A computational model quantifies the effect of anatomical variability on velopharyngeal function

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ABSTRACT

Purpose: This study predicts the effects of velopharyngeal (VP) anatomical parameters on VP function to provide a greater understanding of speech mechanics and aid in the treatment of speech disorders.

Methods: We created a computational model of the VP mechanism using dimensions obtained from MRI measurements of 10 healthy adults. The model components included the levator veli palatini (LVP), the velum, and the posterior pharyngeal wall and the simulations were based on material parameters from the literature. The outcome metrics were the VP closure force and LVP muscle activation required to achieve VP closure.

Results: Our average model compared favorably with experimental data from the literature. Simulations of 1,000 random anatomies reflect the large variability in closure forces observed experimentally. VP distance had the greatest effect on both outcome metrics when considering the observed anatomic variability. Other anatomical parameters were ranked by their predicted influences on the outcome metrics.

Conclusions: Our results support the implication that interventions for VP dysfunction that decrease anterior to posterior VP portal distance, increase velar length, and/or increase LVP cross-sectional area may be very effective. Future modeling studies will help to further our understanding of speech mechanics and optimize treatment of speech disorders.
INTRODUCTION

Several studies have examined the variability in velopharyngeal (VP) muscle measures in normal individuals (Perry, Kuehn, Sutton, & Gamage, 2014; Perry, Kuehn, & Sutton, 2013), and yet the direct effects of this variability on normal and abnormal function are not well understood. One study demonstrated a significant gender effect for VP muscles among an adult population (Perry, Kuehn, Sutton, & Gamage, 2014). These findings were not observed in a pre-pubertal child population (N=34) demonstrating gender effects appear to be dependent upon age (Kollara, Perry, & Hudson, 2014). Significant variation in VP muscle anatomy compared to non-cleft anatomy has been associated with hypernasal speech among adults with repaired cleft palate (Ha, Kuehn, Cohen, & Alperin, 2007). Furthermore, variations in cleft infant anatomy compared to non-cleft controls has been demonstrated (Kuehn, Ettema, Goldwasser, & Barkmeier, 2004; Kuehn, Ettema, Goldwasser, Barkmeier, & Wachtel, 2001; Perry, Kuehn, Sutton, Goldwasser, & Jerez, 2011). Understanding the effect of anatomical variability on VP mechanics is essential for developing effective treatments and interventions for VP dysfunction. The development of these treatments can be accelerated by using advanced imaging (Perry et al., 2013; Sutton, Conway, Bae, Seethamraju, & Kuehn, 2010) and computational modeling techniques (Inouye, Pelland, Lin, Borowitz, & Blemker, 2014) that can reveal important insights into the mechanical interactions between VP anatomy and function.

Magnetic resonance imaging (MRI) has been used to study the geometry of the VP mechanism and the surrounding structures (e.g., Akgüner, 1999; Bae, Kuehn, Sutton, Conway, & Perry, 2011; Beer et al., 2004; Kollara & Perry, 2013; Tian & Redett, 2009). Specifically, MRI studies have examined the soft palate (velum), VP port, and the levator veli palatini (LVP) muscle, which is the primary muscle for VP closure. It has been hypothesized that specific dimensional features of VP anatomy are essential to producing VP closure necessary for normal speech
production (Perry et al., 2011; Perry, Sutton, Kuehn, & Gamage, 2014). These MRI studies have identified morphological variations between normal and cleft palate VP anatomy. Perry, Sutton, et al. (2014) used structural and dynamic MRI to assess LVP muscle contraction at the sentence-level with high imaging speeds among 10 children with normal anatomy. These and other recent dynamic imaging advances (e.g., Scott, Boubertakh, Birch, & Miquel, 2013) provide insight into the relationship between VP anatomy and function in normal speech. Because dynamic MRI methods for LVP muscle contractions have been limited to small homogenous sample sizes, studies have been unable to demonstrate a connection between variable anatomies, such as cleft palate anatomy, and the effect of these variations on the VP function.

