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Bilateral asymmetry of tooth formation is elevated in children with simple hypodontia

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ABSTRACT

Objective: Tooth formation normally progresses symmetrically between sides; the goal in this study was to test the clinical impression that left–right asymmetry in tooth formation is elevated in children with simple hypodontia.

Materials and methods: Data from panoramic X-rays of American white children (5–14 years of age) with simple hypodontia ($n = 158$) were compared to a comparable group from the same practises with all teeth present ($n = 206$). Children with hypodontia were otherwise phenotypically normal, with no cleft or recognized syndrome. Crown–root formation of each tooth (ignoring third molars) was scored using an 11-grade scheme. Analysis relied on chi-square goodness-of-fit tests and odds ratios.

Results: Hypodontia typically occurs unilaterally; it is more common in girls than boys; and it most frequently affects second premolars (omitting third molars). No evidence of a side preference was found as regards absence of the tooth or tooth formation. Tooth formation was decidedly more frequently asymmetric in those with hypodontia, though again the distribution by side was random in the sample. Summed over all tooth types, asymmetric formation occurred in 18.6% of cases with hypodontia compared to 11.9% in controls, and this is significant by chi-square ($P = 0.03$), with an odds ratio of 1.43 (CL: 1.02, 2.04). All tooth types exhibit elevated developmental asymmetry in the hypodontic sample despite only one or a few teeth being agenic.

Conclusions: Increased asymmetry suggests a breakdown in the rigour of developmental timing in cases with simple hypodontia. In concert with increased frequencies of other growth issues in such cases, such as side differences in size and morphology, hypodontia is best viewed as a symptom of an anatomically broad relaxation of developmental canalization between homologous structures, not an isolated dental feature.

1. Introduction

Hypodontia—the congenital absence of one or a few teeth[1]—has been labelled the most common developmental anomaly in humans.[2] The frequency of missing teeth varies by sex and race, and reported frequencies vary appreciably depending on sampling fluctuations and the inclusion criteria used. In Caucasians, simple (nonsyndromic) hypodontia affects about 7% of the population (ignoring third molars).[3]

Hypodontia can result from various causes. Failure of innervation is one problem.[4–6] Defects of molecular signalling and transcription factors, notably of PAX9 and MSX1, can be the proximate cause,[2,7] and numerous other genes are

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essential for proper development.[8,9] Environmental stressors (teratogenic chemicals, severe malnutrition) also have been implicated, but the evidence here is not strong.[10,11]

It is intriguing that hypodontia follows no clear mode of inheritance.[12] Indeed, phenotypes (i.e., which and how many teeth are absent) can vary considerably even within monozygotic twin pairs[13–15] and within family members with the same mutation.[16] Moreover, numerous researchers note that hypodontia often occurs unilaterally—even though the body's genetic information is presumed to be identical on both sides.[17] Formation of a tooth but not its antimere in the opposing quadrant seems to be due to local differences in genetic–environmental interactions between the two sides. Environmental factors probably influence the frequency of hypodontia and the risk of developmental asymmetry, but controlled animal studies suggest that tooth size is more commonly affected by stress than is the actual failure of tooth formation.[10,11] Comparable results are derived from clinical studies, where common environmental stressors, such as malnutrition and infectious disease, can influence size, but cessation of tooth formation seems uncommon. Exceptions are restricted to events that directly kill tissues rather than stress them.[18,19]

The familial aggregation of hypodontia is well documented,[12,20–22] which argues for a genetic influence on the congenital absence of teeth, even though the specific mode of inheritance remains a moot issue. It appears that hypodontia is multifactorial both in the sense that (A) various causes (genetic and environmental) can result in congenital absence and (B) various gene defects along the developmental pathway can abort tooth development. Consequently, single-gene models[23–25] do not fit the actual pedigrees as well as a polygenic threshold model.[26] The threshold model was originally developed by Wright[27,28] and applied to minor skeletal and dental features by Grüneberg.[29,30] Brook[31–33] has applied a polygenic threshold model to hypodontia and related dental features.

The observation that hypodontia is frequently unilateral is intriguing, and the purpose of the present study was to explore the frequencies of developmental asymmetry in children with simple hypodontia. We tested our clinical impression that left–right asymmetry in tooth formation is elevated in children with hypodontia compared with those with complete dentitions.

2. Materials and methods

This was a retrospective case–control study. Panoramic radiographs of otherwise normal American white children with simple hypodontia were collected from paediatric and orthodontic practises in Arkansas and Tennessee. Total sample was 158 children between 5 and 14 years of age in whom between 1 and 4 permanent teeth were congenitally absent (omitting third molars). These were compared with 206 children with full dentitions from the same practises (ignoring M3s). This retrospective study was HIPAA compliant and approved by the institutional review board.

The 11-grade ordinal scale of Haavikko[34] was used to score all permanent teeth (Fig. 1). (Third molars also were scored

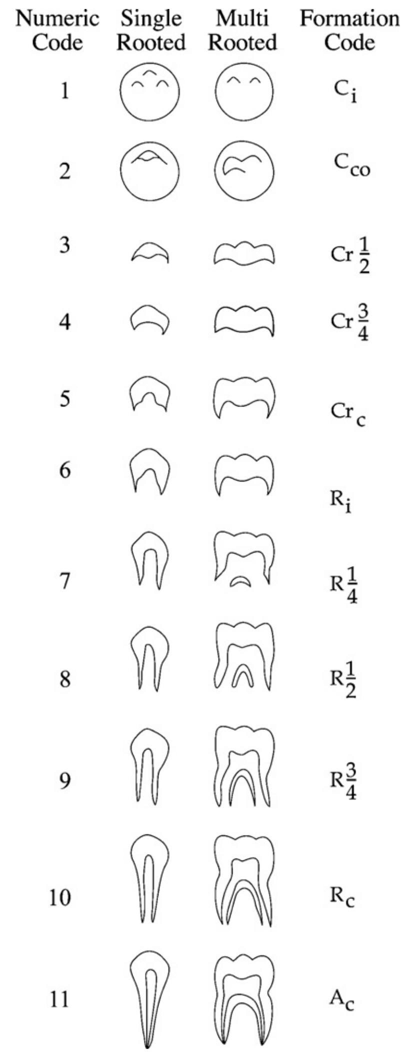

Fig. 1 – Diagrams of the 11 ordinal stages of crown–root mineralization[34] used to score each tooth's extent of formation.

when both were forming to assess left–right asymmetry.) These morphological grades are distinguished visually by differences in shape of the mineralized crown and root portions of each tooth.[35] The highest grade actually attained by each tooth was recorded.[36] Teeth were left unscored if film quality or image quality (due to overlapping structures) prevented firm assignment. There was no way to be blinded as to the group (because of the missing teeth), but the films (cases and controls) were intermingled, and data were collected for a different purpose so there was no reason a priori to favour a difference between groups. Several cases (228 teeth) were re-scored after a wash-out interval of 4 months. Repeatability was high (kappa = 0.975; se = 0.0145), and none of the differences (7/228) exceeded one grade.

Hypodontia is more common in girls than boys in the general population,[3,37] and this is mirrored in this selected sample with more girls (63%; 100/158) than boys (37%; 58/158) with hypodontia.

The hypodontic cases were counted for each tooth type regarding whether the missing tooth occurred only on the left