Original article

Sella turcica morphology and the pituitary gland—a new contribution to craniofacial diagnostics based on histology and neuroradiology

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Summary

The present review summarizes two decades of published and unpublished studies on normal and pathological development of sella turcica and pituitary gland in humans. The pathological conditions are studied in known genotype deviations, syndromes, and other malformations. The studies include histological analyses of human prenatal material and profile radiographic analyses of human postnatal material, supplemented in a few cases with neuroradiology. Prenatal and postnatal results are compared. Similarities between prenatal and postnatal deviations in sella turcica morphology were demonstrated. Malformations in the pituitary gland were observed in several cases. For diagnostic purposes, the review distinguishes between deviations in the anterior wall and in the posterior wall of the sella turcica. Deviations in the anterior wall seem to be associated with deviations specifically in the frontonasal developmental field, while deviations in the posterior wall are often connected with malformations in the posterior structures, e.g. the cerebellum. In normal cases, minor variations in morphology are observed. In each pathological case, a specific malformation pattern was observed in sella turcica morphology, varying from mild to severe phenotype. The malformation in the sella turcica/pituitary gland can be associated with a malformation within a developmental field that forms the craniofacial region (frontonasal, maxillary, palatal, and mandibular fields), sometimes also involving the brain stem, thymus, thyroid, and heart (velocardiofacial syndrome). Pathological sella turcica morphology can also be associated with malformations in the cerebellum and larynx (Cri-du-Chat syndrome). This review demonstrates the value of combining profile radiographic diagnostics with neuroradiological diagnostics in cases with malformed sella turcicae.

Introduction

During the last two decades, the morphology of the sella turcica has been studied on profile radiographs. Studies describe normal conditions and deviations in known and unknown genotypes. In several cases, the description of the shape of the sella is based on previous prenatal observations in the region. These studies supplemented with new observations are summarized in the present review.

An overview of normal morphological changes during growth has recently been described in detail by Axelsson et al. (2004a). They described the size and morphology of the sella in a longitudinal cephalometric study on Norwegians, 6–21 years of age. The main morphological characteristics are schematically shown in Figure 1. Some deviations, described by Axelsson et al. (2004a), were rare findings and it may be presumed that such variations in morphology are in fact signs of pathology.
Normal morphology and growth of the sella turcica
Changes in the sella turcica during growth in childhood have been studied radiographically, e.g. in the implant study by Björk and Skieller (1983), and histologically, e.g. by Melsen (1974). These studies showed that the sella turcica increases in size during childhood. The increase occurs as a result of resorption at the anterior wall of the dorsum sella, while the anterior wall appears stable during growth. This stable structure is useful for radiographic superimposition used in evaluation of craniofacial growth (Björk and Skieller, 1983). As the posterior wall undergoes resorptive changes during growth, the sella point gradually moves in the dorsal-caudal direction (Björk and Skieller, 1983). Accordingly, the anterior wall of the sella is used in craniofacial growth analysis, performed when two or more profile radiographs taken years apart are available.

Even after more than 60 years of intense interest and research concerning the location of the s-point and the growth of the sella, important questions still remain: when is the morphology of the anterior and posterior wall in the sella turcica normal and when is it pathological? How is the s-point defined if the sella turcica has deviant morphology? Is the anterior wall reliable as a structure for superimposition if it has an abnormal morphology?

This review article focuses on the first of the three questions: When is the morphology normal and when pathological?

It was hypothesized in the mid 1990s that histological analysis of prenatal sella turcica and pituitary gland development could be a useful method for answering the question concerning normal or pathological morphology of the sella turcica (Kjær and Hansen, 1995). Histological examinations of foetuses with different phenotypes were supposed to help classify morphological deviations in the region. In the following, normal prenatal development of the sella turcica/pituitary gland will be described and illustrated. Then a series of sella turcica deviations from foetal pathological conditions will be described and illustrated. After these overviews of the sella turcica and pituitary gland before birth, postnatal conditions seen on profile radiographs will be discussed. In a few cases, the profile radiographs were supplemented by neuroradiographs, and the condition was explained and illustrated.

