

Functional appliance treatment and stability in Class II/1 malocclusion, and masticatory muscle characteristics

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ABSTRACT

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Aims: To evaluate the short-term antero-posterior effects on Class II division 1 malocclusion in growing children using functional appliances, and investigate whether the functional capacity of the masticatory musculature can be used as a predictive variable in determining the treatment and post-treatment effects following functional appliance treatment.

Material and Methods: Firstly, a literature search was carried out identifying prospective clinical trials on the treatment of Class II malocclusion using functional appliances or/and headgear in growing children. The data provided in the publications underwent meta-analysis using the random effects model with regard to SNA, SNB, ANB, and overjet. Then, two samples of Class II malocclusion growing children, 22 treated with twin-block appliances and 25 with activators, were examined and associations between treatment outcomes and masseter muscle thickness measured by ultrasound or maximal molar bite force, respectively, were determined. Finally, 28 Class II malocclusion growing children having undergone activator treatment were followed-up post-treatment and relationships between maximal molar bite force and post-treatment outcomes and stability were determined.

Results: Functional appliances used in the treatment of Class II division 1 malocclusion growing children may bring about an improvement in sagittal intermaxillary relationships mainly by acting on mandibular position. Twin-block appliances also seem to act on the maxilla. During and following this treatment, an adaptation of the masticatory muscles is observed, namely a decrease in masseter muscle thickness and in maximal molar bite force during treatment, and an increase in maximal molar bite force once appliances are discontinued. Children with thinner pre-treatment masseter muscles show a greater proclination of mandibular incisors, distalisation of maxillary molars and posterior displacement of the cephalometric A point during treatment, as well as a less pronounced increase in posterior facial height, condyle-ramus height, and mandibular unit length. Likewise, children with weaker maximal molar bite force pre-treatment show greater improvement in dentoalveolar sagittal relationships, as well as greater changes in SNB and ANB angles. Following activator treatment, children who show dentoalveolar sagittal relapse are more likely to have a lower maximal molar bite force pre-treatment. Moreover, children with an obtuse gonial angle are more likely to show greater incisor compensation during treatment, as well as a greater risk of relapse post-treatment.

Conclusions: Mild atrophy of the masticatory muscles may occur due to their decreased functional activity during functional appliance treatment. The functional capacity of the masticatory muscles, and their impact on mandibular morphology and gonial angle shape, may play a role in contributing to the variation seen as regards treatment outcomes and stability.

Keywords: Class II malocclusion, functional appliances, masticatory muscles, stability, ultrasonography, bite force

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PREFACE

The present thesis is based on the following papers, which will be referred to in the text by their Roman numerals (I-IV):

I. Antonarakis GS, Kiliaridis S (2007) Short-term anteroposterior treatment effects of functional appliances and extraoral traction on Class II malocclusion. A meta-analysis. *Angle Orthodontist* 77: 907-914.

II. Kiliaridis S, Mills CM, Antonarakis GS (2010) Masseter muscle thickness as a predictive variable in treatment outcome of the twin-block appliance and masseteric thickness changes during treatment. *Orthodontics and Craniofacial Research* 13: 203-213.

III. Antonarakis GS, Kjellberg H, Kiliaridis S (2012) Predictive value of molar bite force on Class II functional appliance treatment outcomes. *European Journal of Orthodontics* 34: 244-249.

IV. Antonarakis GS, Kjellberg H, Kiliaridis S. Bite force and its association with stability following Class II/1 functional appliance treatment. *European Journal of Orthodontics* (accepted for publication 2012).

