INNOVATION

THEORY AND CONCEPT

The Functional Matrix Hypothesis Revisited. 5. Orofacial Capsular Matrices Defined

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ABSTRACT

Objective: The objective of this communication is to define the functional matrices of the orofacial capsules. The functional matrix hypothesis (FMH) was introduced by Melvin L. Moss in the 1960's, and has been an enduring concept for explaining the compensatory growth and development of the craniofacial complex in general, and the facial skeleton in particular. Expansion of orofacial capsular matrices have historically been explained as intrinsically-derived spaces that satisfy the metabolic demands of the body. However, these spaces have matrices overlooked in earlier research.

Methods: Precepts of hard tissue biology based on the authors' experience and the literature are reviewed that describe properties of consistent with the existence of functional orofacial capsular matrices.

Results: The results of our inquiry are an appreciation for how evolved bone/tooth and upper airway structures and functions develop and maintain the orofacial capsules.

Innovation Statement: Orofacial capsules, once thought to be intrinsically-derived spaces, are instead explained to develop from functional matrices. These capsules enclose a mass or otherwise fill a volume within their respective functional spaces. Orofacial capsular matrices do indeed have contents that furnish the pressures required to form these spaces.

Conclusion: The oropharyngeal capsule is mechanically challenged by chewing a hard and tough diet, responding during growth by rendering a normal occlusion. The functional matrix of the oral cavity is thus hard and tough food. The nasopharyngeal capsule is mechanically challenged by air pressures elicited by vigorous nasal breathing. While chewing forces play a role in development of the nasopharyngeal passage, nasal breathing is likely primary. The functional matrix of the nasal cavity is thus air. The orthodontic community must transition from treating only the symptoms of perturbed facial growth, to acknowledging the public health benefit of identifying the causes of maxillary and mandibular insufficiencies and tooth crowding, and interventional approaches that intercept growth anomalies and reestablish normal function.

Background & Justification[i]

Conceptualization of the functional matrix hypothesis (FMH) by Melvin L. Moss remains a pillar of orthodontic theory as an explanation for compensatory growth of the craniofacial skeletal complex principally in response to the growth and function of soft tissue matrices. Excellent historical accounts of this concept may be found in the literature [1-4]. The expression "functional matrix" was introduced to the orthodontic community and described by Moss in 1962 [2] as a tissue mass enclosed by bones to form a functional unit. This concept was operationalized in an analysis of the developing maxilla in 1967 [5]. In the following year, whilst performing a functional analysis of the mandible, the FMH concept adopted a more complete view, detailing the primacy of the functional matrix to elicit secondary growth responses by its corresponding skeletal unit [6]. In that study, teeth were introduced as the functional matrix of the alveolar skeletal unit of the mandible. It is also noteworthy that while Moss described the FMH at the macro scale, in this publication he referred to supporting research on bone growth remodeling at the microscopic scale by Enlow [7]. The support and strength that this dyad provided would become a staple of developing theory in publications by both Moss and Enlow throughout their careers.

In 1969 Moss and Moss-Salentijn formalized the capsular matrix [8] and provided the relatively advanced explanation of the FMH that remains the core of the concept today [9]. Functional matrices were said to be of two types; periosteal matrices serve as the functional muscle/tendon attachments to skeletal units, and capsular matrices enclose a mass or volume within a functional space. Because it is easy to intuit, the neurocranial capsular matrix was heralded to convey the concept of the FMH. However, an operational description of the oronasopharyngeal functional space was needed [8]:

> Operationally, the form (the size and the shape) as well as the spatial location of the orofacial capsule, and therefore of any of its completely embedded and included functional cranial components, is determined primarily by the operational volumetric demands of the enclosed patent functioning spaces. (p. 478). For the moment, we wish to state only that the human oronasopharyngeal functioning space alters in size alone, not in shape, after the beginning of the third month of pregnancy. This morphogenetically primary volumetric increase causes a compensatory increase in the size of the orofacial capsule. Growth of the enveloping capsule is produced by mitosis of both its epithelial and mesenchymal cellular elements and the consequent increase in intercellular materials, which results in an expansion of the capsule as a whole. Within the capsule are situated a number of mandibular functional cranial components, periosteal matrices together with their respective skeletal units. (p. 483).

