stimulus	0.23	.64	0.43	.53
		Concentration	0.11	.75	0.28	.61
		Time	0.27	.89	0.13	.97
		Stimulus x Conc	0.04	.85	0.07	.79
		Stimulus x Time	2.01	.12	1.05	.40
		Concentration x Time	0.50	.73	0.14	.88
		Stim x Conc x Time	1.20	.33	0.91	.47
	Stimulus by time	Stimulus	2.69	.10	2.73	.10
		Time	0.26	.90	0.51	.73
		Stimulus x Time	0.46	.88	0.59	.78

Note: For immediate effect, where sphericity is assumed, F^a = F(1, 8) and F^a = F(2, 16) for main effect; F^a = F(1, 8) and F^a = F(2, 16) for interactions. For late effect, where sphericity is assumed, F^a = F(1, 8), F^a = F(2, 16), and F^a = F(4, 32) for main effect; F^a = F(1, 8), F^a = F(4, 32), and F^a = F(8, 64) for interactions.*p < .05. Stim, stimulus; Conc, concentration; Cond, condition.

4.6.1   Volitional Contraction

The mean MEP amplitude and latency for low odour, high odour, low tastant, high tastant, and combined stimulation during volitional contraction are presented in

Appendix H. The *F-* and *p*-values of repeated-measures ANOVAs for MEP amplitude and latency during contraction are presented in Table 1.

MEP Amplitude during Volitional Contraction: Immediate Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation) revealed no effects or interactions of concentration (Table 4). Therefore, low and high concentrations odour and tastant were collapsed. Repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by condition (control, stimulation) also revealed no significant effect.

MEP Amplitude during Volitional Contraction: Late Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by time (5-, 30-, 60-, and 90-min poststimulation) for contraction showed no effects or interactions with concentration (Table 4). Therefore, low and high concentrations odour and tastant were collapsed. Another repeated-measures ANOVA was performed for stimulus (odour, taste, combined stimulation) by time (5-, 30-, 60-, and 90-min poststimulation). A significant interaction of Stimulus x Time; $F(3.48, 52.24) = 3.23$, $p = .02$, $r = .42$ was found. Further, posthoc one-way repeated-measures ANOVAs for each of the stimulus were done. Results for the analyses of tastant and combined stimulation revealed no differences in MEP amplitude across time, $F(3, 45) = 0.35$, $p = .79$, $r = .15$ and $F(3, 45) = 1.98$, $p = .13$, $r = .34$, respectively. Repeated-measures ANOVA of odour revealed a significant time effect on MEP amplitude; $F(1.74, 26.05) = 3.63$, $p < .05$, $r = .44$.

Table 4

F- and p- values of repeated-measures ANOVAs of MEPs during volitional contraction

Repeated-measures ANOVAs		Main and interaction effects	Amplitude		Latency	
			F^a	p	F^a	p
Immediate effect	Stimulus by concentration by condition	Stimulus	0.39	.54	1.13	.30
		Concentration	2.00	.18	0.37	.55
		Condition	4.17	.06	1.33	.27
		Stimulus x Conc	3.82	.07	0.61	.45
		Stimulus x Condition	0.57	.46	0.94	.35
		Conc x Condition	3.83	.07	0.15	.71
		Stim x Conc x Cond	0.05	.83	**7.00**	**.02***
	Stimulus by condition	Stimulus	0.56	.58	0.64	.53
		Condition	< 1.0	.99	0.19	.67
		Stimulus x Condition	2.78	.08	3.15	.06
Late effect	Stimulus by concentration by time	Stimulus	0.63	.44	0.14	.72
		Concentration	0.05	.83	0.72	.41
		Time	3.06	.08	0.85	.47
		Stimulus x Conc	1.24	.28	0.93	.35
		Stimulus x Time	2.32	.09	1.79	.16
		Concentration x Time	0.68	.49	0.63	.52
		Stim x Conc x Time	0.13	.86	0.45	.72
	Stimulus by time	Stimulus	2.25	.12	0.09	.92
		Time	1.71	.21	0.20	.90
		Stimulus x Time	**3.23**	**.02***	1.77	.11

Note: For immediate effect, where sphericity is assumed, $F^a = F(1, 15)$ and $F^a = F(2, 30)$ for main effect; $F^a = F(1, 15)$ and $F^a = F(2, 30)$ for interactions; when two or three factors were considered, respectively. For late effect during volitional contraction, where sphericity is assumed, $F^a = F(1, 15)$, $F^a = F(2, 30)$, and $F^a = F(3, 45)$, for main effect; $F^a = F(2, 30)$, $F^a = F(3, 45)$, and $F^a = F(6, 90)$ for interactions; when two, three, or four factors were considered, respectively. *$p < .05$. Stim, stimulus; Conc, concentration; Cond, condition.

Posthoc one sample *t*-tests for odour stimulation revealed increased MEP amplitude at 90 min poststimulation compared to baseline; $t(15) = 2.18$, $p < .05$, Cohen's $d = 0.77$, $r = .36$ (95% CI -58.5 to -0.60, Figure 12). The barely significant result of one sample *t*-test for MEP amplitude following odour stimulation at 90 min

poststimulation did not follow the same pattern of change seen in other studies. As the *p* value was just under .05 with very large standard deviation and the data do not fit with prior research, there may be a possibility that this is a Type I error. Therefore, this *t*-test result was not taken into consideration.
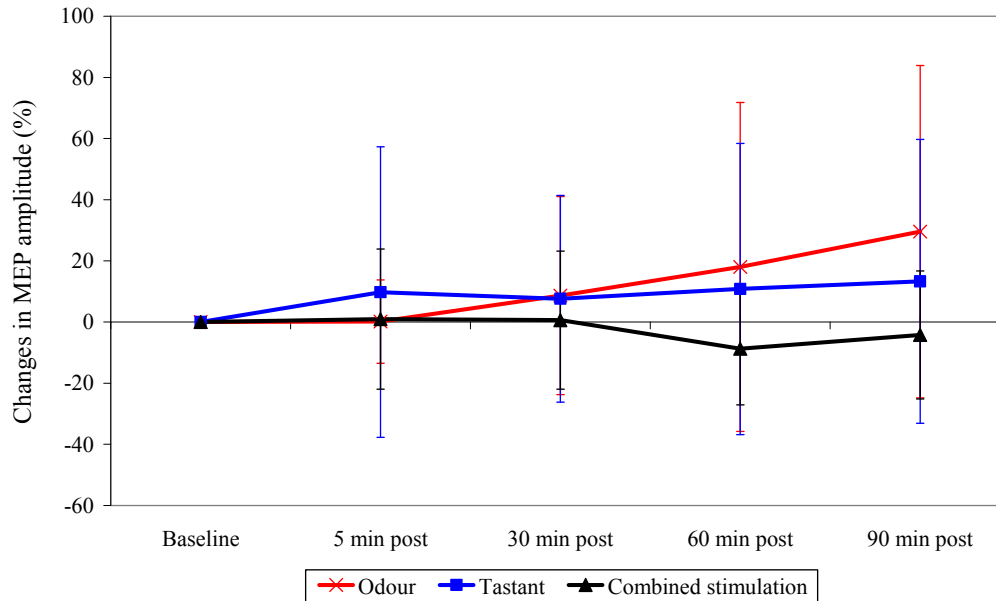
Figure 12. Mean percent changes from baseline (error bar as SD) in MEP amplitude for odour, tastant, and combined stimulation during volitional contraction at 5-, 30-, 60-, and 90-min poststimulation.

As one of the hypotheses stated that there would be a change in MEP up to 90 min poststimulation, one-sample *t*-tests at 30-, 60-, and 90-min poststimulation were also conducted for tastant and combined stimulation at these time points. However, none of the results were significant.

MEP Latency during Volitional Contraction: Immediate Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation) showed no main effect of concentration but there was a significant interaction of Stimulus x Concentration x Condition (Table 4). MEP latency was decreased during presentation of low concentration odour compared to control condition. The presentation of high concentration tastant decreased MEP latency compared to control condition (interaction effect of Stimulus x Concentration x Condition shown in Figures 13 and 14).
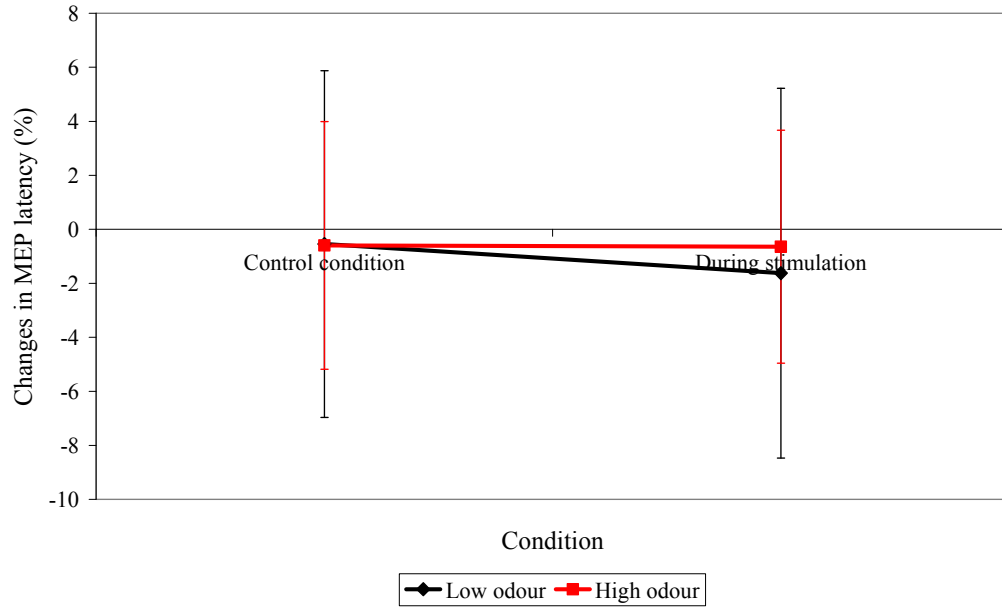
Figure 13. Figures 13 and 14 illustrate the interaction of Stimulus x Concentration x Condition. The latency tends to decrease when low odour was presented but no latency changes were apparent with high odour (compare with Figure 14 where high tastant tends to decrease the latency but not low tastant). Paired *t*-tests for low and high odours comparing control and during stimulation were not significant ($p = .45$ and $p = .98$ for low odour and high odour, respectively).
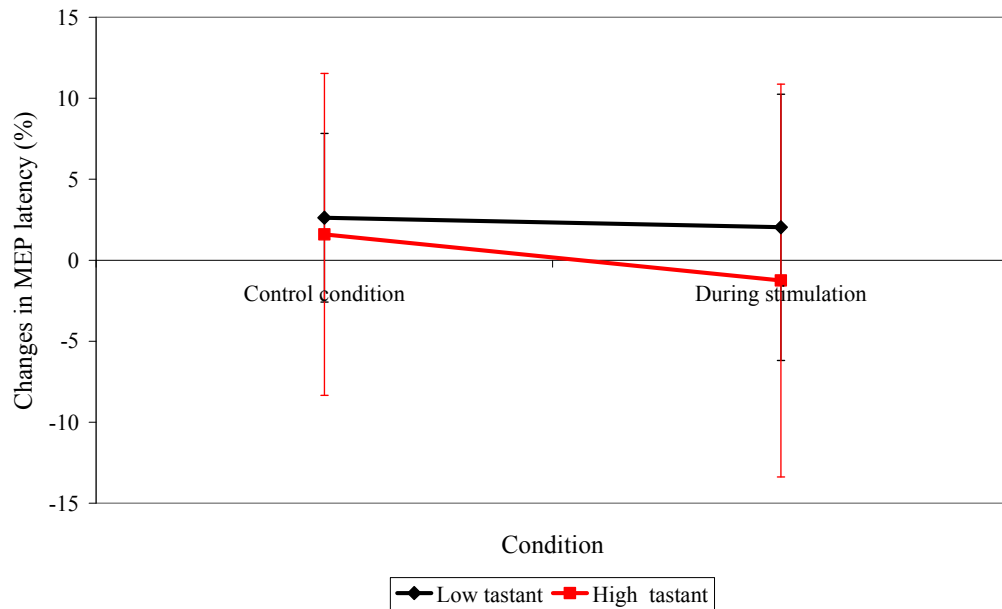
Figure 14. Figures 13 and 14 illustrate the interaction of Stimulus x Concentration x Condition. The latency tends to decrease when high tastant was presented but no latency changes were apparent with low tastant (compare with Figure 13 where low odour decreased the latency but not high odour). Paired *t*-tests for low and high tastants comparing control and during stimulation were not significant ($p = .68$ and $p = .07$ for low tastant and high tastant, respectively).

As there was no main effect of concentration and interaction of Stimulus x Concentration, the low and high concentrations odour and tastant were collapsed. Repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by condition (control, stimulation) showed no significant effects (mean data showed in Table 5).

Table 5

Mean (SD) MEP latency during volitional contraction for immediate effect

	Mean MEP latency (ms) (SD)		
	Odour stimulation	Tastant stimulation	Combined stimulation
Baseline	9.43 (0.87)	9.23 (0.75)	9.46 (0.84)
Control condition	9.37 (0.96)	9.39 (0.67)	9.33 (0.78)
During stimulation	9.31 (0.79)	9.23 (0.86)	9.51 (0.89)

MEP Latency during Volitional Contraction: Late Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by time (5-, 30-, 60-, and 90-min poststimulation) showed no effects or interactions with concentration. Therefore, the low and high concentrations odour and tastant were collapsed (Table 4). Repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by time (5-, 30-, 60-, and 90-min poststimulation) also showed no significant effect (mean data showed in Table 6).

Table 6

Mean (SD) MEP latency during volitional contraction for late effect

	Mean MEP latency (ms) (SD)		
	Odour stimulation	Tastant stimulation	Combined stimulation
Baseline	9.43 (0.87)	9.23 (0.75)	9.46 (0.84)
Poststimulation	9.39 (0.71)	9.20 (0.79)	9.34 (0.78)
30 min post	9.53 (0.77)	9.22 (0.90)	9.29 (0.85)
60 min post	9.29 (0.81)	9.22 (0.98)	9.36 (1.03)
90 min post	9.15 (0.82)*	9.16 (0.89)	9.50 (0.94)

*$p < .05$ compared to baseline.

As one of the hypotheses stated that there would be a change in MEP up to 90 min poststimulation, one-sample *t*-tests at 30-, 60-, and 90-min poststimulation were also conducted for odour, tastant, and combined stimulation at these time points. Results indicated that MEP latency following odour stimulation at 90 min poststimulation was significantly decreased from baseline; $t(15) = 2.81$, $p = .01$, Cohen's $d = 0.99$, $r = .44$ (95% CI -4.77 to -0.65, Figure 15).
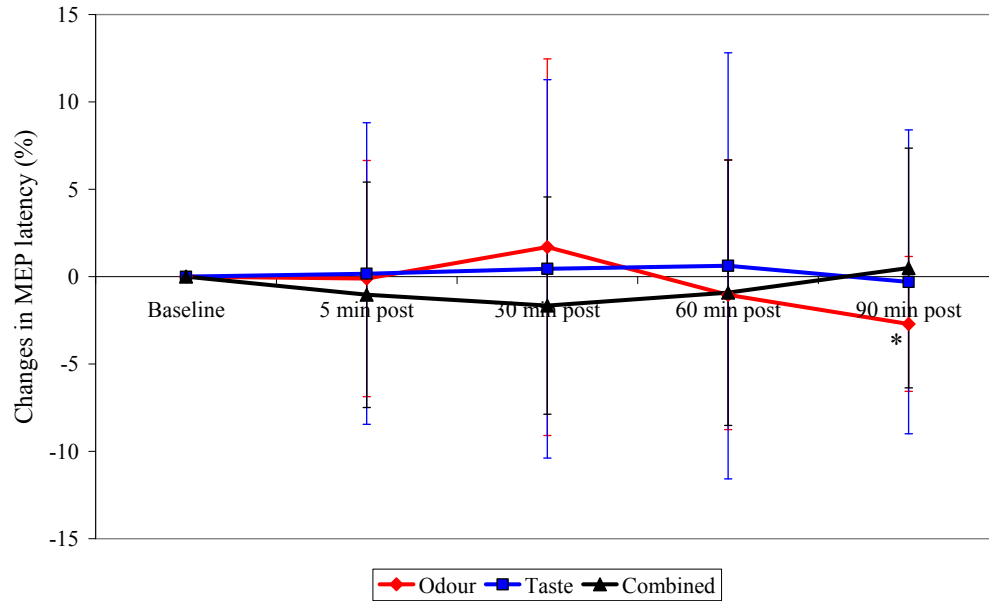
Figure 15. Mean percent changes from baseline (error bar as SD) in MEP latency for odour, tastant, and combined stimulation during volitional contraction at 5-, 30-, 60-, and 90-min poststimulation. *$p < .05$.

4.6.2 Volitional Swallowing

The mean MEP amplitude and latency for low odour, high odour, low tastant, high tastant, and combined stimulation during volitional swallowing are presented in Appendix I. The *F*- and *p*-values of repeated-measures ANOVAs for MEP amplitude and latency during swallowing are presented in Table 4.

MEP Amplitude during Volitional Swallowing: Immediate Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation) showed no effects or interactions with concentration (Table 7). Therefore, low and high concentrations odour and tastant were collapsed. Repeated-measures ANOVA of stimulus (odour, taste, combined

stimulation) by condition (control, stimulation) also showed no significant effect (mean data shown in Table 8).

Table 7

F- and p- values of repeated-measures ANOVAs of MEPs during volitional swallowing

Tasks and repeated-measures ANOVAs		Main and interaction effects	Amplitude		Latency	
			F^a	p	F^a	p
Volitional swallowing: Immediate effect	Stimulus by concentration by condition	Stimulus	2.54	.15	0.07	.80
		Concentration	1.26	.29	0.04	.85
		Condition	0.23	.65	0.01	.93
		Stimulus x Conc	0.21	.66	<1.0	.99
		Stimulus x Condition	0.11	.75	0.30	.60
		Conc x Condition	0.27	.62	4.74	.06
		Stim x Conc x Cond	1.13	.32	0.02	.91
	Stimulus by condition	Stimulus	1.85	.19	1.86	.19
		Condition	1.22	.30	0.01	.95
		Stimulus x Condition	0.16	.76	0.07	.93
Volitional swallowing: Late effect	Stimulus by concentration by time	Stimulus	0.42	.53	0.11	.75
		Concentration	1.40	.27	0.81	.40
		Time	1.45	.25	1.31	.30
		Stimulus x Conc	4.73	.06	0.04	.85
		Stimulus x Time	1.30	.30	1.77	.21
		Concentration x Time	0.84	.49	0.69	.57
		Stim x Conc x Time	2.99	.051	0.93	.44
	Stimulus by time	Stimulus	1.28	.31	0.21	.82
		Time	0.82	.50	1.05	.39
		Stimulus x Time	1.04	.37	1.19	.33

Note: For immediate effect, where sphericity is assumed, $F^a = F(1, 8)$ and $F^a = F(2, 16)$ for main effect; $F^a = F(1, 8)$ and $F^a = F(2, 16)$ for interactions; when two or three factors were considered, respectively. For late effect, where sphericity is assumed, $F^a = F(1, 8)$, $F^a = F(2, 16)$, and $F^a = F(3, 24)$, for main effect; $F^a = F(2, 16)$, $F^a = F(3, 24)$, and $F^a = F(6, 48)$ for interactions; when two, three, or four factors were considered, respectively. Stim, stimulus; Conc, concentration.

Table 8

Mean (SD) MEP amplitude during volitional swallowing for immediate effect

	Mean MEP amplitude (µV) (SD)		
	Odour stimulation	Tastant stimulation	Combined stimulation
Baseline	453.6 (234.9)	424.6 (152.3)	440.1 (180.0)
Control condition	419.8 (178.3)	450.5 (107.0)	496.5 (189.1)
During stimulation	405.1 (159.4)	442.4 (136.1)	464.7 (148.8)

MEP Amplitude during Volitional Swallowing: Late Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by time (5-, 30-, 60-, and 90-min poststimulation) for swallowing showed no significant effects or interactions with concentration. Therefore, the low and high concentrations odour and tastant were collapsed. Repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by time (5-, 30-, 60-, and 90-min poststimulation) also showed no significant effect (Table 7). However, as one of the hypotheses stated that there will be a change in MEP up to 90 min poststimulation, one-sample *t*-tests at 30-, 60-, and 90-min poststimulation were conducted for odour, tastant, and combined stimulation at these time points. Results showed significant differences following the presentation of combined stimulation at 30-, 60-, and 90-min poststimulation; $t(8) = 2.72$, $p = .03$, Cohen's $d = 1.28$, $r = 0.54$ (95% CI 2.56 to 31.46); $t(8) = 2.36$, $p < .05$, Cohen's $d = 1.11$, $r = .49$ (95% CI 0.53 to 44.90); and $t(8) = 2.92$, $p = .02$, Cohen's $d = 1.38$, $r = .57$ (95% CI 4.47 to 37.67); respectively (Figure 16). To illustrate this effect, the mean MEP waveforms of one participant during volitional swallowing are shown in Figure 17.
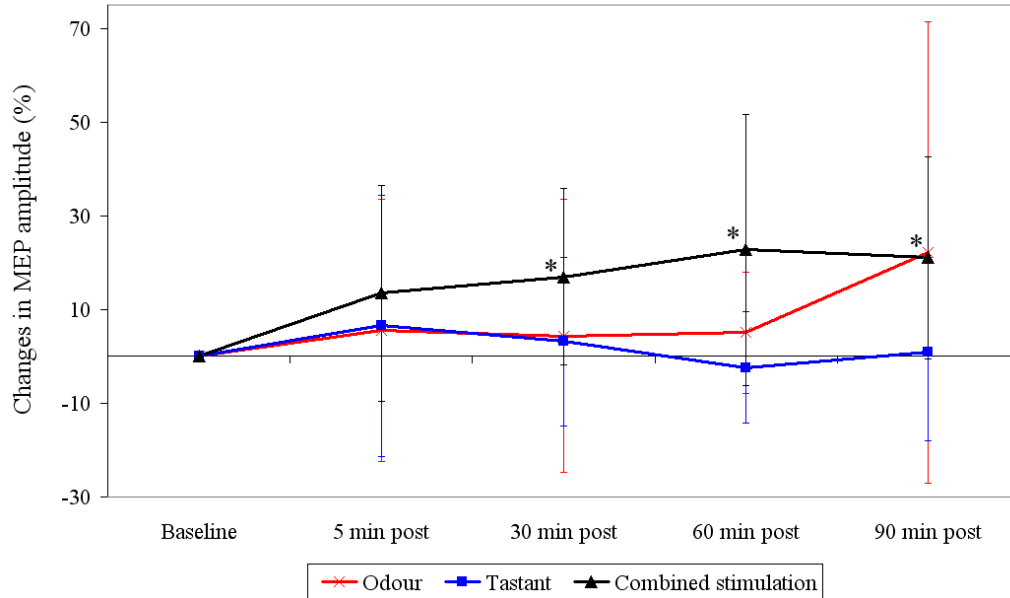
Figure 16. Mean percent changes from baseline (error bar as SD) in MEP amplitude for odour, tastant, and combined stimulation during volitional swallowing at 5-, 30-, 60-, and 90-min poststimulation. *$p < .05$ compared to baseline.
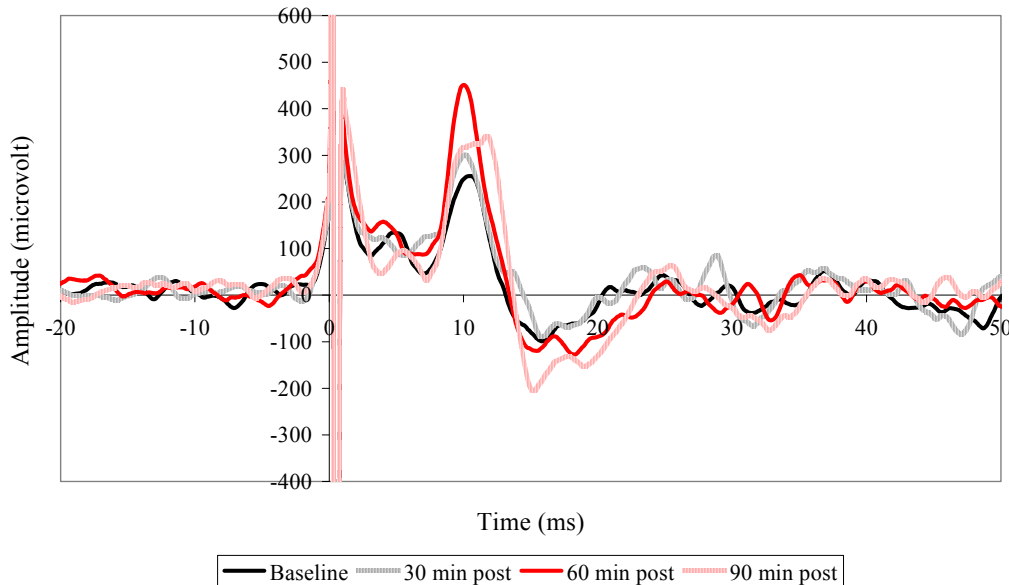
Figure 17. Mean MEP waveforms of one participant during volitional swallowing at baseline and at 30-, 60-, and 90-min following simultaneous odour and tastant presentation.