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INTRODUCTION

Mode of action of functional appliances used in Class II malocclusion

Functional appliances are designed to alter the mandibular position both sagittally and vertically (Woodside, 1977), and are thus used for treatment of sagittal and vertical malocclusions in growing patients. These appliances act via a displacement of the mandible downwards and forwards causing a corresponding stretching of the orofacial soft tissues and muscles, as well as myotatic reflexes, i.e. active muscle contraction evoked by muscle stretching (Carels and van der Linden, 1987; Bishara and Ziaya, 1989; Aelbers and Dermaut, 1996; Dermaut and Aelbers, 1996). Thus, myotatic reflexes in combination with the viscoelastic properties of muscles may be responsible for the tension exerted on teeth and bony structures during treatment. This muscle action may be an important factor producing the desired orthodontic or orthopaedic force. These forces are directly or indirectly transmitted to the underlying dentoskeletal tissues, hopefully resulting in a correction of the malocclusion (Woodside, 1977) by improving the sagittal intermaxillary relationship namely by a change in molar relationship and a reduction in overjet. Beside the small sagittal skeletal base improvement influencing overjet, the dentoalveolar effect on overjet is also brought about by palatal tipping of maxillary and labial tipping of mandibular incisors respectively (Björk, 1951; Trayfoot and Richardson, 1968; Vargervik and Harvold, 1985; Macey-Dare and Nixon, 1999). The skeletal changes are thought to be brought about by stimulation of condylar growth (Baume and Derichsweiler, 1961; Charlier *et al.*, 1979; McNamara and Carlson, 1979; Williams and Melsen, 1982; Woodside *et al.*, 1983; Rabie *et al.*, 2003) as well as a contribution by a certain amount of fossa advancement (Birkebaek *et al.*, 1984; Vargervik and Harvold, 1985; Woodside *et al.*, 1987; Voudouris *et al.*, 2003). Functional appliances also seem to display a growth restraining headgear-like effect on the maxilla (Jakobsson, 1967; Harvold and Vargervik, 1971; Pancherz, 1982; Pancherz, 1984; Vargervik and Harvold, 1985; Jakobsson and Paulin, 1990; Macey-Dare and Nixon, 1999; Collett, 2000; Voudouris *et al.*, 2003).

Functional characteristics of the masticatory muscles

Muscles involved in the process of mastication and jaw movements include the masseter, temporalis, medial pterygoid, lateral pterygoid, digastric, geniohyoid, mylohyoid, and stylohyoid muscles. Clinically, masticatory muscles can be divided into elevator or jaw closing muscles (primarily the masseter, temporalis, and medial pterygoid) and depressor or jaw opening muscles.

Clinical methods for evaluating masticatory muscle characteristics, mainly focusing on the jaw elevator muscles, are numerous. Muscle biopsy has been used to determine characteristics such as the type or thickness of muscle fibers, and can be carried out on human masticatory muscles also in an

orthodontic setting in cases where patients are undergoing orthognathic surgery for example (Tippet *et al.*, 2008). This is however an invasive technique and thus not for routine use. Apart from muscle biopsy, one can try to evaluate the activity of the masticatory muscles, the force outcome of muscle activity, or evaluate the muscle characteristics using various imaging techniques.

Electromyography

Electromyography is a method used for recording and evaluating the electric potential generated by muscle fibers when they are electrically stimulated or neurologically activated. This method can be used to assess the activity of a muscle fiber, a motor unit, a single muscle, or a group of muscles, or to detect differential muscle activity when performing certain functions. The muscle activity can be recorded under various conditions such as at rest (postural activity), or during chewing, swallowing, or maximal clenching. Assessing the activity of a muscle fiber or a motor unit accurately requires intramuscular electromyography which implies that a needle electrode or a needle containing electrodes is inserted through the skin into the muscle tissue. This is an invasive technique, useful for specific circumstances but not for routine use in the field of orthodontics. Surface electromyography on the other hand can be used to measure the activity of a muscle or a group of muscles, depending on the location of electrode placement. The most simple and frequently used method of recording surface electromyographic activity, as far as the electrodes are concerned, is a bipolar system where the electric potential difference (denoted by voltage) between two electrodes is measured (Lapatki *et al.*, 2010). Otherwise, more complex methods using multiple electrodes have been applied, which can either be linear (a series of electrodes along a line) or bi-dimensional (electrodes located in a grid) (Lapatki *et al.*, 2004; Castroflorio *et al.*, 2008). Surface electromyography measurements, however, are reported to be not very reproducible and associated with a larger error of the method, possibly due to factors such as electrode placement, impedance of the skin, the subcutaneous fat layer and the depth of the muscle under study (Tzakis *et al.*, 1994; Cecere *et al.*, 1996; Georgiakaki *et al.*, 2007). This is especially true for longitudinal measurements where exact electrode placement must be reproduced. Though more accurate and reproducible results may be obtained in adult patients, where changes due to growth of the face are minimal and precise electrode placement is both possible and realistic for example by the use of templates, in growing children this presents major difficulties due to growth of the face and the absence of a reproducible system to minimize measurement error.