The operational demands of the respiratory and digestive systems creating patency of the oronasopharyngeal functional space were aptly described as related to the metabolic demands of the body [8]. However, attributes of the capsular matrices themselves were not described, other than to claim primacy as an intrinsic space, a throughway, from which its tissue boundaries grew mitotically from early embryonic life. Therein is the first irony that partly prompted this communication. It is well understood that anomalies of functional matrices are responsible for abnormal growth, such as was discussed by Moss regarding defects in neural mass [10] and by Young regarding experimental research on the rat neurocranial capsular matrix [11]. Then why do perfectly normal teeth that comprise the functional matrix of the alveolar bone become crowded? If growth of the oronasopharyngeal functional space is intrinsic, then why are there anomalous mismatches between large tongues and relatively small oral volumes? Despite these and other questions, we are sure Moss would have agreed that extrinsic environmental factors were at work. If so, it suggests that the orofacial capsular matrices that make up the oronasopharyngeal functional space do in fact contain something, and until we describe what that something is, the FMH remains incomplete.

Indeed, our purpose is to describe and analyze hard tissue biological evidence supporting the contents and nature of orofacial capsular matrices and advance our understanding of FMH and its importance to improve clinical practice of Orthodontics and Dentofacial Orthopedics. The position taken in this communication is that growth of the orofacial capsular matrices must be explained in exactly the same fashion that Moss and colleagues have described for the neurocranial capsular matrix, which is an enclosure having contents that exert pressure, which in turn stimulates compensatory growth of its skeletal unit.

Above we mention one reason for undertaking the present analysis. The other reason concerns the opening three sentences of Moss and Moss-Salentijn's 1969 paper on the capsular matrix [9], which was a shout-out from the basic sciences to the orthodontic community, that a knowledge and theory of cranial growth is fundamental to clinical practice:

> It is commonly agreed that a comprehensive knowledge of cranial growth is a sine qua non for any rational approach to orthodontic therapy. Quite apart from the intrinsic value of such information, many aspects of orthodontic diagnosis, therapy, and prognosis are based firmly on this aspect of cranial

[i]This communication is in response to enthusiastic readers of an editorial who requested to have a more in depth and referenced examination of the subject: Bromage TG. The oronasopharyngeal space and renewed formalization of the functional matrix hypothesis. CRANIO: The Journal of Craniomandibular & Sleep Practice. 2021;39:275-277.

> biology. Far from being an academic matter, it is easily demonstrated that the fundamental conceptualizations of the orthodontist concerning the process of cranial growth strongly influence his therapeutic techniques. (p. 474).

If it was commonly agreed in 1969, it is no longer. The orthodontic community failed to appreciate this guidance. Therein emerges the second irony prompting the purpose of this communication, which is that such knowledge and theory would have helped to mitigate the mishaps of orthodontic therapy, such as relapse, root resorption, failure to achieve desired tooth movement(s), and more, as recently reviewed [12]. More significantly, such knowledge and theory would have been used in campaigns to reduce the prevalence of dental crowding, maxillary and mandibular insufficiencies, and other craniofacial skeletal anomalies in the general public; orthodontics would have transitioned to preventative dental medicine, thus minimizing iatrogenic harm.

Or maybe not. At least not if general agreement with a reviewer for the American Journal of Orthodontics and Dentofacial Orthopedics of a previously submitted version of this manuscript is held to be true: [13]

> The FMM (functional matrix model) is untestable. There was never anything substantial about the model that could be tested empirically. Instead, you either were an advocate or a naysayer, with almost no evidence on either side. Having read through this manuscript, I see that nothing much has changed since 2006 when Dr. Moss passed away. (parenthetical explanation added)

That the American Journal of Orthodontics,- as it was then named when Moss was publishing - would be the main heralder of functional matrix theory, then to be abandoned by its reviewers today, is a disingenuity that should concern dental practitioners who depend upon the advancement of theory. The sentiment expressed above is thus a wakeup call, and what follows are descriptions of the contents of orofacial capsular matrices in order that the FMH may be better understood and hopefully applied in clinical practice.