MEP Latency during Volitional Swallowing: Immediate Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation) showed no effects or interactions of concentration (Table 7). Therefore, low and high concentrations odour and tastant

were collapsed. Repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by condition (control, stimulation) also showed no significant effect (mean data shown in Table 9).

Table 9

Mean (SD) MEP latency during volitional swallowing for immediate effect

	Mean MEP latency (ms) (SD)		
	Odour stimulation	Tastant stimulation	Combined stimulation
Baseline	9.23 (1.04)	9.47 (0.88)	9.40 (0.85)
Control condition	9.29 (0.80)	9.69 (0.97)	9.12 (0.85)
During stimulation	9.28 (0.89)	9.59 (0.98)	9.14 (1.22)

MEP Latency during Volitional Swallowing: Late Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by time (5-, 30-, 60-, and 90-min poststimulation) for swallowing showed no significant effects or interactions with concentration. Therefore, the low and high concentrations odour and tastant were collapsed. Repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by time (5-, 30-, 60-, and 90-min poststimulation) also showed no significant effect (Table 7). However, as one of the hypotheses stated that there will be a change in MEP up to 90 min poststimulation, one-sample *t*-tests at 30-, 60-, and 90-min poststimulation were conducted for odour, tastant, and combined stimulation at these time points. Results showed no significant differences in any of the analyses (mean data shown in Table 10).

Table 10

Mean (SD) MEP latency during volitional swallowing for late effect

	Mean MEP latency (ms) (SD)		
	Odour stimulation	Tastant stimulation	Combined stimulation
Baseline	9.23 (1.04)	9.47 (0.88)	9.40 (0.85)
Poststimulation	9.16 (0.73)	9.45 (1.08)	9.29 (1.23)
30 min post	9.35 (0.73)	9.14 (1.11)	9.05 (1.13)
60 min post	8.97 (0.59)	9.11 (1.09)	9.17 (1.39)
90 min post	8.92 (0.74)	9.35 (1.04)	9.05 (1.04)

4.6.2   Volitional Contraction versus Volitional Swallowing

The *F*- and *p*-values of repeated-measures ANOVAs for MEP amplitude and latency during both contraction and swallowing tasks are presented in Table 11.

MEP Amplitude: Immediate Effect

In nine participants who had recordable MEPs during both contraction and swallowing, repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation) showed significant main effect of concentration and the interaction of Task x Condition (Table 11). The low concentration generally produced lower MEP amplitude compared to the high concentration stimuli. The interaction effect showed that volitional contraction generally produced higher MEP amplitude compared to MEP during swallowing (Figures 18 and 19). The interaction effect also indicates that contraction tends to increase MEP amplitude during stimulation, whilst swallowing has no apparent effect on the MEP amplitude.

Table 11

F- and p-values of repeated-measures ANOVAs for analyses of MEPs during both contraction and swallowing in one model

Repeated-measures ANOVAs	Main and interaction effects	Amplitude		Latency	
		F^a	p	F^a	p
Immediate effect	Task by stimulus by concentration by condition	Task	2.57	.15	1.76	.22
		Stimulus	3.63	.09	0.25	.63
		Concentration	**7.84**	**.02***	0.57	.47
		Condition	0.56	.48	0.37	.56
		Task x Stimulus	0.38	.55	<1.0	.994
		Task x Concentration	2.15	.18	0.98	.35
		Stimulus x Conc	3.98	.08	0.42	.54
		Task x Stimulus x Conc	1.34	.28	0.90	.37
		Task x Condition	**8.48**	**.02***	0.56	.48
		Stimulus x Condition	2.82	.13	1.71	.23
		Task x Stimulus x Cond	4.09	.08	0.004	.95
		Conc x Condition	0.43	.53	1.07	.33
		Task x Conc x Cond	2.30	.17	**6.56**	**.03***
		Stim x Conc x Cond	0.43	.53	1.10	.33
		Task x Stim x Conc x Cond	0.33	.58	0.54	.48
	Task by stimulus by condition	Task	-	-	0.45	.52
		Stimulus	-	-	0.98	.40
		Condition	-	-	0.05	.82
		Task x Stimulus	-	-	1.41	.27
		Task x Condition	-	-	0.03	.86
		Stimulus x Condition	-	-	0.73	.50
		Task x Stim x Condition	-	-	0.36	.71
Late effect	Task by stimulus by concentration by time	Task	1.05	.34	0.87	.38
		Stimulus	0.46	.52	0.24	.64
		Concentration	2.57	.15	3.32	.11
		Time	1.58	.22	0.83	.43
		Task x Stimulus	0.19	.68	0.01	.94
		Task x Concentration	0.56	.48	0.01	.94
		Stimulus x Conc	0.25	.63	0.01	.93
		Task x Stimulus x Conc	1.55	.25	0.07	.80
		Task x Time	1.29	.30	0.35	.79

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	Stimulus x Time	3.47	.03	3.56	.07
	Task x Stimulus x Time	1.48	.25	0.37	.77
	Concentration x Time	0.46	.61	0.74	.54
	Task x Conc x Time	0.27	.84	0.56	.64
	Stimulus x Conc x Time	1.43	.26	1.56	.23
	Task x Stim x Conc x Time	0.53	.67	0.30	.83
Task by stimulus by time	Task	0.19	.68	0.01	.92
	Stimulus	0.54	.59	0.17	.85
	Time	1.70	.19	0.72	.55
	Task x Stimulus	**4.12**	**.04***	1.18	.32
	Task x Time	0.57	.65	0.23	.88
	Stimulus x Time	2.39	.12	1.84	.16
	Task x Stimulus x Time	1.77	.13	0.42	.86

Note: For immediate effect, where sphericity is assumed, $F^a = F(1, 8)$ and $F^a = F(2, 16)$ for main effect; $F^a = F(1, 8)$ and $F^a = F(2, 16)$ for interactions; when two or three factors were considered, respectively. For late effect during volitional contraction, where sphericity is assumed, $F^a = F(1, 8)$, $F^a = F(2, 16)$, and $F^a = F(3, 24)$, for main effect; $F^a = F(2, 16)$, $F^a = F(3, 24)$, and $F^a = F(6, 48)$ for interactions; when two, three, or four factors were considered, respectively. *$p < .05$. Stim, stimulus; Conc, concentration; Cond, condition.
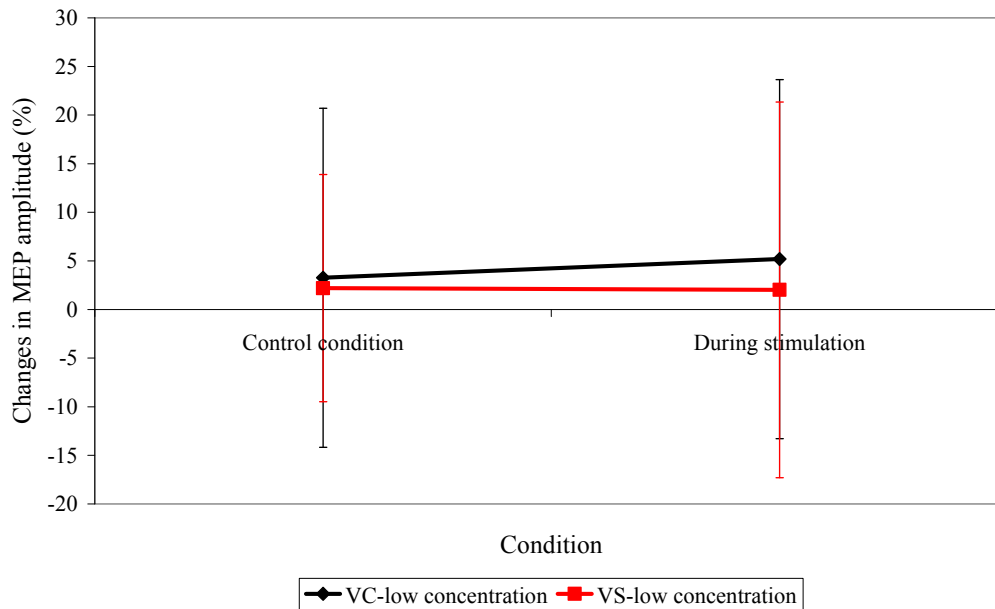
Figure 18. Condition x Task x Concentration graph for low concentration stimuli showing the differences in MEP amplitude between volitional contraction (VC) and volitional swallowing (VS).
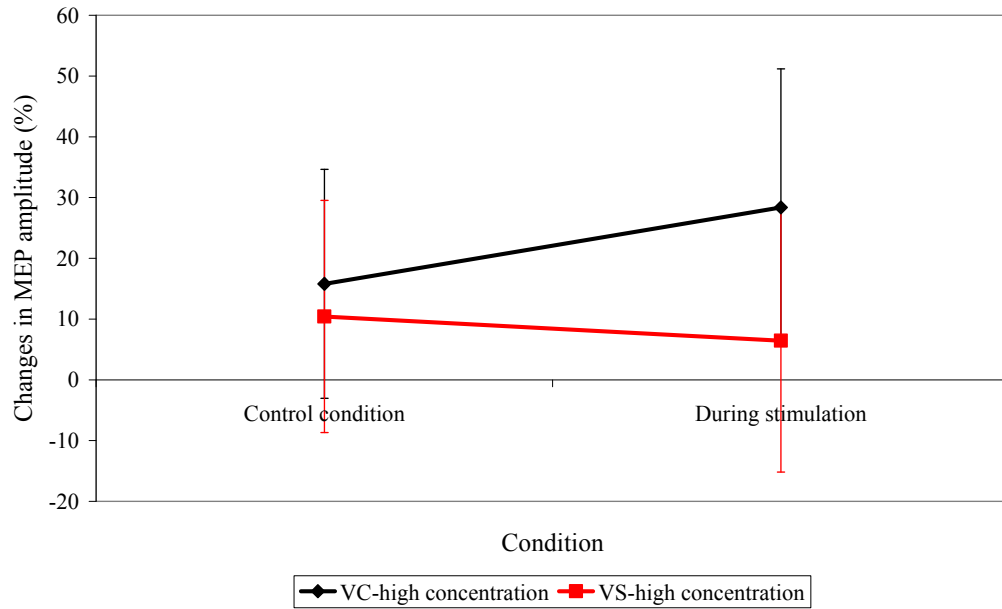
Figure 19. Condition x Task x Concentration graph for high concentration stimuli showing the differences in MEP amplitude between volitional contraction (VC) and volitional swallowing (VS).

MEP Amplitude: Late Effect

Repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste) by concentration (low, high) and by time (5-, 30-, 60-, and 90-min poststimulation) showed no significant effects or interactions with concentration. Therefore, the low and high concentrations odour and tastant were collapsed. Another repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste, combined stimulation) by time (5-, 30-, 60-, and 90-min poststimulation) was performed; it revealed significant interaction between Task x Stimulus (Table 11). MEP amplitudes for odour and tastant were higher during contraction compared to during swallowing (Figures 20 and 21). However, when combined stimulation was used, the MEP amplitude was higher during swallowing compared to during contraction (Figure 22).
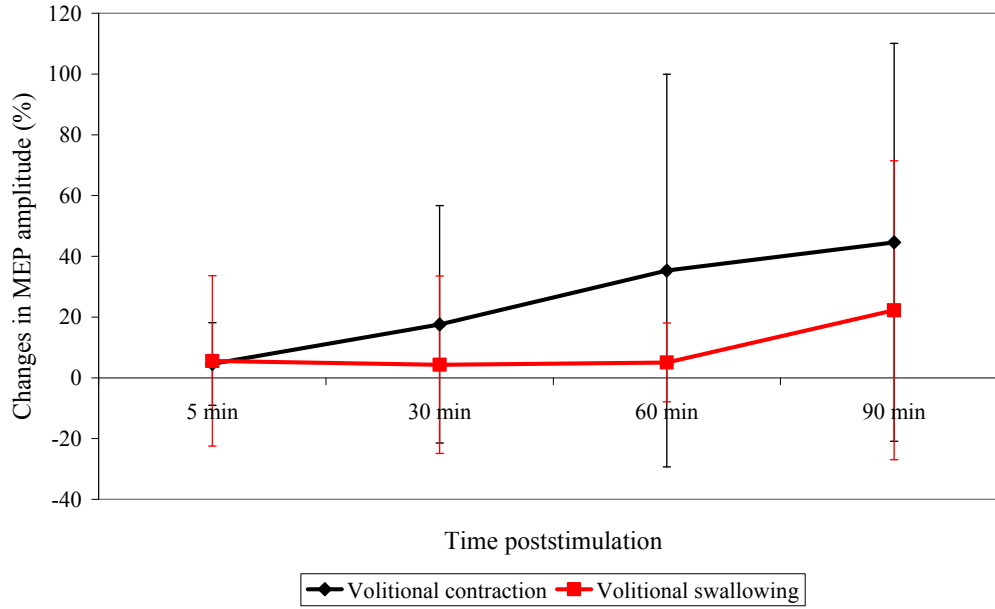
Figure 20. Time x Task x Stimulus graph when odour was presented. Volitional contraction produced higher MEP amplitude compared to volitional swallowing.
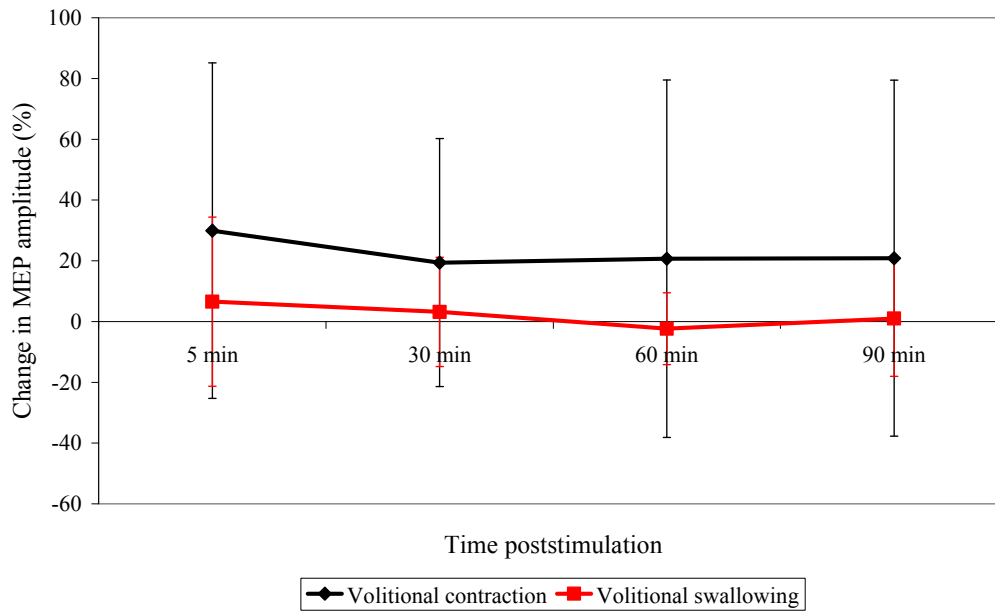
Figure 21. Time x Task x Stimulus graph when tastant was presented. Volitional contraction produced higher MEP amplitude compared to volitional swallowing.
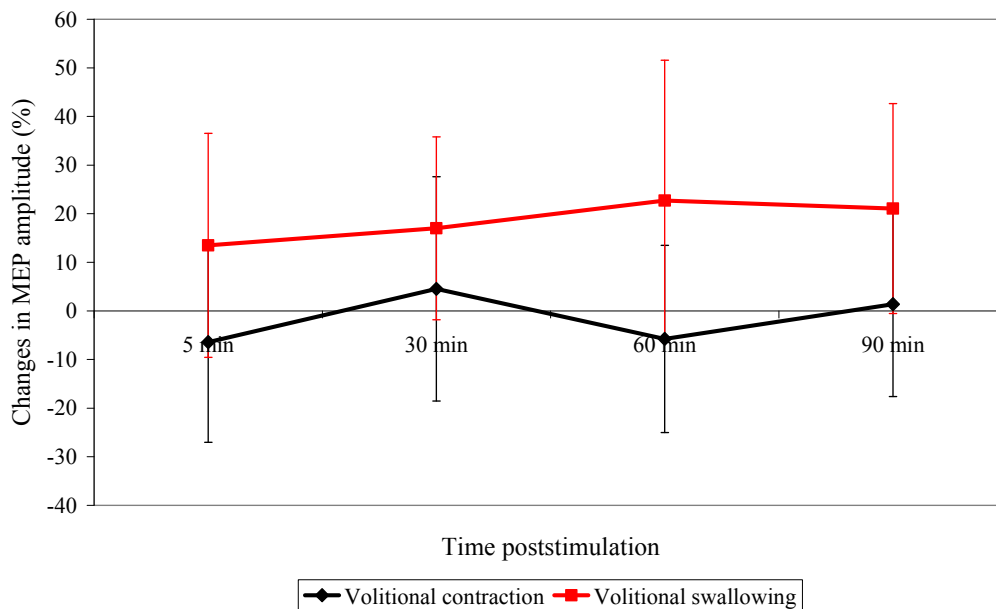
Figure 22. Time x Task x Stimulus graph when combined stimulation was presented. Volitional swallowing produced higher MEP amplitude compared to volitional contraction, compare Figure 22 to Figures 20 and 21 where the opposite was true when odour or tastant was presented independently.

MEP Latency: Immediate Effect

Repeated-measures ANOVA of stimulus (odour, taste) by concentration (low, high) by condition (control, stimulation) showed no main effect of concentration or interactions of Task x Concentration and Stimulus x Concentration. However, the interaction of Task x Concentration x Condition was significant. Latency was reduced during contraction and increased during swallowing when low concentration stimulus was presented, in contrast to no apparent effect during contraction and reduced latency during swallowing when high concentration was presented (Figures 23 and 24). As the main effect of concentration was not significant, the low and high concentrations were collapsed. Repeated-measures ANOVA of stimulus (odour, taste, combined stimulation) by condition (control, stimulation) also showed no differences in latencies (Table 11).
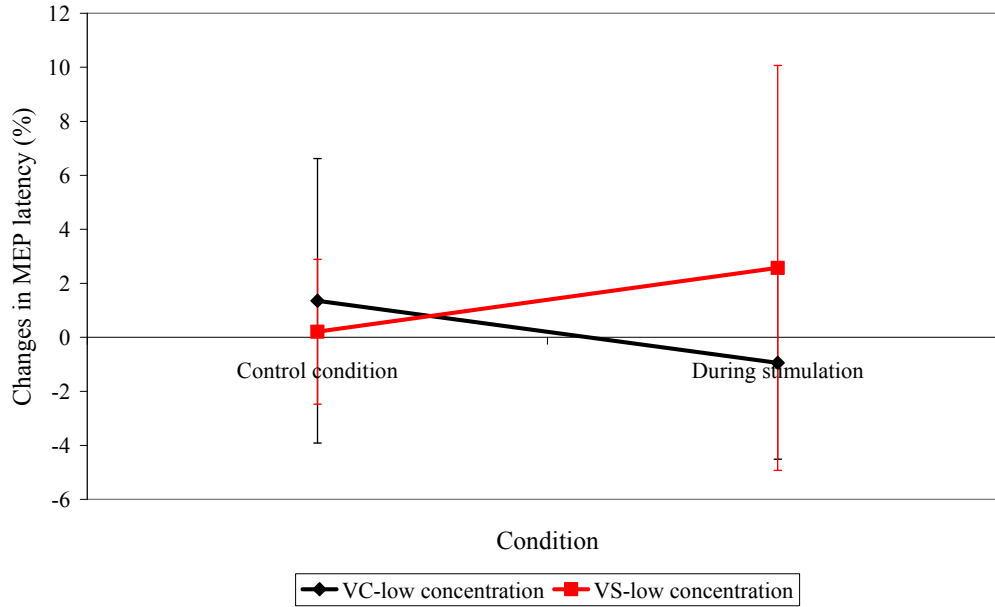
Figure 23. Graph to illustrate the interaction of Task x Concentration x Condition for low concentration stimuli. Latency was reduced during contraction and increased during swallowing when stimuli were presented.
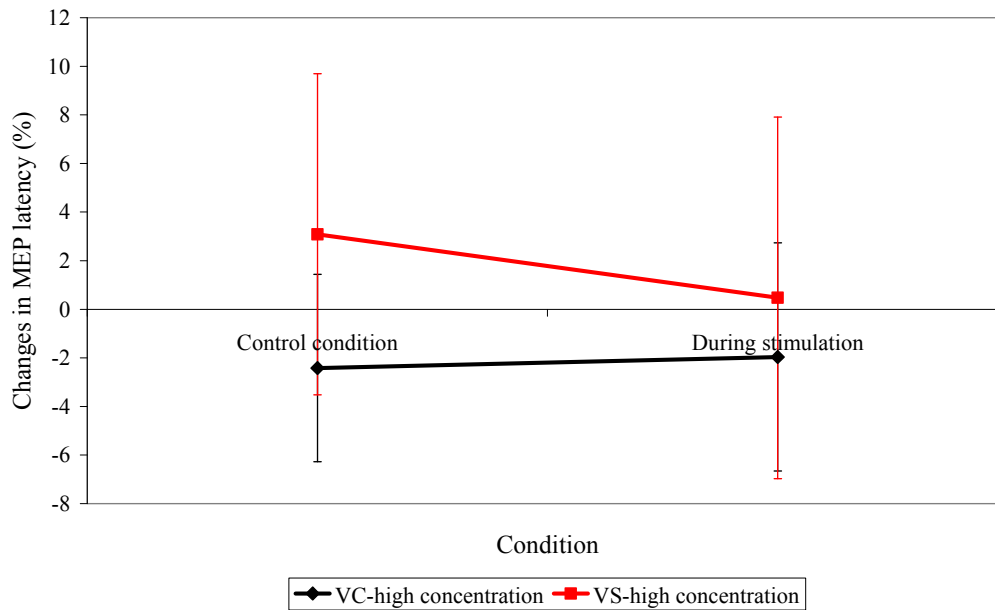
Figure 24. Graph to illustrate the interaction of Task x Concentration x Condition for high concentration stimuli. Latency was reduced during swallowing when high concentration stimuli were presented, in contrast to increased latency during swallowing when low concentration stimuli were presented (Figure 23).

MEP Latency: Late Effect

Repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste) by concentration (low, high) by time (5-, 30-, 60-, and 90-min poststimulation) showed no significant effects or interactions with concentration. Therefore, the low and high concentrations odour and tastant were collapsed. Repeated-measures ANOVA of task (contraction, swallowing) by stimulus (odour, taste, combined stimulation) by time (5-, 30-, 60-, and 90-min poststimulation) also showed no differences in latencies (Table 11).

4.7   Discussion

This is the first study to demonstrate changes in MEP amplitude during volitional swallowing following simultaneous presentation of odour and tastant stimuli. It has also shown that these increases in MEP amplitude are not present immediately poststimulation but are evident from 30- to 90-min poststimulation. No long-term effects were found when tastant was presented independently. However, odour presentation was found to influence the excitability of the neural pathway during volitional contraction but the effect was only evident at 90 min poststimulation. As the odour presentation was nebulized via nasal cannula inserted into both nares, odour molecules may also have stimulated some taste receptors in the nasopharynx. Tastant stimulation alone did not stimulate the odour receptors as the filter paper was placed anteriorly on the tongue surface, which may not stimulate the retronasal odour receptors.