Prenatal development of the sella turcica and pituitary gland
The normal sella turcica develops in the most rostral part of the germ sheet in the area where the notochord ends cranially (Kjær and Hansen, 1995a; Müller and O’Rahilly, 2003; Figure 2). The development takes place in the embryonic period beginning at Carnegie stage 19 at approximately 44th post-fertilization day when the longest part of the embryo is 16–18 mm (O’Rahilly and Müller, 1999). In the very beginning of the foetal period, the pituitary gland has attained normal morphology (Kjær and Hansen, 1995).

The anterior and posterior walls of the sella turcica have different developmental origins. The cartilage forming the posterior wall develops in the same way as the corpora of the vertebra under direct influence from the notochord. In the prenatal period, notochordal remnants are seen in the cartilage of the dorsum sella on midaxial histological sections (Kjær et al., 1997b). In normal cases, the notochordal remnant is slightly curved with the hollow of the curvature facing anteriorly. In pathological cases, this notochordal remnant appears with different malformations (non-straight course, such as s-shaped, y-shaped, or multibranched). The para-notochordal tissue forms the posterior wall, the dorsum sella (Kjær et al., 1997b).

In contrast to the posterior wall, the cartilage forming the anterior wall develops from neural crest cells (Figure 3). The sonic hedgehog

Figure 1. Schematic drawings of sella turcica contours observed in different profile radiographs of normal, young individuals. Anterior direction to the left. (a) This contour was observed in approximately 70% of the cases. (b) Slightly oblique anterior wall was observed in approximately 20% of the cases. (c) Slightly abnormal posterior wall was observed in approximately 10% of the cases.

In a study on the sella turcica morphology in a group of monozygotic twins, it was shown that the size of the sella turcica was predominantly similar in individuals within a twin pair (Brock-Jacobsen et al., 2009). Meanwhile, within some twin pairs, the sella turcica was different in the two individuals. These findings indicate that malformations in the sella turcica are not solely genetically determined. The question raised in this study is to which extend the morphology is inherited and to which extend affected by external factors.

Another interesting question also is to what degree the pituitary gland is normal or abnormal in a malformed sella turcica.

The present review focuses on how to determine the morphology of the sella turcica and how the relationship is between deviations in the sella turcica and general craniofacial deviations. Focus is also on how abnormal morphology of the sella turcica is interrelated with the morphology of the pituitary gland. New findings on these inter-relationships are presented in this review. Even though new insight has been gained in this specific field, a complete overview of this complex region has not yet been achieved.

The present review aims to focus on the shape and size of the sella turcica and on the pituitary gland located in the sella turcica. The purpose is to draw attention to the importance of these aspects by focusing on prenatal cases that show a connection between the shape and size of the sella turcica and the location of the pituitary gland. It is also the intention to demonstrate how prenatal and postnatal development of the sella turcica/pituitary gland is associated. The review suggests how brain-imaging techniques may inspire and renew the field of orthodontics as an association is demonstrated between osseous contours normally analysed only by orthodontists and brain contours normally analysed only by neurologists.

The main sections in this review include the postnatal registration of sella turcica, prenatal development of sella turcica/pituitary gland, and pathological conditions associated with abnormal development of the sella turcica/pituitary gland.

Morphology and postnatal development of the sella turcica
The sella turcica serves as an important anatomical reference in orthodontics partly because the s-point, placed centrally in the sella region, is a central fix point in cephalometric analysis and partly because the contour of the anterior wall is used in evaluation of craniofacial growth.