Methods, Results, and Discussion & Innovation

What follows is a review of hard tissue biology precepts that justify the existence of functional orofacial capsular matrices. The approach taken in this revision of the FMH is exclusive to the authors' experience as an evolutionary biologist, all concepts and details fully referenced in the attending bibliography. The results of this inquiry lead to an understanding of how evolved structures and functions develop and maintain the capsules, which are discussed at length.

THE FUNCTIONAL MATRIX OF THE ORAL CAVITY IS HARD AND TOUGH FOOD.

The oropharyngeal cavity.

What are teeth for?

To understand what contents fill and regulate growth of the oropharyngeal cavity, we begin by addressing what teeth are for, an innovation rarely – if ever – explored in the orthodontic literature, but which has been considered in bioceramic design [14]. Human enamel is a biological material made of approximately 95% by weight carbonated hydroxylapatite $Ca_{10}(PO_4)_6(OH)_2$ (hydroxyapatite), with the remaining 3-4% being protein and a 1-2% fraction of water. The hierarchy of attributes that convey mechanical efficacy from the macro- to the nanoscopic scale of enamel will reveal attributes of the functional matrix. At the macroscopic end of the spectrum are the loads and stresses absorbed by an intact tooth due to the incursive, intercuspal, and excursive contacts that distinguish an individual's unique masticatory function [15].

A level down the hierarchy is enamel thickness. Human enamel is among the thickest of all primates, being 2 mm thick and more on molars [16]. This is an adaptation to a hard and tough diet [17] in order to survive the lifetime of wear. Until the exposure of dentine, enamel also retains highly decussated enamel prisms, or rods, at the inner enamel (Fig. 1). Mammalian species with hard and tough diets develop this architecture wherein groups of enamel prisms cross at some angle to one another and are observed as Hunter-Schreger bands (HSBs) [18, 19]. Human molar HSBs originate at the enamel-dentine junction (EDJ), coursing toward the outer enamel but typically dispersing into a zone of parallel rods before reaching the surface in an unworn tooth [19]. In the lower enamel, the junctions between decussating groups of prisms forms an enamel prism discontinuity that serves to resist the propagation of cracks [20] (Fig. 1). Occlusal loads drive the enamel shell into the significantly softer underlying dentine, causing peak tensile stress of the enamel situated at the EDJ, to which brittle solids like enamel are vulnerable. The HSBs and their enamel prism discontinuities are thus situated in exactly that region of the enamel volume to serve as an adaptation to resist the propagation of bottom surface cracks [21, 22].

Prism orientation at wear surfaces also confers resistance to load and functional wear [23-26] especially as regards a diet of hard and tough food. Adaptations of prism orientation have been shown to vary in relation to dietary niches of early humans [27].

When materials embody a sharp transition in density, differential strains cause fracture or separation at the transition under load. Human molar enamel thus contains another discontinuity in a zone whose gradients in hardness and elastic modulus diminish from the outer surface toward the inner enamel [28], the enamel becoming more compliant at the EDJ. The dentine side of the EDJ is itself graded too, it initially having mechanical properties quite similar to enamel, but then becoming softer and more stress-tolerant some tens of micrometers away from

