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ORIGINAL ARTICLE

*S Daugaard*
*IJ Christensen*
*I Kjær*

# Delayed dental maturity in dentitions with agenesis of mandibular second premolars

**Authors' affiliation:**
*S. Daugaard, I.J. Christensen, I. Kjær,* Department of Orthodontics, Institute of Odontology, University of Copenhagen, Copenhagen, Denmark

**Correspondence to:**
*Inger Kjær*
Department of Orthodontics
Institute of Odontology
The Faculty of Health Sciences
University of Copenhagen
20 Nørre Allé
DK-2200 Copenhagen N
Denmark
E-mail: ik@sund.ku.dk

**Structured Abstract**

***Authors –*** Daugaard S, Christensen IJ, Kjær I

***Objectives –*** To evaluate dental maturity in the mandibular canine/premolar and molar innervation fields in children with agenesis of the 2nd mandibular premolar and to associate these findings with normal control material.

***Setting and Sample Population –*** Department of Orthodontics, Institute of Odontology, University of Copenhagen. Eighty-three panoramic radiographs (27 girls and 31 boys with agenesis of one mandibular 2nd premolar and 17 girls and eight boys with agenesis of both mandibular 2nd premolars) represented all mandibular second premolar agenesis cases from a material of 2847 radiographs.

***Material and Methods –*** On each radiograph, dental maturity of all available mandibular premolars, canines and 2nd molars was evaluated and categorized in maturity stages according to Haavikko whose material served as control material. Descriptive statistics given by sample mean, standard deviation and range for each tooth stratified by gender and agenesis. Ninety-five percentage confidence limits and T-statistics were used. $p$-values <5% were considered significant.

***Results –*** In unilateral agenesis, the canines are specifically delayed in both girls and boys, with a larger delay in girls ($p = 0.009$). The second molar is not delayed in boys ($p = 0.98$) but is in girls ($p = 0.04$). The differences in delay for the canine compared to the second molar are significant for both girls and boys. The results show a considerable delay in tooth maturation within the canine/premolar innervation field predominantly in girls. The 2nd molar is delayed in girls but not in boys.

**Key words:** agenesis; development; maturation; radiography; tooth

## Introduction

In a study on 24 737 Danish children, Parner et al. (1) showed a strong correlation between tooth eruption times within the dental developmental fields, which are defined by Kjær (2) as areas in the dental arch with separate main innervations branches. Meanwhile, the study by Parner et al. (1) also showed weak correlation between the eruption of teeth located in different developmental fields. The study was based on clinical observations of tooth eruption. The developmental fields in the mandibular arch are innervated and determined by different nerve

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branches departing at different times from the prenatal development of the mandible (3). Correlated tooth eruption within fields, as demonstrated by Parner et al. (1), may be because of the common innervation branch in the developmental field.

The clinical study on eruption by Parner et al. (1) was followed up by a radiographic study by Andersen et al. (4) on 365 radiographs focusing on the influence of jaw innervation on the dental maturation pattern, also of unerupted teeth in the mandible. This study focused on all stages in tooth maturation observed radiographically. The study concluded that there was a strong association between the development of mandibular teeth in the same individual. The associations between dental maturation and jaw innervation within and between areas with different innervation observed in the study by Andersen et al. (4) are depicted graphically in Fig. 1A. Although the maturation curves are comparable to Parner et al.'s (1) curves for associations in eruption, Andersen et al. (4) did not find statistically significant differences in maturation within and between the different fields. The innervation of the different fields is schematically illustrated in Fig. 1B.

The eruption process itself is not known in detail, but different factors that influence the eruption are known. One of these factors is the innervation, which has been demonstrated experimentally (5) and on a molecular basis (6). The innervation of tooth primordia in humans (7) and in mice (6) has been shown to play a decisive role in tooth formation. It could be questioned whether agenesis of the mandibular 2nd premolar can be explained by deviations in innervation. The mandibular 2nd premolar develops as the last tooth on the main nerve branch of the canine/premolar developmental field.