Sour taste has been shown to have widely differing effects on swallowing biomechanics, which could reflect methodological differences between the studies. Some authors have reported better swallowing function when healthy participants or patients were given sour tastant (Ding et al., 2003; Leow et al., 2007; Logemann et al., 1995; Palmer et al., 2005; Pelletier & Lawless, 2003), whereas another reported poorer swallowing behaviour (Chee et al., 2005), and yet another reported no changes (Hamdy et al., 2003). No study has reported the effect of sour taste on neural transmission during swallowing; however, there is a study which evaluated corticobulbar excitability in healthy adult males following pleasant (sweet) and aversive (bitter) taste stimuli by measuring pharyngeal MEP triggered with TMS

(Mistry et al., 2006). A delayed—30 min—inhibitory effect on pharyngeal MEP amplitude for both stimuli, was reported. The conclusion from that study was that taste stimuli directly reduced activity in the NTS, which then caused a "reduction in the activity of cortical swallowing centres" (Mistry et al., 2006, p. G670). However, no follow up study was carried out to confirm this assumption. Mistry et al. attributed their results to a behavioural consequence of the strong flavour used. Indeed, individual preferences towards the stimuli could account for the differences observed in swallowing studies. For example, smell and taste may be differently perceived by individual and consequently may have an effect on his/her swallowing; which is, to slow down or speed up swallowing. These changes may be attributed to the behavioural aspect; for instance, the participants who dislike the taste would take more time to swallow as they may be considering spitting it out (Leow et al., 2007). Chee et al. (2005), who reported poorer swallowing outcome following taste stimulation, have also proposed that some aspect of compensatory strategy was employed when food with strong flavour was consumed; the authors suggested that this may be a kind of safety mechanism to avoid harmful food. The effect of different tastes on swallowing has been reported by Miyaoka et al. (2006), where reportedly, sweet food was easier to swallow compared to bitter and sour tasting foods. Likewise, a treatment may potentially slow down swallowing in some patients and speed it up in others, based on their preference towards the stimulus.

Chee et al. (2005) reported that glucose, citrus, and saline decreased the rate of ingested bolus per swallow during a water swallow test in normal adults, the effect being similar to that of anaesthesia. The authors proposed that as most of the participants rated the tastants as intense, the "heightened sensory input" (p. 398) increased the participants' alertness as a protective mechanism towards noxious stimuli, thus the decreased rate of ingested bolus. The results seen in these studies (Chee et al., 2005; Mistry et al., 2006) were thought to be due to the participants' perception of the stimuli as being noxious. Another explanation was that the stimulus has an effect on trigeminal stimulation, which is mediated by free nerve endings of trigeminal nerve axons in the olfactory mucosa and oral cavity (Prescott et al., 1984), usually as a result of irritating chemicals. To ensure that this problem was minimized, a pilot study was conducted to identify a suitable stimulus (see Chapter 3). In the current study, two concentrations of each olfactory and gustatory

stimulus were used: a higher concentration which was rated by participants as acceptable but not pleasant, and a lower concentration which was deemed acceptable and more pleasant. Sensation of taste is a combination of gustatory and olfactory information (Steward, 2000); therefore, an odour that resembles the sour tastant was used, hence the use of nebulized lemon odour from the same source.

The finding from this study that smell and taste increased MEP amplitude differs from previous results (Mistry et al., 2006) which reported decreased pharyngeal MEP following taste stimulation alone. The differences may be explained by the different stimuli used and the fact that the MEPs were recorded from different sites under a different condition (at-rest versus voluntary contraction). The excitability of neural pathways from pharynx (Mistry et al.) and submental muscles (this current study) may be differently affected by sensory stimulation. Furthermore, the current study incorporated two different sensory stimuli, which are known to excite a different brain region than if given independently. Moreover, Mistry et al. used a strong flavour in contrast to the current study where the stimuli used were deemed acceptable as they were chosen based on their ratings of intensity, pleasantness, and tolerability. Unfortunately, Mistry et al. did not extend their research to include biomechanical data; therefore, no conclusions can be made as to the effectiveness of their stimulation in changing swallowing behaviour. Although increased MEP has been associated with improved swallowing function (Hamdy et al., 1996), there are studies that do not support this view (Doeltgen, Heck, & Huckabee, 2010; Power et al., 2004). Power et al. documented increased pharyngeal MEP following 0.2 Hz of electrical stimulation to the faucial pillars but no changes in the biomechanics of swallowing following the same stimulation was reported. Another study on the effects of electrical stimulation to the submental muscles found increased MEP amplitude poststimulation (Doeltgen, Dalrymple-Alford et al., 2010) but the same stimulation decreased pharyngeal pressure poststimulation (Doeltgen, Heck et al., 2010).

Enhanced neural activation following taste stimulation has been suggested to result from increased NTS excitation (Ding et al., 2003; Pelletier & Lawless, 2003). Furthermore, it has been shown that excitation of corticobulbar pathway following peripheral stimulation is due to coincident afferent input to the sensorimotor cortex, which then modulates swallowing (Gow, Hobson, Furlong, & Hamdy, 2004).

Behavioural preference towards these stimuli may play a role in modulating these changes. Results from this study seem to support the clinical suggestion that a sour bolus facilitates swallowing (Logemann et al., 1995). A model of swallowing modulation following sensory stimulation, which integrates these findings from those documenting biomechanical changes in Chapter 5, is proposed in Chapter 6.

4.7.1   Immediate Effects of Sensory Stimulation

Following odour and taste stimulation, there were no significant immediate effects on corticobulbar excitability despite the fact that other studies found immediate biomechanical changes during swallowing with other sensory stimulation (Ding et al., 2003; Hamdy et al., 2003; Leow et al., 2007; Logemann et al., 1995; Palmer et al., 2005; Sciortino et al., 2003). Besides differences in the stimuli used, the immediate biomechanical measures of swallowing may be affected by behavioural changes, in contrast to neural change which may not be influenced by immediate behaviour change. However, the immediate findings from this study are comparable to Miyaoka et al. (2006) who also reported no immediate effect of taste on swallowing activity. The authors measured the duration of oral phase and the amplitude of peak suprahyoid muscle activity when sweet, sour, salty, bitter, and umami taste qualities were used, compared to distilled water. Unfortunately, Miyaoka et al. did not extend their study to include poststimulation data, thus the late results from this study could not be compared with theirs.

The finding of no immediate effect in this study may simply reflect the high variability of MEPs (Darling et al., 2006; Kiers et al., 1993; Thickbroom, Byrnes, & Mastaglia, 1999; Wassermann, 2002). This variability may increase further in the presence of multiple sensory stimuli. Large variances in the data would likely lead to nonsignificant differences for the case of sample size and any effect sizes being small. Other swallowing MEP studies have measured outcome after intervention was performed (Doeltgen, Dalrymple-Alford et al., 2010; Fraser et al., 2002; Fraser et al., 2003; Mistry et al., 2006). No MEPs were measured during intervention/stimulation itself, as was done in this study, unless they were using TMS to locate the topography of swallowing musculature. Thus, the immediate effect data from this study cannot be compared with other MEP studies.

4.7.2   Late Effects of Sensory Stimulation

Increases in MEP amplitude were significant following simultaneous odour and tastant stimulation, suggesting that the presentation of a single modality is insufficient to evoke changes in the MEP during swallowing. However, independently presenting odour stimulus is enough to change the MEP during volitional contraction, albeit with a more prolonged delay in the change (90 min for contraction compared to 30 min for swallowing). As no MEP changes were seen with tastant presentation, and odour can stimulate taste buds in the nasopharynx, it was proposed that single sensory modality is also not enough to change the MEP during volitional contraction. The simultaneous presentation of odour and tastant is flavour, which is considered to represent a separate sensory stimulus, rather than merely a combination of the independent stimuli of smell and taste (Rolls, 2005; Small et al., 1997).

The olfactory and gustatory pathways converge onto neurons in the endopiriform nucleus. Human interest in food is modulated by mechanisms related to the cortical integration of olfactory and gustatory information in this nucleus, which is located between the piriform cortex and caudate-putamen (Fu et al., 2004). The insula has also been implicated as an area where smell and taste information are integrated. Lesions in the anterior insula are related to dysphagia but not when confined to the posterior insula (Daniels & Foundas, 1997), suggesting that the anterior insula is an important area in regulating swallowing function. Furthermore, a gustatory aura has been noted to precede epileptic convulsions in people with injury to the anterior insula (Augustine, 2008). It has been shown that information from the anterior insula travels to the NTS in the brainstem (Willett et al., 1986). Activities in the NTS have been suggested to modulate the brainstem interneurons, hence the muscles involved in swallowing (Mistry et al., 2006). Additionally, the NTS may receive increased information from other brain areas activated by flavour stimulation. Signals from the piriform cortex travel via the mediodorsal nucleus of the thalamus to the prefrontal cortex (Parent, 1996) and, in turn, to the supplementary motor area (Bear et al., 2007). Information from the supplementary motor area may be directly channeled to the brainstem (Huckabee et al., 2003). Furthermore, the reticular area in the brainstem also receives information from the frontal part of the cortex (Kuypers,

1958). Specifically for swallowing, it has been suggested that information from the cortex can modulate interneuronal activities in the dorsal swallowing group (NTS), which can then change neuronal activities in the nucleus ambiguus (Jean, 1984a). Furthermore, it has been reported that information from the dorsal medullary area ventral to the NTS has connections to the trigeminal, facial, and hypoglossal motor nuclei (Cunningham & Sawchenko, 2000). Therefore, changes in brainstem neuronal activity can modify the contraction of muscles innervated by these motor nuclei.

Multiple cortical regions, as described in the preceding paragraph, may all contribute to adaptation in the NTS, probably through increased number of motoneurons activated. Thus, it can be speculated that the increased MEP amplitude seen in this study during swallowing was due to increased activation in the NTS following simultaneous odour and tastant stimulation.

A decreased MEP amplitude following taste stimulation 30 min poststimulation has been previously reported (Mistry et al., 2006). Conversely, electrical stimulation applied to the submental muscles increased the MEP amplitude 60 min poststimulation (Doeltgen, Dalrymple-Alford et al., 2010). Late changes in the MEP amplitude may be explained by residual odour and tastant molecules that were present after the stimulus was taken away, allowing the receptors to be activated poststimulation. However, given the long latency of response, it is proposed that changes in the MEP amplitude at 30-, 60-, and 90-min poststimulation are most likely explained by way of LTP, which has been implicated as one aspect of neural plasticity (Cooke & Bliss, 2006). LTP is an increase in synaptic strength transmission, which can be achieved with persistent stimulation of a synapse. Repetitive activation can lead to several mechanisms which would eventually change the physiology of the synaptic membrane for a more efficient transfer of neural signals by, for example, increasing the number of receptors in the membrane (Cooke & Bliss, 2006).

LTP can be divided into early and late phases. Early LTP is the immediate effects seen at the synapse, while late LTP (> 60 min), which is the extension of the early LTP, is when gene transcription and protein synthesis occur in the postsynaptic cell. This can lead to changes in the morphological structure of the neural cell—for example, increase in dendritic spine number and surface area—to increase synaptic

efficiency. However, Ziemann, Iliac, Pauli, Meintzschel, and Ruge (2004) cautioned the use of the term LTP plasticity because this cannot be proven. They proposed the term LTP-like plasticity instead.

Studies in an animal model have shown that LTP is present long after the stimulation is removed (Kajii et al., 2002), indicating auto-regulation of the sensory-motor network towards the initial stimulus (Le Ray & Cattaert, 1999). This evidence of neural plasticity may thus contribute to long-term rehabilitative recovery in patients with swallowing impairment.

4.7.3   Volitional Contraction versus Volitional Swallowing

Motor-evoked potentials during volitional contraction were recorded from all 16 participants but only nine participants had recordable MEPs during volitional swallowing. This finding was consistent with prior research (Doeltgen, Ridding, Dalrymple-Alford, & Huckabee, 2011) which found MEPs to be more robust during volitional contraction than during swallowing. It has been hypothesized that this may be due to greater cortical drive utilization during the contraction condition, compared to the brainstem-activated swallowing condition which uses less cortical input. If the corticobulbar pathway is not substantially preactivated during swallowing, the MEP output from TMS is not boosted, resulting in very small or immeasurable MEPs at the periphery (McMillan et al., 2001). Another interpretation is that the primary motor cortex exerts an inhibitory influence on swallowing neural networks, thereby minimizing the measured MEP output from the excitatory TMS input (Mistry et al., 2007).

In general, results from this study showed that volitional contraction produced higher-amplitude MEPs than MEPs during swallowing, and this was the case for both immediate and late effects. This finding is similar to previous research which has reported larger MEPs during contraction compared to swallowing (Doeltgen et al., 2011). The authors attributed their findings to the differences in motor cortex excitability in executing the contraction and the swallowing tasks.

Another interesting finding from this study was that a larger late-effect MEP amplitude is associated with swallowing when combined stimulation is used

compared to MEP during contraction (Figure 22). This cannot be explained by the theory proposed by Doeltgen et al. (2011) that the motor cortex has less input during swallowing compared to contraction but the finding supports results from research in flavour stimulation which documented that other brain regions were also stimulated when flavour was presented compared to independent presentation of odour or tastant (Babaei et al., 2010; Small et al., 1997).

4.7.4   Methodological Aspects and Limitations

MEPs are a measure of neural excitation from the motor cortex to the target muscles (Doeltgen et al., 2009; Mistry et al., 2007). This study evaluated MEPs when the submental muscles were partially contracting for two reasons. First, it is known that MEPs are larger when recorded during preactivation (Hallett, 2007; Maertens de Noordhout, Pepin, Gerard, & Delwaide, 1992) and prior research on MEPs associated with muscles of the head and neck has shown that MEPs can best be elicited when background muscle contraction is present (Cruccu et al., 1997; McMillan et al., 2001). Studies on the cricopharyngeal and cricothyroid muscles have also documented that MEPs are larger when TMS is elicited during swallowing (Ertekin, Turman et al., 2001).

The variability in MEP responses is quite large (Kiers et al., 1993); however, no control experiment was done to evaluate MEP changes across time. This may be a limitation in this project but prior research in this laboratory using very similar methods (Al-Toubi et al., 2010) has demonstrated no significant modulation of submental MEPs with time. Although findings by Al-Toubi et al. were nonsignificant, large variations in the data may have resulted in a Type II error with true changes masked by noise. As the current study did not have its own control over time for MEP variability, findings from Al-Toubi et al. were used to support the current data as the same protocols were used in the two studies. Gallas et al. (2009) have also reported stable mylohyoid MEPs over time following TMS to the motor cortex.

A custom-built trigger system was used to monitor muscle contraction and ensure that the TMS output was triggered at the same level of muscle contraction for both tasks to avoid a systematic measurement error. More importantly, using this

method, the cortical contribution during brainstem-controlled swallowing activity may be evaluated and compared to a less complex and better defined pyramidal motor task of the corticobulbar pathway during volitional contraction of the submental muscles. The research results justify this approach as there were notable differences in task-related MEPs.

After analysis of preliminary data, the odour and tastant that maximally influenced the MEP in each participant were then presented simultaneously, irrespective of excitatory or inhibitory response. If no effects were seen, the higher concentration stimulus was used. This method was chosen as the study's main objective was to evaluate if sensory stimulation had any effects on corticobulbar excitability, hence the inclusion of any responses that could change the MEP. Furthermore, when odour and tastant are combined, the cumulative effect is not merely the sum of its individual effect, as have been proven by other researchers (Grabenhorst et al., 2008; Small, 2004; Small et al., 1997). This method is not without complications, as the excitatory and inhibitory effects could cancel each other out. However, to divide participants into excitatory, inhibitory, and no effects was not feasible as there were participants who had the opposite effects when odour or tastant were independently presented or they had the opposite effects during contraction and swallowing when the same stimulus was used. For example, one participant produced an excitatory response to odour but an inhibitory response to tastant, and these two stimuli were selected as the combined stimulation because the method used was to choose any stimuli that maximally influenced the MEP. Another problem in choosing the combined stimulation occurred when a participant produced an excitatory effect during contraction but an inhibitory effect during swallowing with the same stimulus. Nevertheless, the participants were grouped into "excitatory, inhibitory, and no effects" and it was found that the participants who had mixed effects on independent odour/tastant stimulation all showed excitation during swallowing when combined stimulation was presented.

Several *t*-tests were performed to evaluate changes at 30-, 60-, and 90-min poststimulation as previous researchers have documented similar pattern of changes in corticobulbar excitability with time following other sensory stimulation (Doeltgen, Dalrymple-Alford et al., 2010; Fraser et al., 2002; Fraser et al., 2003; Mistry et al.,

2006). However, Bonferroni correction was not reported in the analyses as using it may increase Type II error (Field, 2005). Other statisticians also agree that using Bonferroni correction in clinical studies with repeated measurements may not be appropriate as the data are highly correlated (Bland & Altman, 1995; Perneger, 1998). Furthermore, three consecutive poststimulation effects during swallowing (30-, 60-, and 90-min poststimulation) were significant with t-tests; this may indicate true changes in the data instead of a random significant point. To further strengthen the analyses, 95% CI of the mean differences and the effect size of each analysis were included. Indeed, the CI did not include zero, which suggests that there are true differences between the datasets. Furthermore, the effect sizes were fairly large, ranging from .49 to .57.

MEPs during swallowing could be detected in only 9 of the 16 participants as opposed to MEPs being measured in all 16 participants during sustained contraction. It is considered that this imbalance would not have biased the swallowing versus contraction results other than to reduce sensitivity to any differences. Fraser et al. (2002) gave a zero amplitude value for MEPs when no response to TMS was recorded in their mapping study but their method is not the direct equivalent to the current study. Nevertheless, this analysis is not a direct comparison of neural representation of swallowing and muscle contraction, as it is known that muscle contraction utilizes direct pyramidal pathway from motor cortex to the muscle, whereas swallowing is a brainstem-driven act.

4.8   Conclusion

Simultaneous stimulation of smell and taste may provide an optimal sensory condition for mimicking real food which would increase swallowing efficiency. This may offer significant opportunities, in particular, for patients in whom cognitive deficits inhibit participation in more behaviourally-focused rehabilitation programmes. To further translate these data into dysphagia management, a follow-up study was designed to define the biomechanical changes produced by similar sensory stimulation.

Chapter 5

The Effects of Olfaction and Gustation on the Biomechanics of Swallowing[2]

5.1   Background

Combined olfactory and gustatory stimulation (flavour) can modulate neural excitability in healthy participants, as measured by the amplitude of MEPs recorded from the submental muscles (Chapter 4). Increased MEP amplitude has been associated with neuroplastic changes in the intact hemisphere of nondysphagic poststroke patients compared to patients with dysphagia following stroke who showed no changes in their intact hemisphere (Hamdy et al., 2000; Khedr et al., 2008). However, changes in neural transmission do not directly imply functional changes in swallowing. Similarly, an absence of change in neural excitability would not necessarily suggest an absence of functional change in swallowing. Therefore, further studies were carried out to evaluate the influence of the same stimuli used in the prior study on swallowing function.

The current studies investigated the biomechanical aspects of swallowing via: (a) surface EMG of the submental muscles, (b) lingual manometry of tongue-to-palate (glossopalatal) pressures, and (c) pharyngeal manometry of the pressures in the pharynx and the dynamics of the UES.

5.2   Electromyography of Swallowing Muscles

EMG is a measure of electrical activity in muscles (Bolek, 2010). Electrodes can be attached to the skin surface overlying the muscle of interest or a collection of

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[2] This study was published in *Physiology and Behavior* (Appendix J, Abdul Wahab, Jones, & Huckabee, 2011)

muscles for a measure of sEMG, or embedded directly into a muscle by a hooked wire to get a more focal measure of electrical activity from one muscle.

The submental muscles, comprised of the anterior belly of digastric, mylohyoid, and geniohyoid muscles, are involved in the superior and anterior excursion of the hyolaryngeal complex, which is an important biomechanical event to facilitate opening of the UES for bolus transfer (Cook et al., 1989; Kahrilas et al., 1991). Surface EMG of the submental muscles is a noninvasive method to study swallowing function (Vaiman, Eviatar, & Segal, 2004a, 2004c, 2004d). Identification of a swallow in sEMG recordings from the submental muscle is more specific than sensitive (Crary et al., 2007); that is, it is more likely to miss a swallow than misidentify it as a nonswallow. However, when sEMG is paired with other tools to assess swallow-related measurements—for example, the manometer—identification of a swallow may be more accurate. The use of paired assessment of investigative tools to increase interrater reliability in assessing swallowing function has been recommended by Pelletier and Lawless (2003). Although normal swallowing function is highly variable across individuals, sEMG can be used to compare within-subject swallowing behaviour (Vaiman et al., 2004d).

The sEMG amplitude of several muscles was studied in 420 adults, separated into different age groups, during dry swallowing, normal swallowing (swallowing mean volume of water for the age group), "stress test" water swallowing (swallowing a large bolus), and continuously drinking 100 ml of water (Vaiman et al., 2004c). Two surface electrodes placed on the right side of midline were used to collect the EMG data. This placement may not be the best position to record submental activities as the muscles are recorded only from one side; recording muscle activities concurrently at the right and left sides may be preferable. The authors reported substantial variability in the range and mean of sEMG measures among subjects and concluded that the range of sEMG amplitude "is more informative than its mean" (p. 780). No differences were reported between males and females for all swallowing conditions and for all age groups. The authors reported decreased submental sEMG amplitude in the older group (age 70+ years) compared to the younger group (age 18-30 years) for both dry and normal swallowing conditions. The amplitude of submental sEMG during the "stress test" was significantly lower compared to normal, discrete swallowing in the younger age group. In another report, Vaiman,

Eviatar, and Segal (2004b) indicated that the duration of sEMG activity in the older population is prolonged compared to the younger population. This finding is similar to Humbert et al. (2009) who reported increased effort by their elder participants in initiating dry swallowing compared to the younger participants.

Crary and Baldwin (1997) evaluated sEMG activities from the perioral, masseter, and infrahyoid muscles in six healthy controls and in six patients with dysphagia due to unilateral brainstem stroke (mean age for both groups was 66.8 years). SEMG measurements were recorded at baseline, while holding a 5- or 10-ml bolus in the mouth, during dry swallow, and during 5- and 10-ml water bolus swallows. The authors reported that infrahyoid muscles in the patient group had higher sEMG baseline activity and bigger peak and average sEMG compared to the control group. Moreover, they reported "more variable amplitude characteristics" (p. 185) of the sEMG signals in the patient group. The duration of the infrahyoid sEMG was also shortened in the dysphagia group. Crary and Baldwin concluded that "stroke patients use more myoelectric activity over a shorter time period with poorer coordination" (p. 186) compared to age- and gender-matched controls. However, the interpretation of this study must be taken with caution as only six patients were included in the study. Although all of them had unilateral brainstem stroke, the "pattern of neurological involvement was variable" (page 180), which may pose a confounding factor in this study.

Several studies have evaluated sEMG of submental muscles following sour taste stimulation (see Section 2.3.4.2). Ding et al. (2003) found earlier submental muscle contraction when sour taste was ingested, compared to a no-taste condition. Sciortino et al. (2003) evaluated changes in the sEMG of submental muscles following mechanical, cold, and/or sour stimulation to the anterior faucial pillars. They reported shorter latency to the first swallowing activity when all three conditions were combined, compared to no stimulation, but there were no changes in the duration of submental contraction. On the other hand, Miyaoka et al. (2006) found no differences in sEMG recordings when either high or low concentration of sour food was swallowed, or when sour food was compared to tasteless food. Miyaoka et al.'s findings were contradictory to the two previously reported studies; however, different methodologies were used in the studies. In Ding et al.'s study, participants were required to hold a 5-ml bolus in their mouth before an instruction to

swallow was given. This could potentially increase both cortical preparation and the activation of sensory receptors as they are exposed to the stimulation longer compared to participants who were told to swallow the stimulus quickly as in Miyaoka et al.'s study. In Sciortino et al. study, taste stimulation was not ingested, it was presented to the faucial pillars and the authors reported significant findings only when all three stimuli were combined (that is, the mechanical, cold, and sour stimulation).