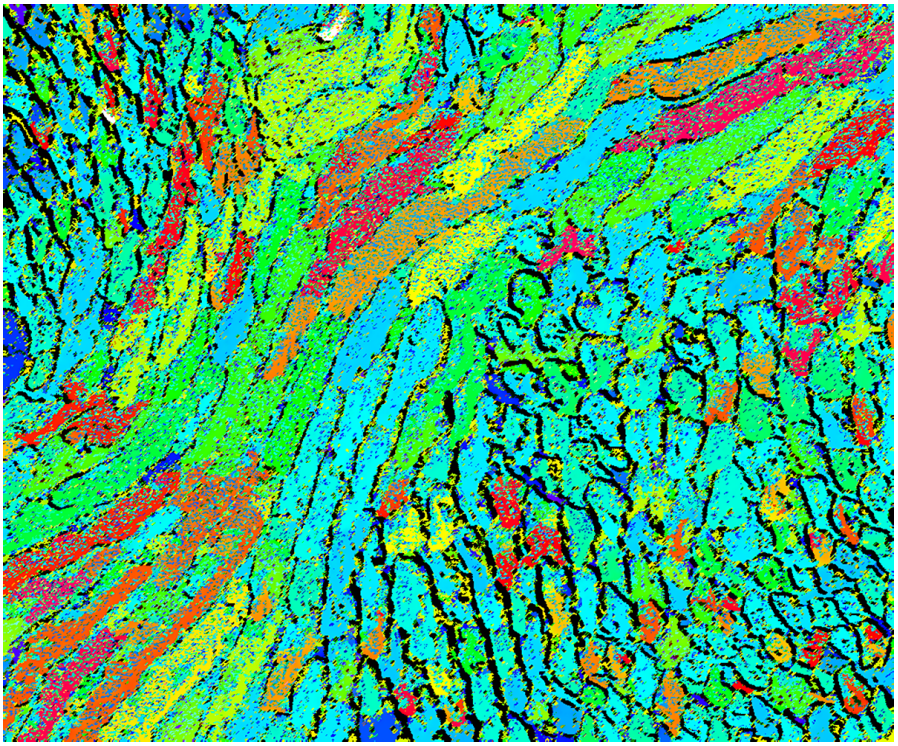

Figure 1: Human enamel microanatomical structure. *In this example of modern human enamel deep to the surface of a transversely cut and polished tooth and imaged by backscattered electron imaging in the scanning electron microscope, we see that the prisms have divergent courses. Some prisms are seen to course longitudinally and wander lengthwise in the plane of the image while others course in and out of the plane of the image and appear semicircular. This heterogeneity provides crack propagating resistance to a tooth, enabling it to withstand the mechanical forces of chewing. Color was imparted to the image by an image analysis program for measuring prism orientation. Field width 180 µm.*

the EDJ [29-31]. This is an adaptation to a diet of hard and tough food.

There are further enamel discontinuities at the microscopic scale that confer mechanical efficacy [24, 32]. Enamel prism structures are about 5 µm in diameter, which are packed with crystallites around 20-40 nm in width. The crystallographic c-axes of these crystallites are formed perpendicular to the secretory surface of the ameloblast's Tome's process. Because this process is asymmetrical, a complex arrangement of crystallite orientations within prisms creates enamel crystallite discontinuities at the junctions between prisms [32]. These discontinuities are anti-crack propagating at the micrometer scale. Enamel crystallites are hexagonal and are packed so that their flat surfaces against one another will provide sliding planes at the nanometer scale, offering resistance to strains in bulk enamel by absorbing stress under high biological loading conditions. Cracks that might emerge at the nanometer scale will also arrest at this length scale among the discontinuities between crystallites.

Finally, ameloblast secretory behavior renders incremental lines over daily and near-weekly timescales in humans that produce changes in mineralization chemistry [32, 33], producing compositional discontinuities. In addition, low mineralization density due to porosity, putatively at prism boundaries and their centers [34] (dark prism boundaries and speckling in the centers of prism heads in Fig. 1), is yet another density-dependent discontinuity, which confers mechanical resistance to loading.

In sum, the macro- to nanoscopic arrangement of discontinuities in structure and composition renders human enamel supremely competent at absorbing stresses in the biological loading stress regime encountered with a hard and tough diet. Fractures that may begin at the nanoscopic scale will follow paths of least resistance indicated by the various discontinuities described [35]. The heterogeneity of these discontinuities enables enamel to arrest cracks before becoming catastrophic.

Human teeth are designed for processing hard and tough foods.

What is the relationship between what teeth are for and their bone?