As a conclusion, previous studies have shown that innervation is important for initial tooth formation and for eruption in humans, while seemingly no study has demonstrated if occurrence of agenesis is associated with delay in the ongoing tooth maturation in the dentition. Based on the studies by Parner et al. (1) and by Andersen et al. (4), the hypothesis of the present study is that agenesis of the mandibular 2nd premolar is associated with changes in the maturation pattern within the canine/premolar innervation field although not necessarily with changes in other fields innervated differently. The purpose of this study was to evaluate dental maturity in the mandibular canine/premolar

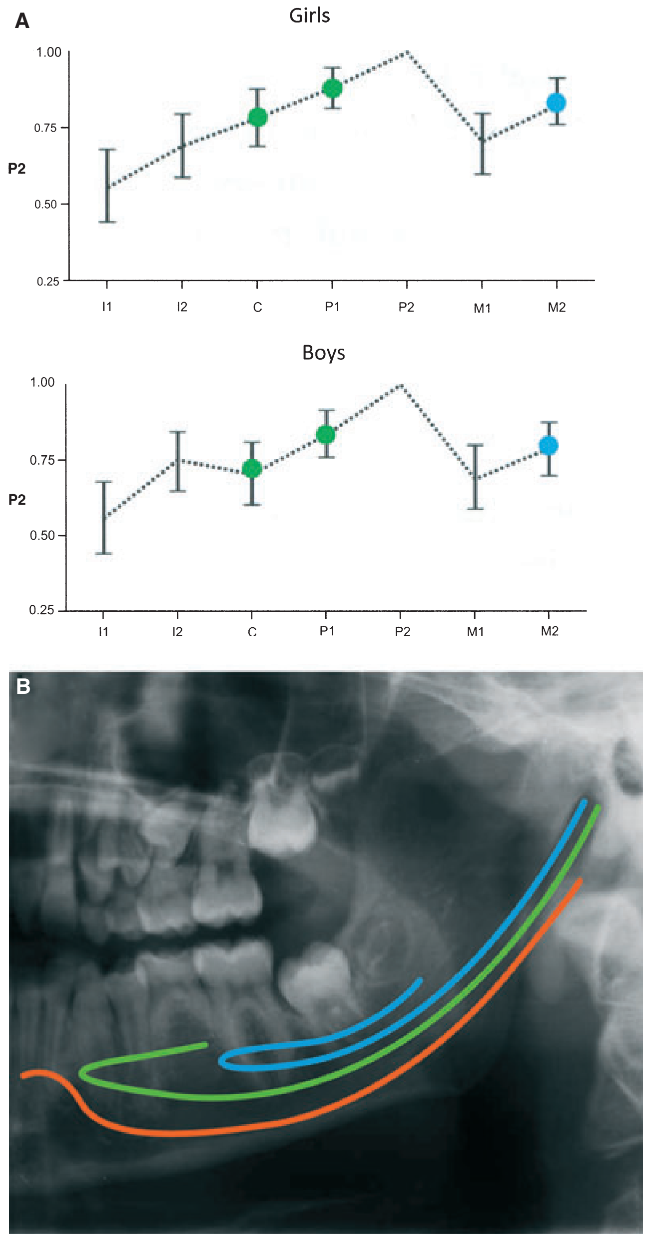


*Fig. 1.* Schematic and radiographic overview of dental maturation in the left side of the human mandible. (A) Correlation between maturation of the 2nd premolar and the six other teeth in the left side of the mandible in girls and boys. The vertical bars indicate the 95% confidence interval. All the correlation coefficients are larger than 0.5 indicating a rather high level of association between development of teeth in the same individual. However, no obvious difference could be shown between maturity of the teeth belonging to the canine/premolar group and molar group. The schematic drawings have previously been published by Andersen et al. (4). Green dots indicate teeth belonging to canine/premolar field, and blue dot indicates second molar located in the molar field. (B) Left side of an orthopantomogram from a girl aged 9 years and 10 months. The colored lines indicate main nerve branches developed since early prenatal life. Blue line indicates innervation path to molar field. Green line indicates innervation path to canine/premolar field. Redline indicates innervation path to incisor field. The figure illustrates that the nerve branches that innervate the mandibular teeth in the canine/premolar field are different from the nerve branches innervating the mandibular teeth in the molar field.

field and in the molar field in children with agenesis of the 2nd mandibular premolar and to compare these findings with normal control material.

## Material and methods

From a material of 2847 panoramic radiographs, the so-called Copenhagen material, all radiographs in which agenesis of one or both mandibular 2nd premolars occurred were selected, in total 83 cases. The Copenhagen material came from a collection of panoramic radiographs taken during the 1960's of children (aged 8 years 8 months–14 years 11 months) with and without indication of orthodontic treatment. When the radiographs were taken no children had received orthodontic treatment. The younger children were predominantly radiographed because of trauma in the maxillary incisor region, while the majority of the children were radiographed at 10–14 years of age. The Copenhagen material also formed the basis for the study by Andersen et al. (4), mentioned earlier.

