Is craniofacial morphology in Apert and Crouzon syndromes the same?

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This article reviews previous research on the craniofacial development in Apert and Crouzon syndromes and adds new roentgencephalometric information. It is concluded that craniofacial development in the two syndromes is not the same. Marked differences were found in the calvaria, cranial base, orbit, maxilla, zygoma, incisal occlusion, and soft tissue profile. In general, abnormal craniofacial morphology was more severe in Apert syndrome than in Crouzon syndrome. □ *Craniofacial morphology; craniosynostosis; roentgencephalometry*

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Since around the beginning of the 20th century, when the French pediatrician Eugène Apert (1) published observations of one case and reviewed earlier known cases of *acrocéphalosyndactylie* (later known as Apert syndrome) and the French neurologist Octave Crouzon (2) published a study of two cases of *dysostose cranio-faciale héréditaire* (later known as Crouzon syndrome), it has been argued whether craniofacial development in these two conditions is the same or different. It appears that Apert and co-workers thought Crouzon's cases represented the same condition as in those reported by Apert, with the exception of syndactyly of hands and feet in Apert syndrome (3). In contrast, Crouzon and co-workers argued that the cases described by Crouzon (2) represented a separate condition because it was inherited, whereas the cases reviewed in Apert's article (1) occurred sporadically. In addition, Crouzon (4–6) thought other clinical features of the two disorders were different.

It has been stated repeatedly in the literature since then that craniofacial morphology in Apert and Crouzon syndromes is the same; in fact, data and analysis in several studies have been pooled (7, 8). The reasons for this are understandable. The two syndromes share a number of clinical and radiographic findings: premature synostosis of sutures of the calvaria, cranial base, orbital region, and maxillary complex; early closure of synchondroses of the cranial base; brachycephaly; increased digital markings; increased size of the sella turcica; shallow orbits; exorbitism; hypertelorism; maxillary hypoplasia; and mandibular overjet (9). However, some qualitative craniofacial traits show marked differences between the two syndromes: cleft palate and bifid uvula are frequent findings in Apert syndrome (10), whereas these traits are extremely rare in Crouzon syndrome (11). In addition, both the frequency and the distribution of cervical spine coalitions differ significantly in the two syndromes (12). We have previously documented a marked difference in skull morphology in infancy and early childhood in the two syndromes (13–15). The infant Apert skull is characterized by premature fusion of the coronal sutures only and by a wide calvarial midline defect extending from the glabella to the posterior fontanelle. In contrast, the infant Crouzon skull shows much more extensive synostosis of calvarial sutures and no midline defect.

Roentgencephalometric findings

In a study of 26 adolescents and adults with Apert syndrome (15 males and 11 females) (16), we compared the craniofacial morphology with that found in Crouzon syndrome (11). The results are shown as superimposed mean diagrams of the lateral and frontal cephalometric projections in the male groups (Figs. 1 and 2).

Analysis showed marked and significant differences in the following morphologic areas: calvaria, cranial base, orbit, maxilla, zygoma, incisal occlusion, and soft tissue profile. In general, abnormal craniofacial morphology was more severe in Apert syndrome than in Crouzon syndrome. These findings corroborate our other studies of infants, children, adolescents, and adults with these syndromes (11, 13–17).

Discussion and conclusion

Apert and Crouzon syndromes are different disorders, and the craniofacial development is not the same. The craniofacial phenotypes are distinct at all ages. The differences are most pronounced during infancy but become less exaggerated with age (18) (Fig. 3). Since both syndromes show a high degree of variable expression, clinical evalua-

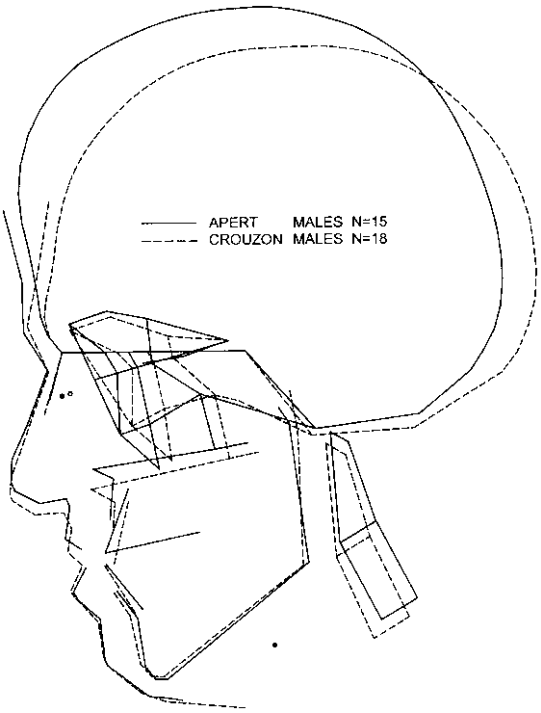

Fig. 1. Mean diagram for lateral projection for males with Apert syndrome superimposed on mean diagram for males with Crouzon syndrome. Superimposition was made on nasion-sella line (NSL), registered at sella (s). Source: Kreiborg et al. (16).

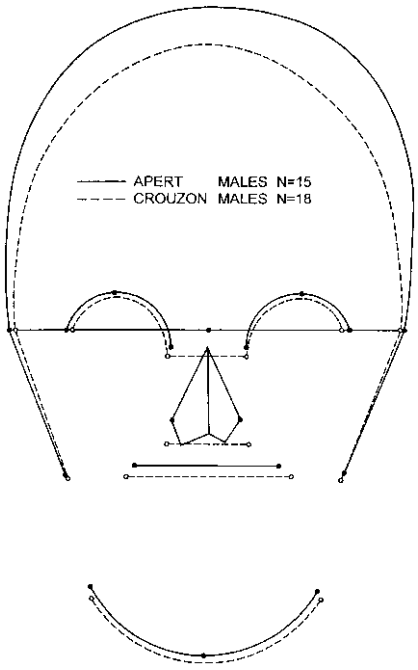

Fig. 2. Mean diagram for frontal projection for males with Apert syndrome superimposed on mean diagram for males with Crouzon syndrome. Superimposition was made on line connecting lod (latero-orbitale dexter), and los (latero-orbitale sinister), registered at the center point (c). Source: Kreiborg et al. (16).

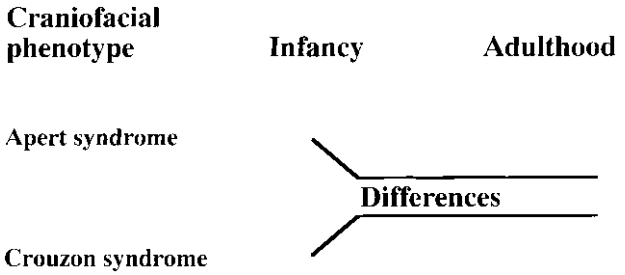

Fig. 3. Craniofacial phenotypes of Apert and Crouzon syndromes, distinct at all ages, show most pronounced differences during infancy, but become less exaggerated with age. Source: Cohen (18).

tion of them has to be individualized for treatment planning and care.

Biologic differences observed in craniofacial development in Apert and Crouzon syndromes are consistent with the different types of mutations known to cause these disorders. The two mutations that cause Apert syndrome are located in the linker region between immunoglobulin-like loops II and III on fibroblast growth factor receptor 2. More than two dozen mutations known for Crouzon syndrome are located within immunoglobulin-like loop III of the same receptor (19). However, the pathogenesis of both syndromes is incompletely understood at present.

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