It is an axiom of hard tissue biology attributed to Wolf's Law [36] that bone adapts its architecture to the habitual intensity and frequency of mechanical loads to which it is subject. Frost [37] specifically targeted an explanation of Wolff's Law to the orthodontic community to enhance the clinicians' understanding of its concepts. Mechanically-mediated effects by biological loads and mildly overloaded biological regimes will have a positive

effect on bone growth of the jaws (e.g., [38]). We are speaking of sufficient mechanical forces transmitted through teeth, that is, through the enamel, EDJ, dentine, periodontal ligament, and ultimately to the maxillary and mandibular bones, which experience the stress and strains that stimulate growth and expand the oral cavity and oropharynx. Strong support for this derives from studies of the positive association between masticatory muscle shape and cross sectional area with mandibular shape characteristics, such as a wider ramus, more rectangular body, and more curved basal arch [39], which are anticipated to provide the tissue space required to accommodate a complete and uncrowded adult dentition. Clinically, in both the child and the non-grower, orthodontic tooth movement is only possible because of the maxillary and mandibular bone threshold for receiving mildly overloaded forces to enable modeling drift of the tooth through tissue space. These concepts dominate much of the basic science and clinical literature on bone, particularly in respect to exercise, e.g. [40-42].

Underloading has no effect on modeling drift to change shape or increase bone size [37]. A bone that does not experience the strain thresholds to which it was adapted during growth will not stimulate modeling sufficiently to increase in size to whatever its genetic potential may be. In a study of 104 pairs of siblings receiving orthodontic treatment, King and coauthors concluded that environmental factors operating on similar genetic backgrounds aided the alteration of physiological parameters leading to similar malocclusions [43]. Underloading of the jaws will lead to maxillary and mandibular insufficiencies and tooth crowding. Biological loading and mildly overloaded force regimes will subject a bone to strains that promote size and shape change consistent with the demands of the mechanical environment [44]. Meeting or mildly exceeding the biological strain threshold of the jaws will cause the maxillary and mandibular bones to grow sufficiently and to permit all teeth to erupt into a normal uncrowded occlusion.

To understand what mechanical environment human teeth and maxillary and mandibular bones are adapted to, modern-day hunters and gatherers provide the grist for a comparison of their diet with industrialized people. In a study of the Hadza people of northern Tanzania, the average fracture toughness of various underground plant species consumed was about 2000 Jm^2 [45], even after processing by roasting to make the food softer. In a sample of store-bought cheeses, vegetables, and nuts typically available in the industrialized world, the average fracture toughness is roughly 200 Jm^2 [46], the highest value of 647.9 Jm^2 given for the green turnip. There is an order of magnitude difference between the mechanical properties of what the Hadza eat and what is available to industrialized people. But as both communities of people process their food, this may reveal a common human behavioral response to effect a reduction in mechanical properties, perhaps because of the metabolic cost associated with mastication. We know that orofacial muscle tonus is positively associated with mechanical food properties [47]. A focus group asked to rate the preferred cooking time of noodles chose around 7 minutes in boiling water, which is at just that moment when they reach the minimum toughness value of about 140 Jm^2 from the uncooked value of about 200 Jm^2 [48].

Research on the consequences of a soft diet to orofacial growth tend to offer support. A softer diet is associated with a posterior location of the teeth and reduced oral processing [49]. However, it should be noted that this study found a significant degree of variability in cranial form, suggesting that phenotypic plasticity also require consideration of diet-related effects on the masticatory system. Toro-Ibacache has also noted that mandibles are more gracile in low masticatory loading individuals, having a lower relative amount and distribution of bone than higher loading individuals [50]. An exception to this was a significantly more robust symphysis, but this apparent anomaly may be the response of a gracile mandible to "wishboning" forces. As for the aforementioned research, because of substantial variability, this study also concluded that there must be other as yet unresolved factors responsible for malocclusions. Nevertheless, we find it interesting that the Food and Drug Administration, which provides the food industry with detailed guidance documents, completely fails to address that specific property of processed foods most relevant to its effects on orofacial health, namely that they are invariably less hard and tough [51].

