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ORIGINAL ARTICLE

Root length in the permanent teeth of women with an additional X chromosome (47,XXX females)

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Abstract

Objective. Previous studies have demonstrated differential effects of the X and Y chromosomes on dental development. The expression of sexual dimorphism in terms of tooth size, shape, number and developmental timing has been explained especially by Y chromosome influence. The Y chromosome promotes enamel, crown and root dentin development. The X chromosome has an effect on enamel deposition. The aim of this research is to study the influence of the extra X chromosome on the development of permanent tooth root length. ***Material and methods.*** The study subjects (all of whom were from the Kvantti Dental Research Project) were seven 47,XXX females, five female relatives and 51 and 52 population control men and women, respectively. Measurements were made from panoramic radiographs on available permanent teeth by a digital calliper according to established procedures. ***Results.*** The results showed that the maxillary root lengths of the 47,XXX females were of the same magnitude as those in normal women, but the mandibular root lengths were longer in 47,XXX females than in normal men or women. ***Conclusions.*** Increased enamel thickness in the teeth of 47,XXX females is apparently caused by the active enamel gene in all X chromosomes having no increased influence on crown dentin formation. These results in 47,XXX females indicate an increase in root dentin development, at least in the mandible, which together with the data on crown formation reflects a continuous long-lasting effect of the X chromosome on dental development.

Key Words: *Aneuploidy, chromosomes: human, X, growth and development, sex characteristics, tooth root*

Introduction

47,XXX females are women with one extra X chromosome. The incidence of this anomaly among newborn girls is 1/800 according to Therman [1] and 1/1002 according to Nielsen and Wohlert [2] and tends to increase with maternal age [1]. Birth weight, height and head circumference are smaller in individuals with an extra X chromosome, such as 47,XXX girls, than in normal girls. 47,XXX females show a tendency towards an increase in final height [3]. The sitting height of 47,XXX females is already small during childhood and the leg length proportionally long. The face in 47,XXX females is levelled and vertically enlarged in comparison to normal females and occlusion is featured by bimaxillary prognathism, with increased anterior lower face height [4]. 47,XXX females have normal sex hormone conditions and normal children.

The expression of sexual dimorphism in terms of tooth size, shape, number and developmental timing has been explained especially by a Y chromosome influence. Normal men have bigger tooth crowns and longer roots than women [5–10]. The average difference in tooth crown and root size between normal men and women is explainable primarily by a growth-promoting effect of the Y chromosome on enamel and dentin [7,9–13].

Amelogenin is involved in the control of the size, morphology and orientation of the mineral crystals of the dental enamel [14,15]. In addition to the inner enamel epithelial cells during crown formation, amelogenin is found in Hertwig's epithelial root sheath when the dental papilla cells are still undifferentiated, suggesting a role in the induction of root odontoblast differentiation [16]. It has also been suggested that there are both qualitative and quantitative differences in the inductive mechanisms operating in crown and

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root dentin formation [17]. Molecular studies have indicated that the loci for human amelogenin are to be found on the distal short arm of the X chromosome (Xp22.1-p22.3) and on the short arm of the Y chromosome (Yp11.2), although the proximal long arm of the Y chromosome (Yq11) has also been suggested as a locus [18–20]. The coding regions of the X and Y chromosome amelogenin genes are ≈87% homologous [21] and in humans both of them are transcriptionally active [18–20,22]. It has also been suggested that the normal development of the tooth root may be influenced by the same genes on the X and Y chromosomes which promote crown formation [23].

The results of dental studies on individuals with an abnormal sex chromosome constitution and on normal men and women have shown some variation between these groups in terms of tooth crown sizes, enamel and dentin thicknesses, root length and also morphology [7,10–13,18–25]. Permanent tooth root lengths in Turner females, who have a lack of sex chromosome material, are smaller than in normal men or women [26,27], whereas the tooth root lengths of those with extra sex chromosomes, such as 47,XYY and 47,XXY males, are larger than those of normal men, men having longer roots than women [10,23]. Also, the root morphology varies and the prevalence of taurodontism increases with additional X chromosomes, i.e. in 47,XXX females and 47,XXY males [28–30]. All molars of the 47,XXX female shown in Figure 1 are taurodontic. Taurodontism is a morphological tooth variation in a multirooted tooth in which the pulp chamber is long and bifurcates into short root canals near the apical third of the root.

