Premature Fusion of the Spheno-Occipital Synchondrosis (SOS) and Midface Hypoplasia in Syndromic Craniosynostosis

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Background: The spheno-occipital synchondrosis (SOS) is a key driver of cranial base and mid-facial development. Its premature fusion has been associated with midface hypoplasia in animal models, and there is growing evidence that it plays a role in midface hypoplasia associated with syndromic bicoronal craniosynostosis in humans. The purpose of this study was to compare CT scans of patients with Apert's Syndrome, all of whom had midface hypoplasia, to a cohort of non-syndromic bicoronal craniosynostosis patients, none of whom had midfacial hypoplasia, to determine if there is a difference in timing of closure of the SOS.

Methods: CT-scans of Apert's Syndrome patients (47), age-matched non-syndromic bicoronal synostotic (12), and 76 normal age-matched control patients were assessed. There were 32 male and 15 female Apert's patients. The non-syndromic group consisted of 4 males and 11 females. There were 39 males and 37 female controls. SOS fusion on axial images was graded as open, partially closed, or closed by three blinded reviewers. Groups were further assessed according to gender. Special attention was focused on ages 2 to 17 years as no Apert's patients fused prior to age 2 or had failed to fuse after age 17. An unbalanced two-way analysis of variance and a subsequent Tukey-Kramer *post-hoc* test were performed to compare groups.

Results: Both male and female Aperts patients demonstrated partial suture fusion significantly earlier than non-syndromic bicoronal patients ($p<0.001$). No difference was observed in timing of partial closure between genders ($p=0.855$). Apert's patients demonstrated partial fusion as early as age 2 in both genders, whereas the earliest partial fusion for non-syndromic craniosynostotic males and females occurred at 10 and 13 respectively. In unaffected controls, the earliest age for partial suture fusion was 7 for both genders. In all groups, females completed suture fusion earlier than males ($p=0.053$).

Conclusions: The SOS begins to fuse significantly earlier in Apert's patients than non-syndromic bicoronal synostosis patients or controls. This data also confirms earlier SOS closure in females across all groups, as has been shown in the literature. There is a strong association between early fusion of the SOS and midface hypoplasia given that all of the Apert's syndrome patients had midface hypoplasia compared to none of the non-syndromic bicoronals or controls. Further work is needed to establish causality between premature fusion of the SOS and growth arrest of the midface in syndromic craniofacial patients.