The use of computational models to investigate form-function relationships and develop treatment protocols has increased dramatically in the last several decades (Inouye et al., 2014; Neptune, 2000; Valero-Cuevas, Hoffmann, Kurse, Kutch, & Theodorou, 2009), and empower us to develop a mechanistically-based understanding of VP function. For example, computational modeling can systematically investigate cause-and-effect relationships that are impossible to accomplish in vivo and/or take decades of clinical trials to elucidate. Previous computational models have provided insight into the mechanics of the VP mechanism (Berry, Moon, & Kuehn, 1999; Inouye et al., 2014; Srodon, Miquel, & Birch, 2012); however, these models have not explored how anatomical variability influences VP function.

The goal of this work is to integrate quantitative anatomical information obtained from MRI and the known properties of the velum (Birch & Srodon, 2009; Cheng, Gandevia, Green, Sinkus, & Bilston, 2011; Ettema & Kuehn, 1994; Kuehn & Kahane, 1990) and skeletal muscle (Blemker, Pinsky, & Delp, 2005; Gordon, Huxley, & Julian, 1966; Zajac, 1989) into a computational model to investigate how variations in VP anatomy across the normal population influences VP function (Figure 1). In particular, this study aimed to i) develop a model that accurately predicts
experimental data, ii) simulate a large sample of random anatomies based on distributions of MRI data collected from adult subjects, and iii) quantify the effects of isolated anatomical parameter changes on VP function.

METHODS

Subjects

In accordance with the local Institutional Review Boards, 10 healthy male subjects with normal anatomy participated in the study. The use of male subjects eliminated the effect of gender, as it has been shown to have a significant effect on VP parameters (Perry, Kuehn, Sutton, Gamage, & Fang, 2014; Perry, Kuehn, Sutton, & Gamage, 2014) and VP function (Kuehn & Moon, 1998; McKerns & Bzoch, 1970). Subjects were Caucasian, native English speakers, and were between 19 and 24 years of age (mean = 21 years; SD = 1.5 years). Subjects displayed normal head and neck anatomy with no history of neurological, swallowing, or hearing abnormalities. Perceptual speech assessments (by a speech language pathologist) confirmed normal speech and oral-to-nasal resonance.

Magnetic resonance imaging

Methods for imaging subjects have been previously described (Perry et al., 2013; Sutton et al., 2010). In brief, subjects were scanned using a Siemens 3 T Trio and a 12-channel head coil. Imaging was obtained in the supine position while subjects were instructed to breathe through their nose with their mouth closed. A Velcro-fastened elastic strap was placed around the subject’s head, passing over the glabella and fastened to the head coil to reduce motion during the scanning session. A high-resolution, T2-weighted turbo-spin-echo anatomical scan, SPACE (Sampling Perfection with Application optimized Contrasts using different flip angle Evolution), was used to acquire three-dimensional data of the oropharyngeal anatomy (dimensions 25.6 X 19.2 X 15.5 cm) with 0.8 mm isotropic resolution with an acquisition time of slightly less than 5 minutes (4:52). Echo time
was 268 milliseconds, and repetition time was 2.5 seconds. Static MRI data were used for the present study to determine the morphology of the VP mechanism among subjects.

**Model creation from MRI measurements**

Measures used in the present study have been previously described and used routinely in studies of the VP mechanism using MRI (Ettema, Kuehn, Perlman, & Alperin, 2002; Ha et al., 2007; Perry et al., 2013; Perry, Sutton, Kuehn, & Gamage, 2014; Tian & Redett, 2009). Measures from the MR images included the LVP, velum, and posterior pharyngeal wall (Figure 2a, Tables 1 and 2). The LVP major and minor axis measurements—antero-to-posterior and superior-to-inferior distances, respectively, as in Perry et al., (2013)—were combined to calculate the cross-sectional area measurement. Values were used to create line segment representations of the velum, LVP, and posterior pharyngeal wall (Figure 2b). Line segment components were oriented in the corresponding MR image planes (Figure 2c) to create a three-dimensional model (Figure 2d).

