Neuro-Orthodontics-A Sub-Specialty in Orthodontics, Important for Diagnostics and Treatment Planning

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Abstract

The text in this review is divided in three sections, each with results from four decades of research at the borderlines between orthodontics and the medical disciplines: embryology, fetal pathology, endocrinology, neurology, neuro-anatomy, neuro-psychiatry, neuro-radiology, and neuro-anthropology. The focus in this inter-disciplinary collaboration has been on the central nervous system, CNS and the peripheral nervous system (PNS). The three sections are:

1. Section 1: The theoretical background for understanding the normal close interrelationship between CNS/PNS and the hard tissues, based on human fetal studies and human post-natal studies.

2. Section 2: CNS. Clinical examples demonstrating the pathological interrelationships between the brain and the cranial base.

3. Section 3: PNS. Clinical examples demonstrating the pathological interrelationships between the peripheral nerve branches and the jaws, alveolar processes, and teeth.

As the CNS and PNS systems are highly important for orthodontic diagnostics and accordingly for treatment planning in orthodontics, the term neuro-orthodontics is hereby introduced as a subspecialty in orthodontics.

Keywords: Profile Radiograph; Orthopantomogram; Brain; Peripheral Nervous System; Orthodontics

Introduction

Neuro-orthodontics is a sub-specialty in orthodontics, where structures seen on profile radiographs are related to structures in the central nervous system, CNS, and where bone structures and teeth, observed on orthopantomograms are related to the peripheral nervous system, PNS.

By including CNS and PNS in the orthodontic analyses, neurologic fields appear on radiographs. These fields indicate specific CNS-structures or specific areas, indicating specific peripheral branches of innervation, PNS. CNS and PNS fields in the cranium, alveolar processes, and teeth have been documented by Kjær [1-3]. These fields are illustrated in figure 1-3.

Figure 1: The human prenatal axial skeleton.

A schematic drawing of the axial skeleton of a human fetus, about 17 weeks of GA. The spinal cord and the brain stem (except cerebellum) are marked dark yellow, and the hemispheres of the cerebrum and cerebellum are marked light yellow. Green arrows indicate paths of neural crest cell migrations to the jaws and facial bones, coloured green. Red lines mark structures with an ectodermal origin, which includes the notochord, within the vertebral bodies. Peripheral nerves to the jaws are marked orange.

Figure 2: Registration on profile radiographs.

a) A profile radiograph coloured according to craniofacial fields with different embryological origins. The fields in the maxilla are: Frontal nasal field (yellow), maxillary field (red), and palatal field (orange). In the mandible, the incisor field, canine/premolar field and molar field are all marked blue. The occipital field is marked green and the theca region purple.

The interrelationship between the cranial base, jaw bone and teeth is exemplified in the maxillary field (red), where the canine and two premolars are drawn. Newer research [82] has suggested that the canine might have a separate field.

b) A profile radiograph coloured according to craniofacial fields with different embryological origins (same as 2a). Inserted on the figure is the cephalometric landmarks: n(nasion), s(sella), ba(basion), sp(anterior nasal spine), ss(subspinale), pm(ptyerygomaxillare), sm(supramentale), pg(pogonion), gn(gnathion), tgo(gonion tangent point), ar(articulare), o(opisthion), sqo (squamaoccipithale).

Furthermore, the cranial base angle(n-s-ba) is marked, and the occipital angle (the angle between the line s/ba and the line o/sqo). This illustration indicates that the etiology behind deviations in cephalometric distances can be traced back to deviations in different fields. As an example, the etiology behind a short n-s distance is deviation in the fronto-nasal field and the etiology behind a short palate is specifically caused by deviations in the maxillary and/or palatine field. Also the size/shape of the occipital field (green) can be expressed cephalometrically by the occipital angle and s-sqo distance.

c) The same profile radiograph of the craniofacial fields, demonstrated in figure 2a and 2b, now with insertion of the brain: H (cerebrum hemispheres), D (diencephalon with an extension, infundibulum cerebri to the sella turcica, where it forms the neuro-pituitary gland), M (metencephalon), BS (brain stem, including the pons and cerebellum), S (upper and lower spine). Note that the fossa cranii anterior (s-n) (Figure 2c) supports the frontal hemispheres of the cerebrum. Also note, that the fossa cranii posterior, expressed as the angle between s-ba and o-sqa (See figure b) encircles mainly the cerebellum and pons, located in the green craniofacial field (Figure 2a).

