Variation in dentofacial morphology and occlusion in juvenile idiopathic arthritis subjects: a case–control study

Yuqian Hu*, An D. Billiau**, An Verdonck*, Carine Wouters*** and Carine Carels*

*Department of Orthodontics, School of Dentistry, Oral Pathology and Maxillofacial Surgery, Catholic University of Leuven, **Laboratory of Experimental Transplantation, Catholic University of Leuven and ***Department of Paediatric Rheumatology, University Hospitals Leuven, Belgium

SUMMARY Juvenile idiopathic arthritis (JIA) can severely disturb facial growth and affect occlusal development. In this case–control study, facial, functional, and occlusal characteristics of 100 JIA patients (35 males and 65 females; age range: 1.7–19.4 years) comprising all subtypes classified according to the revised classification criteria of the International League of Associations for Rheumatology (ILAR) were studied. They were compared with a mixed orthodontic control group (n = 32; 12 males and 20 females) and with a Class II division 1 malocclusion group (n = 18; eight males and 11 females). The JIA patients and controls were evaluated using clinical assessment, dental pantomograms, lateral cephalograms, lateral cephalograms (LCGs), and dental casts.

Compared with the age- and gender-matched mixed orthodontic controls, JIA patients showed a significantly greater prevalence of anterior open bites (AOBs; P < 0.05; Wilcoxon matched pairs test). Cephalometrically, a larger mandibular plane (P < 0.05) and SNA (P < 0.001) angles and a smaller interincisal angle (P < 0.001) were found. In comparison with the Class II division 1 controls, JIA patients showed a larger SNA (P < 0.001; Wilcoxon matched pairs test) and SNB (P < 0.05) angles and smaller lower anterior face heights (LAFHs; P < 0.05). No differences were found for the mandibular plane, the gonial and the interincisal angles, or total face height.

From this case–control study, it can be concluded that although JIA patients share occlusal characteristics with non-JIA patients with a Class II division 1 malocclusion, they are different with regard to the prevalence of condylar lesions and AOBs, as well as SNA and SNB angles and LAFH.

Introduction

Involvement of the temporomandibular joint (TMJ) in patients with juvenile idiopathic arthritis (JIA) can severely disturb facial growth, especially that of the mandible. Typical characteristics include mandibular micrognathia and retrognathia, a steep mandibular plane angle (MPA), an increase of profile convexity, the presence of a Class II division 1 malocclusion, and an anterior open bite (AOB; Karhulahti et al., 1990; Stabrun, 1991; Kjellberg, 1995, 1998).

TMJ involvement is thought to occur during the active phase of JIA. When swelling within the synovial membrane takes place, the inflammatory condition generates chondral lesions and subchondral bone resorption leading to condylar destruction (Radin et al., 1970; Rönning et al., 1974; Rönning and Valiaho, 1981; Frost, 1986; Pearson and Rönning, 1996; Pedersen et al., 2001; Svensson et al., 2001; Twilt et al., 2004). As the condylar growth cartilage resides beneath the superficial articular cartilage layer, endochondral mandibular growth can be disturbed when the condyle is being resorbed or eroded (Rönning et al., 1974; Rönning and Valiaho, 1981; Pedersen et al., 2001; Svensson et al., 2001).

Condylar growth disturbance can be expressed unilaterally or bilaterally by deceleration of vertical and sagittal growth (Karhulahti et al., 1990; Stabrun, 1991; Kjellberg, 1995, 1998). In children with unilateral condylar destruction, asymmetries develop, with the chin deviating to the affected side (Rönning and Valiaho, 1981; Kjellberg, 1995; Ronchezel et al., 1995; Pedersen et al., 2001; Sidiropoulou-Chatzigianni et al., 2001). The facial morphology of JIA children can become more abnormal (Kreiborg et al., 1990; Kjellberg, 1995), reflected in further posterior mandibular rotation (Stabrun, 1991; Kjellberg, 1995, 1998; Sidiropoulou-Chatzigianni et al., 2001; Svensson et al., 2001; Twilt et al., 2006). An increase of the gonial angle and antegonial notching have also been reported (Kreiborg et al., 1990; Pearson and Rönning, 1996). Other facial components, including the maxilla, alveolar process, occlusion, jaw muscles, and head posture, can also become involved (Barriga et al., 1974; Larheim et al., 1981a, b; Kjellberg et al., 1995a, b; Wenneberg et al., 1995; Bakke et al., 2001).