**Modeling assumptions and intrinsic parameters**

Muscle properties from a previous study (Blemker et al., 2005) were implemented for the LVP, containing both passive (related to passive muscle stretch) and active (related to muscle activation and muscle stretch) nonlinear tensile components. The active tensile component incorporates the known force-length behavior of skeletal muscle (Gordon et al., 1966), where the peak muscle force occurs when the muscle reaches its optimal length (Figure 3) of \( \lambda_{\text{muscle}} = 1 \) (where \( \lambda_{\text{muscle}} \) is the muscle stretch ratio, e.g., \( \lambda_{\text{muscle}} = 1 \) is 100% rest position, no contraction, and \( \lambda_{\text{muscle}} = 0.8 \) is 80% rest position or 20% shortened from rest). Because the muscle fibers run parallel to the line of action of the muscle, we assumed that the maximal muscle force was proportionate to the muscle
cross-sectional area. Cross-sectional area was calculated from the major and minor axis measurements by approximating the cross-section shape as an ellipse:

$$\text{Cross-sectional area} = \frac{\pi}{4} \times \text{Major axis} \times \text{Minor axis}.$$  

We varied the parameter of muscle specific tension (equal to the maximum force per unit area, also called “peak isometric stress”) so the average model (from the 10 subjects) would reproduce previously published experimental data of velopharyngeal closure force (Kuehn & Moon, 1998). In iterating across a range of values, we found that 0.03MPa was able to generate computational data within one standard deviation of all experimental data (Figure 7a). See discussion for further details and a parameter sensitivity analysis.

The velum was modeled as a simple spring with a Young’s modulus of 1kPa (Birch & Srodon, 2009) and a cross-sectional area defined by the multiplication of the velar thickness and the VP width (which we assumed was equal to the velar width). The force exerted by the velum was therefore determined from its extension, with the force equal to

$$F_{\text{velum}} = CSA_{\text{velum}}E_{\text{velum}}(\lambda_{\text{velum}} - 1)$$

where $CSA_{\text{velum}}$ is the velar cross-sectional area, $E_{\text{velum}}$ is the velum stiffness or Young’s modulus, and $\lambda_{\text{velum}}$ is the stretch ratio of the velum.

The posterior pharyngeal wall was modeled as a rigid (non-moving) body (a simplification also employed in Berry et al., 1999) against which the velum would make contact. The width of this contact was set to the VP width measurement. The configurations of the LVP, velum, and posterior pharyngeal wall during LVP relaxation and LVP contraction producing closure were determined (Figure 4a and b) and then the force calculations were based on the geometry of the VP closure configuration and corresponding static force balance (Figure 4c). The force of the velum in the sagittal plane would naturally pull the LVP out of the oblique coronal plane. Therefore, a force equal to the velum force was applied in the downward direction in the sagittal plane to keep the
LVP in the oblique-coronal plane (Figure 4c, sagittal plane). This force represented known contributions (Seaver & Kuehn, 1980) from other soft tissue and palatal muscles that would pull the velum downward (e.g., palatopharyngeus and palatoglossus).

LVP activation, ranging from 0 to 100%, was used as an input variable, and the output quantities of interest were the magnitude of the total force exerted on the posterior pharyngeal wall—VP closure force —and the minimum activation required from the LVP muscle to achieve closure.

*Computational simulations*

We conducted three sets of computational simulations (Figure 5). The first set of “image-based simulations” was composed of 10 models, each from the MR images of the individual subjects. The second set of “randomized simulations” was composed of 1,000 randomized simulations with each parameter drawn independently from a uniform probability distribution varying between the mean ± one standard deviation for each anatomy as in a previous study (Santos & Valero-Cuevas, 2006). The third set of “parameter isolation simulations” consisted of simulations in which each parameter was varied up and down one standard deviation from its mean, holding other parameters at their mean values. These simulations quantified and ranked the importance of each anatomical parameter. Each parameter change affected the model anatomy in different ways, sometimes changing multiple basic measurements simultaneously (Figure 6).

*Definition of anatomical parameter variations*

The anatomical parameter variations in the model were defined such that the combined set of parameters could uniquely define a particular anatomy, and that the anatomical parameters could be varied independently of one another (Figure 6). VP distance (i.e., depth of the VP portal) was
increased by moving the posterior pharyngeal wall posteriorly in the oblique-coronal plane. Extravelar LVP length was increased by moving the points of LVP muscle origin posteriorly in the oblique-coronal plane while keeping the side-to-side distance between points of origin constant. Intravelar LVP length was increased by increasing the width of the intravelar segment while keeping the origin-to-origin distance and extravelar LVP length constant. This moved the points of origin posteriorly in the oblique-coronal plane. VP width was increased by widening the posterior pharyngeal wall contact area. Distance between points of origin was increased while keeping extravelar LVP length constant. The velum-LVP angle was increased by rotating the velum anteriorly in the sagittal plane. Velar length was increased by extending the point of attachment to the hard palate posteriorly and superiorly while keeping the velum-LVP angle constant. Velar thickness was increased in simulation by increasing the velar cross-sectional area. LVP cross-sectional area was increased in simulation by increasing the maximal force of the muscle.