These diagrams a, b, and c can be used in the clinic for etiology based diagnostics.
In cases where patients have congenital or acquired abnormalities in CNS, the radiographic structures on profile radiographs might disclose these abnormalities. Furthermore, abnormalities observed in the alveolar process and teeth, observed on orthopantomograms can in some cases reveal deviations in PNS. These observations make orthodontic analyses important, not only for orthodontic diagnostics and treatment planning, but also for clinical and theoretic neurology.

Based on the reflections above, the text in this review is divided in three sections, each with results from four decades of research at the borderlines between orthodontics and the medical disciplines: embryology, fetal pathology, endocrinology, neurology, neuro-anatomy, neuro-psychiatry, neuro-radiology, and neuro-anthropology. The focus in this inter-disciplinary collaboration has been on the central nervous system, CNS and the peripheral nervous system (PNS). The three sections are:

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3. Section 3: PNS. Clinical examples demonstrating the pathological interrelationships between the peripheral nerve branches and the jaws, alveolar processes, and teeth.

Figure 3: Overview of the peripheral nerves to the alveolar processes and teeth.

a) A frontal radiograph illustrating the bilateral trigeminal ganglia (black) and the schematic innervation paths from the ganglia towards the alveolar bone and dentition. Red lines indicate the nerves to the incisors and green lines indicate the nerves to the canines and premolars. The blue lines indicate the innervation paths to the molars.

b) Orthopantomogram with marking of the peripheral nerves (neuroectoderm) and jaws/alveolar bone fields (ectomesenchyme). The fields arise from migrating cells from the neural crest. Also, the dentition appears in the radiograph. Enamel has arisen from surface ectoderm and dentine/pulp from ectomesoderm from the neural crest.

This diagram can be used in the clinic for etiology based diagnostics.

Dental deviations occurring within fields might have another etiology that deviations occurring sporadically in the dentition.
Section 1

The theoretical background for understanding the normal close interrelationship between CNS/PNS and the hard tissues

CNS/Cranial base

The central nervous system consists of the brainstem, the cerebrum, the cerebellum, and the spine. All structures are developed from the primitive neural tube. This development is controlled by the axially located cell chord, the notochord [3] (Figure 1). In this review, the brain part of the CNS is described. The brain has an axial posterior part, predominantly pons and cerebellum, and an anterior part where bilateral cerebrum structures develop (Figure 2). These bilateral structures are separated mid-axially by the falk cerebrii from the dura mater, which is attached to the crista galli.

Between the posterior and the anterior parts of the brain, the pituitary gland develops from the infundibulum cerebri (Figure 2).

When it comes to cranial development, exactly the same overall structures are seen, with a posterior cranial part, fossa cranii posterior, constituted of mainly clivus and the occipital squama, and an anterior part, mainly fossa cranii anterior, constituted of the body of the sphenoid bone, ethmoid bone and nasal septum.

Pituitary gland and sella turcica

Between the posterior and anterior parts of the cranial base is sella turcica located, enclosing the pituitary gland centrally in the brain (Figure 2). The sella turcica represents the fossa cranii media on the profile radiographs. As sella turcica is a bordering structure between the anterior and posterior fossae, the anterior wall of the sella reflects the development of the fossa cranii anterior; while the posterior wall, including the cranial end of the notochord, reflects the posterior part of the cranial base [3].