The line of argument above leads us inextricably to conclude that the overwhelming prevalence of maxillary and mandibular insufficiencies and commensurate tooth crowding in the industrialized world is linked to a reduction in the mechanical properties of the diet. As in all biological systems, there is variability in tooth size, bone size, and the capacity for what Enlow called "intrinsic compensation" [52] that will permit some people to avoid a problem when it appears they should have one, and for others to have a problem when by all measures they shouldn't. Reasons for this require research, but the vast majority of craniofacial skeletal anomalies of interest to clinicians can be explained by deficiencies in the mechanical properties of the diet alone.

We hope to have provided circumstantial evidence for understanding the relationship between evolutionary adaptations of human enamel to a hard and tough diet and the contents of the oral capsular matrix that meet the mechanical requirements. The innovation of evolutionary medicine emphasizes the need to understand evolutionary adaptations in order to fully comprehend the etiology of malformations, and in the case presented here, especially among industrialized societies whose diets are particularly lacking in the necessary mechanical properties to which the teeth are adapted.

THE FUNCTIONAL MATRIX OF THE NASAL CAVITY IS AIR

The nasopharyngeal cavity.

What is the role of respiration in facial growth?

To understand what contents fill and regulate growth of the nasopharyngeal cavity, we must address the role of respiration in facial growth. We can address this question by outlining its physiologically important attributes in connection with the necessary exchange of carbon dioxide and oxygen to meet the metabolic demands of the body, and olfaction [53-57]: *humidity* added to

the inspired air facilitates lung function; nitric oxide release in the upper respiratory tract destroys pathogens and assists in the regulation of carbon dioxide and oxygen concentrations; *filtering* of particulates from the air protects the lung's delicate structures; *thermal conditioning* of the air by warming facilitates gas exchange in the lungs; *vagal tone* is stimulated during deep diaphragmatic breathing and facilitates health; *immune defenses* are mounted against airborne pathogens.

What distinguishes these features and benefits of the airway as a group is that none of them occur during habitual mouth breathing, but rather describe the purpose of obligate nasal breathing. It is universally appreciated that all mammals are obligate nasal breathers, yet metabolic demands beyond resting levels are said to induce a switch in humans to obligate mouth breathing [58].

> ...the onset of oronasal breathing...was quite consistent individually, but varied considerably between individuals without showing a significant sex difference. The factors most closely related to the switching point were rating of perceived exertion of breathing and nasal work of breathing. (p. 61).

It is extremely unfortunate that our scientific community so readily accepted this line of research without question (e.g., [59]), but it is understandable because, just as humans endeavor to make chewing easy (see section above), so they attempt to make breathing easier too.

Two clues from the quote above illustrate the misapplication of the study results to airway research. The first clue is the considerable variability between subjects independent of sex. If a normal healthy population were sampled, and the switch to obligate mouth breathing was a human metabolic adaptation, then why the tremendous variability between individuals? The second clue is the "perceived" exertion as a function of nasal resistance, which study subjects took to mean more work than necessary, which then caused the switch to mouth breathing despite the important biological functions described above.

That this misapplication continues today defies logic and illustrates where improvements can be made in dental education. Implicit in the first clue above is that the variability among subjects exists because their normal biology, behavior, and health has been modified in whatever direction each individual experienced less respiratory work. They will vary because of the length and duration of their maladaptation, intrinsic facial morphological variability, and their differences in flexibility of metabolic rate. Anomalies of facial development and dental health attributed to mouth breathing - typically in relation to nasal obstruction - include aberrant inferoposterior mandibular rotation, overjet, long face, narrowing of the dental arches, overcrowding, open bite, cross bite, poor lip seal and posture, and relatively small external nares, [60-71], outcomes that have been largely experimentally induced in a primate model [72, 73], and which are universally regarded as harmful to health.