**RESULTS**

The variability of the individual models in the image-based simulations and the randomized simulations mirrors the observed experimental variability (Figure 7a). The standard deviations of the experimental data points are as large as 50% or more of the mean. The individual models also deviate around 50% or more in closure force from the mean. This suggests that the large standard deviations of the experimental data may be a result of anatomic variability. Furthermore, the similar relative variability of closure force in experimental and model data provides further support for the predictive power of the model.

The parameter isolation simulations reveals that decreasing VP distance by one standard deviation increases closure force and decreases minimum activation required more than any other parameter adjustment of one standard deviation from the mean (Figures 8 and 9). This highlights
the importance of VP distance in creating adequate VP closure during speech. The model suggests that increased VP distance may be one of the main contributing factors to velopharyngeal insufficiency.

Following VP distance, the next parameters most influential on closure force differed from those most influential on minimum activation required. Increasing LVP cross-sectional area and extravelar LVP length were the next parameters most influential on VP closure force. Velum-LVP angle and velar length were the next parameters most influential on minimum activation required. Interestingly, the most influential parameters for closure force tended to be those measured in the oblique-coronal plane and related to LVP configuration, while the most influential parameters for minimum activation required tended to be those measured in the sagittal plane and related to velar configuration (Figure 10). VP distance was the most influential predictor of closure force and can be examined in either oblique-coronal or sagittal imaging plane.

DISCUSSION

In this study, we created a computational model of the LVP, velum, and posterior pharyngeal wall using MRI data from 10 adult subjects with normal anatomy to investigate how variability in anatomies affects VP closure. The model was able to predict closure forces that were, on average, consistent with experimental data. Analysis of the model revealed that anatomical variability has a significant impact on VP closure mechanics. In such, the most advantageous anatomies had over twice the closure force of the least advantageous anatomies. Sensitivity analysis of the model reveals that some anatomical parameters have a much greater influence on VP mechanics compared to others, suggesting roles of these parameters of interest in normal and abnormal VP function.

One of our central working assumptions was that a higher closure force and lower minimum activation required are predictors of better VP function, all other variables being equal. If closure
force is higher for a given activation (which our study shows occurs for more advantageous anatomies), then less muscle activation is needed in general to produce the same amount of closure force (Figure 11). This may be important for fatigue avoidance in patients with borderline VP incompetence (Nohara, Tachimura, & Wada, 2006). Furthermore, higher closure force in general should ensure a tighter, more complete VP closure for patients with VP dysfunction. Further validation of these concepts can be achieved in the future by creating models based on anatomical measurements of individuals with VP dysfunction (Drissi et al., 2011; Ha et al., 2007; Ozgür, Tunçbilek, & Cila, 2000). We would predict that, as compared to the normal ranges presented here, closure force would be lower and minimum activation required would be higher in models built from patients with VP dysfunction.

The variability in VP closure metrics for different anatomies in our study is explained by both the geometry of the VP mechanism (Figure 4) and the force-length relationship of the LVP muscle (Figures 3 and 12). For instance, in the case of geometry, if the LVP muscle origin-to-origin distance is decreased, closure force increases (Figures 8 and 9) because of the more favorable angle to produce high closure force. The VP distance had the largest effect on closure force. A large VP distance requires more LVP contraction, thereby decreasing the force capacity of the muscle, and vice-versa (Figure 12). This is due to the intrinsic force-length relationship of muscle.

The geometry and the force-length relationships may also be dependent on each other. For instance, increasing the extravelar LVP length in our model makes the geometry more favorable because the angle of muscle force is more backward and therefore favorable for closure. Furthermore, the amount of muscle contraction (measured by percent of the initial length) required for VP closure is decreased, making the overall LVP muscle force greater.