Bite force

The outcome of the masticatory muscles' activity during contraction is expressed as bite force. Different types of measurements may be carried out when dealing with bite force, such as maximal bite force, chewing bite force, or endurance measurements (either chewing or maximal bite force

endurance). Maximal bite force is often chosen as a measure of the outcome of functional activity of the masticatory muscles because it is said to be a useful indicator of the functional state of the masticatory system (Hagberg, 1987; Kiliaridis *et al.*, 1995). Maximal bite force has been shown to be highest in the molar region (Erhardson *et al.*, 1993; Koc *et al.*, 2010). When dealing with young subjects, this is an advantage since the first molars erupt early and are present in all individuals upon insertion of a functional appliance. Other advantages of performing maximal molar bite force recordings are that it is a simple, quick, direct, and inexpensive method for clinical use. Despite these advantages, this method is associated with a rather large error of the method, often attributed to variation due to factors such as mental conditions, muscle or joint pain, dental or periodontal pain, fear of pain or damage to teeth and restorations, fatigue, and head extension (Carlsson, 1974; Hellsing and Hagberg, 1990; Bakke, 2006).

Imaging techniques

The cross-sectional area of a masticatory muscle is related to both the number and the cross-sectional area of the muscle fibers. Thus, measurement of the cross-sectional area of the masticatory muscles reveals their contraction capacity and the resulting bite force (Weijs and Hillen, 1985; van Spronsen *et al.*, 1989; van Eijden *et al.*, 1997; Tuxen *et al.*, 1999). Various imaging techniques are used to evaluate masticatory muscle contraction capacity. These techniques are for the most part used to measure the cross-sectional thickness of a particular masticatory muscle. The cross-section of masticatory muscles can be measured using methods such as computer tomography, magnetic resonance imaging, or ultrasound imaging. Computer tomography has been found to correlate well with the physiological cross-section of the muscles, and the masseter muscle is proposed to be a muscle well representing all of the masticatory muscles, according to computer tomography studies on cadavers (Weijs and Hillen, 1984; Weijs and Hillen, 1985). Thus, the masseter muscle is often assessed. This method however has the large disadvantage of exposing the patient to radiation, and so being unethical for use in a research setting. Magnetic resonance imaging has been found to correlate well with computer tomography cross-sections of masticatory muscles (van Spronsen *et al.*, 1989), but this method also has disadvantages including cost and its difficult application in children.

Another method, ultrasound imaging, has been suggested to provide quantitative information about the functional capacity of muscles (Sipilä and Suominen, 1991) as found when measuring the cross-sectional area and thickness of the quadriceps muscle. Kiliaridis and Kålebo (1991) applied the ultrasonography method on the masseter muscle, using it to measure muscle thickness, and showed that this method is both reliable and accurate. Cross-sectional area of the masseter muscle has also been correlated to its thickness (Close *et al.*, 1995). Thickness measurements using ultrasonography have furthermore been validated and display a high correlation with magnetic resonance imaging (Raadsheer *et al.*, 1994; Braun *et al.*, 1996), and this method is a simpler, cheaper, quicker, and less

invasive technique to perform. A strong correlation has been found between muscle thickness measurements and electromyographic activity (Georgiakaki *et al.*, 2007). Out of all of the jaw muscles, only the thickness of the masseter muscle correlates significantly with bite force magnitude (Raadsheer *et al.*, 1999). Masseter muscle thickness measurement using ultrasonography has been found to be uncomplicated, easily accessible, reliable and reproducible.

Comments

Many different methods exist to estimate the functional capacity of the masticatory muscles. Muscle thickness measurements using ultrasonography and maximal molar bite force measurements are two methods which are quick, simple, and patient-friendly in their performance, and relatively cost-effective. Maximal molar bite force measurements are the simplest and cheapest to perform but also associated with an error of the method which may be notable.