While sella turcica is an important bone structure post-natally, the sella and the pituitary gland have been ignored in pre-natal autopsy descriptions, because the autopsy procedure does not allow ordinary histological preparation of the pituitary gland region [4].

Studies of sella turcica development have revealed how the posterior wall component developed first from the cartilage encircling the rostral end of the notochord [5]. At that stage, the anterior part of the pituitary gland, composed of adeno-pituitary tissue, attached to the infundibulum cerebrii, is drawn cranially from the pharyngeal mucosa. Thereafter, the complete pituitary gland with the anterior lobe, the adeno-pituitary gland, an intermediate lobe, and a posterior lobe, the neuro pituitary gland was formed [5,6]. Sella turcica morphology and the pituitary gland have formerly been described based on histology and neuro-radiography [7]. Studies have demonstrated that location of the anterior pituitary gland (adenopituitary gland) is interrelated with sella turcica morphology [8]. After this endocrinological developmental process, the anterior wall and lastly the floor of the sella turcica developed [3,9].

According to this developmental process, distinctions are made between bony abnormalities in the anterior wall of the sella turcica, in the posterior wall, and in the bottom (see later). These distinctions are made prenatally as well as postnatally. In prenatal analyses furthermore the location of the pituitary gland tissues have been reported [3,9-15].

PNS/Craniofacial skeleton

From the rim or crest of the early formed neural tube, the neural crest cells migrate anteriorly and gradually form the jawbones [1,3]. This is illustrated in figure 1. The neural crest is composed by a left neural crest, related to the left part of the craniofacial skeleton and a right neural crest, related to the right part of the craniofacial skeleton.

From the neural crest, the multipotential neural crest cells originate. The neural crest is a crest, formed by an inner neuro ectodermal layer and of an outer surface ectodermal layer. Concurrently the cells migrating have the potential for forming ectomesenchymal struc-
tures such as subcutis, muscles, and bones bilaterally and in addition also the ability to form peripheral nerves. It is important to remember that neural crest cells migrate from different caudo-cranial locations on the crest to different areas in the face and jaws (Figure 1). As an example, the cells migrating to form the mandible and the mandibular innervation, are located further caudally of the neural crest than the cells forming and innervating the maxilla (Figure 1). Accordingly, the innervation of the alveolar bone and teeth comes from peripheral nerves with different origins on the neural crest. The different innervation paths from the neural crest can divide the craniofacial hard tissues in innervation fields [2,3,16] (See figure 2 and 3). These fields, useful in diagnostics, can be compared to the fields of dermatomes [17-19].

PNS and maxilla formation

The early close spatial interrelationship between bone formation in the maxilla and innervation is documented prenatally [20,21].

PNS and mandible formation

The formation of the mental foramen demonstrated that the bone gradually encircled the mental nerve and thereby formed the mental foramen [22]. The formation of the mandibular canal was mapped anthropologically in fetal mandibles about 25 - 35 weeks of gestation [23]. This study revealed that stepwise outgrowing peripheral nerves were gradually enrolled in the formation of the mandibular canal. Thus, the inferior mandibular nerve is a bundle of nerve fibers, developed at different periods, and innervating different teeth. Bone spiculae appear between the nerve fibers in the mandibular canal.

PNS/CNS and vomero-nasal organs

In the anterior part of the craniofacial area, the bilateral vomero-nasal organs are developed. These organs, formed early in prenatal life close to the nasal septum, produces Lutenising Hormone Releasing Hormone (LHRH) [24,25]. The LHRH positive cells migrate from the vomero-nasal organ later in prenatal life, cranially along the terminal nerves (PNS), to the olfactory bulbs, and further to the hypothalamus (CNS), from where the hormone, LHRH, postnatally influences the growth hormone production in the pituitary gland [3].

PNS/Dentition

Systematic histological overviews of human tooth formation are always based on early fetal crown formation in the primary dentition, before GA 21 weeks. This is due to limited access to human tissue from the periods, where the permanent teeth develop pre- and postnatally.

