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Review Article

Neuro-osteology – A Discipline of Importance for Evaluation of Human Craniofacial Development

Inger Kjær*

Professor, Institute of Odontology, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

***Corresponding Author:** Inger Kjær, Professor, Institute of Odontology, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark.

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Abstract

Neuro-osteology emphasizes the biological connection during development between nerve tissue and hard tissue. The present review article summarizes neuro-osteological results from more than 25 years of scientific publications by the author and co-workers.

It is highlighted and demonstrated in the review, that there is a relationship prenatally as well as postnatally between the development of the human craniofacial skeleton and the central and the peripheral nervous system, (CNS/PNS). Dermatome-like neural crest developmental fields based on innervation paths have been suggested in the cranium. Furthermore it is demonstrated that interrelationships between CNS/PNS and hard tissue are of importance for human anthropological studies for pathological studies and for clinical etiology based diagnostics.

Keywords: *Neuro-Osteology; Bone; Tooth; Brain; Innervation*

Background

Neuro-osteology emphasizes the biological connection during development between nerve tissue and hard tissue [1].

In the present overview of studies, performed by a research team at the Odontological Institute, Health Science Center, University of Copenhagen, the focus will be on the neuro-osteological aspects in the normal and pathological craniofacial development in humans. The interrelationship between the brain, the central nervous system (CNS) and the neuro-cranium will be described. Also the interrelationship between jaw development including the dentition and the peripheral nervous system (PNS) will be highlighted.

These interrelationships will be described in prenatal and postnatal tissues.

Prenatal neuro-osteological development of the neuro-cranium

Normal prenatal studies have focused specifically on the bone formation of the cranial base during early development [2-5]. The sequence in appearances of bones structures was interrelated with vertebral column development [6]. In the studies, bone development was not coordinated with the early brain development. Later a paper on the relationship between the normal development of the pituitary gland and the osseos sella turcica appeared [7]. Also, the p75-NGF-R (nerve growth factor receptor) expression was documented in the pituitary gland [8]. These studies were the basis of the description of the normal cranial base development.

Among pathological fetuses specific attention was on 15 anencephalic fetuses [9,10] and 8 holoprosencephalic fetuses [11]. In both conditions with CNS malformations the fetal pituitary gland and the sella turcica was described [12,13]. These studies revealed abnormal development in the anterior wall of the sella turcica, in the pituitary gland, and in the anterior mid-axial region (anterior cranial fossa) in holoprosencephaly corresponding to the abnormal development of the frontal lobe of the hemispheres. In opposition to this, the posterior wall of the sella turcica and the occipital bone was malformed in anencephaly, where the neuro pituitary gland was absent and the sella turcica malformed [12]. These studies formed the basis for further studies on the pituitary gland and sella turcica in trisomy 18 [14], trisomy 21 [15], fetuses spina bifida, cranial encephalocele, and myelomeningocele [16,17]. Interestingly these conditions also involved abnormal pituitary/sella turcica formation [17]. Notochordal remnants in these conditions and in human iniencephaly and Meckel syndrome have also been described [18]. In Down syndrome the occipital field of the posterior cranial base revealed abnormal dimensions [19,20].

Postnatal neuro-osteological development of the neuro-cranium

The prenatal studies on the neuro-osteological development of the cranial base was followed-up by postnatal studies. In the SMMCI (Single Maxillary Median Central Incisor) condition (mild degree of holoprosencephaly) studies documented a significant shortening of the anterior cranial fossa [21]. The follow-up MRI (Magnetic Resonance Imaging) scan - study revealed brain malformation in this condition [22]. Studies on the single central incisor have documented the midline skeletodental abnormality [21-24]. A postnatal study on sella turcica has been performed in children with lumbosacral myelomeningocele [25]. This study demonstrated an abnormal anterior wall in sella turcica. Also postnatal follow-up studies on sella turcica have been performed in children with Down syndrome [26].

Prenatal neuro-osteological development of the jaws

In early studies on jaw development a correlated appearance of ossification and PNS tissue was described in the maxilla [4]. In the mandible, formation and early prenatal location of the mental foramen were described [4]. In both the maxilla and in the mandible bone formation appeared close to peripheral nerve paths observed histochemically. Concerning tooth development immunocytochemical demonstrations of NGF-R was observed in early tooth development [27,28]. This was later documented by the PGP 9.5 method (protein gene product) [29].

To understand the interrelationship between the development of the mandibular canal and the inferior alveolar nerve analysis of fetal anthropological material was necessary [30]. This study revealed a surprising developmental spatiotemporal pattern. Separate nerve paths developed consecutively to different tooth groups during prenatal life. This information made it possible to construct an innervation diagram of the mandibular dentition of importance for clinical diagnostics. Concerning the growth of the craniofacial jaw skeleton the immunohistochemical PGP 9.5 positivity in human osteoblasts was suggested as an indicator for compensatory and dysplastic craniofacial growth controlled by peripheral nerves [31].

Postnatal neuro-osteological development of the jaws

The innervation diagrams based on prenatal neuro-osteological observations in the jaws have been clinical useful [1,32-35]. In Cri-du-Chat syndrome and in Velocardiofacial syndrome craniofacial bone analysis has been the basis for describing neural crest developmental fields [36,37].

Conclusion

In this short overview, the relationship between prenatal and postnatal neuro-osteology observations in the craniofacial skeleton has been highlighted and craniofacial neural crest developmental fields have been suggested. It has been demonstrated that interrelationships between CNS/PNS and hard tissue development could be of importance not only for anthropological studies [38], but also for clinical diagnostics [39-42]. If the craniofacial skeleton can predict brain development might be a question for the future. Interestingly, the interrelationship between macrodontic permanent maxillary incisors and neuropsychiatric conditions has been suggested [43].

Studies like the ones mentioned in this overview are of a phenotypic nature. In the future it is desirable to combine these finding not only with experimental studies, but also with genetic studies.

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