Palmer et al. (2005) used hooked wire electrodes to record intramuscular EMG from the anterior belly of digastric, mylohyoid, and geniohyoid muscles in young healthy adults. The participants were asked to swallow a 3-ml water or lemon bolus and the strength and duration of muscle contraction were analysed. The contractions were stronger and the onset was more closely approximated across the three muscles when sour bolus was presented. There was a trend for increased duration but, possibly due to a large variability among participants, the difference was not significant. Leow et al. (2007) also reported stronger muscle contraction in sEMG recordings when a sour taste was swallowed, compared to sweet, salty, and bitter. Although findings of the effects of sour stimulation on submental EMG are contradictory, the majority of studies reported improved swallowing function when sour taste was used. This may indicate that sour stimulation can improve swallowing. Nevertheless, the negative results reported by other researchers cannot be ignored. Besides the different methodology used, there may be mechanisms surrounding perception of taste that led to the contradiction in results. For example, Miyaoka et al. used creamed food as their stimulus; this may be perceived differently by participants—particularly regarding its consistency—compared to a sour bolus as used by Ding et al. and Palmer et al. Another possible limitation in Miyaoka et al.'s study is the use of tea as the rinsing solution in between experiments. The tea itself may have an effect on swallowing, thus confounding the results.

In summary, changes in the submental muscles following an intervention can be studied by measuring its electrical activity via sEMG. Sour taste is shown to influence submental sEMG recordings during swallowing in most studies, but the effect of combined lemon odour and tastant stimulation is not known.

5.3   Lingual Pressure

Prior to swallowing, the tongue generates pressure which propels a bolus into the pharynx by squeezing the tongue to the palate in an anterior to posterior movement (Shaker, Cook, Dodds, & Hogan, 1988). The pattern of pressure generation in the oral cavity has been systematically studied using pressure transducers secured in a base plate, similar to a denture (Kieser et al., 2008; Ono, Hori, & Nokubi, 2004). Ono et al. reported that tongue pressure was first generated at the anterior sensor 5 mm posterior to the incisive papilla and the pressure wave moved posteriorly. The most anterior sensor recorded the highest pressure and longest duration compared to all other sensors. Conversely, Kieser et al. reported a pressure drop at the start of swallowing at all palatal sensors before the pressure rise to reach peak amplitude. Both Ono et al. and Keiser et al. also found "considerable intraindividual variability" (Kieser et al., 2008, p. 242) in the pressure data. The method of incorporating pressure sensors in a base plate guarantees that the transducers are in situ at all times, ensuring the reliability and stability of the recorded pressures; however, it requires custom-fitted hardware.

Measures of pressure data in healthy participants, as well as in patients with head and neck cancers, have also been reported to be reliable and stable when using a commercially available lingual pressure bulb (Kay® Digital Swallowing Workstation, Kay Elemetrics Corporation, Lincoln Park, New Jersey, USA; Ball et al., 2006; White, Cotton, Hind, Robbins, & Perry, 2009). The normal swallowing pattern in healthy individuals was not altered with the presence of the lingual bulb in the mouth (Hind et al., 2005). Using this system, lingual pressure was increased when 10-ml chilled sour boli were presented compared to water (Pelletier & Dhanaraj, 2006). It is possible that retronasal odours may have also contributed to the higher lingual pressures seen in that study. Furthermore, bolus volume or temperature, or both, may have contributed to the increased pressure.

The tongue propels a bolus posteriorly and subsequently into the pharynx. Spatial and temporal tongue propulsion has been evaluated by securing four pellets on selected tongue regions (Wilson & Green, 2006). The vertical movement of these pellets were analysed radiographically. Results showed that the anterior tongue region moved more (vertically) than its posterior counterpart, and the lag time

between the two posterior pellets was shorter than the two anterior pellets. As the posterior tongue is adhered to the pharynx, its movement is somewhat restricted compared to the freely moving anterior tongue. The anterior tongue remained elevated during swallowing to prevent anterior spillage, thus the longer lag time at this region compared to the posterior tongue. Actual tongue movement during swallowing is more complex than just the vertical component (Ono, Hori, Tamine, & Maeda, 2009), which was reported in this study. Nevertheless, the limited information gleaned from this study may help future development of assessment tools for patients with swallowing impairment, particularly for oral stage dysphagia.

The tongue is involved in manipulating food to form a cohesive bolus which is suitable for swallowing. Postswallow, the tongue helps to clear the oral cavity from residues. Patients with oral phase dysphagia can present with reduced tongue strength. Adequate tongue strength is important to prevent premature spillage into the pharynx which can lead to aspiration (Huckabee & Pelletier, 1999; Nicosia et al., 2000). This is achieved by lingual to palatal approximation during oral stage of swallowing, which separates the oral cavity from the pharynx. Although maximal tongue strength is reduced with increasing age, no differences in the functional tongue-to-palate pressures (at the tongue tip, blade, and dorsum) during swallowing have been noted (Nicosia et al., 2000; Robbins et al., 1995). However, the reduced "pressure reserve" (Nicosia et al., 2000, p. M638) may predispose the elderly to swallowing impairment when there is a problem in the normal swallowing system. Indeed, Tibbling and Gustafsson (1991) reported that the self-reported incidence of hypopharyngeal dysphagia is greater in an elderly compared to a younger group based on questionnaires received from 796 participants over 60 years old.

Clinical examination of the tongue is usually comprised of subjective evaluation of movement characteristics such as tongue strength and mobility. There are studies that have looked at objective assessments, such as the lingual swallowing pressures (Ball et al., 2006; Hind et al., 2005; Nicosia et al., 2000; Pelletier & Dhanaraj, 2006; Steele & Huckabee, 2007) but this technique is infrequently utilized during routine clinical examination. The inclusion of objective assessment of tongue function as part of the clinical examination may help clinicians understand the role of lingual pressure in swallowing pathophysiology and develop consequent treatment approaches.

5.4 Pharyngeal Manometry

The pharynx contracts in a superior to inferior direction to ensure safe bolus transport into the oesophagus (Brasseur & Dodds, 1991). Adequate pharyngeal pressure during swallowing clears the pharynx of residue (Pauloski et al., 2009). If inadequate pressure is generated, postswallow residue in the pharynx can enter the airway when the larynx re-opens to resume respiration (Butler et al., 2004; Leslie, Drinnan, Ford, & Wilson, 2002). Therefore, measurement of pharyngeal pressure provides a valuable indicator of successful swallowing.

Pharyngeal pressure can be measured by solid-state manometry (Brasseur & Dodds, 1991), which has been used concurrently with videofluoroscopy to assess the relationship between pressure and biomechanical movement (Boden et al., 2006; Bulow et al., 1999, 2001, 2002; Olsson, Nilsson, & Ekberg, 1995). With simultaneous manofluoroscopy (manometry recording during videofluoroscopy), intrabolus pressure can be evaluated as the researcher can record manometry measures when the bolus surrounds the sensor, as opposed to contact pressure when the pharyngeal wall is directly in contact with the sensor (Olsson, Kjellin, & Ekberg, 1996). In a review article by Castell and Castell (1993), the authors noted that accurate evaluation of pharyngeal and UES pressure measurements can be obtained when the pull-through technique was used to insert the catheter, as confirmed by videofluoroscopy. They suggested that the sensor be positioned just proximal to the high pressure zone of UES such that an "M configuration" (p. 272) of the waveform is obtained during swallowing. They further proposed the use of pharyngeal manometry as an adjunct to assess patients with dysphagia.

Pharyngeal pressure can be modulated by several factors; such as age, gender, bolus type, and the manoeuvres applied during swallowing (Butler et al., 2009; Hiss & Huckabee, 2005; Kahrilas et al., 1991; Perlman et al., 1993; van Herwaarden et al., 2003). In three separate studies, pharyngeal pressures showed a trend to be higher in the elderly compared to the younger participants, but the differences were not significant (Butler et al., 2009; Dejaeger, Pelemans, Bibau, & Ponette, 1994; Perlman et al., 1993). Van Herwaarden et al. (2003) found inverse correlation for resting UES pressure with age; it was lower in the older group (mean age 71.3 years) compared to the younger group (mean age 33.7 years). Butler et al. (2009) reported greater UES

relaxation pressure in saliva swallowing in young adults (mean age 30 years) compared to the elderly (mean age 75 years). The UES relaxation pressures were -8 mmHg in the young and -1 mmHg in the elders. In the elderly, the UES relaxation pressure was less when 10-ml and higher viscosity boli were used compared to 5-ml and lower viscosity boli, respectively. In the durational measures, contact durations at the upper and lower pharynx were longer in older volunteers compared to the younger group. Butler et al. (2009) found that female participants have increased UES relaxation duration with increased age, which is the opposite of that seen in males. The authors acknowledged that the effects seen in their study may be influenced by anatomical differences and changes due to gender and aging. As gender and age may influence manometry measurements, studies evaluating these measures need to consider using participants where these factors are controlled.

Incomplete UES relaxation (where the relaxation pressure does not reach atmospheric level) was recorded in 18% of elderly participants in Dejaeger et al.'s (1994) study. The older participants (mean age 80 years) have decreased UES relaxation pressure compared to the younger participants (mean age 28 years). The authors proposed diminished UES compliance associated with aging as the main factor influencing the results. Dejaeger et al. also reported pharyngeal pressure in the elderly with respect to residues. The elders with postswallow residue have decreased pharyngeal contact pressure compared to the elders without residue. This strengthened the concept that pharyngeal pressure is important to clear the pharynx postswallow.

Perlman et al. (1993) reported longer duration of pharyngeal pressures in the elders (mean age 68.1 years), males, and dry swallow, compared to the young (mean age 23.4 years), females, and bolus swallow, respectively. Witte et al. (2008) also reported increased duration of pharyngeal contact pressures during dry swallows compared to water. The duration of UES relaxation is increased with increasing bolus volume, irrespective of age (Butler et al., 2009; Tracy et al., 1989). In addition, Butler et al. (2009) reported increased peak pressure in the lower pharynx when volume and viscosity were increased; these effects were not seen in the upper pharynx. The UES relaxation duration was longer when 10-ml bolus was used compared to the 5-ml bolus. All of these studies documented changes in manometry measurements during swallowing of a bolus compared to dry swallows, or when

different volume of a bolus was ingested. Thus, swallowing studies may want to incorporate different types of bolus volume or used only one volume/dry swallow to assess changes in swallowing following an intervention.

Hiss and Huckabee (2005) evaluated changes in pharyngeal manometry measures in young healthy adults (mean age 27.9 years) during effortful and normal swallowing. Effortful swallowing produced longer pharyngeal pressure and UES relaxation durations compared to normal swallowing. Duration was longer in the upper pharynx compared to the lower pharynx. In a separate study by Humbert et al. (2009), their participants reported that more effort was needed to initiate dry swallowing as the experiment progress. This may be due to several factors, such as dry oral mucosa, inability to produce more saliva, or fatigue. Participants in a swallowing study of a long duration may be inclined to swallow hard (effortful swallowing) when they are asked to swallow. Thus, participants must be reminded to swallow as normal as possible to ensure that the data collected is from normal swallowing. Another factor that may influence pharyngeal manometry is the manoeuvres applied during swallowing. For example, using the Mendelsohn manoeuvre, Kahrilas et al. (1991) reported that the UES relaxation duration was longer when the manoeuvre was executed compared to normal swallowing. Although the participants were taught how to execute the manoeuvre, their performance of the manoeuvre itself was not documented. Some swallowing manoeuvres are not easy to master, thus participants or patients must be coached of the correct technique to perform the manoeuvres and methods to ensure the correct technique are included in the procedure.

In conclusion, may factors can affect pharyngeal pressure, which can be recorded via pharyngeal manometry. However, no studies have evaluated how these measurements are influenced by odour and tastant stimulation, either during stimulation or poststimulation.

5.5 Aims of Studies

Two studies were carried out: main and supplementary. The main study was designed to investigate the influence of simultaneous odour and tastant stimulation on swallowing biomechanics under the same stimulation conditions known to

modulate the neural substrates of swallowing as measured by increased MEP amplitudes. Specifically, the study aimed to determine whether sensory stimulation would alter biomechanical swallowing function as measured by changes in the contraction of the submental muscles, pressures in the oral cavity and pharynx, and the dynamics of the UES. Additionally, the effects of odour and tastant presented independently were evaluated.

The supplementary study aimed to evaluate the differences between lemon and water as stimuli when either one was presented simultaneously as odour and tastant. Changes in the contraction of the submental muscles, the pressures in the oral cavity and pharynx, and the dynamics of the UES were evaluated.

5.6   Main Study

5.6.1   Hypotheses

The hypotheses for this study have been elaborated in Sections 2.7.4–2.7.6. In this section, only the hypotheses are presented.

5.6.1.1   Hypothesis 4

Olfactory stimulation increases contraction of the submental muscles. The amplitude of the submental sEMG is greater when lemon odour is presented compared to no odour presentation. The duration of the muscle contraction is longer following odour presentation compared to baseline. The increase in amplitude and duration is larger when high concentration odour is presented compared to the presentation of low concentration odour.

5.6.1.2   Hypothesis 5

Gustatory stimulation increases contraction of the submental muscles. There is an increase in the amplitude of the submental sEMG when lemon tastant is presented compared to no tastant presentation. The duration of the submental contraction is longer than the baseline. The increase in amplitude and duration is

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larger when high concentration tastant is presented compared to the presentation of low concentration tastant.

5.6.1.3   Hypothesis 6

Combined olfactory and gustatory stimulation affects the submental muscle contraction more than the independent presentation of either odour or tastant, or when compared to baseline. The amplitude of the submental sEMG is greater when odour and tastant are presented simultaneously compared to baseline. The amplitude is larger when compared to the odour or tastant presented independently. The duration of submental contraction is longer during combined stimulation compared to the independent presentation of either odour or tastant, or when compared to baseline. The effects of combined odour and tastant stimulation are evident even after the stimuli have been removed for at least up to 90 min poststimulation.

5.6.1.4   Hypothesis 7

Olfactory stimulation affects the lingual swallowing pressure. Lingual swallowing pressure amplitude is higher when lemon odour is presented compared to no odour presentation. The tongue-to-palate contact duration is longer following odour presentation compared to no odour presentation. The increase in pressure amplitude and contact duration is greater when high concentration odour is presented compared to the presentation of low concentration odour.

5.6.1.5   Hypothesis 8

Gustatory stimulation affects the lingual swallowing pressure. Lingual swallowing pressure amplitude is higher when lemon tastant is presented compared to no tastant. The tongue-to-palate contact duration is longer following tastant presentation compared to no tastant presentation. The increase in pressure amplitude and contact duration is greater when high concentration tastant is presented compared to the presentation of low concentration tastant.

5.6.1.6   Hypothesis 9

Combined olfactory and gustatory stimulation affects the lingual swallowing pressure more than the independent presentation of either odour or tastant, or when compared to baseline. The amplitude of the lingual pressure is greater when odour and tastant are presented simultaneously compared to baseline. The amplitude is greater when compared to the odour or tastant presented independently. The duration of the tongue-to-palate contact is longer during combined stimulation compared to the independent presentation of either odour or tastant, or when compared to baseline. The effects of combined odour and tastant stimulation are present for at least up to 90 min poststimulation.

5.6.1.7   Hypothesis 10

Pressures in the pharynx and UES are positively affected by olfactory stimulation. There is an increase in the pharyngeal pressure amplitude following lemon odour presentation compared to no odour presentation. There is an increase in the duration of the pressure generation in the pharynx following odour presentation compared to no odour presentation. The high concentration odour produces a greater increase in the amplitude and duration of pharyngeal pressure compared to the low concentration odour. The relaxation pressure in the UES is more negative when lemon odour is presented compared to no odour presentation. The duration of the UES opening is longer following odour presentation compared to baseline. The high concentration odour produces more negative relaxation pressure and longer duration of UES opening than the low concentration odour.

5.6.1.8   Hypothesis 11

Pressures in the pharynx and UES are positively affected by gustatory stimulation. Pharyngeal pressure amplitude increases following lemon tastant presentation compared to no tastant presentation. The duration of pressure generation is longer during tastant presentation compared to baseline. The high concentration tastant produces a greater increase in the amplitude and duration of pharyngeal pressure compared to the low concentration tastant. The relaxation pressure in the UES is more negative when lemon tastant is presented compared to no tastant

presentation. The duration of the UES opening is longer following tastant presentation compared to baseline. The high concentration tastant produces more negative relaxation pressure and longer duration of UES opening than the low concentration tastant.

5.6.1.9   Hypothesis 12

Combined olfactory and gustatory stimulation positively affects the pharyngeal and UES pressures more than the independent presentation of either odour or tastant, or when compared to baseline. The amplitude of the pharyngeal pressure is greater when combined odour and tastant are presented compared to baseline. The amplitude is larger when compared to the odour or tastant presented independently. There is longer duration of the pressure generation when combined stimulation is compared to the independent presentation of either odour or tastant, or compared to baseline. The relaxation pressure in the UES is more negative when combined odour and tastant are presented compared to baseline or when compared to the odour or tastant presented independently. The duration of the UES opening is longer during combined stimulation compared to the independent presentation of either odour or tastant, or when compared to baseline. The effects of combined odour and tastant stimulation are still present after the stimuli are removed, for at least up to 90 min poststimulation.

5.6.2   Study Design

This was a repeated-measures within-subject study designed to evaluate changes in the biomechanical aspects of swallowing as a result of olfactory and gustatory stimulation. Measurements were recorded during and up to 90 min poststimulation and compared with baseline data. Ethical approval was granted by a regional Health and Disability Ethics Committee (see Appendices K and L for advertisement flyer and information sheet for participants, respectively).

5.6.3   Participants

Sixteen healthy participants aged 19-47 years (mean 27.5 years, SD 7.8) were recruited. They reported no previous history of neurological problems or dysphagia

and were not taking medication that could affect swallowing. They were all asked not to ingest caffeine, alcohol, or spicy food one hour prior to the procedures to ensure that the stimuli were not contaminated by chemical residues of food in the mouth.

As anatomical differences among subjects due to gender and aging may influence pharyngeal manometry recordings (Butler et al., 2009; Dejaeger et al., 1994; Perlman et al., 1993; van Herwaarden et al., 2003), equal number of males and females were used in this study. As the MEP study (Chapter 4) evaluated neural changes in healthy young adults, participants in the same age range were recruited.

5.6.4   Instrumentation

The sEMG measuring system, lingual pressure device, and pharyngeal manometer catheter are components of the Kay® Digital Swallowing Workstation (Kay Elemetrics Corporation, New Jersey, USA). Triode surface electrode patches 5.4 cm in diameter (disposable pregelled electrode pads, standard silver/silver chloride EMG electrodes, Multi Bio Sensors, El Paso, Texas, USA) were used to measure electrical activity from the submental muscles. When placed under the chin, the patches pick up differential sEMG signal of the submental muscles. This signal was then amplified, band-pass filtered (50-220 Hz), rectified, low-pass filtered at 3 Hz, and digitized at 1000 Hz.

Lingual swallowing pressures were measured with a three-bulb lingual pressure array placed onto the palatal vault by means of oral adhesive (Stomahesive® strips, ConvaTec, Princeton, New Jersey, USA). It measures glossopalatal pressures corresponding to the anterior, middle, and posterior part of the tongue. Each sensor was 13 mm in diameter and the spacing between sensors was 8 mm. However, as some participants could not tolerate the posterior sensor, which when the array was secured onto the palate was approximately between the junction of the hard and soft palate, it was removed. Thus, data were recorded only from the anterior and middle sensors. An example of the lingual array used in this study is shown in Figure 25.

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Figure 25. Example of the lingual array used in this study.

A 100-cm long solid state pharyngeal manometer 2.1 mm in diameter, with three pressure transducers measuring 2 x 5 mm (Model CTS3 + EMG, Gaeltec, Hackensack, New Jersey, USA), oriented towards the posterior pharyngeal wall was used to record pressures in the pharynx and UES. The sensors on the catheter are spaced according to the proposed catheter standard reported by Salassa, DeVault, and McConnel (1998). There are 2- and 3-cm spaces between sensors 1 and 2 and sensors 2 and 3, respectively.

5.6.5   Stimuli

The same low (25%) and high (100%) concentrations of lemon concentrate (Country Gold lemon juice, Steric Trading Pty Ltd, Villawood, NSW, Australia) used in the MEP study were utilized in this study. Tap water was used as control. Stimulus presentation was also similar to the MEP study. The odour was presented as a mist via nasal cannula attached to a nebulizer (DeVilbiss PulmoMate® compressor/nebulizer, Model 4650I, Sunrise Medical, Somerset, Pennsylvania, USA) and tastant was presented by placing filter paper strip (Genuine Whatman Filter Paper No. 5, W & R Balston, Maidstone, Kent, UK) impregnated with the stimulus on the tongue.

5.6.6   Procedures

Participants provided written informed consent (similar to Appendix E used in the MEP study) prior to the procedures. Additionally, they were asked to complete a brief medical questionnaire (Appendix F) to confirm that they met the inclusion and exclusion criteria to participate in the study. Prior to data collection, the tongue array and pharyngeal manometer were calibrated following the manufacturer's recommendation.

The participants were seated comfortably in a chair and the surface under the chin was cleaned vigorously with an alcohol swab. The triode surface electrode patch was placed under the chin, between the spine of the mandible and the superior border of the thyroid cartilage. The two active electrodes were positioned in the midsagittal plane and the ground electrode was positioned laterally. The averaged and rectified sEMG waveforms were checked to ensure that clear sEMG recordings were achieved.

Next, the pharyngeal manometer was inserted transnasally. The tip of the catheter was lubricated before insertion. As the catheter reached the posterior aspect of the participant's nasal cavity, he/she was asked to look briefly to the ceiling to reduce the nasopharyngeal angle so that the catheter could be inserted into the pharynx. Then, with the head back to neutral position, the participant was handed a glass of tap water and asked to rapidly drink the water through a straw. In doing so, the distal portion of the catheter was swallowed into the oesophagus. Participants were asked to swallow until the catheter was pulled down 30 cm as measured from the tip of the nose. It was then slowly pulled out again until it was in the appropriate location to measure the information needed for this study. When positioned correctly, the first, second, and third sensors recorded pressures from the oropharynx, hypopharynx, and UES, respectively, during swallowing (Huckabee et al., 2005). The M wave (Castell, 1993; Castell & Castell, 1993) was observed in the third sensor during swallowing, indicating its correct placement within the UES. When the catheter was correctly placed, it was taped securely to the external nose with adhesive tape.

The next step was to secure the lingual pressure array onto the palatal vault by means of oral adhesive strip. Consistency in placement was established by placing the anterior sensor 5 mm posterior to the incisive papilla, similar to Ono et al. (2004). All data were recorded concurrently with a sampling rate of 1000 Hz.

When the participant was ready, he/she executed five relaxed dry (saliva) swallows, which were taken as baseline measures. Stimuli were then randomly presented: (a) control odour, (b) low odour, (c) high odour, (d) control tastant, (e) low tastant, and (f) high tastant. The odour stimuli were presented continuously for 1 min, then paused for 15 s to avoid adaptation (Cometto-Muniz & Cain, 1995). The odour was presented again for another minute, and the cycle repeated until all data were recorded. A fresh taste stimulus was used after three swallows to ensure adequate taste stimulation. Participants were asked to breathe normally during stimulus presentation and to swallow their saliva approximately once every 30 s. After the filter paper strip was placed on the tongue or the nebulizer has been switched on for at least 10 s, an instruction to swallow was given. The instruction was: "You may now swallow whenever you are ready". The nebulizer was switched on before instruction to swallow was given to ensure that the odour stimulus has reached the nostrils when participants swallowed.

Participants completed five repetitions of a dry swallow with each stimulus. The concentrations of odour and tastant that best stimulated a participant's swallowing when presented on its own (based on the largest sEMG amplitude) were then combined for the simultaneous presentation of odour and tastant. The high concentration stimuli were used if no differences were detected. Using the same method to present the odour and tastant stimulation as when they were presented independently, five dry swallows were recorded during the combined odour and tastant stimulation, which was denoted as time = 0 min. Five dry swallows were again recorded at 30-, 60-, and 90-min poststimulation, as was done in the MEP study (Chapter 4). Data were saved on the computer for offline analyses. Confidentiality was assured by assigning a coded numerical identification for each participant.