While we have demonstrated that some parameters are more influential than others, the measurement of a particular influential parameter such as VP distance, LVP cross-sectional area, or
extravelar LVP length is not sufficient to predict the VP closure for a given anatomy due to all of
the other factors. For example, there is a significant scatter of closure forces over the range of the
most important parameters (Figure 13). There exist some anatomies that have the greatest VP
distance (a large disadvantage) but still have higher closure forces than those with the smallest VP
distance (a large advantage). This is because other anatomical factors combine to overcome the
large VP distance. One implication of this is, for instance, that VP depth cannot be measured in
isolation to make inferences about how advantageous the anatomy is to produce VP closure overall.
In contrast, if other factors are held constant, our model predicts that decreasing VP depth (e.g., via
surgery) will in general result in an anatomy more advantaged for VP closure.

One of the assumptions of our study is that the LVP resting length corresponds to the
optimal length of the muscle (i.e., that the muscle sarcomeres are at their optimal length for force
production at rest) (Zajac, 1989). Currently, the resting sarcomere lengths of the LVP muscle are
unknown. However, regardless of the actual starting length of the sarcomeres, the force-generating
capacity of the LVP will be highly sensitive to the amount of contraction, making anatomic
variables that affect the amount of required contraction such as VP distance and extravelar LVP
length very influential.

Of interest, the model predicted variability in closure force that resembled the variability in
the published VP closure force data (Kuehn & Moon, 1998), suggesting that variability in VP
function across individuals may be due to anatomical variability. Other studies have found similar
effects of anatomical variability in the context of speech (Brunner, Fuchs, & Perrier, 2009;
Finkelstein, Talmi, Nachmani, Hauben, & Zohar, 1992; Ha et al., 2007). However, it should be
noted that the measurement variability of the electromyography data and closure force sensors,
gender differences, and minor contributions of other palatal muscles to closure are other factors that
could contribute to the scatter of the data in the experimental study (Kuehn & Moon, 1998), in addition to the anatomical variability.

The simplicity of our model has both significant advantages and drawbacks. Advantages include a low computational cost (enabling a thousand simulations in only a few seconds) and ease of adjusting specific parameters in isolation. The main drawback of this approach is that it necessitates exclusion of several more complex factors such as other muscles’ contributions to closure force, curvature of the intravelar LVP segment, dynamic and viscoelastic effects on tissue deformation, consideration of more complex tissue geometries, pharyngeal wall movement, Passavant’s ridge, and movement of the LVP outside the original oblique-coronal plane. Future research that reduces the computational cost of more complex computational modeling techniques such as finite-element models (Blemker et al., 2005; Inouye et al., 2014) will empower the exploration of these complexities.

Because the musculus uvulae is intrinsic to the velum, a line segment model is not conducive for modeling its contribution to closure using the proposed methods. During VP closure, the musculus uvulae likely facilitates in VP closure by adding stiffness to the nasal velar surface and providing additional muscle bulk to fill the VP gap (M. Huang, Lee, & Rajendran, 1997). It has not be confirmed with imaging data in vivo whether individuals with repaired cleft palate demonstrate a musculus uvulae, although fibers have been distinctly reported in one histologic study of cleft infant specimens (Landes et al., 2012). However, nasendoscopy studies providing an indirect view of the musculus uvulae and other histology studies have suggested an absent or hypoplastic musculus uvulae (Azzam & Kuehn, 1977; Lewin, Croft, & Shprintzen, 1980; Pigott, Bensen, & White, 1969). In normal VP function, the actual closure force and minimum activation required are likely representative of the combined contributions of the LVP and musculus uvulae fibers rather than the LVP alone. The contribution of the musculus uvulae to VP function has never
been quantified and is deserving of further research. However, given its very small size relative to the LVP, we assume that variations in the LVP muscle, velum, and VP port geometry contribute more to our quantitative metrics of closure force and minimum activation required than variations the musculus uvulae.