Implicit in the second clue above is that, while nasal breathing is more work [74], it is less efficient. In a study of recreational runners purposefully trained to breathe through their nose during intense exercise, both mouth and nasal breathing were examined for carbon dioxide and oxygen exchange [54]. It was found that the ratio of oxygen intake to carbon dioxide outtake lowered in nasal breathing, suggesting that oxygen was given more time to enter and remain in the bloodstream while at the same time tolerating higher concentrations of carbon dioxide. This is a measure of performance and endurance that benefits nasal breathers and elite athletes. Thus while mouth breathing divests more carbon dioxide during intense exercise, which at first appears to relieve the oxygen debt, it actually makes the oxygenation of our cells more difficult. It is interesting that once trained, any deficits that may otherwise be attributed to nasal breathing are eliminated. Erect posture and exercise actually decrease nasal resistance [75, 76], which is another expression of our adaptation.

To appreciate why humans have maintained the biological necessity explicit in the mammalian adaptation for nasal breathing, one only has to account for our origins in the Great African Rift Valley [77]. Landscapes then, several million years ago, and now, contained a variety of habitats, but semi-aridity is a common feature of many of them for various durations of the year. Water loss in the switch from nasal to mouth breathing increases by 42% [78], which is potentially deadly, particularly during water scarcity. Anyone watching people run across these African landscapes in remote parts of the continent will not have observed any mouth breathing. Elite long distance runners, except perhaps for the final push to the finish line, are also habitual nasal breathers. Amateur runners accompanying the elites in marathons will include many mouth breathers who are losing so much water vapor that the route's water stations cannot be close enough together. The selection pressure to preserve water is by itself extreme enough to explain the evolutionary history of human nasal breathing. It is no wonder that facial growth is perturbed and that dental health is compromised by aberrant "obligatory" mouth breathing, something humans were never adapted to perform.

Obligatory nasal breathing is for promoting normal facial growth and function.

What is the mechanism relating nasal breathing to growth of the facial skeleton?

Regrettably, the research required to solidify an answer to this question does not exist. However, together with our reasoning outlined in the section above, the circumstantial evidence given below strongly suggests that the answer is yes.

Resistance to nasal airflow is borne by the mucosa and other soft tissues overlying bone of the nasal passage. The resistance is not insignificant, requiring about 50% more effort than required for mouth breathing [74]. (it is no wonder that indolent energy-unconscious individuals switch to mouth breathing when physically challenged by exercise).

The results of airflow studies in the literature vary depending

upon anomalies of nasopharyngeal anatomy, but geometry-based simulated breathing flow rates vary from roughly 2 to 8.5 m/s, depending on location, being highest at the nasopharynx [53, 74, 79]. Because of anatomical variations within the nasal passage and the influence that turbinates have on flow patterns, pressure varies from roughly -9 Pa to 7 Pa [53, 79], with nasal mucosal wall shear stresses reaching about 1 Pa [53, 80]. All values are expected to be significantly higher during intense physical exercise, and while this has not been modeled, turbulent nasal airflow is said to occur above 40-80 Pa [57, 81].

We thus anticipate pressure differences during cyclic nasal breathing to be in the vicinity of 100 Pa (=10,000 nN) and higher during intense physical exercise. Bernoulli forces of this magnitude represent 10 grams of compression pressure per square centimeter. This is many orders of magnitude larger than the 100-500 nN proliferative pressure exerted by growing tissues on their surroundings [82]. The airway is incessantly subject to cyclic mechanical stresses such as compression, shear, and stretch during breathing [83]. Cyclic stretch in particular is recognized as one factor mediating cell proliferation [84, 85].

Growth in body mass is linearly related to increases in metabolic rate. Assuming ideal nasal breathing during development, nasal passages must increase in size to maintain homeostasis consistent with higher metabolic rates. Increased ventilatory demand at larger sizes may in tandem increase nasal resistance and increased pressures that stimulate growth. However we rather think that the Bernoulli forces at high levels of physical activity, as might occur during vigorous play, stimulate the increase in size of the nasal soft and hard tissues. We posit that high intranasal pressures may expand the nasal passage, distending sutures that absorb much more of the strain energy than the surrounding bone [86], leading to compensatory modeling of sutures and the delicate bones of the nasal region.

DIET AND THE NASAL CAVITY.