5.6.7   Data Analyses

Preliminary analyses of the mean sEMG amplitudes were completed on the low and high concentrations of odour and tastant for each participant. The concentration that produced greater sEMG amplitude was selected for simultaneous presentation of both stimuli. Data from the combined odour and tastant stimulation were subjected to two separate repeated-measures ANOVAs to evaluate immediate (during stimulation compared to baseline) and late (at 30-, 60-, and 90-min poststimulation compared to baseline measures) effects of sensory stimulation on swallowing biomechanics. Additionally, data from the independent presentation of control odour, low odour, high odour, control tastant, low tastant, and high tastant were subjected to paired *t*-tests compared to baseline measures to evaluate immediate biomechanical changes during the stimulation. Data were analysed with SPSS 17.0 (SPSS Inc, Somers, New York, USA).

Pharyngeal manometry analyses were done separately for the pharyngeal pressures (the first and second sensors) and the pressure in the UES (the third sensor). The time difference between the peak pressures at the first and second sensors was also analysed (the peak-to-peak duration). Lingual pressures and EMG data were analysed separately in two additional analyses. $p < .05$ was taken as significant. For all analyses, Greenhouse-Geisser correction was reported if Mauchly's test of sphericity was significant, suggesting that the assumption of sphericity was violated.

Further *t*-tests comparing baseline measures with during- and post-stimulation data were also carried out even if the ANOVAs showed no significant differences, as data from the MEP study showed significant changes at 30-, 60-, and 90-min poststimulation (Chapter 4). As in the previous chapter, Bonferroni correction was not applied in these analyses as the data are highly correlated (Bland & Altman, 1995; Perneger, 1998). Furthermore, previous research has documented changes in neural substrates of swallowing postintervention (Doeltgen, Dalrymple-Alford et al., 2010; Fraser et al., 2002; Fraser et al., 2003; Mistry et al., 2006), thus it was felt necessary to make a priori hypothesis at these time points. Nevertheless, confidence interval and effect size of each calculation were considered to critically evaluate for Type I error.

5.6.8   Results

5.6.8.1   Intra- and Inter-Rater Reliability

Twenty percent of data were randomly selected and re-analysed by the investigator (Rater 1) and two other persons (an undergraduate student and a speech-language therapist as Raters 2 and 3, respectively) for intra- and inter-rater reliability. Two-way mixed effects model for ICC was used to analyse reliability; results for single-measures ICC are shown in Table 12.

Table 12

Single-measures ICC for intra- and inter-rater reliability

Measurements	Intrarater ICC	Interrater ICC
Submental sEMG: Amplitude	1.00	.99
Submental sEMG: Duration	.93	.63
Lingual pressure: Amplitude	.99	.98
Lingual pressure: Duration	.93	.66
Pharyngeal manometry: Amplitude	1.00	1.00
Pharyngeal manometry: Duration	.99	.94

High intrarater reliability was found for both measurements of amplitude and duration. The interrater reliability among the three raters for amplitude was very good. This may be due to the method used to generate the values for the amplitude, which was automatically computed by the software. The interrater reliability for durational measures was moderate.

Results are presented as immediate (during stimulation) and late (poststimulation) effects. A figure of sEMG, lingual pressure, and pharyngeal manometry waveforms captured concurrently is shown in Figure 26. Although the phases of swallowing cannot be explicitly defined by these methods, one can loosely infer the end of oral phase and the start of pharyngeal phase.
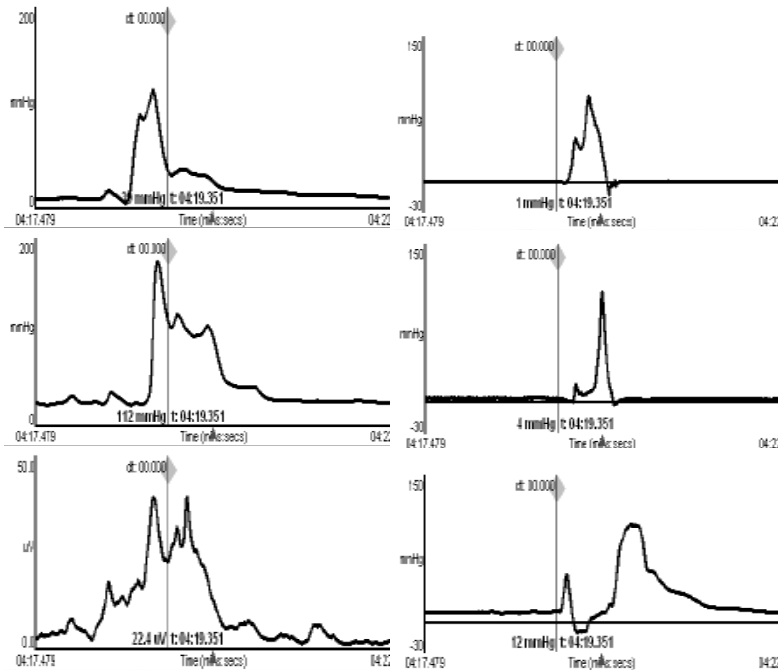
Figure 26. The averaged and rectified waveforms of submental EMG (lower left), anterior and middle lingual pressures (upper and middle left, respectively), and pharyngeal manometry (right, with oropharynx, hypopharynx, and UES pressures sequentially from top to bottom) recorded from one participant. The vertical line indicates the likely boundary between the oral and pharyngeal phases of swallowing. Note the peak of lingual pressures during oral phase of swallowing to the left side of the vertical line and the occurrence of pharyngeal pressure changes during swallowing to the right side of the vertical line. Lingual pressure is apparent during oral phase of swallowing to facilitate bolus transfer into the pharynx and is maintained during the pharyngeal swallow. Submental sEMG and midlingual activation is apparent during both oral and pharyngeal phases of swallowing.

5.6.8.2 Surface Electromyography of the Submental Muscles

The *F*- and *p*-values for repeated-measures ANOVAs are tabulated in Appendix M. SEMG amplitude and duration at baseline, during stimulation, and at 30-, 60-, and 90-min poststimulation are tabulated in Table 13. Paired *t*-test results comparing (a) baseline versus during stimulation and (b) baseline versus poststimulation for both amplitude and duration are tabulated in Appendix N.

Table 13

Mean (SD) of sEMG measurements at baseline, during stimulation, and poststimulation

Time measures were recorded	Amplitude (µV) (SD)	Duration (s) (SD)
Baseline	50.96 (17.31)	1.31 (0.28)
During stimulation		
Control odour	49.07 (15.15)	1.35 (0.28)
Low odour	49.60 (17.74)	1.33 (0.24)
High odour	52.06 (19.14)	1.34 (0.29)
Control tastant	49.57 (15.59)	1.37 (0.26)
Low tastant	54.85 (19.76)	1.37 (0.29)
High tastant	56.39 (21.89)	1.42 (0.35)
Odour + Tastant	55.85 (23.65)	1.45 (0.31)
Poststimulation		
30 min post	53.36 (18.08)	1.39 (0.33)
60 min post	51.53 (17.83)	1.41 (0.32)
90 min post	52.81 (18.01)	1.34 (0.27)

Submental SEMG during Odour Stimulation: Immediate Effect

There were no differences in the sEMG amplitude between baseline and control condition. The sEMG amplitude during low or high odour stimulation also showed no significant differences compared to baseline.

There were no differences in the sEMG duration between baseline and control condition. Similarly, no differences were detected when low or high odour stimulation was compared to baseline.

Submental SEMG during Tastant Stimulation: Immediate Effect

No differences in the sEMG amplitude between baseline and control condition were found. There were no differences in the sEMG amplitude when the low and high tastants were compared to baseline.

The sEMG durations between baseline and control condition were not significantly different. No differences in sEMG duration were present between baseline and the low or high tastants.

Submental SEMG during Combined Stimulation: Immediate Effect

The sEMG amplitude and duration during simultaneous odour and tastant presentation were not different from baseline but there was a trend towards increased duration compared to baseline ($p = .06$, $r = .23$).

Submental SEMG Poststimulation: Late Effect

Repeated-measures ANOVAs for sEMG amplitude and duration across time were not significant. However, t-tests showed increased sEMG duration at 60 min poststimulation compared to baseline, $t(15) = 2.13$, $p = .05$, Cohen's $d = 0.33$, $r = .16$. The 95% confidence interval of the mean difference (CI) for this comparison was -0.195 and 0.00012 for lower bound and upper bound, respectively, with small effect size. As the CI includes zero and the effect size was small, this effect may represent a Type I error.

5.6.8.3 Lingual Pressures

The F- and p-values are tabulated in Appendix M. The amplitude and duration of lingual pressures at baseline, during stimulation, and at 30-, 60-, and 90-min poststimulation are tabulated in Table 11. Paired t-test results comparing (a) baseline versus during stimulation and (b) baseline versus poststimulation for both amplitude and duration are tabulated in Appendix O.

Lingual Pressures during Odour Stimulation: Immediate Effect

There were no differences in the anterior and middle tongue-to-palate pressure amplitude between baseline and control condition for odour. The anterior glossopalatal pressure amplitude during low and high odour stimulation showed no significant differences compared to baseline. The middle tongue-to-palate pressure amplitude during low and high odour stimulation also produced no significant differences when compared to baseline.

No differences were detected in the duration of anterior and middle glossopalatal contact between baseline and control condition for odour. Similarly, no differences in duration were found when baseline measurement was compared with the low or high odour for anterior glossopalatal contact and the middle glossopalatal contact.

Table 14

Mean (SD) tongue-to-palate pressure measurements at baseline, during stimulation, and poststimulation

Time measures were recorded	Anterior tongue		Middle tongue	
	Amplitude (mmHg) (SD)	Duration (s) (SD)	Amplitude (mmHg) (SD)	Duration (s) (SD)
Baseline	150.3 (81.1)	1.50 (0.21)	184.7 (66.9)	1.48 (0.27)
During stimulation				
Control odour	151.2 (105.1)	1.50 (0.27)	167.8 (64.6)	1.53 (0.35)
Low odour	147.9 (83.0)	1.56 (0.32)	170.5 (50.6)	1.50 (0.32)
High odour	159.8 (107.8)	1.50 (0.24)	180.6 (81.5)	1.49 (0.28)
Control tastant	170.1 (82.8)	**1.75 (0.33)***	178.3 (75.3)	1.54 (0.35)
Low tastant	176.5 (92.6)	**1.82 (0.31)***	178.2 (72.0)	**1.63 (0.34)***
High tastant	**197.3 (104.3)***	**1.79 (0.35)***	189.6 (74.6)	1.54 (0.44)
Combined stimulation	**187.4 (98.6)***	**1.73 (0.27)***	162.2 (79.7)	1.49 (0.39)
Poststimulation				
30 min post	134.7 (107.1)	1.41 (0.34)	**156.8 (64.4)***	1.42 (0.35)
60 min post	147.9 (102.1)	**1.35 (0.23)***	161.1 (72.9)	**1.37 (0.32)***
90 min post	150.6 (102.3)	1.29 (0.37)	161.6 (66.7)	1.43 (0.33)

*$p < .05$ compared to baseline.

Lingual Pressures during Tastant Stimulation: Immediate Effect

There were no differences in the anterior and middle tongue-to-palate pressure amplitude between baseline and control condition for tastant. The anterior

tongue-to-palate pressure amplitude during low tastant stimulation showed no differences when compared to baseline but the amplitude was increased when high tastant was presented, $t(15) = 2.6$, $p = .02$, Cohen's $d = 0.50$, $r = .24$ (95% CI -86.01 to -8.00). As the effect size was moderate and the CI did not include zero, this analysis was taken as not representing Type I error. The middle tongue-to-palate pressure amplitude during the presentation of low and high tastants showed no differences when compared to baseline.

No differences were found in the duration of middle glossopalatal contact between baseline and control condition but the duration of anterior glossopalatal contact was increased, $t(15) = 3.5$, $p = .003$, Cohen's $d = 0.90$, $r = .41$ (95% CI -0.40 to -0.10). When compared to baseline, the duration of anterior glossopalatal contact was increased when either low or high tastant was presented, $t(15) = 4.1$, $p = .001$, Cohen's $d = 1.18$, $r = .51$ (95% CI -0.48 to -0.15, and $t(15) = 3.2$, $p = .01$, Cohen's $d = 1.00$, $r = .45$ (95% CI -0.48 to -0.10), respectively. The duration of middle glossopalatal contact was increased only when low tastant was presented, $t(15) = 2.7$, $p = .02$, Cohen's $d = 0.49$, $r = .24$ (95% CI -0.28 to -0.03). In all the t-tests, the effect size was moderate to good and the CI did not include zero; thus, these analyses were taken as having true effect.

Lingual Pressures during Combined Stimulation: Immediate Effect

The analyses for pressure amplitudes and durations were significant for interaction between the tongue sensor (anterior versus middle) and condition (baseline versus during stimulation), $F(1, 15) = 26.3$, $p < .0001$, $r = .80$, and $F(1, 15) = 53.7$, $p < .0001$, $r = .88$, respectively. The durational analysis for the main effect of tongue sensor (anterior versus middle) was also significant, $F(1, 15) = 5.5$, $p = .03$, $r = .52$. Further, t-tests showed increased pressure and duration of glossopalatal contact at anterior tongue when simultaneous odour and tastant stimulation was presented compared to baseline, $t(15) = 2.6$, $p = .02$, Cohen's $d = 0.41$, $r = .20$ (95% CI -67.95 to -6.13), and $t(15) = 2.9$, $p = .01$, Cohen's $d = 0.95$, $r = .43$ (95% CI -0.40 to -0.06), respectively. The t-tests revealed moderate effect size and the CI did not include zero; thus, these analyses were taken as not representing Type I error.

Lingual Pressures Poststimulation: Late Effect

In contrast to the immediate effect, the repeated-measures ANOVAs showed no late effects. However, *t*-tests showed decreased pressure at midglossopalatal contact 30 min poststimulation compared to baseline, $t(15) = 3.2$, $p = .01$, Cohen's $d = 0.42$, $r = .21$ (95% CI 9.45 to 46.34), and decreased duration for anterior and midglossopalatal contact at 60 min poststimulation compared to baseline, $t(15) = 2.3$, $p = .04$, Cohen's $d = 0.68$, $r = .32$ (95% CI 0.01 to 0.29), and $t(15) = 2.2$, $p = .05$, Cohen's $d = 0.37$, $r = .18$ (95% CI 0.001 to 0.21), respectively. The *t*-tests revealed moderate effect size except for midglossopalatal contact duration which has small effect size. However, all CIs did not include zero; thus, these analyses were taken as not representing Type I error.

5.6.8.4   Pharyngeal Manometry

The *F*- and *p*-values are tabulated in Appendix M. The pressure amplitude and contact duration of pharyngeal manometry at baseline, during stimulation, and at 30-, 60-, and 90-min poststimulation are tabulated in Table 12. Paired *t*-test results comparing: (a) baseline versus during stimulation and (b) baseline versus poststimulation for both amplitude and duration are tabulated in Appendix P.

Pharyngeal Manometry during Odour Stimulation: Immediate Effect

There were no differences in the pressure amplitude at sensors 1, 2, and 3 between baseline and control condition for odour. No differences in the pressure amplitude were detected when low or high odour was compared to baseline at all sensors.

No differences were found in the contact duration at sensors 1, 2, and 3 between baseline and control condition for odour. Similarly, no differences in contact duration at all sensors were found when baseline measurement was compared with the low or high odour.

Table 15

Mean (SD) pharyngeal manometry measurements at baseline, during stimulation, and poststimulation

Time measures were recorded	Sensor 1		Sensor 2		Peak-to-peak duration	Sensor 3	
	Amplitude (mmHg) (SD)	Duration (s) (SD)	Amplitude (mmHg) (SD)	Duration (s) (SD)	Duration (s) (SD)	Amplitude (mmHg) (SD)	Duration (s) (SD)
Baseline	92.2 (22.4)	0.48 (0.09)	111.1 (34.0)	0.36 (0.12)	0.25 (0.08)	-9.15 (6.24)	1.07 (0.29)
During stimulation							
Control odour	93.6 (24.7)	0.47 (0.09)	113.4 (43.0)	0.36 (0.13)	**0.24 (0.06)***	-8.48 (6.85)	1.01 (0.25)
Low odour	97.5 (27.4)	0.47 (0.10)	108.2 (35.2)	0.37 (0.13)	0.23 (0.07)	-8.53 (7.06)	1.05 (0.26)
High odour	94.6 (27.3)	0.46 (0.10)	107.7 (34.4)	0.35 (0.13)	0.23 (0.06)	-8.39 (8.12)	1.03 (0.26)
Control tastant	93.4 (26.1)	**0.46 (0.08)***	111.6 (35.3)	0.34 (0.11)	0.25 (0.08)	-9.34 (5.58)	1.03 (0.29)
Low tastant	92.7 (28.3)	**0.46 (0.10)***	108.3 (36.1)	**0.34 (0.13)***	**0.23 (0.06)***	-9.64 (5.99)	1.04 (0.22)
High tastant	90.6 (27.8)	**0.44 (0.08)***	105.3 (36.1)	0.33 (0.11)	0.24 (0.06)	-10.2 (4.92)	1.05 (0.22)
Combined stimulation	92.4 (29.3)	0.45 (0.11)	**94.0 (23.5)***	0.35 (0.12)	0.23 (0.08)	-8.79 (5.59)	1.05 (0.20)
Poststimulation							
30 min post	93.4 (28.8)	0.46 (0.11)	104.2 (32.8)	0.36 (0.11)	0.24 (0.08)	-8.62 (5.17)	1.07 (0.27)
60 min post	92.6 (25.8)	0.46 (0.10)	105.4 (36.8)	0.36 (0.13)	0.24 (0.08)	-9.69 (5.00)	1.14 (0.31)
90 min post	90.4 (24.1)	0.48 (0.10)	113.3 (32.3)	0.37 (0.13)	0.23 (0.08)	-9.41 (6.28)	1.10 (0.31)

*$p < .05$ compared to baseline.

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Pharyngeal Manometry during Tastant Stimulation: Immediate Effect

There were no differences in the pressure amplitude at sensors 1, 2, and 3 between baseline and control condition for tastant. No differences in the pressure amplitude were detected when low or high odour was compared to baseline at all sensors.

No differences were detected in the duration of contact pressure at sensor 2 between baseline and control condition for tastant. The differences in the contact duration at sensor 1 was significant, $t(15) = 3.0$, $p = .009$, Cohen's $d = 0.23$, $r = .12$ (95% CI 0.008 to 0.05), and marginally significant at sensor 3, $t(15) = 2.1$, $p = .051$, when the control condition for tastant was compared to baseline. No differences in contact duration were found when baseline measurement was compared with the low or high tastant at sensor 3. The contact durations at sensor 1, sensor 2, and in the peak-to-peak duration were different when low tastant was presented compared to baseline, $t(15) = 2.3$, $p = .04$, Cohen's $d = 0.21$, $r = .10$ (95% CI 0.002 to 0.05), $t(15) = 3.8$, $p = .002$, Cohen's $d = 0.16$, $r = .08$ (95% CI 0.01 to 0.03), and $t(15) = 2.2$, $p = .04$, Cohen's $d = 0.28$, $r = .14$ (95% CI 0.001 to 0.05), respectively. The presentation of high tastant decreased the contact duration at sensor 1, $t(15) = 3.6$, $p = .003$, Cohen's $d = 0.47$, $r = .23$ (95% CI 0.02 to 0.07), and with marginal significance in sensor 2 and in the peak-to-peak duration, $t(15) = 2.0$, $p = .06$ and $t(15) = 1.9$, $p = .07$, respectively. The CI for all significant comparisons did not cross zero and the effect size was small for all comparisons except during high tastant presentation, which has a moderate effect size. As other studies have also reported immediate changes in the biomechanics of swallowing following tastant presentation, these analyses were taken as not representing Type I error.

Pharyngeal Manometry during Combined Stimulation: Immediate Effect

Repeated-measures ANOVAs for the peak pharyngeal pressures were significant for the main effect of condition (baseline versus stimulation) and the interaction between condition and the sensor (sensors 1 and 2), $F(1, 15) = 5.0$, $p = .04$, $r = .50$, and $F(1, 15) = 8.2$, $p = .01$, $r = .59$, respectively. Further t-tests showed decreased contact pressure at sensor 2 during stimulation compared to baseline, $t(15) = 3.2$, $p = .006$, Cohen's $d = 0.58$, $r = .28$ (95% CI 5.6 to 28.4). This

analysis is taken as having a true difference as the effect size was moderate and the CI did not cross zero. No pressure differences were recorded from sensor 3.

Repeated-measures ANOVAs for durational measures at sensors 1 and 2 showed differences, $F(1, 15) = 21.0$, $p < .0001$, $r = .76$. The contact duration at sensor 1 was longer than sensor 2. Further t-tests comparing durations during combined stimulation with baseline measures showed no differences. Also, no differences in duration were detected for sensor 3 or in the peak-to-peak timing.

Pharyngeal Manometry Poststimulation: Late Effect

Differences were found in the amplitude of contact pressure at sensors 1 and 2, $F(1, 15) = 4.5$, $p = .050$, $r = .48$. Pressures recorded at sensor 2 were higher than sensor 1. No pressure differences were computed for sensor 3. Repeated-measures ANOVA for duration and sensor (sensors 1 and 2) showed a significant main effect of sensor and time, $F(1, 15) = 21.3$, $p < .0001$, $r = .77$, and $F(3, 45) = 3.4$, $p = .03$, $r = .43$, respectively. Pressure durations at sensor 1 were higher than sensor 2. Further t-tests comparing the durations at sensors 1 and 2 at baseline with 30-, 60-, and 90-min poststimulation showed no differences. No durational differences were detected in the UES and peak-to-peak timing.

5.6.9   Discussion

This is the first study to investigate immediate and late changes in the biomechanics of swallowing following odour and tastant stimulation. Some changes were observed following sensory stimulation, which—to some extent—parallels patterns of neural change documented in the MEPs associated with sensory stimulation (Chapter 4).

As this study was an extension of the MEP study where combined smell and taste stimulation increased the MEP amplitude poststimulation, an a priori hypothesis was made before data were gathered and t-tests have been chosen to evaluate the differences. These t-tests were carried out without correcting for multiple comparisons. It has been reported that using Bonferroni correction in clinical studies with repeated measurements may not be appropriate as the data are highly correlated (Bland & Altman, 1995; Perneger, 1998). However, in the absence of alpha level

adjustment, to evaluate the data for potential Type I errors, effect size and confidence interval of the mean differences were evaluated.

Immediate Effects Following Olfactory and Gustatory Stimulation

The MEP study documented no immediate effects of paired olfactory and gustatory stimulation (Chapter 4). However, the current study found immediate biomechanical changes during flavour stimulation. These changes included increased pressure and duration of tongue-to-palate contact at the anterior tongue and decreased contact pressure at the second pharyngeal sensor (in the hypopharynx) when simultaneous odour and tastant stimulation was presented compared to baseline. Similar changes in lingual pressures were recorded with independent taste stimulation. There was a trend towards decreased contact pressure at sensor 2 following tastant stimulation; however, there was decreased duration of contact pressure in the pharynx. Other studies have documented increased submental muscle contraction or lingual pressure when sour taste was presented (Ding et al., 2003; Leow et al., 2007; Palmer et al., 2005; Pelletier & Dhanaraj, 2006). In the current study, there was a trend towards increased duration of submental muscle contraction following simultaneous odour and tastant stimulation compared to baseline but it was not significant (Table 13 and Appendix N). A larger sample size may have revealed a difference.