Functionally, overloading of the joints that accelerates condylar damage may occur. In the later stages of the disease, muscle weakness and decreased functional ability may also contribute to craniofacial growth deviations (Kreiborg et al., 1990; Kjellberg et al., 1995a, b; Wenneberg et al., 1995; Pearson and Rönning, 1996). In the early disease stage, the diagnosis of TMJ involvement may not be obvious as patients often do not complain of pain, and clinical signs of TMJ arthritis are often absent.
As Class II division 1 malocclusions have been reported as the most prevailing malocclusions in JIA subjects, dental and facial characteristics should preferably be compared not only with a random group of orthodontic patients but also with a Class II division 1 malocclusion group.

No case–control study of facial, functional, and occlusal characteristics in a group of JIA patients comprising all subtypes classified according to the revised criteria of the International League of Associations for Rheumatology (ILAR; Petty et al., 2004) and compared with a random mixed orthodontic control group and with an exclusive Class II division 1 malocclusion group appears to have been published. This was the aim of the present study.

**Subjects and methods**

**Patients and controls**

One hundred consecutive patients diagnosed with JIA at the Department of Paediatric Rheumatology at the University Hospital Gasthuisberg of the KU Leuven were included in this study. Written informed consent was obtained from the parents and verbal consent from the children for the purpose of ethical approval as requested by the University Hospital Gasthuisberg Institutional Review Board.

As defined by the ILAR criteria, a diagnosis of JIA applied if the onset of JIA was before 16 years of age and if it had a minimum duration of 6 weeks. Classification of JIA subtypes was made according to the ILAR criteria (Petty et al., 2004). The group included 12 subjects with systemic arthritis, 24 with polyarthritis rheumatoid factor negative (RF−), 39 with oligoarthritis, 22 with enthesitis-related arthritis, two with psoriatic arthritis, and one with rheumatoid factor positive (RF+) polyarthritis. The gender ratio was 1.86/1 (65 females/35 males). The median age of the patients at the first examination was 10.5 years (range: 1.7–19.4 years). Detailed information on the composition of the patient group has been published previously (Billiau et al., 2007). The mean duration of the disease at the first examination was 2.96 years (range: 2 months to 15 years). The current medication of the patients included non-steroidal anti-inflammatory drugs in 66 subjects, low-dose corticosteroids (less than 0.3 mg/kg/day) in 26, methotrexate (MTX) in 30, tumor necrosis factor (TNF) TNF-α-antagonists in nine, sulphasalazine in two, and both thalidomide and cyclosporine in one. Patients taking second-line drugs (MTX, sulphasalazine), TNF-α-antagonists, thalidomide, and cyclosporine were considered to suffer from a severe form of the disease (a total of 43 subjects). In 66, the disease was active (at least one active joint) while the other 34 were in remission (on/off medication). The patient population has been reported previously (Hu, 2005; Billiau et al., 2007). Of the above-mentioned group, 46 consented to further dentofacial radiographic examination. These patients received a separate appointment to obtain impressions for dental casts, a dental pantomogram (DPT), and a lateral cephalogram (LCG). The distribution of JIA subtypes and disease characteristics in this subgroup were not significantly different to those of the total (n = 100) JIA sample (tested by chi-square or Mann–Whitney U-test; Billiau et al., 2007): seven patients were diagnosed with systemic arthritis, 10 with polyarthritis RF−, one with polyarthritis RF+, 10 with enthesitis-related arthritis, 17 with oligoarthritis, and one with psoriatic arthritis. The subgroup included 17 males and 29 females with a median age of 9.3 years (range: 2.2–19.4 years) at the first examination. The median disease duration was 3 years (range: 2 months to 15 years), 33 patients having an active form of disease while 13 were in remission; 14 patients were categorized with a severe form of the disease.