Histochemical methods have demonstrated neuronal markings of human odontoblasts and of nerve fibers apically to the developing crown in a ligament similar structure, presumably the later Hammock ligament [26,27]. This ligament is in this early stage named the root membrane, even though the root has not formed. Further human studies have documented the spatio-temporal expression of innervation in the root membrane [28,29]. How the peripheral nerves find their way (path finding) to the developing tooth buds, have been proved experimentally by Luuko., et al [30] and by Kettunen., et al [31].

Normal dental development, which cannot be studied prenatally

Root formation

Root formation in humans has been studied longitudinally by radiography. Histological studies on root formation have not been possible. For a better understanding of different root abnormalities in the human dentition, a study on extracted teeth with attached periodontal tissue was performed elucidating the cell-layers close to the root surface [32]. These cell layers were innermost towards the root

surface a close network of nerve fibers covered by an ectomesenchymal tissue sheet and outermost by surface ectodermally derived Malassetz epithelium, innervated by tiny nerve fibers. These three main tissue layers, illustrated in figure 4, were named the peri-root sheet [32-34]. A similar root sheet with the same three tissue layers, though morphologically different, was also observed close to the roots of the primary teeth [35].

**Figure 4: Peri-root sheet and eruption.**

*Left: A schematic drawing of the peri-root sheet, covering the root surface. Grey colour indicates the cementum/dentine of the root. The root surface is covered innermost by a layer of peripheral nerves (yellow). This inner layer is covered by a mesodermal layer (ectomesenchyme), coloured green. The outermost layer is indicated by red ectoderm (Malassetz layer) which is also innervated (yellow dots). The vessels are marked by light red capillary structures, which occur in all three layers of the peri-root sheet.*

*Disturbance of the peripheral nerves by virus attack can seemingly provoke inflammation, resulting in resorption.*

*Right: A schematic drawing, demonstrating the tissue types important for normal pre-emergence tooth eruption. Marked is the perforated upper part of the crown follicle (U), the lower part of the crown follicle (L), the periodontal membrane, not fully developed (P) and the root membrane (R). The arrows indicate that the monocytes within the crown follicle penetrate the follicular wall and resorb the overlying bone during pre-emergence eruption.*

**Normal eruption**

Insight in the normal tooth eruption process is fundamental for understanding pathological tooth eruption. The eruption process is still not completely understood, but different theories exist [36]. One of these will be highlighted in the following.

The normal tooth eruption is a physiological process, which depends primarily on innervation of the root membrane, but also on the penetration ability for resorptive cells in the crown follicle and on the periodontic membranes ability to re-generate during the eruption process [3]. Histo-chemical studies have proved the existence of a peri-root sheet with three main cell layers, covering the root surface [36]. The outer cell layer in this sheet is the mucosal layer of Malassetz epithelium. The medium layer is the ecto-mesenchyme fiber layer, and the innermost layer, close to the root surface is rich in innervation [32,34]. Innervation also occurs in the Malassetz epithelium [37]. The re-building ability of the peri-root sheet during tooth eruption, where the tooth moves and the bone stay stable, has been proved by marking of apoptotic reaction in cells close to the root [38]. Permeability of the crown follicle secures mono-nuclear resorptive cells to penetrate the membrane and resorb the over-lying bone, which is important for tooth emergence [1,3]. The root membrane is highly

innervated, similar to innervation observed in the end-pieces of glands. It is hypothesized that the innervation of the root membrane generates a pressure, comparable to the pressure at the highly innervated end-pieces in glands, creating flow of saliva. In the teeth, the pressure from the root membranes creates the force, which is important for tooth movement [36]. Accordingly, the following three eruption factors, illustrated in figure 4, are supposed to interact. The root membrane creates a pressure for eruption movement, the follicle makes a path in the bone for eruption, and the periodontal membrane secures the adaptation process under normal development. It is furthermore hypothesized that if one of these three factors does not function, then tooth eruption stops or deviates. The post-emergence eruption depends on the activity in the root membrane and in the periodontal membrane [36].