Length, depth, and diameter of the sella turcica have been calculated since the 1950s and 1960s (Silverman, 1957; Kisling, 1966). The centre of the sella turcica was defined as the s-point by Björk (1947). The s-point is one of the fix points used for determining the cranial base angle and the nasion–sella line connecting the nasion and the sella point s. This line is important for the expression of jaw prognathia. The accuracy or reproducibility of the s-point has been given great attention in orthodontic research.
gene, SHH, plays a major role in the midaxial development along the notochord. In the rostral end of the notochord, SHH influences the formation of the midaxial part of the cranium extending from the anterior wall of the sella turcica to the midface (Schoenwolf et al., 2009). This midaxial developmental field is also called the frontonasal segment (Figure 3).

The pituitary gland develops before the cartilaginous sella turcica has been formed (Sheng and Westphal, 1999). The adenopituitary gland develops from the oral ectoderm (Rathke’s pouch) and the neuropituitary gland from the infundibulum cerebri (Figure 2).

In conclusion, the development of the pituitary gland is closely coordinated with the development of the sella turcica. The development of the pituitary gland must be completed before the sella turcica can be formed. It is presumed that a deviation in the development of the pituitary gland will result in a deviation in the morphology of the sella turcica. The second hypothesis is thus that there is an interrelationship between the deviations observed in the pituitary gland and the deviations observed in the sella turcica.

Under normal conditions, the thyroid stimulating hormone production in the pituitary gland begins in the 15th week (Dubois et al., 1978). At this time, the sella turcica has formed in cartilage.

The prenatal morphology of the sella, as it appears in cartilage, is similar to the morphology seen in bone tissue after birth (Figure 4). Therefore, foetal pathological studies revealing deviations in the sella turcica form an adequate basis for a better understanding of deviations in the sella turcica seen postnatally. Of particular importance are studies performed on sella turcica morphology in foetuses with well known genotypes. In such studies and also in studies on foetuses with unknown genotypes, it is important to distinguish between deviations in the different parts of the sella that have different embryonic origins (anterior wall, posterior wall, or the border area between these walls). Accordingly, this distinction will be made in this review. Furthermore, morphological deviations in the pituitary gland associated with sella turcica deviations will be described.

Pathological conditions associated with abnormal development of the sella turcica and pituitary gland

Prenatal pathological development of the sella turcica

Pathological morphology of the prenatal sella turcica, observed histologically on human post-mortem material, is summarized and illustrated in this section. Sella turcicae and pituitary glands from foetuses with known and unknown molecular aetiology will be described. The material arose from spontaneous and therapeutically induced abortions and was investigated as part of the required brain autopsy procedure.

As the anterior and posterior walls have different developmental origins, distinction will be made between conditions with malformations in the posterior and anterior walls and conditions with deviation in the bottom of the sella, where the anterior and posterior walls meet. Also morphological malformations in the pituitary gland will be highlighted. An overview of sella turcicae from different pathological conditions compared with normal findings is shown in Figure 5.

Holoprosencephaly

Holoprosencephaly is a condition with severe facial anomalies combined with short stature, pituitary insufficiency, microcephaly, choanal atresia, midnasal stenosis, and congenital nasal perform aperture stenosis (Nanni et al., 2001). Only mild forms of the condition are compatible with life. Thirteen prenatal cases have been investigated. The sella turcica/pituitary gland was analysed histologically in all 13 cases.

In this condition, the anterior wall of the sella turcica is deviant and partly absent, while the posterior wall with the notochordal remnant is completely normal (Kjær and Hansen, 1995b; Kjær et al., 2002; Figure 5 and Supplementary Figure 1). The size of the sella is diminutive. The condition was in all cases associated with severe malformations of the pituitary gland. In this condition, huge amounts of adenopituitary gland tissue are located subpharyngeally
below the external aspect of the cranial base (Kjær and Hansen, 1995b; Supplementary Figure 1).

**Trisomy 21**

Clinical characteristics of Trisomy 21, often called Down syndrome, are mental retardation, short limbs, high arched narrow palate, short fifth finger, and depressed nasal ridge. Forty-eight cases have been investigated. The sella turcica/pituitary gland was analysed histologically in 32 cases.