The facial morphology of JIA patients was compared with that of orthodontic controls of healthy children whose records were selected from the files of the Department of Orthodontics, University Hospital St Rafael, KU Leuven, on the basis of matching gender and age. In total, matched controls were found for 32 of the 46 JIA patients. Again this JIA subgroup exhibited similar distribution of JIA subtypes and similar disease characteristics to that of the total (n = 100) JIA sample and was therefore considered representative for the whole JIA cohort (not significantly different as tested by chi-square or Mann–Whitney U-test). Six patients were diagnosed with systemic arthritis, seven with polyarthritis RF−, one with polyarthritis RF+, 10 with enthesitis-related arthritis, and eight with oligoarthritis. The subgroup included 12 males and 20 females; the median age at the first examination was 11.1 years (range: 3.3–19.4 years). At the clinical dentofacial examination, the median disease duration was 3.1 years (range: 2 months to 15 years), 23 patients had active disease, nine were in remission, and 13 were categorized into the severe disease subgroup.

**Clinical TMJ examination**

The clinical examination was carried out by one author (YH) and was performed according to Truelove et al. (1992), including observation of jaw movements, palpation, and auscultation of the TMJ and jaw muscles and diagnosis of the occlusion. Maximum jaw mobility was assessed by measuring the maximal interincisal mouth opening (MIO). The edge of a millimetre ruler was placed at the incisal edge of the right maxillary central incisor and the MIO was measured vertically to the labio-incisal edge of the opposing mandibular incisor; if the right maxillary and mandibular central incisors were missing, the left maxillary and mandibular central incisors were taken as the reference teeth. According to Olson et al. (1991), restricted mouth opening was diagnosed when the MIO was less than 29.5 mm in 3-year-old patients, less than 34.5 mm in 4- to 6-year-olds, and less than 39.5 mm in those 7 years of age or older.
The presence/absence of TMJ sounds was assessed by auscultation with a stethoscope and the presence/absence of masticatory muscle and TMJ pain by bilateral palpation. Positive symptoms were determined by the appearance of reflex responses such as blinking or flinching. Reproducibility of the TMJ examinations was assessed by repeated measurements of the records in 10 random subjects after an interval of at least 2 weeks; no significant difference between measurements was found (Wilcoxon matched pairs test).

**Radiographic examinations**

The DPT was used to assess condylar morphology and to attribute a score of condylar lesion/destruction. The cortical outline of the mandible was traced with special attention paid to the condyles. The degree of condylar destruction was scored into five grades: 0 = normal, 1 = small cortical bone erosions, 2 = flattened, 3 = flattened condyles combined with erosion, and 4 = complete absence of condylar head (Figure 1).

Both for the JIA patients and orthodontic controls, the LCGs were taken in centric occlusion (Cranex Tome®, Soredex, Helsinki, Finland). The exposure parameters varied depending on the age and gender of the patients. The average KVp was 70 kV and mAs was between 1.8 and 3. All LCGs were traced manually on acetate paper by the same author (YH) and the cephalometric landmarks were determined according to Jacobson and Caufield (1985). To test the reproducibility of the method, 10 LCGs were traced twice with an interval of at least 2 weeks. No significant differences were found between the two series of measurements (Wilcoxon matched pairs test).

**Dental cast analysis**

Molar occlusion, overjet, and overbite were measured on the study casts. Left and right molar occlusion was assessed as distal or mesial if the molar occlusion deviated by more than one-quarter premolar width from neutral occlusion. Deviations in overjet and overbite were considered if more than ± 4 mm. An AOB was defined as an absence of vertical overlap between the upper and lower anterior teeth.

**Statistical analysis**

Statistical analyses were performed with the Statistica package, version 5.1 (StatSoft, Tulsa, Oklahoma, USA). Groups of numerical data from DPTs and cephalometric variables of patient and control groups were tested using the Wilcoxon matched pairs test. The chi-square test was used to evaluate the relationship between the ordinal variables. In view of the large number of tests of the same data set, a correction for multiple testing was introduced. Depending on the number of statistical tests, differences were considered statistically significant either when P-values were smaller than 0.05 or smaller than 0.00625 (after correction).