At baseline, the midglossopalatal contact produced greater pressure than its anterior counterpart, comparable to Shaker et al.'s study (1988). However, a higher pressure was recorded in the anterior tongue during stimulation compared to midglossopalatal contact, similar to that reported by Pelletier and Dhanaraj (2006). It was hypothesized that increased activation of the facial and glossopharyngeal nerves, which carry taste information from the oral cavity and pharynx, would subsequently activate more sensory neurons in the NTS. Moreover, flavour stimulation may have activated other brain areas, such as the insula, which also feeds sensory information into the NTS (Willett et al., 1986). Information from the NTS is conveyed to the motor neurons in the NA, which contains motor neurons involved in swallowing (cranial nerves IX and X). Consequently, there would be more motor neurons activated in the NA; the neural signals may then be conveyed via monosynaptic or interneuronal connections (Cunningham & Sawchenko, 2000; Jean et al., 1983) to

other cranial motor nuclei involved in swallowing (cranial nerves V, VII, and XII). A similar hypothesis has been suggested previously by others (Ding et al., 2003; Leow et al., 2007; Logemann et al., 1995; Pelletier & Dhanaraj, 2006).

The current study found decreased contact pressure at the hypopharynx during stimulus presentation. Pressure at this site has been shown to correlate negatively with oral and pharyngeal transit times and pharyngeal response time (Pauloski et al., 2009) and with submental muscle contraction (Huckabee et al., 2005). Findings from this study are comparable to previous reports where lower hypopharyngeal pressure and increased anterior glossopalatal contact pressure and duration during stimulus presentation were recorded compared to baseline. The decreased hypopharyngeal pressure has been suggested to be due to the close proximity of the second sensor to the UES (Butler et al., 2009). Similarly, a transient negative subatmospheric pressure has been recorded in the hypopharynx during dry swallows, which was suggested as resulting from expansion of pharynx during swallowing (Cook et al., 1989).

Late Effects Following Olfactory and Gustatory Stimulation

Data from the MEP study (Chapter 4) suggested late changes in submental muscle contraction. It was proposed that the mechanism of LTP, a function of neural plasticity (Cooke & Bliss, 2006), was responsible for changes in MEP amplitudes poststimulation. LTP is an increase in synaptic strength transmission which leads to more efficient neural communication. Persistent LTP activity will lead to long-term neural change which may contribute to recovery in patients with dysphagia.

The late effects seen in the current study were detected in the glossopalatal measures but no submental and pharyngeal changes were evident. However, there was a trend of increased duration of submental contraction and UES opening poststimulation compared to baseline, which parallel the increased MEP amplitude seen in previous data. Changes in the cortical areas involved in swallowing have been reported to begin long before changes are seen at the periphery (Humbert et al., 2010). Therefore, although the MEP data showed increased excitability, changes in the muscles and UES may not have been detectable during the course of data collection.

Poststimulation changes in the biomechanics of swallowing were documented up to 60 min poststimulation, in contrast to that seen with the MEP data where changes were recorded at 90 min poststimulation. However, unlike MEPs, which reflect neural excitability and transmission, biomechanical data are highly influenced by variations in voluntary behaviour which may have obscured a small biomechanical effect at 90 min.

Poststimulation changes in submental sEMG and lingual pressures following flavour stimulation have not been previously reported. Submental sEMG and lingual pressures are not highly correlated (Lenius, Carnaby-Mann, & Crary, 2009). Therefore, an increase in one measure does not necessarily imply an increase in the other. In the current study, decreased glossopalatal contact duration compared to baseline was recorded. Conversely, there were no changes in sEMG amplitude or duration compared to baseline. However, the relatively small sample size may have limited the ability to detect differences but there was a trend of increased duration of the sEMG. The poststimulation results showed decreased midglossopalatal pressure and contact duration and decreased anterior glossopalatal contact duration. Decreased durations may be explained by increased efficiency in the oral phase, which appeared as faster oral transit time compared to baseline (Taniguchi, Tsukada, Ootaki, Yamada, & Inoue, 2008). The decreased pressure at midglossopalatal contact could be explained by the existence of negative tongue pressure when the tongue moved away from the palate (Kennedy et al., 2010; Ono et al., 2004), which could not be measured via the current method.

Methodological Aspects and Limitations

Many factors can influence swallowing; for example, the volume and temperature of the bolus. Pelletier and Dhanaraj (2006) found that 10-ml chilled sour boli elicit higher lingual swallowing pressures compared to water. However, they could not separate out the volume and temperature effects, which may have confounded their results. Thus, the present study used filter paper strips impregnated with lemon concentrate at room temperature to ensure that the volume and temperature effects were controlled. However, there is also a taste-salivary gland reflex which stimulates salivary secretion upon taste presentation (Noback et al., 2005), thus the dry swallows measured in this study could have contained a higher

volume of saliva. Nevertheless, increased salivary volume due to taste is minimal (Logemann et al., 1995) and only boluses of more than 1 ml have been reported to affect swallowing function (Logemann et al., 1995; Rademaker et al., 1998).

The interrater reliability for the measurement of sEMG duration was moderate. An objective approach to measure the duration was specified to all raters to be implemented in the analyses; however, no training was provided. The start and end of the duration were gauged when the change in the slope of the waveform was more than 0.2 μV. For improved interrater reliability, raters may benefit from a session of practice before the actual rating is done. Another explanation for the moderate reliability among raters for the duration is the presence of "double-share swallow" (Vaiman et al., 2004d). Double-share swallow is when "after single oral phase, two pharyngeal phases are observed with incomplete muscle relaxation in between" (p. 980), which may cause raters to gauge different start time. An example of a waveform from one of the participant with double-share swallow is shown in Figure 27.
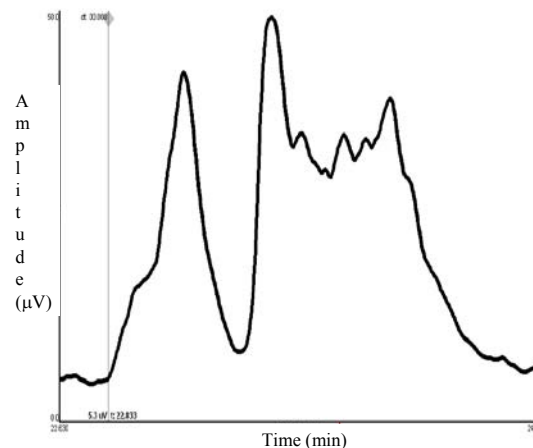
Figure 27. EMG waveform from one participant showing the double-share swallow.

In the current study, changes in the biomechanics of swallowing were primarily identified during the volitional oral stage of swallowing. This may provide further evidence that the different stages of swallowing are controlled by different neural pathways, or utilize different levels of cortical involvement, or both. A similar

hypothesis has been proposed by others (Doeltgen et al., 2011). More work is needed to further explore this hypothesis.

5.7 Supplementary Study

The main biomechanical study was conducted to determine if the effects of simultaneous presentation of odour and tastant on swallowing, as seen in the MEP study, could be measured at the periphery. Therefore, combined stimulation was performed without an equivalent control condition. To address this problem, a supplementary study to evaluate differences between control condition and during simultaneous odour and tastant stimulation was conducted.

5.7.1 Hypotheses

The hypotheses for this study have been elaborated in Section 2.7.7. In this section, only the hypotheses are presented.

5.7.1.1 Hypothesis 13

The presentation of combined lemon odour and tastant affects submental contraction more compared to water. The amplitude of the submental sEMG is greater when lemon odour and tastant are presented simultaneously compared to water. The duration of the submental contraction is longer during lemon stimulation compared to water.

5.7.1.2 Hypothesis 14

The presentation of combined lemon odour and tastant affects lingual swallowing pressure more compared to water. The amplitude of the lingual pressure is greater when combined lemon odour and tastant are presented compared to water. The duration of the tongue-to-palate contact is longer during lemon stimulation compared to water.

5.7.1.3 Hypothesis 15

The presentation of combined lemon odour and tastant affects pressures in the pharynx and UES more compared to water. The amplitude of the pharyngeal pressure is greater when combined lemon odour and tastant are presented compared to water. There is longer duration of the pressure generation when lemon stimulation is compared to water. The relaxation pressure in the UES is more negative when combined lemon odour and tastant are presented compared to water. The duration of the UES opening is longer during lemon stimulation compared to water.

5.7.2 Study Design

A repeated-measures within-subject design was carried out to assess differences between combined presentation of lemon odour and tastant and combined presentation of water mist and water as tastant. Ethical approval was granted by a regional Health and Disability Ethics Committee (see Appendix Q for information sheet for participants).

5.7.3 Participants

Twelve young (mean age 26.6 years, SD 9.8) healthy participants were recruited for this study (gender equally represented); they may have been involved in the MEP study, biomechanical study, or both. The participants reported no respiratory abnormalities on the day data was collected, and they were all informed to refrain from taking any food and/or liquids (except water) one hour prior to the procedures.

5.7.4 Instrumentation and Stimuli

As the objective of this study was to support the findings from the main biomechanical study, the same instrumentation was used. Based on the MEP and biomechanical studies, the combination of low concentration odour and tastant was the most frequently combined stimuli; hence, they were simultaneously presented to all participants in this supplementary study. Water at room temperature was used in the control condition.

5.7.5 Procedures and Data Analyses

The procedures were similar to the main biomechanical study. When the participant was ready, these three conditions were counter-balanced among participants: (a) five relaxed dry (saliva) swallows, which were taken as baseline measures; (b) five dry swallows during combined odour and tastant stimulation; and (c) five dry swallows during control condition which used water as both the odour and tastant stimuli.

Data were saved on the computer for offline analyses. Confidentiality was assured by assigning a coded numerical identification for each participant. Data were analysed with paired t-tests to compare control condition with the experimental condition. $p < .05$ was taken as significant.

5.7.6 Results

Mean data are tabulated in Table 16. Results from paired t-test analyses are tabulated in Appendix R. The EMG amplitude and duration between the control and combined conditions were not different from each other.

The anterior tongue-to-palate pressure during combined stimulation was significantly higher from the control condition, $t(11) = 2.9$, $p = .01$ but no differences were detected in the middle tongue-to-palate pressure. For the analyses of durations, the middle glossopalatal contact during combined stimulation was significantly longer when compared to the control condition, $t(11) = 2.7$, $p = .02$. No differences were detected in the anterior tongue-to-palate contact.

There were no differences in the contact pressure at the first, second, and third sensors when the control and combined conditions were compared. Similarly, no durational differences were detected between the control and combined conditions in the first, second, and third sensors, as well as in the peak-to-peak duration.

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Table 16

Mean (SD) of outcome measurements for supplementary study

Measurements	Control condition		Combined stimulation	
	Amplitude (SD)	Duration (s) (SD)	Amplitude (SD)	Duration (s) (SD)
SEMG (amplitude in μV) Submental muscle	39.7 (12.8)	1.37 (0.22)	40.9 (13.6)	1.42 (0.26)
Lingual pressures (amplitude in mmHg)				
Anterior tongue	97.3 (27.3)	1.64 (0.25)	113.4 (30.4)	1.73 (0.25)
Middle tongue	99.5 (37.7)	1.33 (0.24)	108.2 (40.9)	1.42 (0.25)
Pharyngeal manometry (amplitude in mmHg)				
Sensor 1	81.0 (21.7)	0.45 (0.10)	78.8 (19.3)	0.45 (0.09)
Sensor 2	97.0 (28.2)	0.42 (0.23)	99.0 (28.4)	0.41 (0.22)
Peak-to-peak timing	-	0.22 (0.06)	-	0.21 (0.07)
Sensor 3	-7.30 (6.83)	1.14 (0.26)	-7.57 (6.37)	1.11 (0.27)

5.7.7   Discussion

No differences were found in the sEMG and pharyngeal manometry measures when the control condition was compared to the combined stimulation. However, both pressure amplitude and contact duration of the anterior and middle glossopalatal contact were increased following odour and tastant stimulation, but significant results were computed only for the pressure amplitude at the anterior tongue and contact duration at the middle tongue. Other studies have also reported increased lingual swallowing pressure following tastant stimulation, with the anterior tongue recorded higher pressure compared to the middle tongue (Pelletier & Dhanaraj, 2006). Increased lingual pressure was probably due to increased activation to the NTS, which subsequently increased contraction of the tongue muscles via increased activation of the hypoglossal motoneuron (see Section 2.1.2.2). Another factor that may have contributed to the increased lingual pressure is the presence of the filter paper on the tongue surface. This may have activated other sensory modalities, such as trigeminal stimulation, which may also have contributed to increased NTS activation. However, as the sEMG and pharyngeal manometry measures, which were not directly influenced by the presence of the filter paper, were not different between

the control and combined conditions, it could be speculated that there are no differences between the two conditions. As this supplementary study found that there were no differences between the control and combined conditions, at least in the EMG and pharyngeal manometry measures, data from the combined stimulation can be compared to the baseline.

5.8   Conclusion

In conclusion, the simultaneous presentation of odour and tastant—that is, flavour—can change the biomechanical aspects of swallowing which are under volitional control. As these changes were evident even after the stimulus was removed, its use in therapy could be of great value, particularly for patients with cognitive deficits who have problems following instructions in a standard rehabilitation programme. Follow-up research to investigate the effects of flavour on swallowing function in the elderly and in patients with dysphagia would lend support to the use of sensory stimulation in managing patients with dysphagia.

Chapter 6

Concluding Remarks

The aim of this research programme was to evaluate the role of sensory stimulation—specifically odour and taste—on the neural substrates and biomechanics of swallowing. Submental MEPs were measured to evaluate the effects of smell and taste on neural excitability of the pathways that control swallowing. Submental sEMG and lingual and pharyngeal manometry were utilized to evaluate changes in the biomechanics of swallowing following sensory stimulation.

Fifteen hypotheses were proposed, which collectively posited that smell, taste, and the combined stimulation of smell and taste would affect swallowing. These were partially supported. As a broad summary, independently presenting the odour or tastant did not alter neural excitability of swallowing but when both stimuli were presented simultaneously, the MEP amplitudes were increased at 30-, 60-, and 90-min poststimulation compared to baseline measures. Contrary to the changes in MEPs, the biomechanics of swallowing were altered during combined smell and taste stimulation and when odour and tastant were presented independently. Changes in the biomechanics of swallowing were also seen at 30- and 60-min poststimulation.

6.1   Review of Hypotheses: Neural Effects

Hypothesis 1

Hypothesis 1 stated that olfactory stimulation increases the excitability of neural transmission associated with swallowing.

Review of Hypothesis 1: This hypothesis was largely not supported. Results showed no differences in MEPs between low and high concentrations odour stimulation. Also, no changes in MEP latency and amplitude during olfactory stimulation were detected but there was decreased MEP latency 90 min poststimulation.

Hypothesis 2

Hypothesis 2 stated that gustatory stimulation increases the excitability of neural transmission associated with swallowing.

Review of Hypothesis 2: This hypothesis was also largely not supported. Results showed that a high concentration tastant produced greater MEP amplitude compared to a low concentration tastant. However, no differences in MEPs were apparent when taste stimulation was compared to no stimulation and no poststimulation effects were recorded.

Hypothesis 3

Hypothesis 3 stated that when both olfactory and gustatory stimuli are presented simultaneously there is an increase in the excitability of neural transmission compared to no stimulus and to independent presentation of olfaction or gustation.

Review of Hypothesis 3: This hypothesis was largely supported. Although there were no MEP differences between the stimulation when the stimuli were present, there were differences after stimuli were removed. MEP amplitudes were increased at 30-, 60-, and 90-min poststimulation when combined smell and taste stimulation was presented as opposed to no poststimulation differences following independent presentation of either smell or taste.

Comments

Results from the MEP study suggest that single sensory modality is not enough to change the MEP. Furthermore, the combined stimulation of smell and taste has been shown to activate brain areas not stimulated by either stimulus alone (Fu et al., 2004; Small et al., 1997). Odour may stimulate taste buds in the nasopharynx; therefore, it was proposed that the poststimulation decrease in MEP latency is due to the combined activation of the smell and taste receptors following odour stimulation (see Section 4.7).

Changes in MEPs in the current study were not seen immediately but were evident after the combined odour and tastant stimulation was removed. There was an increase in the MEP amplitudes at 30-, 60-, and 90-min poststimulation compared to

baseline. It is intriguing that these changes lasted long after the stimuli were removed, indicating its potential value in rehabilitation. LTP has been proposed as the mechanism involved in the late changes seen in this study. LTP has been associated with synaptic changes in the neural pathway, which would lead to neural plasticity (Cooke & Bliss, 2006). Studies have indicated that neural plasticity is the mechanism involved in recovery of patients with stroke (Khedr et al., 2008). Moreover, it has been shown that the recovery of swallowing function is related to increased cortical representation of the swallowing muscles in the motor cortex (Gallas et al., 2007).

6.2   Review of Hypotheses: Biomechanics of Swallowing

Hypothesis 4

Hypothesis 4 stated that olfactory stimulation increases contraction of the submental muscles.

Review of Hypothesis 4: This hypothesis was not supported.

Hypothesis 5

Hypothesis 5 stated that gustatory stimulation increases contraction of the submental muscles.

Review of Hypothesis 5: This hypothesis was also not supported.

Hypothesis 6

Hypothesis 6 stated that combined olfactory and gustatory stimulation affects the submental muscle contraction more than the independent presentation of either odour or tastant, or when compared to baseline.

Review of Hypothesis 6: This hypothesis was not supported. However, the data showed a trend of increased sEMG duration when combined odour and tastant stimulation was presented compared to no stimulation.

Hypothesis 7

Hypothesis 7 stated that olfactory stimulation affects lingual swallowing pressure.

Review of Hypothesis 7: The present data did not support this hypothesis.

Hypothesis 8

Hypothesis 8 stated that gustatory stimulation affects lingual swallowing pressure.

Review of Hypothesis 8: This hypothesis was partially supported. The data showed increased lingual swallowing pressure amplitude and duration in the anterior tongue when high concentration tastant was presented compared to no stimulation. An increase in the duration of lingual swallowing pressure was detected in the anterior and middle tongue when low concentration tastant was presented compared to baseline. Contrary to the hypothesis, there was greater increase in contact duration when low tastant was presented compared to high tastant. However, the increase in amplitude was larger when high tastant was presented compared to low tastant, which supports the hypothesis. It is not known why these differences were recorded; other authors investigating the effects of sour taste on swallowing biomechanics have also reported contradictory results (see Section 2.3.4.2).

Hypothesis 9

Hypothesis 9 stated that combined olfactory and gustatory stimulation affects the lingual swallowing pressure more than the independent presentation of either odour or tastant, or when compared to baseline.

Review of Hypothesis 9: This hypothesis was partially supported. Results showed that the amplitude and duration of anterior glossopalatal contact were increased when combined stimulation was compared to no stimulation, which support the hypothesis. However, no differences were detected at middle glossopalatal contact during the stimulation. Also, contrary to the hypothesis, poststimulation results showed decreased contact duration at anterior and middle tongue and decreased amplitude of lingual swallowing pressure at middle glossopalatal contact after removal of stimuli.

Hypothesis 10

Hypothesis 10 stated that pressures in the pharynx and UES are positively affected by olfactory stimulation.

Review of Hypothesis 10: This hypothesis was not supported by the present data.

Hypothesis 11

Hypothesis 11 stated that pressures in the pharynx and UES are positively affected by gustatory stimulation.

Review of Hypothesis 11: This hypothesis was not supported. In fact, the duration of the pharyngeal pressure was decreased following both low and high tastant stimulation compared to no stimulation.

Hypothesis 12

Hypothesis 12 stated that combined olfactory and gustatory stimulation affects pharyngeal pressures and the UES more than the independent presentation of either odour or tastant, or when compared to baseline.

Review of Hypothesis 12: This hypothesis was not supported. Contrary to the hypothesis, results showed a decreased duration of contact pressure at oropharynx and a decreased pressure amplitude at hypopharynx during combined stimulation of smell and taste compared to no stimulation.

Hypothesis 13

Hypothesis 13 stated that the presentation of combined lemon odour and tastant affects submental sEMG more compared to water.

Review of Hypothesis 13: This hypothesis was not supported, with the data showing no differences between the two conditions.

Hypothesis 14

Hypothesis 14 stated that the presentation of combined lemon odour and tastant affects lingual swallowing pressure more compared to water.

Review of Hypothesis 14: This hypothesis was partially supported. The amplitude of anterior lingual pressure and duration of middle lingual swallowing pressures were increased when combined lemon smell and taste stimulation was compared to water.

Hypothesis 15

Hypothesis 15 stated that the presentation of combined lemon odour and tastant affects pharyngeal pressures and the UES more compared to water.

Review of Hypothesis 15: This hypothesis was not supported.

Comments

In contrast to the MEP study where changes were only significant poststimulation, results from the biomechanical study showed that immediate changes occur to facilitate swallowing. Specifically, there was increased pressure and duration of tongue-to-palate contact at the anterior tongue, which is similarly reported by other researchers when sour taste was presented (Pelletier & Dhanaraj, 2006). The discrepancy between the two current studies may be explained by the methods used during recordings of the outcome measures; participants were instructed to limit tongue movement in the MEP study as opposed to the biomechanical study where no such instruction was given. Furthermore, the MEP study measured neural excitability as opposed to the biomechanical study which measured the functional use of swallowing muscles. These are related but clearly do not have a one-to-one equivalence. Nevertheless, the main aim of this project was to evaluate the effectiveness of sensory stimulation as a tool for rehabilitation of patients with dysphagia—in particular, long-term effect of stimulation—which was significant in the two studies. The inability to detect differences during stimulation in the MEP study may have been due to the relatively small sample size used in this study. However, the sample size was based on a priori data analysis using data from a previous MEP study (Doeltgen, 2009).

6.3   A Proposed Model for Sensory Integration in the

Neural Control of Swallowing

The findings from both the MEP and biomechanical studies following combined olfactory and gustatory stimulation are summarized in Table 17.

Table 17

Summary of significant findings from the MEP and biomechanical studies for combined stimulation

Measures	Immediate effects		Late effects	
	Amplitude	Temporal	Amplitude	Temporal
MEP study				
Submental MEP	-	-	Increased	-
Biomechanical study				
Submental EMG	-	-	-	-
Anterior glossopalatal pressure	Increased	Increased	-	Decreased
Middle glossopalatal pressure	-	-	Decreased	Decreased
Oropharyngeal pressure	-	-	-	-
Hypopharyngeal pressure	Decreased	-	-	-
Dynamics of the UES	-	-	-	-

No immediate effect of sensory stimulation was recorded in the MEP study. In contrast, the biomechanical changes seen during sensory stimulation were increased in the amplitude and duration of tongue-to-palate contact at anterior tongue and decreased pressure at the hypopharynx. Late effects seen in the MEP study were increased submental MEP amplitudes following sensory stimulation compared to baseline. The submental sEMG measures from the biomechanical study showed a trend towards increased duration following simultaneous odour and tastant stimulation compared to no stimulation; however, it was not significant. It was proposed that increased NTS activation plays a role in the changes seen in this study. Other poststimulation changes seen in the biomechanical study were decreased

amplitude of middle glossopalatal contact and decreased duration of anterior and middle tongue-to-palate contact, which have been previously discussed (Section 5.6.8).

This research provides new information on the role of smell and taste in swallowing modulation. Based on results from this project, an enhanced model for the neural control of swallowing is proposed as in Figure 28.
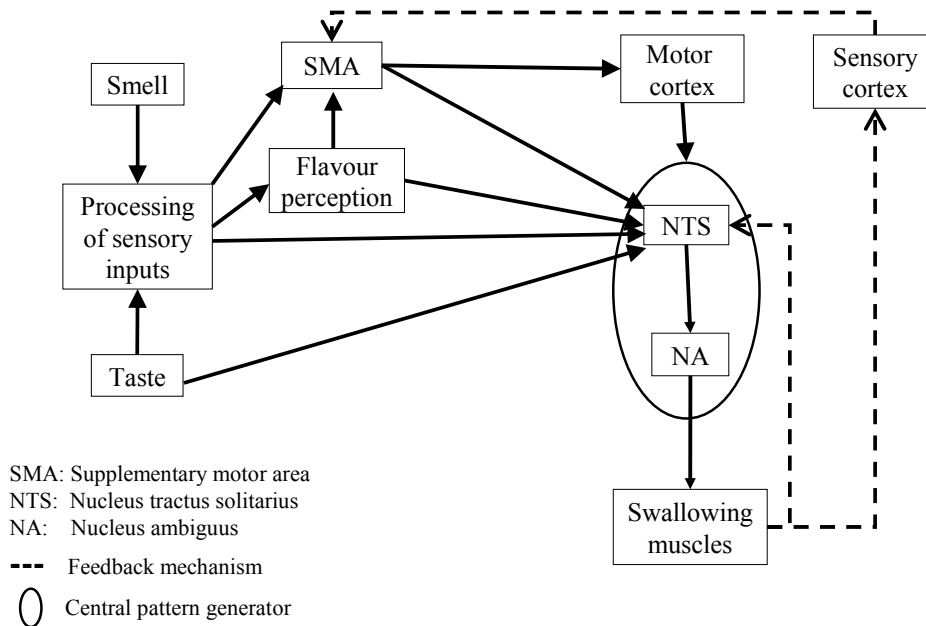
Figure 28. Proposed model for neural control of swallowing following sensory stimulation.