The anterior wall of the sella turcica is affected in different degrees in this genotype from a slight depression in the lower aspect of the anterior wall to more severe cases where the anterior wall is completely separated from the posterior wall (Kjær et al., 1998b). In the different degrees of severities, the posterior wall and the notochordal remnant will appear either normal or with minor malformations (Figure 5 and Supplementary Figure 2). Adenopituitary gland tissue is located in the fossa of the sella turcica and, in some cases, also located subpharyngeally (Kjær et al., 1998b).

**Myelomeningocele/spina bifida**

Spina bifida is a congenital anomaly in which the neural tube has not closed during early foetal life. The genotype has not been determined. In most cases of spina bifida, the only phenotypic sign is non-closure of the vertebral arches. When the neural tissue protrudes through the opening, the condition is more severe and is called Myelomeningocele. Twenty-seven cases have been investigated. The sella turcica/pituitary gland was analysed histologically in 21 cases.

The closure of the neural tube is the result of a complex interaction at the molecular level between the notochord, the neural tissue, and the surface ectoderm. In this process, the gene sonic hedgehog, SHH, also plays a role. At the cranial end of the notochord, the posterior wall of the sella turcica is formed. This wall has a wide, cone-shaped morphology, and the remnant of the notochord in the dorsum appears with a jagged course (Figure 5 and Supplementary Figure 3). Furthermore, the anterior wall is undermined, and the bottom of the sela is thin. Large amounts of adenopituitary gland tissue are seen subpharyngeally (Kjær et al., 1996, 1999a; Supplementary Figure 3).

**Meckel–Gruber syndrome**

Children with Meckel–Gruber syndrome are born with multiple severe malformations of which occipital encephalocele, enlarged kidneys, and polydactyly are the most common. Frequently, also cleft lip and palate and microcephaly are observed. Mutations in the MKS1-6, mapped to six different chromosomal loci, have been shown to cause Meckel–Gruber syndrome. MKS1 is mapped to 17q21. The condition is never compatible with life. Six cases have been investigated. The sella turcica/pituitary gland was analysed histologically in five cases. Genotype was not determined.

The morphology of the sella turcica is characterized by a wide basis in the dorsum sella with sharply angulated notochordal remnant. The anterior wall of the sella is uneven (Figure 5 and Supplementary Figure 4). Absence of neuropituitary gland tissue and abnormal location of adenopituitary gland tissue on top of the dorsum sella was observed in two cases (Kjær et al., 1999b).

**Anencephaly**

This is a severe congenital malformation with complete absence of the hemispheres. The condition is never compatible with life. Thirty-six cases have been investigated. The sella turcica/pituitary gland was analysed histologically in 30 cases.
The brain stem and the cerebellum have developed. This means that the anterior wall of the sella formed by neural crest is without major malformations, while the posterior wall is short, broad, and malformed (Figure 5 and Supplementary Figure 5). The notochordal remnant in the posterior wall appears with different extensions (star-like shape). The neuropituitary gland is absent, and the adenopituitary gland tissue is observed in the sella area, as well as subpharyngeally. A large cleft is often observed between the anterior and posterior aspects of the sella (Kjær and Hansen, 1995b; Figure 5).

Trisomy 18

Major characteristics of Trisomy 18 are mental retardation, failure to thrive, congenital heart disease, low-set malformed ears, prominent occipital region, long skull, small biparietal diameter and overlapping fingers. Forty-one cases have been investigated. The sella turcica/pituitary gland was analysed histologically in 27 cases.

The sella turcica appears with a malformed posterior wall, with a broad base and often with several notches in the posterior aspects (Supplementary Figure 1). The notochordal remnant appears v-shaped. There is no or only a very slight connection between the anterior and posterior walls, and the adenopituitary gland tissue is displaced subpharyngeally through the opening in the bottom of the sella turcica (Kjær et al., 1998a, Figure 5 and Supplementary Figure 6).

Chondrodystrophy

The main clinical signs are disproportionally large head, prominent forehead, depressed nasal bridge, and short stature. Seven cases have been investigated. The sella turcica/pituitary gland was analysed histologically in all seven cases.