The radiographs in the present study were from 27 girls with agenesis of one mandibular 2nd premolar and from 17 girls with agenesis of both premolars and 31 boys with agenesis of one mandibular 2nd premolar and eight boys with agenesis of both premolars. Example of the left side of an orthopantomogram, including schematically marked innervation patterns, is shown in Fig. 1B. The only agenesis registered was mandibular 2nd premolar agenesis. No other deviations in the dentitions were registered.

On each of the 83 panoramic radiographs, dental maturity of all available mandibular premolars, canines and second molars was evaluated and categorized in maturity stages according to Haavikko (8). These stages are Crc (crown formation completed), Ri (root formation initiated), R¼ (the root has obtained ¼ length), R½ (the root has obtained ½ root length, R¾ (the root has obtained ¾ length), Rc (root formation completed and Ac (apex closed).

All analyses were performed twice by author SD under supervision of author IK. When minor disagreements between the first and second observations were observed, the respective radiographs were controlled by author IK. When uncertainty of a maturation stage occurred, the least mature stage was decided upon.

### Control material

#### Haavikko material

In the present study, Haavikko's material of 1162 Finnish children (8) was used as a large control material after having been compared, at the stage 'root length R½', with the Copenhagen material from which the agenesis cases came. No systematic differences were seen between Haavikko's Finnish material and the Copenhagen material ($p = 0.20$).

#### Statistical methods

The data used for the statistical analyses were the age minus the expected age for the observed stage for each tooth. The expected age was obtained from a previously published reference material (8). Descriptive statistics were given by the sample mean, standard deviation and the range for each tooth stratified by gender as well as agenesis. The estimates were presented using the 95% confidence limits, and T-statistics were used to test the hypothesis that the age was equal to the expected age for each tooth. A general linear model was used for comparison across strata. Calculations were made using SAS (v9.1; SAS Institute, Cary, NC, USA). $p$-values <5% were considered significant.

## Results

The results showed delayed tooth maturation in cases with agenesis of one or two mandibular 2nd premolars. The delay is different in the different teeth. The results are demonstrated in Table 1. It appears that the delay was more significant in unilateral agenesis cases and in women.

In unilateral agenesis, the canines are specifically delayed in both girls and boys, with a larger delay in girls ($p = 0.009$). Delays with 95% confidence intervals are shown in Table 1. The second molar is not delayed in boys ($p = 0.98$) but is delayed in girls ($p = 0.04$). The differences in delay for the canine compared to the second molar are significant for both girls and boys (Table 1). This difference is not significant between genders ($p = 0.98$). In boys, the difference between the canine and the 1st premolar is not significant ($p = 0.72$), but it is in girls ($p = 0.0004$). In boys, the difference between the 1st premolar and the 2nd molar is significant, but not in girls ($p = 0.60$). Estimates are presented with 95% confidence limits (Table 1).

***Table 1.*** **Overview of delay (years) in dental maturation of mandibular canines, 1st premolar and 2nd molar cases with agenesis of mandibular 2nd premolars**