**Results**

**Dentofacial findings in JIA patients**

Fifty-five of the 100 JIA patients showed at least one symptom compatible with TMJ arthritis. Restricted MIO was the most frequent finding (28%); muscle tenderness...
JIA patients, however, demonstrated an AOB signiﬁcantly more often (22%), opening pattern deviation (21%), TMJ tenderness (14%), and joint sounds (10%) were less frequently found. A neutral (Class I) molar occlusion was prevalent in 56 per cent of the patients, a distal (Class II) molar occlusion in 39 per cent, and a mesial (Class III) molar occlusion in 5 per cent. Despite the prevalence of a distal occlusion, an increased overjet was present only in 26 per cent of the patients. An increased overbite was observed in 39 per cent, and 12 per cent showed an AOB. Overbite, overjet, and AOB were not found to be statistically more frequent in severe, longstanding or active disease patient groups. None of the occlusal patterns were found more frequently in association with either one of the JIA subtypes except for an AOB being signiﬁcantly more prevalent in systemic-onset JIA patients (P < 0.001).

Comparison of occlusal relationship in JIA patients and orthodontic controls

Of the 32 JIA patients with a matched control, 18 showed a distal occlusion and 14 a neutral occlusion, while in the control group there were 19 subjects with a distal, six with a mesial, and seven with a neutral occlusion.

In the JIA group, the median values for overjet and overbite were 2.8 and 3.5 mm, respectively. Compared with age- and gender-matched orthodontic controls, JIA patients showed no statistical differences in overjet and overbite. JIA patients, however, demonstrated an AOB signiﬁcantly more often (P < 0.05).

Radiographic ﬁndings

Condylar scores in JIA patients and matched orthodontic controls. Comparing the DPTs of the 32 JIA patients with their orthodontic age- and gender-matched controls, it was found that condylar lesions were signiﬁcantly more prevalent (P < 0.001; chi-square test). Of the 32 JIA patients, 24 (75 per cent) exhibited condylar damage, while this was the case for only ﬁve of the 32 orthodontic controls (15.6 per cent). Condylar damage in JIA patients was bilateral in 74 per cent (17 patients) and unilateral in 26 per cent (six patients). In one subject, this could not be evaluated. These proportions were not found to be different in the total radiographed group (n = 46): condylar damage in 78 per cent, bilateral in 70 per cent (25 patients), and unilateral in 30 per cent (11 patients).

The degree of condylar damage varied from score 1 to 4; 38 per cent exhibited score 1, 25 per cent score 2, 19 per cent score 3, and 4 per cent score 4 (one not evaluated). This distribution did not differ from that of the affected patients in the total radiographed group (n = 46), in which 34 per cent of condyles exhibited score 1, 27 per cent score 2, 19 per cent score 3, and 4 per cent score 4 (one condyle could not be evaluated; chi-square test).

Facial morphology on cephalograms in JIA patients and orthodontic controls. Comparing the cephalometric parameters in JIA patients with the orthodontic controls, using the Wilcoxon matched pairs test, revealed that the JIA patients showed a signiﬁcantly larger SNA and MPA compared with the orthodontic controls (P = 0.0003 and P = 0.006, respectively; Table 1). JIA patients showed a smaller interincisal angle (P = 0.0003) and a smaller LAFH (P = 0.0002) and TAFH (P = 0.002) than the orthodontic controls. SNB and gonial (Go) angle did not differ signiﬁcantly (Table 1).

Facial morphology in JIA patients and Class II division 1 orthodontic controls. For 19 of the 32 JIA patients, the matched orthodontic control exhibited a Class II division 1 malocclusion. In order to compare cephalometric parameters of JIA patients with controls exhibiting this particular type of malocclusion, Wilcoxon matched pairs test were performed between these 19 pairs of JIA patients and their respective (Class II division 1) orthodontic controls. SNA and SNB angles were signiﬁcantly larger in the JIA group (P = 0.0004 and P = 0.004, respectively) and LAFH was signiﬁcantly smaller in the JIA group (P = 0.002; Table 2). No signiﬁcant differences were found for MPA, Go, interincisal angle, or TAFH (Table 2).

