

Normal and increased functional asymmetries in the craniofacial area

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Normal asymmetry in the area of the craniofacial skeleton can be directional or fluctuating in nature. Directionality can in principle be found in three dimensions: anteroposterior, cranio-caudal, and asymmetries in the left–right dimension. When it comes to directional left–right differences, an explanation has been difficult to find, although expressions of this type are obvious. Recent findings made in molecular genetics strongly support the genetic inheritance pattern of laterality. When functionally increased asymmetries of facial structures are concerned, it is often difficult to determine the exact contribution of each factor involved. In the light of recent experimental data, however, it seems that the influence of occlusion on the development of balanced facial structures is highly important during the early periods of life. A review of these factors is given in this article. □ *Asymmetry; craniofacial growth; crossbite; malocclusion; mandible*

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Types of normal asymmetry

Normal asymmetry in the area of the craniofacial skeleton can be directional or fluctuating in nature. Directionality can in principle be found in three dimensions: anteroposterior, cranio-caudal, and asymmetries in the left–right dimension. The differences in the anteroposterior and cranio-caudal dimension can be explained by early embryonic regulation by a group of homeobox control genes. Various explanatory models suggest that these genes specify positional identity along the anteroposterior (A-P) axis of the body and limb (1, 2).

When it comes to directional left–right differences, an explanation has been difficult to find, although expressions of this type are obvious (3–7). Most internal organs show consistent laterality, which is very stable within species. There is clear evidence for directionality in cranial and craniofacial structures, which can be explained, at least where the skull base and cranium are concerned, by the asymmetry in brain structure (8–10). The function of the brain has long been known to be asymmetric, and recent advances in soft tissue analyses and diagnostics have made it possible to show that the highly asymmetric brain function correlates with anatomic and behavioral expression. Brain asymmetry has been found to be associated with handedness (11). This link involves not only the larger cortex areas of the brain, as a similar, associated asymmetry has also been found in the more primitive cerebellar areas of brain (12). The directionality in left–right dimension is found in a variety of species, including primitive animals, and is typically found in mammals (4, 13, 14). A genetic background for the phenomenon has been suggested, although until recent years no specific gene has been found to cause the lateralization.

Genetic background for normal asymmetry

Because no clear genetic background for laterality had been found, many different theories were put forward to explain these phenomena (3, 4, 6). A widely discussed topic has been the possible effect of early hormonal effects on the developing fetus. According to the Geschwind–Galaburda hypothesis (7, 9), an exposure to testosterone prenatally would affect neuronal growth in the cerebral hemispheres differentially and would have an effect on brain asymmetries and handedness.

Recent advances in molecular biology have made it possible to identify important sequences during early embryogenesis, when laterality is formed. These phenomena are obviously based on genetic regulation. Two members of TGF-beta superfamily, called *nodal* and *lefty*, are expressed asymmetrically during early organogenesis, when directionality in the heart and lower brain structures is formed (15, 16). A gene has also been found whose expression can be changed experimentally to cause a condition in which the normal side of laterality is randomized (17, 18). It is noteworthy that asymmetry is not lost in these embryos; only the direction of asymmetric growth is randomized. These findings strongly support the genetic inheritance pattern of laterality (19).

Associated craniofacial asymmetries

When the facial and craniomandibular asymmetries have been correlated to other skeletal asymmetries, these have been found to be associated. Huggare & Houghton (20) found a general asymmetric tendency in the skeletal structures, including long bones and vertebrae. It is

interesting that these general asymmetries were found to correlate with side differences in dental occlusion and mandibular ramal length asymmetries. Another interesting finding in their work (20) is that there was a difference in the degree of measured asymmetry between two studied racial groups, Polynesians and Thais.

In our study on Lapp skulls (8) we found systematic directional asymmetries in all measured skull structures, including skull base foramina and the glenoid fossa. The lower incisal midline was found to be more on the right, and the mandible was longer on the left in the frontal plane. In the axial plane the mandible was longer on the right, possibly because the fossa was found to be more posteriorly located on the right. Also, the fossa was located more laterally on the right than on the left, which correlated with the other asymmetries found in skull base structures. Thus, the general finding that dental occlusion normally is more posterior on the right (8, 20) may be related to the skull base asymmetry, which in turn is correlated with neural asymmetries. This does not necessarily mean that brain asymmetry will induce occlusal asymmetries, but they do seem to be related. The confusing aspect in this regard is that the normal directional asymmetry may well be of functional origin. This may have implications not just for craniofacial structures but for the whole body, as there is a definite right-side preference in chewing in humans and in higher primates (21–23). Keles et al. (11) have reported that, in a normal population, facial asymmetries are related to handedness and that right-handed persons had a larger facial area on the left side whereas the left-handed had larger facial area on the right. This asymmetry was consistent in right-handed persons, while in the left-handed it was more variable. This finding is consistent with observations made concerning asymmetries of the brain. In right-handed humans brain asymmetry is functionally and anatomically relatively stable, whereas in the non-right-handed population this asymmetry is often found to be inversed to some degree (7, 9, 10).