In these cases, the sella turcica is enlarged and the inner contour of the sella is uneven. The notochordal remnant can be hook shaped (Figure 5 and Supplementary Figure 7). This has been observed in two cases and has not been published previously.

Hydrocephalus

A major characteristic is the abnormal enlargement of the head due to ventricular dilations. Thirty-one cases have been investigated. The sella turcica/pituitary gland was analysed histologically in 22 cases.

The posterior wall of the sella is broad and abnormal. The notochordal remnant has several extensions (star-like shape), and there is no connection between the anterior and posterior walls (Figure 5 and Supplementary Figure 8). The neuropituitary gland can be absent, and the adenopituitary gland can be located in the lower space between the two walls. This condition has been observed in three cases demonstrating slightly different phenotypes (Supplementary Figure 8).

Cleft lip and palate

Eleven cases of cleft lip or combined cleft lip and palate have been investigated. The sella turcica/pituitary gland was analysed histologically in 10 cases.

Cleft lip (four cases): The morphology of the sella is close to normal though a short and uneven anterior wall can be seen in some cases. Normal position and morphology is observed of the pituitary gland. The notochordal remnant has normal morphology.

Combined, isolated cleft lip and palate (six cases): In these cases the bottom of the sella appears narrow, seemingly due to malformations of the anterior and posterior walls. The pituitary gland may partly be located subpharyngeally (Figure 6). An extended study of the sphenoid bone was not performed.
adolescence, and ovarian dysgenesis. Thirteen cases have been investigated. The sella turcica/pituitary gland was analysed histologically in all 13 cases.

The sella turcica appears larger and more open cranially than normal, with or without a cleft in the bottom. A notch can appear at the posterior border in the dorsum sella. The pituitary gland is located normally in the fossa. This condition has not been published previously (Figure 8).

Severe facial malformations
The sella turcica and pituitary gland have been investigated in 15 cases where the autopsy diagnosis was severe facial malformation without other visible malformations. The severe malformations are incomparable and the genotype is not known. Two malformations are described. One malformation is characterized by hypertelorism and malformed external nose (Kjær et al., 1997a) and the other by an oro-ocular cleft (Kjær and Hansen, 2000). In both cases, both the anterior and posterior walls are malformed. There is no sella fovea, but a wide, channel-like malformation. The pituitary gland is located partly in the channel and partly subpharyngeally in one case and as an adenoid extension from the pharyngeal mucosa in the other case (Figure 9). Neuroradiological gland tissue can be absent.

Postnatal pathological development of the sella turcica
In the following, the postnatal sella turcica morphology will be described in five of the conditions analysed prenatally and is described in the previous section. Furthermore, the sella turcica morphology will be described in the following conditions, not analysed prenatally: Cri-du-Chat syndrome, Williams syndrome, Arnold Chiari syndrome, velocardiofacial syndrome, Kallmann syndrome, severe skeletal malocclusions, and Acromegaly.

Conditions previously described prenatally are the following.

Holoprosencephaly/single-median maxillary central incisor
Single-median maxillary central incisor (SMMCI) with gene location 7q36.3 can be a mild form of Holoprosencephaly. Characteristic findings are short stature, close set eyes, abnormal lip contours, absent anterior frenulum labii superior, one maxillary central incisor in the midaxis, and absence of incisive papilla.

The postnatal appearance of the sella turcica in these cases is characterized by a small sella with an abnormal anterior wall and a pointed (not curved) bottom (Kjær et al., 2001a). The malformation is associated with other malformations in the frontonasal field of the cranium. The frontonasal field extends backwards into the cranium reaching and including the anterior wall of the sella (Figure 3). The posterior wall is in most cases normal. Neuroradiological studies have demonstrated a diminutive pituitary gland in the fovea. Furthermore, partly non-separated hemispheres were observed (Kjær et al., 2009; Figure 10). Growth hormone substitution can improve the height and general development (Kjær et al., 2009).