Conclusion: CNS/PNS and orthodontic analyses

The profile radiograph, the orthopantomogram, and the cone beam radiograph are usually the radiographs used in orthodontic diagnostics.

On profile radiographs, the cephalometric landmarks and lines are used for expressing normal and abnormal craniofacial development, but the etiology is normally not expressed.

In this first section, the prenatal developmental fields with common origins are incorporated in the post-natal profiles and orthopantomograms (Figure 2a and 3).

If the fields are added to the cephalometric analyses on profile radiographs (Figure 2b), then the abnormal cephalometric measurements can directly be interrelated to the fields. If furthermore, the brain is inserted in the “empty” cranium (Figure 2c), observed on the profile radiograph, then the cephalometric measurements can be interrelated also to the brain. Accordingly, the figure 2a-2c are used in the evaluation of craniofacial etiology. If also the developmental fields are added to the orthopantomograms (Figure 3), then the evaluation of jaw bone and dental etiology can be expressed.

The background for this present short overview is mainly the author’s scientific observation of dental and craniofacial findings in human fetuses and individuals with normal development in the central nervous system (CNS) and normal development in the peripheral nervous system (PNS). These findings in large material form the basis for diagnostics of pathological cases [18,39], highlighted in the following two sections.

Section 2

CNS. Clinical examples demonstrating pathological interrelationships between the brain and the cranial base

Fossa cranii anterior/cerebrum

Associated with the observation of a single mid-axially located maxillary central incisor (SMMCI) in the fronto-nasal field is a significant shorter fossa cranii anterior (sella-nasion distance) [40]. Also, absence of the inter-maxillary suture, short or absent nasal bone and abnormal crista galli are skeletal signs observed in SMMCI patients. According to figure 2a and 2b, the fronto-nasal field is reduced or malformed.

The SMMCI condition has been observed in several cases with mental retardation. Neuro-radiographical observations have in these cases revealed non-separated bilateral cerebral hemispheres [41]. The involvement of the cerebral hemispheres is illustrated in figure 2c. The severe type of this condition called holoprosencephaly has been proved neuro-embryologically with unseparated cerebral hemispheres and the presence of a single median centrally located eye (cyclopia) [42].

Fossa cranii posterior/cerebellum, pons

In patients with Down syndrome a reduced volume/size in the occipital region, where the pons and cerebellum are located has been described by cephalometry [43]. The length of the clivus (sella-basion distance) was reduced, compare to normal standard. The cranial base angle (s-n-a) was enlarged, and the occipital area reduced, compared to non-Down individuals. This morphological deviation was first described prenatally [44]. Interestingly, MR-studies of individuals with Down syndrome have demonstrated that the size of the cerebellum is less than 75% compared to the size in non-Down individuals [45].

Also, complete CLP patients can be diagnosed with cerebellum abnormalities [46]. In these cases, deviant shape abnormalities have been observed cephalometrically in the fossa cranii posterior [47].

Sella turcica/pituitary gland

The pituitary gland is normally located within the sella turcica, where the cephalometric important sella point, S, is constructed for cephalometric measurements of the cranial base angle (Figure 2b and 5). In many orthodontic cases abnormal morphology of the sella turcica makes the exact location of the s-point difficult. This influences the cephalometric analyses and conclusions. Normal post-natal size and morphology of the sella turcica have been elucidated, according to age and gender in an extensive study [48], while the location and morphology of the postnatal pituitary gland, have only been sporadically described. The postnatal pituitary gland is not included in the present overview.

In profile radiographs of patients with severe craniofacial deviations, abnormal sella turcica morphology characterized by sella bridges have been described in 18.6 per cent out of 177 individuals, undergoing orthognathic surgery [49].

According to the prenatal development of the sella turcica, described in section 1, the description of pathological sellae focuses on deviations in the anterior sella wall, the posterior sella wall and deviations in the floor [3] (Figure 4).