The presentation of stimuli will increase the processed information that feed into the NTS (Ding, et al., 2003; Leow, et al., 2007; Logemann, et al., 1995; Pelletier & Dhanaraj, 2006; Pelletier & Lawless, 2003). The NTS also receives direct taste stimulation from the cranial nerves (Miller, 1999; Rolls, 1998). The processed sensory input will simultaneously be transmitted to the supplementary motor area (SMA), which will then integrate the information into the motor plan and convey the adapted motor plan to the motor cortex. Additionally, sensory information from the muscles involved in swallowing may directly communicate with the sensory cortex. Indeed, it has been shown that excitation of the corticobulbar pathway following peripheral stimulation is due to coincident afferent input to the sensorimotor cortex, which then modulates swallowing (Gow et al., 2004). This constitutes a closed-loop sensory feedback system whereby the "feedback is involved in planning an execution

of [the] movement" (Rose & Christina, 2006, p. 5). This information will be used to adapt the motor plan that was previously formed in the SMA. Motor cortex will then execute the adapted motor plan and send that information to the CPG. Sensory information from the muscles may also directly influence the NTS to further modulate the swallowing performance. NTS also receives information from the insula, which is known to be activated during flavour stimulation (Willett et al., 1986). Thus, sensory stimulation is integrated within the motor planning of swallowing to modulate its function.

6.4   Limitations and Critique of Studies

There were some limitations in the two main studies which deserve discussion. The lemon concentrate used in these studies is sour. The use of sour stimuli can increase salivation (Lee & Linden, 1992) and, in turn, the volume of ingested saliva and spontaneous swallowing. However, the increase in saliva flow following lemon juice stimulation is reported to be less than 0.3 ml/30 s (Lee & Linden, 1992). Although bolus volume is known to affect swallowing function, anything less than 1 ml is considered too small to have any effect (Logemann, et al., 1995; Rademaker et al., 1998).

This project evaluated the effects of sensory stimulation on swallowing; thus, measurements were recorded during cued swallowing. Participants were asked to swallow when the recording system is ready. Spontaneous swallowing was not controlled for in the study but MEPs were only recorded when the system was activated by breaching the EMG threshold. By using the same threshold for both swallowing and contraction conditions, it can be assumed that the amount of muscles preactivated when TMS was triggered is the same.

The number of odour molecules stimulating a person's olfactory neurons depends on the concentration of the stimulus. A person may sniff to improve olfaction, as less than 10% of the air we breathe in reaches the olfactory epithelium (Carlson, 2001). Although sniffing may have increased excitation of olfactory neurons, the participants were given instructions to breathe normally through their nose during all procedures to ensure that the amount of odour molecules reaching odour receptors was constant. Therefore, it can be assumed that the odour stimuli

given to participants were equal. However, there may have been some who sniffed the odour, thus getting more sensory neurons activated, which may have caused the neurons to adapt earlier (Cometto-Muniz & Cain, 1995; Coren et al., 2004). Furthermore, as the depth of inspiration could not be controlled or measured, the consistency of inspired volume cannot be assumed.

Only young healthy volunteers were recruited in this project. Although age has been shown to have some effects on swallowing (see Section 2.3.1), elderly participants were not included. Therefore, the findings from the two studies do not necessarily apply to the older population.

6.5 Directions for Future Research

This project has demonstrated the effects of simultaneously presenting odour and tastant on swallowing behaviour. Specifically, combined odour and tastant stimulation can enhance neural excitability and improve some biomechanical aspects of swallowing. However, the participants in these studies were young healthy volunteers and, hence, their swallowing behaviour may not represent swallowing in the elderly population (Dejaeger et al., 1994) who are more at risk of having swallowing disorders (Nicosia et al., 2000; Robbins et al., 1995). Thus, extension of this research to elderly participants is very desirable.

No previous studies have investigated long-term neural effects following flavour stimulation on swallowing function. A study on electrical stimulation therapy for a duration of one hour, five times a week for two weeks, to the neck muscles, showed increased cortical representation using TMS (Oh, Kim, & Paik, 2007). Similar changes are postulated when sensory stimulation is given, which is beneficial in rehabilitation of swallowing disorders as increased cortical representation of swallowing musculature has been correlated with better swallowing performance in poststroke patients with dysphagia (Gallas, et al., 2007). Thus, investigating the effects of smell and taste on swallowing function in patients with dysphagia is highly desirable and could substantially increase our knowledge on sensory manipulation in the treatment of dysphagia.

Only lemon odour and tastant were utilized in the study; therefore, the findings may only be applicable to lemon. Thus, the extension of this research using different flavours is recommended. The use of food in dysphagia therapy has been described as the "ultimate stimuli" by Pelletier (2007, p. 261). She further proposed that "future products may be developed that are not only palatable but also increase safe swallowing just by eating or drinking … [as] starter foods or beverages" (p. 261). Thus, extension of this research to include *therapeutic foods* is strongly recommended.

6.6　Conclusion

This is the first project to investigate the effects of odour and tastant and the combined stimulation of odour and tastant—that is, flavour—on the neural excitability and biomechanics of swallowing. More importantly, this is the first study to demonstrate that the effects of flavour stimulation were present poststimulation, suggesting mechanisms of neural plasticity which may be of great benefit in the rehabilitation of patients with swallowing problems. Thus, this project provides strong justification for the use of combined smell and taste in the rehabilitation of patients with dysphagia.

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Appendices

Appendix A: Visual analogue scale used in the Pilot Study

Smell stimuli

0% smell stimulus   Cough? YES / NO

Not perceived _____ Strongly
                                                                perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

100% smell stimulus   Cough? YES / NO

Not perceived _____ Strongly
                                                                perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Smell stimulus 1: (%)   Cough? YES / NO

Not perceived _____ Strongly
                                                                perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Smell stimulus 2: (%)   Cough? YES / NO

Not perceived _____ Strongly
                                                                perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Smell stimulus 3: (%)   Cough? YES / NO

Not perceived _____ Strongly
                                                                 perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Smell stimulus 4: (%)   Cough? YES / NO

Not perceived _____ Strongly
                                                                 perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Smell stimulus 5: (%)   Cough? YES / NO

Not perceived _____ Strongly
                                                                 perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Smell stimulus 6: (%)   Cough? YES / NO

Not perceived _____ Strongly
                                                                  perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Taste stimuli

0% taste stimulus Gag? YES / NO

Not perceived _____ Strongly
perceived

Unpleasant _____ Pleasant

Intolerable _____ Tolerable

100% taste stimulus Gag? YES / NO

Not perceived _____ Strongly
perceived

Unpleasant _____ Pleasant

Intolerable _____ Tolerable

Taste stimulus 1: (%) Gag? YES / NO

Not perceived _____ Strongly
perceived

Unpleasant _____ Pleasant

Intolerable _____ Tolerable

Taste stimulus 2: (%) Gag? YES / NO

Not perceived _____ Strongly
perceived

Unpleasant _____ Pleasant

Intolerable _____ Tolerable

Taste stimulus 3: (%)   Gag? YES / NO

Not perceived _____ Strongly
                                                                 perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Taste stimulus 4: (%)   Gag? YES / NO

Not perceived _____ Strongly
                                                                 perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Taste stimulus 5: (%)   Gag? YES / NO

Not perceived _____ Strongly
                                                                 perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Taste stimulus 6: (%)   Gag? YES / NO

Not perceived _____ Strongly
                                                                 perceived

Unpleasant   _____ Pleasant

Intolerable   _____ Tolerable

Appendix B

Paper published on the MEP study

Effects of olfactory and gustatory stimuli on neural excitability for swallowing

- Norsila Abdul Wahab[a, b, c,] 📧,
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Abstract

This project evaluated the effects of olfactory and gustatory stimuli on the amplitude and latency of motor-evoked potentials (MEPs) from the submental muscles when evoked by transcranial magnetic stimulation (TMS). Sixteen healthy volunteers (8 males; age range 19–43) participated in the study. Lemon concentrate at 100% and diluted in water to 25% were presented separately as odor and tastant stimuli. Tap water was used as control. 15 trials of TMS-evoked MEPs triggered by volitional contraction of the submental muscles and volitional swallowing were measured at baseline, during control condition, during stimulus presentation, and immediately, 30-, 60-, and 90-min poststimulation for each of the four stimulus presentations. Experiments were repeated using the combined odor and tastant concentrations that most influenced the MEP independently. Differences in MEP amplitude measured during swallowing were seen at 30-, 60-, and 90-min poststimulation for simultaneous olfactory and gustatory stimulation as opposed to no differences seen at any point for stimuli presented separately. This study has shown that combined odor and tastant stimulation (i.e., flavor) can increase MEP amplitude during swallowing and that this enhancement of MEP can persist for at least 90 min following stimulation. As increased MEP amplitude has been associated with improved swallowing performance, a follow-up study is underway to determine the biomechanical changes produced by altered MEPs to facilitate translation of these data to clinical dysphagia management.

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Appendix C: Advertisement flyer for the MEP study

Research Participants needed

The University of Canterbury Swallowing Rehabilitation Research Laboratory

is looking for participants for a study to investigate

Effects of Smell and Taste on Neural Transmission Associated with Swallowing

We are looking for healthy men and women

aged 18-60 years

This study will take place at the Van der Veer Institute for Parkinson's & Brain Research, 66 Stewart Street, Christchurch, New Zealand.
This study includes 5 sessions of approximately 3 hours duration each.
If you are interested and would like more information, please contact

Norsila Abdul Wahab
Phone: 03 378 6098
Mobile: 021 137 2929
nba38@student.canterbury.ac.nz

Dr. Maggie-Lee Huckabee
Phone: 03 378 6070
Mobile: 021 324 616
Maggie-lee.huckabee@canterbury.ac.nz

This project has been reviewed and approved by the Upper South B Regional Ethics Committee
Advertisement Version 1, January 2008

Swallowing Research
Norsila 378 6098
nba38@student.canterbury.ac.nz

(tear-off strips repeated):

Swallowing Research
Norsila 378 6098
nba38@student.canterbury.ac.nz

Appendix D: Information sheet for MEP study

Research Title:

Effects of smell and taste on neural transmission associated with swallowing

Principal Investigator:

Norsila Binti Abdul Wahab

Ph.D. Candidate, Department of Communication Disorders

University of Canterbury

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart Street, Christchurch, New Zealand

(03) 378 6098

Co-Investigators:

Maggie-Lee Huckabee, PhD

Senior lecturer, Department of Communication Disorders

University of Canterbury

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart Street, Christchurch, New Zealand

(03) 378 6070

Richard Jones, BE(Hons), ME, PhD, FACPSEM, FIPENZ, SMIEEE, FAIMBE

Biomedical Engineer & Neuroscientist, Department of Medical Physics and Bioengineering, Canterbury District Health Board.

Research Director - Brain Research Division,

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart Street, Christchurch, New Zealand

(03) 378 6077

Introduction and aims of the project:

You are invited to participate in a research project that evaluates the effects of smell and taste on swallowing function. The aim of this project is to provide important information about the influence of smell and taste on how the brain controls swallowing. A fuller understanding of how the brain coordinates and controls swallowing promises opportunities for improved therapy approaches for swallowing impairment resulting from various brain disorders (e.g. stroke, traumatic brain injury, Parkinson's disease). The results of this study will help identify the best way to use stimuli such as smell and taste for treating swallowing disorders.

Taking part in this study is voluntary (your choice) and you can withdraw from the study at any time. Any decision not to participate will not affect your current, continuing or future health care or academic progress. We would appreciate a decision regarding your participation within two weeks. This research is part of the principal investigator's PhD (Doctor of Philosophy) project.

Participant selection:

Your participation in this study is due to your reply to advertisements for research participants. Upon your consent, you will be selected for this study if you are aged between 18 and 65, and have no medical problems that may affect your swallowing. The study will include a total of 16 participants of the same age group who have no swallowing problems and will require 5 sessions of approximately 3 hours duration each.

Exclusion criteria:

You may not be eligible to participate in this study if you have or ever have had any of the following conditions:
- seizure
- stroke
- metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork
- implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines
- frequent or severe headaches
- any brain-related condition or illness that caused brain injury

- any cases of epilepsy in your family
- currently pregnant

Completing a simple questionnaire, called the Transcranial Magnetic Stimulation Adult Safety Screen (TASS), will ensure that inclusion criteria are met and risks are minimised.

The research procedure:

The research will take place at the Van der Veer Institute for Parkinson's and Brain Research. If you agree to participate in the study, the following will occur:

1. You will be given an appointment and asked to come to the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute, 66 Stewart Street, Christchurch.

2. After signing the consent form, you will be asked to complete a standard safety questionnaire to screen for risk of adverse events during the procedures (TASS). You will also be asked to fill in a brief questionnaire regarding your ethnic background and any medical conditions that may affect your swallowing.

3. You will then be seated in a comfortable chair and the researcher will ask you if you are ready to start.

4. A small pair of surface electrodes will be secured underneath your chin and one electrode will be placed over the bony aspect of your jaw using a removable adhesive. We will need to identify the correct amount of muscle contraction to trigger the equipment used in the study. To do this, you will be asked to swallow your saliva 10 times at intervals of approximately one minute. As you do this, the electrodes will measure the amount of electrical activity you generate in your muscles during swallowing. This will enable the researchers to adjust the equipment to your individual muscle activity during swallowing. 70% of the average electrical activity (electromyography; EMG) amplitude will be set as threshold for triggering the magnetic stimulator. The

same procedures will be repeated, but instead of swallowing you only need to contract your muscles under the chin.

5.   We measure the efficiency of the communication between your brain and muscles by measuring the electrical activity in your muscles after your brain is stimulated. Your brain will be stimulated using a technique called transcranial magnetic stimulation (TMS). TMS consists of a figure-of-eight coil that is held over your scalp. When you contract the muscles used for swallowing, the electrical activity in these muscles will trigger this coil to stimulate your brain using a magnetic pulse. This will feel like someone is tapping you on the head but it will not hurt. You may also feel a small twitch in the arm opposite the side of the brain being stimulated. When the magnetic pulse is triggered, your brain sends an electric signal to your muscles, which can then be measured using the electrodes placed under your chin. This signal is called the motor evoked potential, or MEP.

6.   At the beginning of each session we will need to identify which areas of the brain are activated by the magnetic stimulation and how to best apply that stimulation. Starting on the left side of your head, and then moving to the right, several steps need to be taken.

> a.   First, the best area for stimulating brain signals will be identified by measuring the electrical signal in your muscles after magnetic stimulation of your brain. Several places on your scalp will be stimulated which will help us find the place that gives the best response. Once this area has been determined, the position of the coil will be marked on the scalp using a water soluble pen.
>
> b.   Next, we will evaluate how strong the magnetic pulse needs to be to stimulate your brain and what level is best for doing the research. Starting with a very soft 'tap', or magnetic pulse, we will slowly increase the intensity until we determine what the lowest level of stimulation needed to still measure the communication between your brain and your muscles. Then we will increase the intensity until your MEPs do not get any larger.

c.   These steps will be completed on both sides of your head. This will help the researchers identify which side of your brain is involved more in controlling the muscles used for swallowing. All further measurements will then be made on that side of your brain.

d.   In order to assess the effect of smell and taste used in this study, the researchers will measure a total of 15 MEPs for each stimulus under each of these 6 occasions: before, during, immediately after, and at 30 min, 60 min and 90 min after the stimulus presentation. The TMS will be triggered by two different events (swallowing and contracting muscles); therefore all the procedures will be repeated for each stimulus. Two concentrations of a lemon smell will be presented in moist air through plastic tubing placed at the entrance to your nose for the smell stimuli. For the taste stimuli, small strips of paper impregnated with two concentrations of lemon juice concentrate will be placed on your tongue. The concentration of smell and taste stimuli that best excited the neural transmission will then be combined and MEP will again be measured. If no excitation is seen with any of the concentrations, the higher concentration will be combined.

7.   We may not be able to measure MEPs in all volunteers. This is because every brain is slightly different. The procedures explained under points 6a-6c will help us identify if we can use the data recorded from your brain for our study. Should we not be able to use your data for our study, you will not have to return for the other four sessions.

The information gathered during the study will be stored in a computer for analysis. Confidentiality will be assured by assigning you a coded numerical identification and data will be stored in the locked Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute.

Risks and Benefits:

You will be part of a study that contributes important information regarding the rehabilitation of patients with swallowing disorders.

There are some risks associated with participation in this research study. Single pulse TMS which is applied in this study, is thought to carry little risk beyond occasionally causing local discomfort at the site of stimulation and headaches that last for a short while in subjects who are prone to headache. There are conditions that may increase the risk for adverse effects of TMS (e.g. history of: seizures, head injury, stroke). Screening you with the Transcranial Magnetic Stimulation Adult Safety Screen (TASS) will identify if you are at risk beforehand.

You will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. The Van der Veer Institute has equipment for dealing with medical emergencies.

Compensation:

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention, Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigator. If you have questions about ACC, contact your nearest ACC officer or the investigator.

Participation:

If you do agree to take part in this study, you are free to withdraw at any time, without having to give a reason. This will in no way affect any future care or treatment.

Your participation in the study will be stopped should any harmful effects appear or if you feel it is not in your best interest to continue.

Confidentiality:

Research findings will be presented at International Research Meetings and will be submitted for publication in relevant peer-reviewed journals. Additionally, research findings will be made available to the local Canterbury Medical Community through research presentation and regional forums. However, no material which could personally identify you will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked swallowing research laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of 10 years after data collection is completed, at which time they will be destroyed.

With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee.

Results:

You will be offered copies of the final manuscript of this project or a summary in lay language. However, you should be aware that a significant delay may occur between completion of data collection and the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the principal investigator.

Questions:

You can contact the principal investigator if you require any further information about the study. The principal investigator, Norsila Binti Abdul Wahab, can be contacted during work hours at (03) 378 6098 or via email: nba38@student.canterbury.ac.nz

If you need an interpreter, this can and will be provided.

If you have any questions or concerns about your rights as a participant in this research study, you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.

Telephone (NZ wide): 0800 555 050

Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT)

Email (NZ wide): advocacy@hdc.org.nz

This study has received ethical approval from the Upper South B Regional Ethics Committee.

Appendix E: Consent form for MEP study

VAN DER VEER
INSTITUTE
for Parkinson's & Brain Research

CONSENT FORM

The effects of smell and taste on neural transmission associated with swallowing

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Oute mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai

I have read and I understand the Information Sheet dated _____ for volunteers taking part in the study designed to evaluate the effects of smell and taste on swallowing function. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.

I have had this project explained to me by Norsila Binti Abdul Wahab.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my current, continuing or future health care. I understand that if I choose to withdraw from the study, I may also withdraw all information that I have provided.

I understand that the information obtained from this research may be published. However, I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

I understand that the investigation will be stopped if it should appear harmful to me and I know whom to contact if I have any side effects to the study or have any questions about the study.

I understand the potential risks of participation in the study as explained to me by the researcher.

I understand the compensation provisions for this study.

I have had time to consider whether to take part.

I wish to receive a copy of the results / summary of research findings.
YES / NO
* Please note that a significant delay may occur between data collection and publication of the results

I would like the researcher to discuss the outcomes of the study with me.
YES / NO

I, _____ hereby consent to take part in this study.

Signature:_____   Date:_____

Signature of researcher:_____
Name of primary researcher and contact phone numbers:
Norsila Binti Abdul Wahab
Work phone no.: 03 378 6098
Mobile phone no.: 021 137 2929

(Note: A copy of the consent form to be retained by participant)

Appendix F: Health questionnaire

> **QUESTIONNAIRE**
> **EFFECTS OF SMELL AN TASTE ON NEURAL TRANSMISSION**
> **ASSOCIATED WITH SWALLOWING**

Identifying number:_____

Which ethnic group do you belong to:

☐ New Zealand European	Niuean
☐ Maori	Chinese
☐ Samoan	Indian
☐ Cook Island Maori	Tongan
☐ Other _____	

Do you suffer from the effects of any of the following medical problems?