Trisomy 21
Shortly after birth, the sella appears with exactly the same bone morphology as seen prenatally in the cartilage morphology. This can be with a broad cranial opening, with a cavity in the frontal wall or with a slight channel in the bottom (Russell and Kjær, 1999).

Myelomeningocele/spina bifida
In 18 cases with different degrees of Myelomeningocele, the anterior wall appeared sloped and the fovea was in most cases diminutive (Kjær et al., 1998c).
Cleft lip and palate
In cleft lip, the contour of the sella turcica was close to normal though the anterior wall seemed short and in a few cases sloped (Nielsen et al., 2005).

In combined cleft lip and palate the anterior wall was sloped and curved in most cases. In several cases, the dorsum sella had a broad basis (Nielsen et al., 2005).

Fragile X syndrome
In Fragile X syndrome the anterior wall of the sella was very high compared with the length of the posterior wall. The anterior wall was curved, and the posterior wall appeared short with a notch in the posterior aspect (Kjær et al., 2001b).

Conditions not previously described prenatally are the following.

Cri-du-Chat syndrome
This syndrome is a genetic disorder, involving partial deletion of the short arm of chromosome 5. Clinically, the patients have a cat-like cry; growth retardation; and severe mental retardation, microcephaly, and hypertelorism.

In Cri-Du-Chat syndrome a new cranial developmental field was described, extending from the cerebellum through the dorsum sella to the laryngeal region (Kjær and Niebuhr, 1999). The dorsum sella was in all cases broad, short, plump, and often with a notch in the posterior aspect.

Williams syndrome
This is a rare congenital disorder with distinctive craniofacial features, cardiovascular abnormalities, mental retardation, and behaviour characteristics. The gene has been mapped to 7q11.23.

The morphology of the sella varied from normal to shapes with abnormal posterior walls. A notch was often seen in the posterior aspect of the dorsum (Axelsson et al., 2004b).

Arnold Chiari syndrome
In this condition, the caudal parts of the brain stem and cerebellum are displaced through the foramen magnum into the upper cervical area with or without myelomeningocele. Clinically, a short neck is observed. The genotype is unknown.

A single case has been analysed but not described previously. A very short, nearly absent posterior wall led to a neuroradiographic analysis, which demonstrated a mild type of the Arnold Chiari malformation where the lower parts of the cerebellum are dislocated through the foramen magnum into the cervical spine (Figure 11).

Velocardiofacial syndrome
Velocardiofacial syndrome also known as chromosome 22q11.2 deletion syndrome has the following main manifestations: impairment of speech (palatal abnormalities), cardiac anomalies, and abnormal facial features. Furthermore, thymic hypoplasia/aplasia and brain abnormalities specifically involving the hindbrain are observed.

In velocardiofacial syndrome a new developmental field has been described, extending from the hindbrain area through the posterior aspect of the palate, thyroid, and thymus to the conotruncal septum of the heart (Mølsted et al., 2010). In these cases, the upper part of the dorsum sella was narrow and short.

Kallmann syndrome
Kallmann syndrome is characterized by the association of hypogonadotropic hypogonadism and anosmia or hyposmia. The gene mutations responsible for Kallmann syndrome are KAL1, FGFR1, PROKR2, and PROK2, located in four different chromosomal loci. KAL1 is mapped to Xp22.32.

Kallmann syndrome involves abnormal development of the bilateral vomeronasal organs. In these organs, GnRH neurons are formed that migrate to the hypothalamus where GnRH is synthesized and later released. This in turn stimulates the pituitary gland to secrete luteinizing hormone and follicle-stimulating hormone.

Prenatally, the vomeronasal organs are located on both sides of the cartilaginous nasal septum (Kjær and Hansen, 1996a). In cases with anosmia, the rhino-olfactorium epithelium is also malfunctioning. The gland and the rhino-olfactorium epithelium both belong to the frontonasal field studied prenatally in normal foetuses (Kjær and Hansen, 1996a, b). According to these deviations observed in the frontonasal field, a deviant contour of the sphenoid planum connected to the anterior wall of the sella is observed (Mølsted et al., 1997).
Severe skeletal malocclusions
Severe skeletal malocclusions include extreme maxillary and mandibular skeletal deviations.