Assumptions regarding specific parameters in the model – in particular the stiffness of the velum and the specific tension of the LVP muscle – should be considered when interpreting the results of this study. The Young’s modulus of the velar tissue was assumed to be 1kPa, which was based on what was found from *ex vivo* mechanical testing (Birch & Srodon, 2009). Other studies have found a wide range of palate stiffnesses (from approximately 0.5 to 100 kPa, depending on the location in the velum) (Berry et al., 1999; Cheng et al., 2011; L. Huang, 1995; M. Huang, Riski, Cohen, Simms, & Burstein, 1999; Liu, Luo, Lee, & Lu, 2007; Malhotra et al., 2002). Moreover, our use of 0.03MPa for the specific tension of muscle is smaller than reported in previous muscle experimental studies (Fukunaga, Roy, Shellock, Hodgson, & Edgerton, 1996) (0.11-0.47MPa) and used in modeling studies (Arnold, Ward, Lieber, & Delp, 2010; Blemker et al., 2005) (0.3MPa-0.61MPa). This parameter tuning was used to reproduce the experimental data to provide physiological relevance for the predicted results. This necessary tuning could be due in part to muscle activation measurement factors in the experimental data (Kuehn & Moon, 1998) used for comparison, since the activation levels were measured relatively rather than absolutely. For instance, the maximum activation measured experimentally for a subject may have been 20% of physiological maximum, but was reported as 100% activation because the data were normalized. Furthermore, the specific tensions of palate muscles have never been measured, but using 0.03MPa in our models resulted in predictions that correspond well with experimental data. The velum stiffness also plays a role, as simulating a stiffer velum would require more specific tension to stretch the velum for a specific activation.
To quantitatively investigate the model’s dependence on these parameter values, we performed a sensitivity analysis by multiplying the velum stiffness or specific tension by 10x (i.e. 10kPa stiffness and 0.3MPa specific tension). The data for percent decrease in minimum activation required were identical to the nominal results (Figure 9a). Interestingly, for closure force, 10kPa of velar stiffness (10x nominal) combined with 0.03MPa specific tension (nominal) significantly changed the magnitude and the ranked importance of some parameters, but VP distance remained most important for all cases (Figure 14). The magnitudes of all parameter influences were about five times that of nominal with the stiffer velum. For instance, the closure force increases almost 80% when VP distance is decreased by one standard deviation for the stiffer velum, as compared with 18% for the nominal velum stiffness. VP distance remained as the most influential factor, followed by velum-LVP angle, velar length, LVP cross-sectional area, extravelar LVP length, VP width, origin-to-origin distance, velar thickness, and intravelar LVP length. These data suggest that if the velum is stiffer than modeled (e.g., because of increased stiffness in normal individuals or because of the stiffening effects of scar tissue (Birch & Srodon, 2009) in individuals with repaired cleft palate), VP distance, velum-LVP angle, and velar length may be even more influential for closure force than if the velum is more compliant.

The clinical relevance of findings from this study is the potential impact of computational modeling using MRI data in understanding surgical intervention for cleft palate repair and treatment of VP dysfunction. The use of MRI and computational modeling provide a novel method to patient-specific assessments of VP anatomy and the changes required during surgery to create normal VP function for speech. This approach could be used to decrease the overall failure rate (25-35%, McWilliams, 1990) of primary palate repair, thus reducing the need for secondary speech surgeries (e.g., pharyngoplasties). More specifically, the methods in this proposed study can provide insights into which surgical maneuvers are likely contributing to the success of one surgery procedure over
another. Our results suggest that decreased VP distance may be strongly associated with proper VP function. Surgical outcome studies have shown an association of improved speech outcomes with decreased VP portal distance during phonation (Deren et al., 2005) and at rest (Pet et al., 2013). Decreasing VP distance has been proposed through retropositioning and/or overlap of the LVP muscle bundles during cleft palate surgery (Pet et al., 2013; Woo, Skolnick, Sachanandani, & Grames, 2014) and by lengthening the velum through posterior displacement of the LVP muscle bundle (Furlow Jr, 1986; Sommerlad et al., 2002). Also, our results suggest that velar length is very influential for closure force (if velar stiffness is increased, Figure 14), and minimum activation required (Figure 9a), supporting the findings that increased velar length is associated with successful Furlow re-repair procedures (D’Antonio et al., 2000). In general, surgical techniques manipulate multiple anatomical parameters simultaneously (e.g., velar length and VP distance being changed by LVP retropositioning), while some anatomical parameters cannot be practically modified by surgery (e.g., distance between points of origin). Future work will model these possible simultaneous parameter changes in response to surgeries to understand the potential outcomes of various repair techniques with full consideration of cleft palate patient-specific anatomical variations.