Abnormal anterior wall of the sella turcica

Absence or low-slanting anterior wall has been reported in SMMCI, holoprosencephaly and combined cleft lip and palate [42,50] (Figure 5). Also, in body axis abnormalities, such as seen in prenatal and postnatal encephaloceles and myelomeningoceles oblique anterior wall, deviations have been observed [51,52]. In pathological prenatal cases, such as anencephaly where the adeno-pituitary gland tissue is absent, also the anterior wall of sella turcica is absent [53]. In this case the necessary early attachment between the pharyngeal located adeno-pituitary gland tissue and the infundibulum cerebri failed. When comparing the sella turcica morphology in fetuses with trisomy 21 and trisomy 18, it is obvious that there is a difference, which seemingly is genetically determined [13]. When comparing the prenatal morphology of the sella turcica with the postnatal morphology of the sella turcica in Down syndrome, the morphologies are mainly identical [54,55].

Figure 5: Sella turcica development and morphology.

a) Sella turcica marked with coloured developmental fields, illustrated in figure 2, inserted in the upper right corner. The anterior wall of the sella turcica (left) is formed by neural crest cells from the fronto-nasal field (upper part, yellow), from the maxillary field (medial part, red), and the palatine field (lower part, orange). The cephalometric landmark sella (s) is inserted in the figure.

b) A section of a profile radiograph from a 12 years old girl with SMMCI (single Medial Maxillary central Incisor) illustrates the sella turcica. Note the slanting anterior wall. In this condition, the fronto-nasal field is abnormal.

c) A section of a profile radiograph from a 11 years old boy with congenital hearing deficit. The section illustrates the sella turcica. Note the absence of the posterior wall (right). In this condition, the occipital field including the mastoid process with the inner ear is abnormal.

Abnormal posterior wall of the sella turcica

Abnormal morphology of the posterior wall with shortness or posterior concavities in the wall has been described in Down Syndrome [55] and in Cri du Chat syndrome [56]. This was also observed in Velocardiofacial syndrome [57]. Recently an observation of absence of the posterior sella turcica wall has been described in children with congenital inner ear hearing deficit [58]. This indicates that the inner ear and the mastoid process protecting the inner ear and the posterior wall of the sella turcica (green field) are affected (Figure 5).

Abnormal development of the floor in the sella turcica

A funnel shaped floor has been described with laryngeal location of adeno-pituitary gland tissue in prenatal combined cleft lip and palate [59] and in other severe craniofacial malformations [59].

Section 3

PNS. Clinical examples demonstrating the pathological interrelationships between the peripheral nerve branches and the jaws, alveolar processes, and teeth

Jaws and alveolar bone/PNS

It has been hypothesized by neural cell markings of human osteoblasts with PGP9,5 that compensatory and dysplastic growth of the jaws could be under control by peripheral nerves [60].

A malformed human anthropological mandible confirmed the prenatally described formation of the mandibular canal. This case further demonstrated the dependence of innervation for tooth formation [61].

Postnatally, Arne Björk demonstrated in his lifelong cephalometric studies with metal markers inserted in the jaws, that the mandibular canal stayed stable during growth, and therefore usable for super-imposing of radiographs for growth analysis [62]. The shape of the mandibular canal observed on radiographs expresses the mandibular growth pattern [63].

Human palatal growth has been evaluated on medieval crania using nerve canal openings (PNS) as references [64]. On a reduced number of human anthropological maxillae, the direction of the infraorbital canal expressed the maxillary growth pattern [65]. Post-natally the direction of the orbital canal has been suggested as a stable structure in the maxilla important for revealing the maxillary growth pattern. As the orbital canal is not visible on patient radiographs, this observation can only be used on anthropological material.

Dentition/PNS

In this short review, focus will be on selected examples of dental deviations, associated with abnormal jaw development and dental deviations in individuals with abnormal PNS development.