| Gender | Agenesis of mandibular 2nd premolar | Number of patients | Delay in dental development | Number observed | Mean | Minimum | Maximum | Lower 95% CL for mean | Upper 96% CL for mean | Pr > \|t\| |
|---|---|---|---|---|---|---|---|---|---|---|
| Female | Bilateral | 17 | C same side | 17 | −1.06 | −2.37 | 0.97 | −1.55 | −0.57 | 0.0003 |
| | | | P1 same side | 17 | −0.56 | −1.57 | 1.07 | −0.90 | −0.23 | 0.0026 |
| | | | M2 same side | 17 | −0.98 | −2.33 | 0.40 | −1.39 | −0.56 | 0.0002 |
| | | | P2 opposite side | 0 | – | – | – | – | – | – |
| | | | C opposite side | 17 | −1.06 | −2.37 | 0.97 | −1.55 | −0.57 | 0.0003 |
| | | | P1 opposite side | 17 | −0.56 | −1.57 | 1.07 | −0.90 | −0.23 | 0.0026 |
| | | | M2 opposite side | 17 | −0.99 | −3.33 | 0.40 | −1.51 | −0.46 | 0.0010 |
| | | | C compared to P1 | 17 | −0.49 | −2.30 | 1.00 | −0.98 | −0.01 | 0.0450 |
| | | | C compared to M2 | 17 | −0.08 | −2.00 | 1.30 | −0.64 | 0.48 | 0.5789 |
| | | | P1 compared to M2 | 17 | 0.41 | −1.10 | 1.40 | 0.03 | 0.80 | 0.0382 |
| | Unilateral | 27 | C same side | 26 | −1.25 | −3.67 | 1.92 | −1.70 | −0.81 | <0.0001 |
| | | | P1 same side | 27 | −0.56 | −3.07 | 1.52 | −0.98 | −0.15 | 0.0097 |
| | | | M2 same side | 27 | −0.67 | −2.67 | 1.72 | −1.10 | −0.23 | 0.0041 |
| | | | P2 opposite side | 27 | −1.70 | −5.57 | 0.10 | −2.21 | −1.18 | <0.0001 |
| | | | C opposite side | 24 | −1.17 | −3.67 | 1.92 | −1.65 | −0.68 | <0.0001 |
| | | | P1 opposite side | 27 | −0.56 | −3.07 | 1.52 | −0.97 | −0.16 | 0.0084 |
| | | | M2 opposite side | 26 | −0.65 | −2.67 | 0.90 | −1.07 | −0.23 | 0.0040 |
| | | | C compared to P1 | 26 | −0.67 | −2.30 | 1.00 | −1.10 | −0.33 | 0.0004 |
| | | | C compared to M2 | 26 | −0.57 | −2.00 | 1.30 | −0.87 | −0.27 | 0.0006 |
| | | | P1 compared to M2 | 27 | 0.10 | −2.00 | 2.30 | −0.30 | 0.50 | 0.5988 |
| Male | Bilateral | 8 | C same side | 8 | −1.26 | −4.55 | −0.13 | −2.53 | 0.02 | 0.0525 |
| | | | P1 same side | 8 | −1.28 | −4.95 | 0.57 | −2.73 | 0.16 | 0.0743 |
| | | | M2 same side | 8 | −1.11 | −4.35 | 1.37 | −2.53 | 0.32 | 0.1090 |
| | | | P2 opposite side | 0 | – | – | – | – | – | – |
| | | | C opposite side | 8 | −1.26 | −4.55 | −0.13 | −2.53 | 0.02 | 0.525 |
| | | | P1 opposite side | 8 | −1.28 | −4.95 | 0.57 | −2.73 | 0.16 | 0.0743 |
| | | | M2 opposite side | 8 | −1.11 | −4.35 | 1.37 | −2.53 | 0.32 | 0.1090 |
| | | | C compared to P1 | 8 | 0.02 | −0.80 | 0.40 | −0.28 | 0.33 | 0.8505 |
| | | | C compared to M2 | 8 | −0.15 | −1.60 | 0.80 | −0.98 | 0.68 | 0.6824 |
| | | | P1 compared to M2 | 8 | −0.17 | −1.60 | 0.60 | −0.84 | 0.49 | 0.5529 |
| | Unilateral | 31 | C same side | 31 | −0.57 | −1.97 | 0.87 | −0.86 | −0.29 | 0.0003 |
| | | | P1 same side | 31 | −0.63 | −1.87 | 0.80 | −0.89 | −0.37 | <0.0001 |
| | | | M2 same side | 31 | −0.01 | −2.27 | 1.70 | −0.40 | 0.39 | 0.9760 |
| | | | P2 opposite side | 31 | −1.33 | −2.67 | 0.35 | −1.65 | −1.02 | <0.0001 |
| | | | C opposite side | 26 | −0.52 | −1.63 | 0.87 | −0.81 | −0.23 | 0.0010 |
| | | | P1 opposite side | 31 | −0.60 | −1.87 | 0.52 | −0.83 | −0.36 | <0.0001 |
| | | | M2 opposite side | 31 | 0.07 | −2.27 | 1.70 | −0.33 | 0.46 | 0.7264 |
| | | | C compared to P1 | 31 | 0.06 | −2.20 | 1.60 | −0.27 | 0.38 | 0.7168 |
| | | | C compared to M2 | 31 | −0.57 | −2.50 | 2.20 | −1.01 | −0.12 | 0.0141 |
| | | | P1 compared to M2 | 31 | −0.63 | −2.90 | 2.20 | −1.05 | −0.20 | 0.0055 |

C, canine; P1, 1st premolar; M2, 2nd molar; P2, 2nd premolar.