Treatment effects in Class II malocclusion using functional appliances

The treatment of Class II malocclusion is aimed at improving or masking the often-existing skeletal discrepancy. In the treatment of Class II malocclusion in growing children, treatment possessing the capability to alter patients' differential maxillo-mandibular growth is of particular interest, namely by means of functional appliances, headgear appliances, or a combination. Numerous investigations, over the last few decades, have evaluated the possibility of growth modification. Results are, however, generally equivocal, with conflicting evidence as to the use and effectiveness of these appliances (Bishara and Ziaja, 1989; Tulloch *et al.*, 1997a; Tulloch *et al.*, 1997b; Keeling *et al.*, 1998; Woodside, 1998; Kluemper and Spalding, 2001; Meikle, 2005). Some studies report significant effects, while others fail to demonstrate any consistent change. On the whole, reports demonstrate that some improvement in jaw relationships can be achieved during early treatment with functional appliances (Schudy, 1968; Tulloch *et al.*, 1997a; Tulloch *et al.*, 1997b; Keeling *et al.*, 1998; Ghafari *et al.*, 1998; Ehmer *et al.*, 1999; Wheeler *et al.*, 2002; O'Brien *et al.*, 2003a; Meikle, 2005). Studies suggest, nevertheless, that the changes, albeit present, are neither very predictable nor always significantly different from those occurring either without treatment or with conventional fixed appliance systems (Tulloch *et al.*, 1990). A large variation in inter-individual response (Woodside, 1998) and small mean changes could suggest that differences may be attributable to factors such as study design (Phillips and Tulloch, 1995; Illing *et al.*, 1998), patient compliance, as well as the inability to control the amount and direction of mandibular growth (Schudy, 1968; Ghafari *et al.*, 1998).

Comments

In individual studies looking at Class II treatment with functional appliances, one can often observe small mean treatment changes and large standard deviations. Individual studies separately recruit a limited number of patients, and this number is often not very large, meaning that the results obtained may not be applicable to a different or a larger population sample. Several studies have tried to group together research focusing on treatment in Class II individuals, in order to arrive at a less biased conclusion. They often focus on a particular type of appliance, for example the Andresen and Fränkel appliances (Mills, 1991), Bionator appliances (Flores-Mir and Major, 1996a; Jacobs and Sawaengkit, 2002), twin-block appliances (Flores-Mir and Major, 1996b), Herbst appliances (Flores-Mir *et al.*, 2007), or combine all types of functional appliances (Chen *et al.*, 2002; Cozza *et al.*, 2006). These studies often aim to combine findings from individual studies but fail to do so using statistically sound methodology. Combining the data from individual studies to increase the total sample size seems to be a reliable means of more powerfully estimating the true effect of a certain type of treatment, as opposed to a less precise estimation derived from a single study under a single set of assumptions and conditions. This is most reliably done using meta-analysis methodology. Several studies have previously been carried out on Class II functional appliance treatment using meta-analysis methodology. Nguyen *et al.* (1999) investigated the relationship between overjet and traumatic dental injuries, Perillo *et al.* (2011) investigated mandibular changes following Fränkel appliance treatment, Marsico *et al.* (2011) investigated short-term mandibular growth following functional appliance treatment, and Harrison *et al.* (2007) looked into early versus late Class II malocclusion treatment. The conclusions of these studies often state that more research is needed, that results are variable, and that changes are statistically significant but their clinical significance is doubtful. A meta-analysis which examines removable functional appliances with respect to changes in the sagittal position of the jaws, to our knowledge, has not been carried out previously.

The masticatory musculature and its relation to functional appliance treatment response

Functional appliances have been extensively investigated with regard to skeletal and dentoalveolar changes in response to treatment. Much clinical research attention has been focused on the effect of different clinical growth patterns on treatment results with functional appliances (Pancherz, 1979; Malmgren and Ömblus, 1985; Ruf and Pancherz, 1996). Although the treatment results obtained with functional appliances are often satisfactory, skeletal treatment changes occurring with their use are, on average, not very large, and not very predictable, with large inter-individual variation (Carels and van der Linden, 1987; Bishara and Ziaja, 1989; Tulloch *et al.*, 1990; Woodside, 1998). Not all individuals respond the same way to functional appliance treatment. The large variation seen amongst

patients is often attributed to compliance issues, but evidence of this variation is also found in studies where fixed functional appliances are used and thus the influence of patient compliance is excluded (Hansen and Pancherz, 1992; Wieslander, 1993; Manfredi *et al.*, 2001).