Seemingly, all pathological dental deviations can be inborn and/or acquired.

Pathological tooth development can be caused by a disruptive factor, such as virus infection, or by an inborn malformation with one or more tissue types involved in the tooth formation [3].

Tooth agenesis

Maxillary central incisor

SMMCI, Single Median Maxillary Central Incisor, is a specific type of incisor agenesis, interrelated with brain malformation [41]. This condition is also associated with bone malformations in the fronto-nasal field [66] (Figure 6a). In these cases only one mid-axially located central maxillary incisor exists.

Maxillary lateral incisor agenesis in Combined CLP

Maxillary lateral incisor agenesis is a common finding in combined CLP-patients [67], while not common in other cleft types [67]. In combined CLP, abnormal cerebellar fields occur. Also, abnormal brain development has been reported [68,69]. This is a subject which needs to be sorted out, but seemingly the findings support the theory of different genotypic origins of the three cleft types in the maxilla.

Premolar agenesis

The most common types of agenesis (third molar, second premolar, and maxillary lateral incisor) seems to be agenesis, located at the site of nerve ending within a developmental field [1,70]. The etiology behind inborn agenesis seems to be genetic, but the field patterns support that the innervation or the borderlines between fields are important factors in tooth development. If theses borderlines between developmental fields influence the local growth of the alveolar bone, then it is questioned whether the different areas of initial reduced bone levels in juvenile periodontitis occur at the borderline between fields [71]. If it is so, then the initial stages of juvenile periodontitis are local disturbances in alveolar bone growth [71].

Gender differences in the intra-jaw and inter-jaws occurrences of agenesis of the second pre-molars have been studied [72]. This study seemingly indicated the intra-jaw and inter-jaw influence of innervation on agenesis. Craniofacial development in multiple agenesis cases is different in patients with different numbers of congenitally missing permanent teeth [73].

Third molar agenesis

Third molar agenesis has been studied in CNS deviations, such as in Down syndrome, where the occurrence of agenesis was significantly higher, compared to individuals without Down syndrome [74]. How the CNS condition is interrelated with third molar agenesis has not been determined.

Maxillary canine agenesis

Agenesis of the maxillary canines is a seldom phenomenon (prevalence 0.07 - 0.13 per cent). Except for the canine agenesis, these denitions appeared normal [75]. This could be the reason for defining a specific etiology behind maxillary canine agenesis and for presuming a specific canine PNS innervation field. Retrognatia of the maxilla appears in bilateral maxillary canine agenesis [75], which could indicate a close interrelationship between regional tooth and jawbone development.

Tooth malformations

Macrodontic incisors

Macrodontic incisors have been observed in patients with enlarged craniofacial dimensions [76] (Figure 6b). A later study on the same group of patients demonstrated that out of 22 cases with macrodontic central incisors, 11 cases had neuro-psychiatric diagnoses [77].

En coup de sabre

Tooth malformation has been described in the condition “En coup de sabre,” characterized by areas with abnormal skin formation, specifically in the face. It has been demonstrated that the tooth malformations occurred in the dental arch, exactly in the same region, where the facial skin affection occurred.

In a recent study of six patients with “En coup de sabre” it was documented that the contours of the facial skin abnormalities were identical to the cranial regional fields and associated with tooth abnormalities within the affected fields [78,79]. In two cases with identical skin affections the pre-sphenoidal bone area demonstrated identical bony malformations [79]. Neurological complications, including epilepsy, have been reported in this condition [79]. The interrelationship between the skin, teeth and bone, abnormalities, and the CNS and PNS abnormalities should be highlighted in future studies.

Arrested tooth formation in fields

Arrested tooth formation regionally was first documented in a case after virus affecting the peripheral nervous system, seemingly by destruction of the swan cells. In this case, the virus infection also resulted in temporary hearing loss in the same side where the arrested tooth formation occurred [80]. After the swan cell has regained and more or less normalized the PNS function, the hearing improved, and the tooth formation caught up. The result of this temporary arrest in innervation was abnormal tooth morphologies (taurodontia) and, in some teeth, arrested root development [80].