Discussion

Similar to previous reports (Rönning et al., 1974; Ronchezel et al., 1995; Pedersen et al., 2001), a higher frequency of TMJ symptoms (55 per cent) was found in the JIA patient group. In the present sample, only 22 per cent of the patients suffered muscle pain, which was lower than in a previous study (Twilt et al., 2004). The recent evolution towards early administration of more aggressive drug therapy may have inﬂuenced the prevalence of pain. Moreover, quantitative assessment of pain is difﬁcult, especially in young children (Twilt et al., 2004); they also complain less of joint discomfort and pain due to arthritis than adults (Radin et al., 1970).

Like most other JIA samples (Barriga et al., 1974; Karhulahti et al., 1990; Olson et al., 1991), the present patients also manifested features similar to healthy children with a Class II division 1 malocclusion; TMJ involvement might therefore be missed by clinicians if patients do not complain of TMJ symptoms. A differential diagnosis between JIA patients and healthy children with a Class II division 1 malocclusion is, however, crucial for decision making on follow-up in the early stage of the disease; appropriate treatment minimizes the secondary effects of JIA on facial growth (Svensson et al., 2000). Therefore, co-operation between paediatricians and dentists and/or orthodontists is necessary for early diagnosis and eventual interceptive orthodontic treatment. Clinical examination alone is inadequate for detecting condylar damage in
The frequency of condylar lesions on the DPTs of JIA patients (±80% per cent) is in agreement with previous studies (Rönning et al., 1974; Rönning and Valiaho, 1981; Karhulahti et al., 1990; Olson et al., 1991; Ronchezel et al., 1995a; Hu et al., 1996; Pearson and Rönning, 1996; Nordahl et al., 1997; Svensson et al., 2000; Pedersen et al., 2001; Sidiropoulou-Chatzigianni et al., 2001; Twilt et al., 2006). Similar to Ronchezel et al. (1995) and Pearson and Rönning (1996), lesions were found bilaterally in 74% and unilaterally in 26% per cent. As the majority of the patients were symmetrically affected (two patients showed a 4 unit score difference of left and right condylar lesion), it was assumed that TMJ involvement starts as an asymmetric feature and becomes increasingly symmetric in the later stages (Pearson and Rönning, 1996).

Although some studies suggest that polyarticular JIA carries a higher risk of TMJ involvement, and that the effects on occlusion, facial form, and oral function are more pronounced with polyarticular than with pauciarticular onset (Mericle et al., 1996), this was not the case in the present study, except for the prevalence of an AOB, which was significantly more frequent in the group with systemic onset. AOBs have also frequently been associated with JIA (Karhulahti et al., 1990).

Of the semi-randomly selected age- and gender-matched orthodontic controls, 59% (19/32) presented a Class II division 1 malocclusion, a similar rate as in the JIA group. Another notable finding was the presence of a significantly larger SNA angle in the JIA group, pointing to a more ventral position of the maxilla and/or the maxillary alveolar process. Compensatory ventral growth of the maxilla or the need for a larger functional intra-oral space (for the growing tongue) could both explain this finding.

Mandibular retrognathia, reflected by a small SNB angle, seems to be the most widespread facial feature in JIA patients.
patients with condylar damage. It has, however, been shown that condylar abnormality is detectable in 10.9 per cent of children with normal facial growth (Pearson and Rönning, 1996) and that mandibular retrognathia is also highly prevalent in children without JIA (Proffit and Fields, 2000).

Although Class II division 1 development in JIA patients has been demonstrated in many studies (Barriga et al., 1974; Larheim et al., 1981a,b, 1982; Stabrun, 1991; Kjellberg et al., 1995a,b; Kjellberg, 1995, 1998; Hu et al., 1996; Nordahl et al., 1997; Svensson et al., 2000, 2001; Sidiropoulou-Chatzigianni et al., 2001), the relatively short mean disease duration in the present sample (median 2.9 years) prevented a more significant mandibular retrognathia and micrognathia than in average healthy Class II division 1 patients seeking orthodontic treatment.