- ☐ Stroke
- ☐ Nasal obstruction/history
- ☐ Heart Attack
- ☐ Asthma
- ☐ Chronic Obstructive Pulmonary Disorder (COPD)
- ☐ Swallowing difficulties
- ☐ Head and/or neck injury
- ☐ Head/ and/or neck surgery
- ☐ Neurological disorders (eg. Multiple Sclerosis etc.)
- ☐ Gastroesophageal Reflux Disease
- ☐ Paralysis of the diaphragm
- ☐ Chronic Fatigue Syndrome
- ☐ Do you have any other medical problems which you feel may impact on your ability to participate?   Yes / No (Please circle one)
  If yes, please describe

_____

Are you currently taking any medications that may affect your swallowing?
Yes / No   (Please circle one)
If yes, please describe
_____

Appendix G: TMS safety screen

Transcranial Magnetic Stimulation[†] (TMS) Adult Safety Screen

Name:	
Date:	
Age:	

Please answer the following:

Have you ever:

Had an adverse reaction to TMS?	◯Yes	◯No
Had a seizure?	◯Yes	◯No
Had an electroencephalogram (EEG)?	◯Yes	◯No
Had a stroke?	◯Yes	◯No
Had a serious head injury (include neurosurgery)?	◯Yes	◯No

Do you have any metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork?	◯Yes	◯No
Do you have any implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines?	◯Yes	◯No
Do you suffer from frequent or severe headaches?	◯Yes	◯No
Have you ever had any other brain-related condition?	◯Yes	◯No
Have you ever had any illness that caused brain injury?	◯Yes	◯No
Are you taking any medications?	◯Yes	◯No
If you are a woman of childbearing age, are you sexually active, and if so, are you *not using* a reliable method of birth control?	◯Yes	◯No
Does anyone in your family have epilepsy?	◯Yes	◯No
Do you need further explanation of TMS and its associated risks?	◯Yes	◯No

*If you answered **yes** to any of the above, please provide details (use reverse if necessary):*

_____
_____
_____
_____
_____

[†] *For use with single-pulse TMS, paired-pulse TMS, or repetitive TMS.*

Appendix H: Mean (SD) MEP data for volitional contraction

Stimulus	Time	Amplitude (µV)		Latency (ms)	
		Mean	SD	Mean	SD
Low odour	Baseline	475.9	297.2	9.33	1.05
	Control condition	492.9	293.7	9.27	1.16
	During stimulation	487.9	328.3	9.13	0.84
	Poststimulation	472.0	258.4	9.23	0.96
	30 min post	497.9	260.6	9.34	0.86
	60 min post	539.9	316.8	9.10	0.99
	90 min post	552.4	351.8	9.14	0.97
High odour	Baseline	528.8	381.3	9.53	0.98
	Control condition	517.1	368.6	9.48	1.08
	During stimulation	566.5	449.5	9.48	1.13
	Poststimulation	513.9	402.3	9.56	1.10
	30 min post	539.9	424.5	9.72	1.31
	60 min post	564.6	462.5	9.48	1.04
	90 min post	593.2	418.8	9.16	0.92
Low tastant	Baseline	565.4	322.1	9.19	0.80
	Control condition	532.5	309.7	9.41	0.79
	During stimulation	545.4	309.9	9.36	0.95
	Poststimulation	556.6	379.8	9.08	0.89
	30 min post	549.4	360.3	8.95	0.83
	60 min post	584.8	414.9	8.97	1.15
	90 min post	589.4	413.4	8.97	1.14
High tastant	Baseline	514.7	369.2	9.27	0.95
	Control condition	530.2	292.8	9.36	0.78
	During stimulation	564.2	304.2	9.11	1.04
	Poststimulation	565.0	381.8	9.32	1.06
	30 min post	567.8	392.9	9.48	1.76
	60 min post	512.8	331.8	9.47	1.38
	90 min post	545.7	348.8	9.35	1.00
Combined stimulation	Baseline	601.4	263.2	9.46	0.84
	Control condition	673.7	271.2	9.33	0.78
	During stimulation	627.7	270.9	9.51	0.89
	Poststimulation	616.8	340.0	9.34	0.78
	30 min post	624.2	381.8	9.29	0.85
	60 min post	551.8	285.4	9.36	1.03
	90 min post	590.1	325.1	9.50	0.94

Appendix I: Mean (SD) MEP data for volitional swallowing

Stimulus	Time	Amplitude (μV)		Latency (ms)	
		Mean	SD	Mean	SD
Low odour	Baseline	453.0	205.1	8.64	0.63
	Control condition	421.0	182.7	8.58	0.43
	During stimulation	412.5	120.1	8.83	0.75
	Poststimulation	416.4	168.5	8.76	0.68
	30 min post	382.1	122.5	8.88	0.46
	60 min post	453.9	179.6	8.34	0.56
	90 min post	449.0	176.1	8.59	0.69
High odour	Baseline	454.1	313.5	9.83	1.60
	Control condition	418.7	235.0	10.0	1.38
	During stimulation	397.7	236.8	9.74	1.15
	Poststimulation	475.5	272.6	9.56	1.22
	30 min post	468.9	244.4	9.82	1.14
	60 min post	444.9	246.2	9.59	1.16
	90 min post	523.3	246.2	9.26	1.07
Low tastant	Baseline	453.5	203.0	9.52	0.93
	Control condition	460.6	151.1	9.59	1.04
	During stimulation	442.7	154.4	9.76	1.09
	Poststimulation	492.7	297.5	9.73	1.12
	30 min post	473.6	219.1	9.18	0.99
	60 min post	437.4	192.7	9.21	1.05
	90 min post	488.6	237.0	9.36	1.15
High tastant	Baseline	395.7	146.9	9.43	1.14
	Control condition	440.5	110.2	9.78	1.31
	During stimulation	442.1	146.5	9.42	1.11
	Poststimulation	413.4	144.6	9.18	1.33
	30 min post	398.0	146.3	9.10	1.42
	60 min post	384.9	158.2	9.00	1.48
	90 min post	355.5	122.0	9.35	1.27
Combined stimulation	Baseline	440.1	180.0	9.40	0.85
	Control condition	496.5	189.1	9.12	0.85
	During stimulation	464.7	148.8	9.14	1.22
	Poststimulation	494.6	233.5	9.29	1.23
	30 min post	508.8	206.8	9.05	1.13
	60 min post	537.6	245.0	9.17	1.39
	90 min post	538.0	230.9	9.05	1.04

Appendix J

Paper published on the biomechanical study

Effects of olfactory and gustatory stimuli on the biomechanics of swallowing

- Norsila Abdul Wahab[a, b, c], 👤, ✉,
- Richard D. Jones[a, b, d],
- Maggie-Lee Huckabee[a, b]

- [a] Van der Veer Institute for Parkinson's and Brain Research, Christchurch 8011, New Zealand

- [b] Department of Communication Disorders, University of Canterbury, Christchurch 8140, New Zealand

- [c] School of Dental Sciences, Universiti Sains Malaysia Health Campus, Kota Bharu 16150 Kelantan, Malaysia

- [d] Department of Medical Physics & Bioengineering, Christchurch Hospital, Christchurch 8011, New Zealand

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Abstract

We have previously documented increased amplitude of motor-evoked potentials (MEPs) from the submental muscles during volitional swallowing following simultaneous odor and tastant stimulation. The MEP denotes neural excitability from the motor cortex to the target muscle(s). However, it is unknown if changes in the MEP transfer to the swallowing muscles to facilitate improved swallowing. Thus, we sought to evaluate changes in the biomechanics of swallowing following stimulation protocols that are known to influence neural excitability. Sixteen healthy participants were exposed to low and high concentrations of lemon odor and tastant. The odor and tastant concentrations which produced the highest amplitude of submental electromyography (EMG) were then combined for simultaneous stimuli presentation. Outcome measures included EMG from the submental muscles, as well as lingual and pharyngeal manometry. Poststimulation results showed decreased midglossopalatal pressure at 30 min and decreased duration at anterior and midglossopalatal pressure and increased EMG duration at 60 min. This study strengthens the justification for the use of flavor in managing patients with dysphagia as long-term changes were present in the poststimulation period.

Research Highlights

► Swallowing can be modulated by sensory stimulation. ► Smell and taste—i.e., flavor—can influence swallowing biomechanics. ► The findings justify the use of flavor stimulation in dysphagia rehabilitation.

Keywords

- Olfaction;
- Gustation;
- Deglutition;
- Sour;
- Electromyography;
- Lingual pressure;
- Manometry

Appendix K: Advertisement flyer for biomechanical study

Research Participants needed

**The University of Canterbury Swallowing Rehabilitation Research Laboratory
is looking for participants for a study to investigate**

The Effects of Smell and Taste on Swallowing

**We are looking for healthy men and women
aged 18-60 years**

This study will take place at the **Van der Veer Institute for Parkinson's & Brain Research, 66 Stewart Street, Christchurch, New Zealand.** This is a **one session** study of approximately **2 hours** duration. We will evaluate the influence of smell and taste on the pressure generated by the tongue and throat muscles during swallowing. The results of this study will help identify the best way to use stimuli such as smell and taste for treating swallowing disorders. If you are interested and would like more information, please contact:

Norsila Abdul Wahab
Phone: 03 378 6098
Mobile: 021 137 2929
nba38@student.canterbury.ac.nz

Dr. Maggie-Lee Huckabee
Phone: 03 378 6070
Mobile: 021 324 616
maggie-lee.huckabee@canterbury.ac.nz

**This project has been reviewed and approved by the Upper South A Regional Ethics Committee
Advertisement January 2009**

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Appendix L: Information sheet for biomechanical study

INFORMATION SHEET FOR HEALTHY PARTICIPANTS

Research Title:

The effects of smell and taste on swallowing

Principal Investigator:

Norsila Binti Abdul Wahab

Ph.D. Candidate, Department of Communication Disorders

University of Canterbury

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart Street, Christchurch, New Zealand

(03) 378 6098

Co-Investigators:

Maggie-Lee Huckabee, PhD

Senior lecturer, Department of Communication Disorders

University of Canterbury

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart Street, Christchurch, New Zealand

(03) 378 6070

Richard Jones, BE(Hons), ME, PhD, FACPSEM, FIPENZ, SMIEEE, FAIMBE

Senior Biomedical Engineer & Neuroscientist

Department of Medical Physics & Bioengineering

Canterbury District Health Board

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart Street, Christchurch, New Zealand

(03) 378 6077

Introduction and aims of the project:

You are invited to participate in a research project that evaluates the effects of smell and taste on swallowing function. The aim of this project is to provide important information about the influence of smell and taste on the pressure generated by the tongue and throat muscles during swallowing. These pressures are part of the determining factors of a successful swallow. The results of this study will help identify the best way to use stimuli such as smell and taste for treating swallowing disorders.

Taking part in this study is voluntary and you can withdraw from the study at any time. Any decision not to participate will not affect your current, continuing, or future health care or academic progress. We would appreciate a decision regarding your participation within two weeks. This research is part of the principal investigator's PhD project.

Participant selection:

Your participation in this study is due to your reply to advertisements for research participants. Upon your consent, you will be selected for this study if you are aged between 18 and 65, and have no medical problems that may affect your swallowing. The study will include a total of 16 participants of the same age group who have no swallowing problems and will require a session of approximately 3 hours duration.

The research procedure:

The research will take place at the Van der Veer Institute for Parkinson's and Brain Research. If you agree to participate in the study, the following will occur:

1. You will be given an appointment and asked to come to the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute, 66 Stewart Street, Christchurch.

2. After signing the consent form, you will be asked to complete a brief medical questionnaire to confirm that you meet the inclusion criteria to participate in the study.

3. You will then be seated in a comfortable chair and the researcher will ask you if you are ready to start. The surface under your chin will be cleaned with alcohol and a patch will be secured underneath your chin using a

plaster-like adhesive. This patch contains small discs (electrodes) that measure the amount of electricity in the muscles under your skin.

4. A very thin tube (2.1 mm in diameter) will be placed in your nose. As the tube reaches the back of your nose at the top of your throat you will be handed a glass of tap water and asked to rapidly drink the water through a straw. In doing so, the tube will be swallowed into your oesophagus. You will be asked to swallow until the tube has been pulled down 40 cm as measured from the tip of the nose. The tube will then be slowly pulled out again until it is in the appropriate location to measure the information needed for this study. During this procedure, you will be asked not to swallow, speak, or cough. When the tube is correctly placed in your throat, it will be taped securely to the external nose with adhesive tape. This tube will measure the amount of muscle activity and the amount of pressure created in your throat during swallowing.

5. Next, a small strip of soft plastic will be secured to the roof of your mouth using a removable adhesive. The strip has sensors to measure the amount of pressure created by your tongue during swallowing.

6. You will then be asked to complete five repetitions of each research tasks:

    i. relaxed dry (saliva) swallows

    ii. dry swallows during random presentation of either smell or taste stimuli. 25% and 100% concentration of commercially-available lemon concentrate will be used as the smell and taste stimuli. The lemon smell will be presented in moist air through plastic tubing placed at the entrance to your nose; small strips of paper soaked with lemon juice concentrate will be placed on your tongue as the taste stimulus.

    iii. dry swallows during presentation of combined smell and taste stimuli that best stimulate your swallowing in 6b when presented on its own. If no effect was seen, the high concentration will be used.

    iv. dry swallows 30-, 60-, and 90-min after the procedures in 6c.

7. When you have finished these swallows, the equipment will be removed and you are free to go. The information from the electrodes and the tube will be stored on the swallowing workstation for subsequent analysis. No

audio- or video-recordings of the testing session will be made. The only data recorded will be the line tracings that represent the pressure in your mouth and throat, and the electrical activity in the muscles under your chin. Confidentiality will be assured by assigning you a coded numerical identification and data will be stored in the locked Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute.

Risks and Benefits:

There will be no direct benefit to you but you will be part of a study that contributes important information regarding the rehabilitation of patients with swallowing disorders.

There are no documented complications of pharyngeal manometry (measuring the pressure in the throat) using this small 2.1 mm diameter tube. However, you might experience some very short-lived discomforts associated with the tube, for example, gagging, or nosebleeds.

You will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. Facilities for emergency medical management, including suctioning and intubation, are available in the Swallowing Research Laboratory where the experiment is completed. Further medical help will be available from the patient care wards and the Emergency Cardiac Response team at hospital should any complications arise.

Compensation:

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention, Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigator. If you have questions about ACC, contact your nearest ACC officer or the investigator.

Participation:

If you do agree to take part in this study, you are free to withdraw at any time, without having to give a reason. This will in no way affect any future care or treatment, and/or academic progress (if applicable).

Your participation in the study will be stopped should any harmful effects appear or if you feel it is not in your best interest to continue.

Confidentiality:

Research findings will be presented at International Research Meetings and will be submitted for publication in relevant peer-reviewed journals. Additionally, research findings will be made available to the local Canterbury Medical Community through research presentation and regional forums. However, no material which could personally identify you will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked swallowing research laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of 10 years after data collection is completed, at which time they will be destroyed.

With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee.

Results:

You will be offered copies of the final manuscript of this project or a summary in lay language. However, you should be aware that a significant delay may occur between completion of data collection and the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the principal investigator.

Questions:

You can contact the principal investigator if you require any further information about the study. The principal investigator, Norsila Binti Abdul Wahab, can be contacted during work hours at (03) 378 6098 or via email: nba38@student.canterbury.ac.nz

If you need an interpreter, this can and will be provided.

If you have any questions or concerns about your rights as a participant in this research study, you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.

Telephone (NZ wide): 0800 555 050

Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT)

Email (NZ wide): advocacy@hdc.org.nz

This study has received ethical approval from the Upper South A Regional Ethics Committee.

Appendix M: *F*- and *p*-values of repeated-measures ANOVAs from the biomechanical study

Outcome measures		Effect	Amplitude		Duration	
			F^a	*p*	F^a	*p*
Submental EMG	Immediate effect	Baseline vs Combined stimulation	0.65	.43	4.17	.06
	Late effect	Time	0.29	.70	1.89	.15
Lingual pressures	Immediate effect	Baseline vs Combined stimulation	0.24	.63	2.90	.11
		Anterior vs Middle tongue	0.07	.80	**5.53**	**.03***
		Condition*Tongue	**26.28**	**< .0001***	**53.70**	**< .0001***
	Late effect	Time	2.12	.14	2.27	.12
		Anterior vs Middle tongue	1.13	.30	0.41	.53
		Time*Tongue	2.16	.11	2.76	.053
Pharyngeal pressures	Immediate effect	Baseline vs Combined stimulation	**5.01**	**.04***	3.00	.11
		Sensors 1 vs 2	1.49	.24	**20.99**	**< .0001***
		Condition*Sensor	**8.21**	**.01***	1.93	.19
	Late effect	Time	0.34	.70	**3.38**	**.03***
		Sensors 1 vs 2	**4.53**	**.05***	**21.30**	**< .0001***
		Time*Sensor	1.06	.36	0.42	.74
Peak-to-peak duration	Immediate effect	Baseline vs Combined stimulation	-	-	2.92	.11
	Late effect	Time	-	-	1.40	.26
UES	Immediate effect	Baseline vs Combined stimulation	0.09	.77	2.21	.10
	Late effect	Time	0.28	.76	0.22	.65

Note: Where sphericity is assumed, F^a for EMG and UES analyses = $F(1, 15)$ for immediate effect and $F(3, 45)$ for late effect. F^a for lingual pressures = $F(1, 15)$ for immediate effect and main effect in the analyses for late effect; $F(3, 45)$ in the interaction Time*Tongue for late effect. *p < .05.

Appendix N: Paired *t*-test results comparing (a) baseline versus during stimulation and (b) baseline versus poststimulation for both amplitude and duration of sEMG

EMG at baseline compared with:	Amplitude		Duration	
	$t(15)$	p value	$t(15)$	p value
Control odour	1.31	.21	1.22	.24
Low odour	0.57	.58	0.39	.70
High odour	0.28	.78	0.58	.57
Control tastant	0.49	.63	1.33	.20
Low tastant	0.95	.36	1.13	.28
High tastant	1.09	.29	1.32	.21
Combined stimulation	0.81	.43	2.04	.06
30 min post	0.74	.47	1.37	.19
60 min post	0.13	.90	2.13	.05
90 min post	0.59	.57	0.46	.65

Appendix O: Paired *t*-test results comparing (a) baseline versus during stimulation and (b) baseline versus poststimulation for both amplitude and duration of lingual pressures

Lingual pressures at baseline compared with:	Amplitude		Duration	
	t(15)	*p* value	*t*(15)	*p* value
Anterior tongue				
Control odour	0.07	.95	0.13	.90
Low odour	0.31	.76	0.97	.35
High odour	0.69	.50	0.15	.88
Control tastant	1.24	.23	**3.53**	**.003***
Low tastant	1.60	.13	**4.12**	**.001***
High tastant	**2.57**	**.02***	**3.21**	**.006***
Combined stimulation	**2.55**	**.02***	**2.85**	**.01***
30 min post	1.19	.25	1.00	.33
60 min post	0.21	.84	**2.32**	**.04***
90 min post	0.02	.99	2.04	.06
Middle tongue				
Control odour	1.08	.30	0.83	.42
Low odour	1.24	.23	0.43	.67
High odour	0.26	.80	0.37	.72
Control tastant	0.50	.62	1.21	.25
Low tastant	0.46	.65	**2.69**	**.02***
High tastant	0.35	.73	1.06	.30
Combined stimulation	1.29	.22	0.27	.79
30 min post	**3.22**	**.006***	0.95	.36
60 min post	1.91	.08	**2.16**	**.05***
90 min post	1.90	.08	0.78	.45

*p < .05.

Appendix P: Paired *t*-test results comparing (a) baseline versus during stimulation and (b) baseline versus poststimulation for both amplitude and duration of pharyngeal manometry

Pharyngeal pressures at baseline compared with stimuli	Amplitude		Duration	
	t(15)	*p* value	*t*(15)	*p* value
Sensor 1				
Control odour	0.33	.75	1.22	.24
Low odour	1.49	.16	0.93	.37
High odour	0.62	.54	1.30	.21
Control tastant	0.37	.71	**3.01**	**.009***
Low tastant	0.11	.92	**2.31**	**.04***
High tastant	0.40	.69	**3.55**	**.003***
Combined stimulation	0.04	.97	1.93	.07
30 min post	0.28	.79	1.47	.16
60 min post	0.11	.91	1.75	.10
90 min post	0.46	.65	0.10	.92
Sensor 2				
Control odour	0.31	.77	0.04	.99
Low odour	0.37	.72	0.50	.62
High odour	0.61	.55	0.99	.34
Control tastant	0.11	.91	1.53	.15
Low tastant	0.42	.68	**3.82**	**.002***
High tastant	1.27	.23	2.04	.06
Combined stimulation	**3.19**	**.006***	0.92	.37
30 min post	0.78	.45	0.18	.86
60 min post	0.61	.55	0.45	.66
90 min post	0.27	.79	0.96	.35

Pharyngeal pressures at baseline compared with stimuli	Amplitude		Duration	
	$t(15)$	p value	$t(15)$	p value
Sensor 3				
Control odour	1.03	.32	1.58	.13
Low odour	0.59	.56	0.53	.61
High odour	0.70	.49	0.88	.39
Control tastant	0.28	.78	2.12	.05
Low tastant	0.56	.58	0.94	.36
High tastant	1.28	.22	0.62	.55
Combined stimulation	0.29	.77	0.47	.65
30 min post	0.35	.73	0.11	.91
60 min post	0.38	.71	1.73	.10
90 min post	0.21	.84	0.81	.43
Duration from peak of sensor 1 to peak of sensor 2				
Control odour	-	-	**3.28**	**.005***
Low odour	-	-	1.62	.13
High odour	-	-	1.40	.18
Control tastant	-	-	0.53	.60
Low tastant	-	-	**2.22**	**.04***
High tastant	-	-	1.92	.07
Combined stimulation	-	-	1.71	.11
30 min post	-	-	1.00	.32
60 min post	-	-	0.62	.55
90 min post	-	-	1.75	.10

*$p < .05$.

Appendix Q: Information sheet for supplementary study

INFORMATION SHEET

Research Title: The effects of smell and taste on swallowing: Supplementary study

Principal Investigator:

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Canterbury District Health Board

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66 Stewart Street, Christchurch, New Zealand

(03) 378 6077

Introduction and aims of the project:

You are invited to participate in a research project that evaluates the effects of measurement of smell and taste on swallowing function. The specific aim of this project is to determine if the presence of nasal cannula (tube) used to present smell, and filter paper used to present taste, influences the pressures generated by the tongue and throat muscles during swallowing. These pressures are part of the determining factors of successful swallowing.

Taking part in this study is voluntary and you can withdraw from the study at any time. Any decision not to participate will not affect your current, continuing, or future health care or academic progress. We would appreciate a decision regarding your participation within two weeks. This research is part of the principal investigator's PhD project.

Participant selection:

Your participation in this study is due to your reply to advertisements for research participants. Upon your consent, you will be selected for this study if you are aged between 18 and 65, and have no medical problems that may affect your swallowing. The study will include a total of 12 participants of the same age group who have no swallowing problems and will require a single session of approximately 30 minutes.

The research procedure:

The research will take place at the Van der Veer Institute for Parkinson's and Brain Research. If you agree to participate in the study, the following will occur:

1. You will be given an appointment and asked to come to the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute, 66 Stewart Street, Christchurch.

2. After signing the consent form, you will be asked to complete a brief medical questionnaire to confirm that you meet the inclusion criteria to participate in the study.

3. You will then be seated in a comfortable chair and the researcher will ask you if you are ready to start. The surface under your chin will be cleaned with alcohol and a patch will be secured underneath your chin using a plaster-like

adhesive. This patch contains small discs (electrodes) that measure the amount of electricity in the muscles under your skin.

4. A very thin tube (2.1 mm in diameter) will be placed in your nose. As the tube reaches the back of your nose at the top of your throat, you will be handed a glass of tap water and asked to rapidly drink the water through a straw. In doing so, the tube will be swallowed into your oesophagus. You will be asked to swallow until the tube has been pulled down 30 cm as measured from the tip of the nose. The tube will then be slowly pulled out again until it is in the appropriate location to measure the information needed for this study. During this procedure, you will be asked not to swallow, speak, or cough. When the tube is correctly placed in your throat, it will be taped securely to the external nose with adhesive tape. This tube will measure the amount of muscle activity and the amount of pressure created in your throat during swallowing.

5. Next, a small strip of soft plastic will be secured to the roof of your mouth using a removable adhesive. The strip has sensors to measure the amount of pressure created by your tongue during swallowing.

6. You will then be asked to complete five repetitions of each research task, which will be randomly presented:

    a. relaxed dry (saliva) swallows

    b. dry swallows during simultaneous presentation of combined smell and taste stimuli. Commercially-available lemon concentrate at 25% concentration will be used as the smell and taste stimuli. The lemon smell will be presented in moist air through plastic tubing placed at the entrance to your nose; small strips of paper soaked with lemon juice concentrate will be placed on your tongue as the taste stimulus.

    c. dry swallows with water mist and filter paper moistened with water as a control condition.

7. When you have finished these swallows, the equipment will be removed and you are free to go. The information from the electrodes and the tube will be stored on the swallowing workstation for subsequent analysis. No audio- or video-recordings of the testing session will be made. The only data recorded will be the line tracings that represent the pressure in your mouth and throat, and the electrical activity in the muscles under your chin. Confidentiality will

be assured by assigning you a coded numerical identification and data will be stored in the locked Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute.

Risks and Benefits:

There will be no direct benefit to you but you will be part of a study that contributes important information regarding the rehabilitation of patients with swallowing disorders.

There are no documented complications of pharyngeal manometry (measuring the pressure in the throat) using this small 2.1 mm diameter tube. However, you might experience some very short-lived discomforts associated with the tube, for example, gagging, or nosebleeds.

You will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. Facilities for emergency medical management, including suctioning and intubation are available in the Swallowing Research Laboratory where the experiment is completed. Further medical help will be available from the patient care wards and the Emergency Cardiac Response team at hospital should any complications arise.

Compensation:

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention, Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigator. If you have questions about ACC, contact your nearest ACC officer or the investigator.

Participation:

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Confidentiality:

Research findings will be presented at International Research Meetings and will be submitted for publication in relevant peer-reviewed journals. Additionally, research findings will be made available to the local Canterbury medical community through research presentation and regional forums. However, no material which could personally identify you will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked swallowing research laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of 10 years after data collection is completed, at which time they will be destroyed.

With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee.

Results:

You will be offered copies of the final manuscript of this project or a summary in lay language. However, you should be aware that a significant delay may occur between completion of data collection and the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the principal investigator.

Questions:

You can contact the principal investigator if you require any further information about the study. The principal investigator, Norsila Binti Abdul Wahab, can be contacted during work hours at (03) 378 6098 or via email: nba38@uclive.ac.nz

If you need an interpreter, this can and will be provided.

If you have any questions or concerns about your rights as a participant in this research study, you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.

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This study has received ethical approval from the Upper South A Regional Ethics Committee.

Appendix R: Paired *t*-test results comparing control (water) and lemon stimulation for both amplitude and duration of sEMG, lingual pressure, and pharyngeal manometry

	Amplitude		Duration	
	t(11)	*p* value	*t*(11)	*p* value
Submental sEMG	0.56	.59	1.04	.32
Lingual pressure				
Anterior	**2.93**	**.01***	1.73	.11
Middle	1.31	.22	**2.72**	**.02***
Manometry				
Sensor 1	0.65	.53	0.36	.72
Sensor 2	0.52	.61	0.41	.69
Sensor 3	0.23	.82	0.91	.38
Peak-to-peak timing	-	-	0.91	.38

*p < .05.