The X chromosome mainly promotes the formation of enamel during crown development [11,25,31–33], which manifests in the tooth crown size of 47,XXX females as a thicker enamel layer [14]. The aim of this study was to determine permanent tooth root lengths in 47,XXX females, or females with one extra X chromosome. It was assumed that the X chromosome has an increased influence on root development.

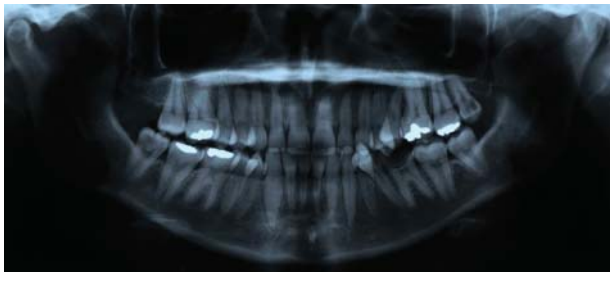

Figure 1. An orthopantomogram of a 47,XXX female aged 26 years. The outlines of the teeth were marked using a special pencil for plaster, as also was a line connecting the mesial and distal cervical margins of the enamel.

Material and methods

The retrospective study material consisted of tomographic radiographs (orthopantomographs) covering both jaws and the dentition of the study subjects. 47,XXX females, their first-degree relatives and population controls from different parts of Finland (of European ancestry) were all participants in the Kvantti Dental Research Project headed by L. J. A. on individuals with sex chromosome abnormalities. The karyotyping of 47,XXX females had been made primarily for medical reasons by cytogenetic testing of skin fibroblasts. The population controls comprised the relatives of individuals with sex chromosome abnormalities in the Kvantti Dental Research Project who were not part of the present group of 47,XXX females. The numbers of study subjects and their age distribution are shown in Table I. The Institutional Review Board of the Faculty of Medicine, University of Turku reviewed and approved the protocol informing the patients and their relatives of the nature and mode of implementation of the research. All the examinations were carried out after individual agreements were obtained.

The same person had taken all the radiographs at the Institute of Dentistry, University of Turku following a standardized procedure and with the same machine (Orthopantomograph 3; Palomex, Helsinki, Finland). The magnification ranges between 1.28 and 1.31 throughout the image layer of the panoramic radiograph (Figure 1). All the drawings and measurements were made by one of the authors (R. E. L.). Tooth root lengths in the maxilla and mandible were measured from orthopantomograms, and crown heights were measured at the same time for further studies [10]. The reliability of the measurements was examined by performing double determinations on a total of 45 dental radiographs from the Kvantti research material [10,24].

Teeth that were partly outside the image layer in the panoramic radiograph or showed obvious distortion because of being on its inner or outer surface [34] and teeth with incomplete root formation were excluded. The dilacerated roots were measured as perpendicular lengths. Permanent tooth root lengths may be affected by several external factors, which could bias the results. Orthodontic treatment, especially

Table I. Mean ages, age ranges and numbers of study subjects.

	Mean age (years)	Age range (years)	*n*
47,XXX females	16.5	9.0–26.1	7
Female relatives (one sister, four mothers)	37.0	24.7–55.5	5
Population control females	28.7	13.3–51.8	52
Population control males	30.9	11.6–67.5	51

with fixed appliances, may cause root resorption, as can traumatic occlusion, bruxism, nail-biting, trauma, apical infection or root treatment for instance. Teeth with root resorption occurring for any reason were not included.

Statistical analysis

The SPSS package 10.0 (SPSS Inc, Chicago, IL) was used for the statistical analysis. The mean values for root lengths were calculated and compared between the 47,XXX females, their female relatives and the population control males and females. In the statistical testing of the results, two-way ANOVA was used to indicate the significance of differences between the groups. $P \leq 0.05$ was considered statistically significant.