Eruption deviations

Arrested molar eruption

All 3 tissue types mentioned as important for normal tooth eruption (section 1) can result in arrestment in the eruption process. In this short overview, only the influence of innervation on tooth eruption will be highlighted. If the swan cells are destroyed by virus attack, e.g. mumps virus, then the periodontal membrane will be affected, resulting in eruption deviation, and sometimes in ankylosis in the innervation fields. It has been highlighted how arrestment of the first molar often is followed by arrestment of the second and third molars within the same innervation field [3] (Figure 6c). This can also appear in more than one field.

Figure 6: Morphological deviations in the dentition.

- a) A single mid-axially located central maxillary incisor SMMC (single Medial Maxillary central Incisor) from a 12 years old girl. The midline structures in the maxilla, nasal bones and frontal bones are missing. These structures are the inter-incisive suture, the inter-nasal suture, and the lower part of the inter-frontal suture. The nasal spine is short and so are the nasal bones. The profile radiograph reveals a severely short maxilla. Neurologically the condition can be associated with fusion (or non-separation) of the frontal hemispheres and sometimes with mental retardation. SMMC is a developmental defect in the fronto-nasal field.
- b) Macrodontic maxillary central incisors can be associated with ADHD or other diagnoses of mental disorders. Maxillary dimensions measured on profile radiographs are significantly enlarged.
- c) Two sections from the same orthopantomograms, demonstrating primary arrested first mandibular molar and delay in the development of the second mandibular molar in the right side, when compared to the left side. The difference in dental development was seemingly caused by a virus-attack(mumps) affecting the right side. The red arrows mark the root membrane (second molars) and stage of root closure (first molars).
Transpositions

Transposition is a specific eruption deviation, often observed in a maxillary canine region, when a maxillary canine erupts between premolars or between incisors. It has been hypothesized in a study of 63 dentitions with maxillary canine transpositions, that a separate canine field during development overlaps either distally to the premolar field or mesially to the incisor field [81]. These processes can be compared to overlapping fields, observed in dermatomes along the body axis [82]. A dermatome is defined as a specific skin region, innervated by a specific nerve branch. The same definition is used for craniofacial fields, where each field is innervated by a specific nerve fiber.

Resorption

It is not known if root resorption occurs in dentition with abnormalities in the root dentine/cementum or if it is the periodontal membrane which is abnormal. Resorption can be provoked by pressure, but it can also be a finding in dentitions where pressures have never occurred. The influence by the inner innervation layer in the periodontal membrane can result in inflammation, followed by root resorption, often occurring within fields [83]. The virus attacks the swan cells, which are disturbed, resulting in a non-functioning peri-root sheet. This type of resorption starts as severe column resorptions, and spreads along nerve paths [81] (Figure 7). Column resorption can also occur sporadically in the dentition, and in these cases, there is still not an etiologic explanation.

Figure 7: Two dental films, registered severe column resorption at the initial stages. The resorption processes are spread along the innervation fields in the maxilla until the midline and in the mandible, restricted to the incisor field. The resorbed teeth where replaced by dental implants, which are observed in the orthopantomogram.

Conclusion

In this present overview, selected examples from four decades of human prenatal and postnatal studies are presented. These studies cross the borderline between odontology and medicine by focusing on human neuro-anatomy, neuro-embryology, neuro- psychiatry, neuro-radiology, neuro-pathology, fetal pathology, neuro-anthropology and neuro-endocrinology. All studies are performed in relation to orthodontic diagnostic problems. The presentation focuses on how information from medical disciplines can add new insight to the orthodontic craniofacial diagnostic material.

As the central and peripheral nervous systems are highly important for diagnostic and accordingly for treatment planning in orthodontics, the term neuro-orthodontics is hereby introduced as a subspecialty in orthodontics.
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