Sella bridges uniting the anterior wall with the posterior wall in the sella turcica have been described with different morphology in 18.6% of orthodontic/surgical cases (Becktor et al., 2000). Later, this sella malformation, seen on profile radiographs, has also been related to deviations in the dentition (Leonardi et al., 2006).

Acromegaly
Acromegaly is caused by a functional GH-secreting adenoma originating in the adenohypophysis. This results in an enlargement of the sella turcica and secretion of growth hormone after the physiological growth of the adenohypophysis has arrested. Before surgical and/or endocrinological treatment is introduced for this condition, a severe enlargement of the sella turcica occurs.

Conclusion
The morphology of the prenatal sella turcica formed in cartilage determines the morphology seen postnatally in osseous tissue. The sella turcica has been described in histological studies on prenatal tissue histologically and in radiological studies on postnatal tissue. Examples of such connections between pre- and postnatal findings show the importance of prenatal analysis in craniofacial biology. It can be concluded that

1. The anterior and posterior walls in the sella turcica have different embryological origins and must therefore be diagnosed individually.
2. Malformations in the pituitary gland may secondarily cause malformations in the sella turcica.
3. There are similarities in the morphology of the sella turcica before and after birth.
4. Deviations in the anterior wall appear to be associated with deviations in the frontonasal fields and in some cases also with malformations in the body axis.
5. Deviations in the posterior wall appear to be associated with brain malformations.
6. In each syndrome or other pathological cases, a specific malformation pattern was observed in the sella turcica morphology, varying from mild to severe phenotype.
7. In normal cases, minor variations in morphology of the anterior and posterior walls were observed.
8. The location of the landmark s depends on the morphology of the sella turcica.

In conclusion, this overview of 22 years of research performed on pre- and postnatal sella turcica and pituitary gland cases illustrates the importance of including the morphology of the sella turcica in orthodontic diagnostics. Even so, there are still unknown aspects in the understanding of how genotype influences this morphology. In a recent overview of craniofacial patterning (Kjær, 2010), it appeared that all craniofacial fields were developmentally interrelated with the sella turcica region (Figure 12). It is therefore clear that malformations in the frontonasal, the maxillary, and the palatinal fields are combined with malformations in the anterior wall. We know that malformations located in the frontonasal field (e.g., SMMCI and cleft lip) have a different genetic background than malformations in the maxillary and palatinal fields (e.g., cleft palate and velocardiofacial syndrome). The most posterior part of the frontonasal field is the anterior wall of the sella turcica, genetically influenced by the SHH gene (Schoenwolf et al., 2009). This is the same gene that is involved in the neural tube closure along the body axis. When the neural tube does not close, as in Myelomeningocele, the SHH may interact. This could be a possible explanation for the finding of a malformed anterior wall in Myelomeningocele (Kjær et al., 1999c).

The influence of genotypes on the morphology from mild to severe expressions remains unexplained. In that context, it is interesting that monozygotic twins often, but not always, have the same sella turcica morphology (Brock-Jacobsen et al., 2009). Another challenge for future studies is to understand how deviations in the body axis and in the central nervous system are associated with anterior and posterior wall malformations.

The SMMCI condition described illustrates how it is possible from a profile radiograph to extend the diagnostics to pituitary gland malformations. It has been demonstrated in SMMCI that growth hormone substitution was necessary in a case with pituitary malformation (Kjær et al., 2009). It is important that specialists in orthodontics as a routine measure the growth in height of patients with significant deviations in the sella turcica. This is considered the first step towards controlling the endocrinological function.

This review demonstrates that it is valuable to expand our understanding of craniofacial deviations by combining profile radiographic diagnostics of the sella turcica morphology with neuroradiological diagnostics.

Supplementary material
Supplementary material is available at European Journal of Orthodontics online.

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