Results

The mean lengths of the permanent tooth roots of the 47,XXX females and the normal men and women are shown in Table II. The results indicated that the root lengths of the maxillary teeth of the 47,XXX females

Table II. Mean permanent tooth root lengths (mm) in the maxilla and mandible in 47,XXX females and population control males (normal men) and females (normal women).

	47,XXX females			Population control females				Population control males			
Tooth root length/mm	Mean	SD	*n*	Mean	SD	*n*	P^a	Mean	SD	*n*	P^b
Maxillary											
Right second molar	16.0	0.8	4	14.5	1.9	46	0.023*	15.7	2.1	39	0.756
First molar	13.4	1.6	6	14.5	1.9	41	0.151	15.3	1.8	38	0.016*
Second premolar	18.2	2.5	4	17.2	1.9	45	0.300	17.4	2.5	37	0.523
First premolar	18.5	1.2	4	17.2	1.9	41	0.182	18.7	2.3	33	0.864
Canine	21.3	3.7	5	21.6	2.1	50	0.797	23.9	2.2	38	0.034*
Lateral incisor	18.2	1.8	7	18.2	1.6	46	0.998	19.7	2.3	35	0.124
Central incisor	18.6	1.7	6	18.8	1.5	49	0.750	20.3	2.4	42	0.090¶
Left central incisor	18.9	1.9	6	19.0	1.3	48	0.911	20.3	2.3	39	0.164
Lateral incisor	18.5	1.0	6	18.4	1.6	46	0.906	19.5	2.0	40	0.239
Canine	19.7	2.4	5	21.8	2.1	47	0.038*	24.0	1.9	40	0.000***
First premolar	16.5	2.0	4	17.0	1.9	43	0.666	18.6	2.3	35	0.092¶
Second premolar	17.4	1.9	5	17.1	1.7	42	0.678	17.5	2.5	38	0.976
First molar	11.8	0.8	5	14.2	1.9	39	0.000***	15.0	2.0	36	0.001***
Second molar	15.7	2.8	4	14.3	1.7	39	0.165	15.0	2.6	37	0.642
Mandibular											
Right second molar	17.7	0.3	3	17.2	1.4	40	0.564	17.2	2.4	29	0.721
First molar	19.2	2.0	7	17.9	1.3	37	0.029*	18.9	1.7	33	0.748
Second premolar	19.0	2.2	4	18.1	1.9	45	0.354	19.4	2.8	43	0.788
First premolar	19.1	2.1	4	17.5	1.8	48	0.086¶	18.9	2.5	49	0.881
Canine	21.8	1.2	4	19.6	2.1	50	0.038*	21.7	2.6	49	0.927
Lateral incisor	17.4	1.5	7	15.9	1.8	51	0.040*	17.6	2.2	47	0.826
Central incisor	17.8	1.6	6	14.5	1.8	51	0.000***	15.8	2.0	45	0.021*
Left central incisor	18.5	1.6	6	14.5	1.8	48	0.000***	16.1	2.0	46	0.008**
Lateral incisor	19.3	2.2	6	16.0	1.9	49	0.000***	17.6	1.8	50	0.038*
Canine	23.8	1.6	3	19.4	1.9	47	0.000***	22.4	2.2	48	0.310
First premolar	20.6	2.4	5	17.7	1.8	48	0.002**	18.8	2.4	46	0.123
Second premolar	19.9	1.1	3	18.6	1.8	48	0.236	19.3	2.7	40	0.700
First molar	19.6	2.5	7	18.0	1.4	38	0.015*	19.0	2.2	33	0.494
Second molar	18.2	1.7	4	17.2	1.9	40	0.165	17.8	2.2	31	0.756

Statistical testing by two-tailed *t*-test: ¶$P < 0.1$; *$P < 0.05$; **$P < 0.01$; ***$P \leq 0.001$.
[a]47,XXX females versus population control females.
[b]47,XXX females versus population control males.

were mainly close to those of normal women. The root lengths in the mandible were longer than those in normal men or women. The difference was significant in 9/14 cases when 47,XXX females were compared with normal women, and the measured values in 12/14 teeth in the mandible were longer than those in normal men. The mean root lengths of antimeric teeth in 47,XXX females differed more than in normal control men and women.