The results show a considerable delay in tooth maturation in dentitions with agenesis of a mandibular 2nd premolar. The delay is most pronounced within the canine/premolar field. Gender differences indicate that the delay is larger in girls. Also, the maturation of the 2nd molar is delayed in girls but not in boys.

## Discussion

The present study demonstrates different patterns of delay in tooth maturation in dentitions with agenesis of one or two mandibular 2nd premolars. The study showed that the pattern of tooth maturation was different in unilateral and bilateral agenesis. The pattern was more significant in unilateral agenesis.

Teeth within the developmental field to which the 2nd premolar belongs, i.e. the canine and the first premolar, are significantly more delayed than the 2nd permanent molar, which belongs to the mandibular field (9). Similar observations have been seen in tooth eruption within and between fields (1). In the study by Parner et al. (1), agreement between eruption times within a field was significant. Parner et al.'s study (1) showed for example that early eruption of the 1st molar was followed by early eruption by the 2nd molar while the same interrelationship was not observed between the 1st molar and teeth belonging to the premolar/canine or incisor fields. The innervation of the different mandibular fields is different (3), and the pattern of eruption, as observed by Parner et al. (1), was associated with the different innervation paths. These observations indicate that innervation is not only important for early tooth formation (6, 7) but also for eruption. As innervation has recently been observed in the close proximity of the root surface (10), it is suggested that the innervation plays a role not only in the onset of tooth formation and for the eruption process but also for the ongoing root formation or maturation.

The 83 cases analyzed in the present study came from the Copenhagen material. As only 244 children from the Copenhagen material could form the basis of a normal control material (11), it was decided to use the Haavikko (8) material as normal control material. The Haavikko material was much larger and based on Finnish children with an ethnic background close to that of the Danish children. Another argument was that the radiographic material of both the Haavikko study and that of the present study was from the late 1960s. The comparison between Haavikko's material (1162 children) and the Copenhagen material (244 children) showed no systematic differences (11).

In the present study, agenesis in the premolar/canine field is associated with delayed tooth formation in the remaining teeth within the field. It is thus interesting that the 2nd premolar is the last tooth to develop from the nerve branch supplying the field (2) and that the nerve branch may influence both late maturity and absence of a tooth. Thus, the present study may illustrate that agenesis of the mandibular 2nd premolar is associated with delayed development of the innervation, which again could result in late dental maturity. This aspect ought to be further elucidated. Particularly, bilateral agenesis needs to be analyzed on a larger material. The present study included only 17 women and eight men with bilateral agenesis. The gender difference between the groups of bilateral mandibular 2nd premolar agenesis may express the more frequent occurrence of agenesis in girls (12). Gender differences observed in the present study within and between fields are also remarkable. The delay was significantly larger in girls than in boys. Again, this supports the general observation that deviations in the dentition occur more often in women than in men. Bilateral differences in dental maturation have been described in congenital hemifacial microsomia (13). As the etiology of congenital hemifacial microsomia is not known, this study cannot directly be compared to the present study. Also, a study by Nyström and Ranta (14) demonstrated asymmetry in the formation of mandibular teeth in twins with different types of oral clefts. As agenesis occurs more frequently than normal in these patients, the present study may be relevant for a future understanding of the different phenotypes in cleft lip and palate.

The hypothesis of this study was that agenesis of the mandibular 2nd premolar is associated with changes in the maturation pattern within the canine/premolar field, although not necessarily with changes in other fields. This hypothesis is confirmed in the present study. For women as well as for men, delay was observed within the canine/premolar field. In the molar field, delay was observed in women but not in men. Further studies are needed to verify the observed gender differences in the present study.

## Clinical relevance

In cases with agenesis of the mandibular 2nd premolar, it can be expected that the canine and the first premolar are delayed in development in men and women compared to dentitions without agenesis. Delay of the mandibular 2nd molar is seen in women but not in men. The study is important for orthodontic treatment planning for children with agenesis as the age for onset of treatment and the duration of the treatment are factors dependent on dental maturity. The study raises the question whether and how the innervation influences the occurrence of agenesis and the maturity process.

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