Fluctuating asymmetry

Another type of asymmetry normally found in the craniofacial structures is fluctuating asymmetry, where the side of the larger and smaller paired structure is randomly determined. The degree of this randomly sided asymmetry is shown to be related to the stress level of the population (24). Fluctuating asymmetry has been shown to be most easily detected in strongly genetically coded tissues like tooth enamel and cartilage; in structures where growth is mainly functionally regulated, the incidence of fluctuating asymmetry is rare (24–26). A significant factor in fluctuating asymmetry is the 'threshold phenomenon', whereby an increased magnitude of stress or a low genetic buffering capacity due to inbreeding or genetic aberration reaches a level at which the phenotypic expression of fluctuating asymmetry is seen (26–28).

Reasons for normal orofacial asymmetry

In the orofacial area normal manifestations of laterality include slight midline deviations in dentition and size differences between the bilateral craniomandibular structures. The causes of these slight deviations are largely unresolved, but side differences in muscular function are evidently the most important factors. Good evidence for this is the normal bilateral side difference in the sizes of human mandibular halves (8, 20). In comparisons between medieval and modern skull samples for condylar and mandibular size, a clear reduction in size has been a common finding. This reduction is related to less use and smaller forces required in modern human occlusal function (29). Thus, analogously, since the joint structures on the right side are normally subjected to greater forces, the right–left size difference can be easily explained. Some facial asymmetries can also be explained merely by this normally asymmetric muscular balance, as facial structures have been shown in humans and animals to be strongly dependent on the muscular balance (30–33). Experimentally induced change in one critical muscle, for example the temporalis muscle, can cause fundamental changes in facial structures during the subsequent growth (34).

Another normally occurring asymmetric sequence during growth is the bilateral variation in brain development. The neurocranial structures and the skull base follow changes in the neural tissues, and the temporomandibular joint is a part of the skull base where only a narrow bony structure is found between the articular fossa and the cranial fossa. As the brain is normally asymmetric both anatomically and functionally, and its asymmetry is linked to the handedness of the individual, it would not be surprising if some craniofacial asymmetries primarily originated from brain asymmetry.

Functional reasons for increased orofacial asymmetry

A greater variety of possible causes can be found when the limits of normal asymmetry are exceeded and pathologic reasons for increased levels of asymmetric formations are suspected. When it comes to the most frequent pathologic asymmetries in the craniofacial region, a functional cause is readily found to be a major etiologic factor. In conditions with normal transversal occlusion, the occlusal relations are for the most part symmetric, except for the slight normal dental midline deviation (8, 20). However, in unilateral malocclusions, in which lateral crossbites are most frequently found, the level of asymmetry in craniofacial or temporomandibular structures and muscular function reaches a significant degree (35–40). Expressions of these asymmetries, which can be clearly visible, are the tilting of the occlusal and the mandibular planes when examined in the frontal view (35, 41). Furthermore, the asymmetric sequence that develops leads to asymmetry in the condylar path, which may become

irreversible if the lateral malocclusion is not corrected early enough (35–37). The condylar position relative to the fossa remains asymmetric since the condyle on the ipsilateral side of the lateral malocclusion is located in an anterior position. This disharmony can be resolved only if the malocclusion is corrected (37, 42). The results of Poikela et al. (43, 44) experimentally confirm the earlier findings made in humans that occlusal disharmony can be a major cause of facial and even some craniofacial asymmetries that disturb normal development. In the works of Poikela et al. (43, 44) experimentally induced lateral malocclusion in rabbits caused a significant increase in the asymmetry of the mandible and the condylar path. Another very important finding was that the maxilla remained narrower in the case of unilateral malocclusion. If the side of malocclusion was reversed, the narrowing was seen on both sides; if the side of malocclusion was constant, the narrowing of the maxilla was strongly unilateral. The width of the maxilla was not recovered, even if the malocclusion was corrected in 50-day-old rabbits and growth was followed until 100 days with normal lateral occlusion. In addition to this clinical and experimental evidence, new functional studies on the masticatory performance in relation to unilateral malocclusion in humans are still needed.

In general, where functionally increased asymmetries of facial structures are concerned, it is often difficult to determine the exact contribution of each factor involved. Given recent experimental data, however, it seems that the influence of occlusion on the development of balanced facial structures is highly important during the early periods of life.

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