The permanent tooth root lengths were also determined for five pairs of 47,XXX females and their first-degree female relatives (sister in preference to mother). The mean values were higher in the 47,XXX female in seven comparisons (versus six in normal control females) in the maxilla and in nine cases (versus 14 in normal control males) in the mandible out of 14 teeth in the jaw by comparison with a female relative.

Discussion

Neural crest-derived homeobox-containing genes, especially *Msx-2*, have an important role in specifying each tooth identity [35,36]. Dental development is mainly determined by genetic influence and in the last resort by the mitotic activity of the inner enamel epithelial cells and the secretory effect of the ameloblasts during crown development. Coordinated interactions between the epithelial and mesenchymal tissue components of developing teeth are mediated by signal molecule pathways regulating the formation of morphogenesis, cell differentiation and hard tissues [37,38]. When the crown is complete and the root begins to grow in length, Hertwig's epithelial root sheath (HERS) is formed from the inner and outer enamel epithelial cells and begins to divide until apexification occurs. After the apex is closed, the size and morphology of a tooth are final. In terms of population developmental standards, the achievement of final sizes of the permanent crown and root development becomes evident between the ages of 3 and 14 years depending on individual teeth (excluding third molars) [39].

Huang and his research group [40] have shown that neural crest-derived mesenchymal cells from the dental follicle are critical for root formation. They showed in mice molars a continuous network of HERS during the whole period of the root development which could be a signal centre of interaction between the dental epithelium and mesenchyme during root dentin and cementum formation. On the other hand, the network of signal molecules is responsible for the regulation of epithelial stem cells. Suzuki et al. [41] have shown in porcine molars the differentiation of dental papilla cells into odontoblasts following their connection to HERS through the basement membrane.

The double amount of X chromosome in normal women (46,XX) compared with men (46,XY) is compensated for by random inactivation of one X chromosome in each somatic cell [42], particularly in humans. Several genes are known to escape X inactivation, however, and are expressed in both X chromosomes; a dozen pseudoautosomal genes have been identified, most of them on the short arm [43]. An example of a gene that escapes X inactivation is given by the amelogenin gene. Also, a multifunctional role has been suggested for amelogenin, as it is expressed during the formation of other dental structures, hard tissues of the body and the cells of non-mineralizing soft tissues [44]. Interestingly, increases in anterior lower face height and body height, particularly leg length, are also obvious in these 47,XXX females. Zeichner-David et al. [45] have shown that active ameloblastin is synthesized and secreted by HERS in both *in vitro* and *in vivo* studies. Results show that the X chromosome has an increasing influence mainly on mandibular permanent tooth root lengths and earlier studies have shown its increasing influence on coronal enamel thickness. The extra length of 47,XXX females apparently results from the always active region in all three of the X chromosomes.

The root length differences observed between the antimeric teeth in this study may have been due to the sample sizes, the varying numbers of measurements available and general technical reasons. Epigenetic and environmental factors may have contributed to the final size of the roots as the measurements of natural teeth have also shown differences between the mean root lengths for antimeric teeth [5]. Anamnestic information for these study subjects did not reveal orthodontic treatment, at least not with fixed appliances, before the examination procedures. Regarding the possible effects of other external factors, the assumption was made of an even distribution between the study groups.

An earlier report on the thick enamel layer in the tooth crowns of 47,XXX females suggested an enamel gene effect of the three X chromosomes [25]. However, the additional X chromosome seemed not to have any increasing influence on crown dentin development. These results in 47,XXX females indicate an increase in root dentin length, at least in the mandible. The combined data on the formation of crown size and root length reflects the long-lasting effect of the X chromosome on dental development.

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