Our model shows that increasing LVP cross-sectional area (or strength) can have a large effect on VP closure. One effective non-surgical intervention for the treatment of VPI is continuous positive airway pressure therapy (Kuehn, Moon, & Folkins, 1993). This can be likened to resistance training for the VP muscles, and therefore continuous positive airway pressure therapy may increase the LVP cross-sectional area (or at least LVP strength), improving VP closure. Overlap of the muscle during surgery (Nguyen et al., 2014; Woo et al., 2014) would also increase LVP cross-sectional area in the overlapped segment, possibly leading to increased strength and force
production in that area. Other methods such as drug therapy that may increase LVP cross-sectional area or strength are likely to improve VP closure as well.

Future modeling studies will elucidate the effects of anatomic variations on predicted VP function in populations differing in categories such as gender and race. Our use of male subjects in this study eliminated the effect of gender, as it has been shown to have a significant effect on VP parameters (Perry, Kuehn, Sutton, Gamage, et al., 2014; Perry, Kuehn, Sutton, & Gamage, 2014) and VP function (Kuehn & Moon, 1998; McKerns & Bzoch, 1970). Modeling the differences in VP morphology and function among populations in future studies may reveal the optimality of different surgical procedures for different groups.

We have shown that i) observed anatomical variability in normal adults results in large differences in VP closure, mirroring the high amount of observed experimental closure force variability and ii) VP distance, and LVP cross-sectional area are perhaps the most influential factors on VP closure force in normal adults given observed variability. From these results, we conclude that interventions for VP dysfunction that decrease VP distance (e.g., autologous fat transplants, surgery with LVP overlap, retropositioning) or increasing LVP cross-sectional area (e.g., via continuous positive airway pressure therapy) may be very effective in improving VP function. Furthermore, because certain anatomies are naturally less anatomically advantaged with respect to VP closure, consideration of these weaker anatomies, such as those occurring in cleft patients, may influence surgery selection. Future modeling studies including more anatomical complexity to simulate normal and pathological VP function as well as surgeries will further elucidate speech mechanics and lead to improved treatment for individuals born with cleft palate.

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REFERENCES


Figure captions

Figure 1. Inputs of VP anatomical parameters and mechanical properties of muscle and the soft palate were used to create a computational model for assessing VP function.
Figure 2. (a) MRI measures in the sagittal and the oblique-coronal image planes (b) line segments represent the velum, LVP, and posterior pharyngeal wall. Width of posterior pharyngeal wall line segment was based on the VP width measurement. Velum line segment extends down to middle of LVP, not along nasal surface. (c) orientation of the components with the MRI planes (d) computational model in the orientation shown in image-c. (e) Model components reflect anatomical representation. Adapted from (Perry & Kuehn, 2007).
Figure 3. The force-length properties of skeletal muscle were used to calculate active muscle tension based on the amount of contraction. A higher amount of contraction from 100% rest position lessens muscle force-generating capacity.
Figure 4. Line segment model configuration for (a) relaxed LVP (b) LVP during VP closure, and (c) determining closure force calculations using a simple force balance.
Figure 5. We conducted three sets of computational simulations with our model. The first simulation set was composed of 10 image-based simulations, each from the MR images of the individual subjects, as well as an averaged simulation. The second set was 1000 randomized simulations with each parameter drawn independently from a uniform probability distribution varying between the mean ± one standard deviation for each anatomy. The third set was parameter isolation simulations that adjusted each parameter up and down one standard deviation from the mean while holding other parameters constant to determine sensitivity of VP closure to individual parameters.
Figure 6. Effects of parameter adjustments on model anatomy. VP distance: increased by moving the posterior pharyngeal wall posteriorly in the oblique-coronal plane. Extravelar LVP length: increased by moving the points of origin posteriorly in the oblique-coronal plane. Intravelar LVP length: increased by increasing the width of the intravelar segment while keeping the origin-to-origin distance and extravelar LVP length constant. This moved the points of origin posteriorly in the oblique-coronal plane. Distance between points of origin remained constant. VP width: increased by widening the posterior pharyngeal wall contact area. Distance between points of origin: increased while keeping extravelar LVP length constant. Velum-LVP angle: increased by rotating the velum anteriorly in the sagittal plane. Velar length: increased by extending the point of attachment to the hard palate posteriorly and superiorly while keeping the velum-LVP angle constant.
Figure 7. (a) The average model agrees well with experimental data, falling within one standard deviation of all data points. (a) Individual models from MRI scans and (b) randomized models show variability similar to that observed experimentally.