Corruccini (1999) hypothesized that the cause for the high prevalence of Class II division 1 malocclusions could be due to a reduction in the use of the masticatory muscles as a result of decreasing food consistency. In animal experiments, softening the diet resulted in a tendency towards skeletal open bites (Kiliaridis, 1995). As in JIA patients, the masticatory muscles might be underused due to pain; 22% in this JIA sample (Kjellberg et al., 1995a,b; Wenneberg et al., 1995; Bakke et al., 2001), it was hypothesized that in the initial disease stage after the condyle became affected, first a pure positional mandibular rotation occurred (Figure 2A,B); with longer disease duration, adaptive posteriorly directed ramus remodelling probably takes place (Björk and Skieller, 1985; Twilt et al., 2003; 2006; Figure 2C).

As in other studies (Larheim et al., 1982; Kreiborg et al., 1990; Kjellberg, 1995; Mericle et al., 1996; Ince et al., 2000; Sidiropoulou-Chatzigianni et al., 2001; Twilt et al., 2004), the MPA was significantly larger in the JIA patients than in the orthodontic subjects. Comparison of the MPA in the JIA group with the Class II division 1 controls resulted in a trend difference (Table 2).

Contrary to expectations, the JIA patients did not demonstrate a larger Go angle compared with either of the control groups. The recent evolution towards earlier and more aggressive medication and the age distribution in the sample (a large number of young patients) could both explain this finding. It has been found that MTX therapy is effective in minimizing TMJ destruction in patients with polyarticular JIA (Ince et al., 2000). From their research on serial dental panoramic radiographs of 71 children with juvenile chronic arthritis, Pearson and Rönning (1996) concluded that systemic administration of corticosteroids appeared to have little or no effect on the condyle or mandibular growth.

In this study, JIA patients showed lower values for LAFH and TAFH compared with the general orthodontic controls as well as for LAFH compared with the Class II division 1 controls. Both could be a consequence of growth retardation reported in JIA patients (Liem and Rosenberg, 2003; MacRae et al., 2006).

Figure 2 Proposed mechanism of sequential effects in temporomandibular joint (TMJ) arthritis and condylar damage on mandibular growth and dentofacial morphology. (A) Normal dentofacial relationship before the onset of juvenile idiopathic arthritis. (B) First stage of TMJ arthritis suggestive of cranioventral true rotation of the mandibular condyle around a fulcrum * located in the molar area due to flattening of the condyle. This results in a steeper inclination of the mandibular plane. (C) Second stage of TMJ arthritis suggestive of adaptive remodelling of the ramus in a posterior direction resulting in an increase of the gonial angle, around a fulcrum * located in the retromolar area.
Conclusions

1. The majority of the examined JIA patients showed at least one symptom of TMJ arthritis; restricted mouth opening was the most frequent clinical finding.
2. Significantly more condylar lesions were present in the JIA patients than in the random orthodontic controls.
3. Asignificantly steeper mandibular plane was documented in the JIA patients with TMJ arthritis compared with age- and gender-matched random orthodontic controls.
4. Mandibular retrognathia was present, but significantly less than in healthy Class II division 1 controls.
5. No significant relationship was found between the JIA subtypes and the prevalence of different dentofacial deviations, except for the prevalence of an AOB, which was more frequently found in the group with systemic-onset JIA.
6. The absence of a correlation with the subtypes should be interpreted with caution as this could be due to small sample sizes in the subgroups.

Address for correspondence

Professor Carine Careas
Department of Orthodontics
School of Dentistry
Oral Pathology and Maxillofacial Surgery
Katholieke Universiteit Leuven
Kapucijnenvoer 7
3000 Leuven
Belgium
E-mail: Carine.Careas@uz.kuleuven.ac.be

References

Frost HM 1986 The intermediary organization, osteoporosis, osteomalacias, and other matters. Intermediary organization of the skeleton. CRC Press, Boca Raton, pp. 207–208
MacRae V E, Farquharson C, Ahmed S F 2006 The pathophysiology of the growth plate in juvenile idiopathic arthritis. Rheumatology 45: 11–19