We do not discount the contributions from chewing a hard and tough diet on the size of the nasal cavity for a few additional reasons. 1) The high principle tensile strains noted over sequential cross sections of the human nasal passage [87] will distend the sutures during growth that then respond by compensatory modeling. 2) The number of chews is significantly decreased during mouth breathing compared with nasal breathing, which may reduce the mechanical environment and lead to malocclusion [88]. 3) The anthropological literature notes that a variety of skulls ranging from the eleventh-eighteenth centuries exhibit a correlation between nasal breadth and the distance between the canines of the upper jaw [89]; these people surely had a significantly harder and softer diet than present day industrialized people. We do not discount these mechanical explanations, but because the upper respiratory airway is only improved in the grower treated artificially by rapid maxillary expansion [90], we regard the effects of Bernoulli forces and the stresses and strains we believe they cause to be primary in the development of the nasal cavity.

THE CASE FOR CONSTITUTIONAL CAUSES OF MALOCCLUSIONS.

In respect of the role of environment in relation to epigenetic regulation of normal growth, Moss was clear; both intrinsic genetic and extrinsic epigenetic factors were understood to be necessary interacting causes of craniofacial growth [91-93]. Masseter muscle genetic variants, fiber phenotype, and physiology, as well as salivary genotypes have been shown to vary in relation to skeletal growth, facial morphology, and malocclusion groups, all of which suggest an epigenetic effect on development of the jaws and face [94-97]. Therein is an important distinction between the thesis explored here and this line of skeletal muscle and physiology research. First, the effects on facial morphology of the aforementioned muscular anomalies are mediated via periosteal matrices, not capsular matrices, the latter of which is the subject of our concern. Second, we have described deficiencies of oral and nasal cavities in relation to aberrant capsular matrices that concern the greater preponderance of people that would otherwise be considered "normal". Nearly all of the research investigations concerning genetic sequence and physiological variants mentioned above compare controls to people who would be deemed by these researchers to require orthognathic surgery. Such cases may 1) be constitutional and syndromic, potentially irrespective of the contents of their capsular matrices, but 2) in any case, may also be treated non-surgically.

Conclusion

The title of this communication extends the series of four papers published by Moss in 1997 [92, 93, 98, 99]. In these four papers, Moss reached out to new and exciting avenues of research that dovetailed with and supported the FMH. The merits of this forward thinking gained strength by the American Journal of Orthodontics and Dentofacial Orthopedics having asked Enlow to write an introduction for the first of the four papers. At that time all four papers had been written, and Enlow concluded with an expression of interest in Moss's final words on complexity in the fourth paper to be published months later.

In fact, complexity science was only just coming into mainstream thinking in the late 1990's, and it was prescient of Moss to include some remarks. There is not yet a formal definition of complexity, and the nature of such systems may even preclude one, but in general terms complex systems share the following features: They are composed of numerous parts (potentially at hierarchies of scale obeying a power law distribution), these parts are diverse, connected, and interdependent, which adapt to changes and perturbations [100]. Insight is also gained by recognizing that all complex systems have a function, or purpose [101].

Anyone who accepts this characterization will agree that the craniofacial complex is, indeed, a complex system. What is also common to complex systems is their robusticity to

failure, which, in the case of the facial skeleton, is exhibited by the whole system remaining in satisfactory function even though some of the parts are perturbed, as described throughout this paper. Perturbations exist because the purpose of the craniofacial complex has changed. Its purpose was to engage in chewing hard and tough food, and to breathe primarily and intensely through the nose. Changing the purpose by chewing a soft diet and, for many, to breathe through the mouth, has led to the current suboptimal health of the human industrialized population.

In our view, the orthodontic community has failed to address the public health advantages of treating to the purpose of the orofacial capsules of the craniofacial complex. It is wonderful that the community itself acknowledges the risks of treatment [12], but it is not healthy that such risks endure by treating symptoms in deference to acknowledging causes and doing something about it. Sir Arthur Keith wrote: “Civilization… is anti evolutionary in its effects; it works against the laws and conditions which regulated the earlier stages of man’s ascent” [102] (p. 76). Recognizing this statement as quintessential evolutionary medicine will help to transform the community’s perceptions of improvements it can make to better human health.

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