(a) Average and individual models

(b) Randomized models
Figure 8. Parameter isolation simulations: (a) Ranked parameter sensitivities measured by percent increase in closure force when varying parameters up or down one standard deviation from the mean with other variables held constant. (b) Closure force has positive relationships with isolated increases in some variables and negative relationships in others.
Figure 9. Parameter isolation simulations: (a) Ranked parameter sensitivities measured by percent decrease in minimum activation required. (b) Minimum activation required has positive relationships with isolated increases in some variables and negative relationships in others.
Figure 10. Parameter isolation simulations (Figures 8 and 9) enable identification of the most influential aspects of VP closure. Interestingly, the most influential parameters for closure force (Figure 8) tended to be those measured in the oblique-coronal plane and related to LVP configuration, while the most influential parameters for minimum activation required (Figure 9) tended to be those measured in the sagittal plane and related to velar configuration.
Figure 11. Randomized simulation set, with each data point representing one random anatomy. Higher closure force at full muscle activation, in general, correlates with a lower minimum activation required in our model.
Figure 12. Effect of VP distance. A large VP distance requires more LVP contraction, resulting in less force capacity, and vice-versa.
Figure 13. Three plots of randomized simulation set, with each data point representing one random anatomy. While the above anatomical parameters are the most influential, they cannot be considered in isolation of the other parameters since there is considerable variability of closure force for a given value of each individual parameter. Closure force measured at 100% muscle activation.
Figure 14. Tissue parameter sensitivity analyses on closure force. VP distance remains most important in all cases. Increasing velar stiffness by 10x relative to nominal while keeping specific tension at nominal value (upper right) increases the effects of parameter variations around 5x. Moreover, velum-LVP angle and velar length increase in relative importance to second and third most influential, respectively.
Tables

Table 1. MRI measures for model creation.

<table>
<thead>
<tr>
<th>Sagittal plane measures</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVP major axis</td>
<td>Largest cross-sectional diameter of the LVP along the midline of the velum</td>
</tr>
<tr>
<td>LVP minor axis</td>
<td>Smallest cross-sectional diameter of the LVP along the midline of the velum.</td>
</tr>
<tr>
<td>Velum-LVP angle</td>
<td>Angle between the line connecting the tip of the posterior nasal spine and the middle of the LVP and the line of the oblique-coronal plane.</td>
</tr>
<tr>
<td>Velar length</td>
<td>Effective velar length extending from the posterior nasal spine to the velar knee</td>
</tr>
<tr>
<td>Velar thickness</td>
<td>Thickness of the velum measured from the velar dimple to the velar knee (coursing through the bulk of the cross-sectional LVP muscle)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oblique-coronal plane measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance between points of origin</td>
</tr>
<tr>
<td>VP width</td>
</tr>
<tr>
<td>VP distance</td>
</tr>
<tr>
<td>Extravelar LVP length</td>
</tr>
<tr>
<td>Intravelar LVP length</td>
</tr>
</tbody>
</table>
Table 2. VP dimensions based on MRI measurements from 10 healthy adults.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVP cross-sectional area (mm²)</td>
<td>35.0</td>
<td>4.65</td>
</tr>
<tr>
<td>Velum-LVP angle (degrees)</td>
<td>78.5</td>
<td>5.23</td>
</tr>
<tr>
<td>Velar length (mm)</td>
<td>13.6</td>
<td>1.82</td>
</tr>
<tr>
<td>Velar thickness (mm)</td>
<td>12.0</td>
<td>1.34</td>
</tr>
<tr>
<td>Distance between points of origin (mm)</td>
<td>59.3</td>
<td>4.89</td>
</tr>
<tr>
<td>VP width (mm)</td>
<td>17.2</td>
<td>3.57</td>
</tr>
<tr>
<td>VP distance (mm)</td>
<td>10.9</td>
<td>2.27</td>
</tr>
<tr>
<td>Extravelar LVP length (mm)</td>
<td>35.3</td>
<td>3.08</td>
</tr>
<tr>
<td>Intravelar LVP length (mm)</td>
<td>26.5</td>
<td>1.60</td>
</tr>
</tbody>
</table>