One factor that could in part explain inter-individual differences in response to functional appliance treatment may be the masticatory musculature and its functional capacity. Antero-posterior intermaxillary forces exerted by functional appliances during treatment display a wide variation and can vary in magnitude between 0.25 and 5 Newtons as well as in direction (Katsavrias and Halazonetis, 1999; Noro *et al.*, 1994). This variation is present both between patients as well as for the same patient during the treatment period. In parallel, it is known that masticatory muscle capacity varies significantly between growing individuals, as measured both by bite force (Proffit and Fields, 1983; Kiliaridis *et al.*, 1993; Braun *et al.*, 1995; Ingervall and Minder, 1997) and masseter muscle thickness (Raadsheer *et al.*, 1996). In view of the fact that masticatory muscle capacity varies significantly between growing individuals, it has been speculated that the considerable variability seen in individual response to functional appliance treatment is possibly related to both the magnitude and the direction of forces, and may thus be directly related to the individuals' muscular and soft tissue characteristics (Kiliaridis, 1998).

Comments

A large variation exists amongst patients with regards to the treatment outcome following functional appliance treatment. A large variation also exists in the masticatory musculature characteristics amongst patients, and these characteristics, namely muscle strength and masseter muscle thickness, have been proposed to be under genetic control (Lauweryns *et al.*, 1995). Based on the current knowledge, it is unclear whether variations in masticatory muscle characteristics in Class II malocclusion growing children, such as masseter muscle thickness and maximal molar bite force can be one of the possible causes of the reported variation of treatment results with functional appliances.

Functional appliance treatment and its effects on the masticatory musculature

Another important question is how the soft tissues respond after a period of using functional appliances and what happens to the magnitude and direction of these forces during treatment. Kiliaridis *et al.* (1990), based on data from patients wearing a posterior bite-block, suggest that muscles do not exert the same forces at the beginning and later on during treatment, since changes occur to re-establish functional balance. There is adaptation over time of the soft tissues and muscles, meaning that if the length of a muscle is changed, this induces initial stretching followed by adaptation of the muscle.

Several electromyographic studies have been carried out looking into muscle function during functional appliance treatment, but the results are sometimes contradictory. Sessle *et al.* (1990) and

Yamin-Lacouture *et al.* (1997) found, with the use of implanted electrodes in monkeys, an initial decrease in swallowing and postural masticatory muscle activity following appliance wear, but this returned to pre-appliance levels after approximately six weeks. Pancherz and Anehus-Pancherz (1980) and Pancherz and Anehus-Pancherz (1982) found a decrease in chewing and maximal biting electromyographic activity of the masticatory muscles during Herbst appliance treatment, but this increased and sometimes exceeded pre-treatment levels after the end of Herbst appliance treatment. Miralles *et al.* (1988) on the other hand found similar electromyographic tonic activity with and without functional appliance wear in a cross-sectional study looking at children undergoing functional appliance therapy during a period of three and a half to forty-two months, which was in agreement with Thilander and Filipsson (1966). Freeland (1979) also found little difference in swallowing and chewing masseteric activity in Class II subjects treated with activators over a twelve month period. On the other hand, Ahlgren (1960), Moss (1975), Ahlgren (1978), as well as McNamara (1980) report an increase in muscular activity with functional appliance use, which may return to normal levels once treatment progresses. Due to the issues of reproducibility and reliability in measuring electromyographic activity associated with the large measurement error, the findings recorded to date on increased, static, or decreased masticatory muscle activity after functional jaw orthopedics are highly contradictory.

Comments

Physical activity can modify certain properties of a muscle, and thus changes in muscle activity during functional appliance wear may have an effect on the masticatory muscles. The current data available is contradictory, mainly due to the methodological difficulties in performing electromyographic studies in humans in a reliable manner. Changes in masticatory muscle activity during functional appliance treatment may cause alterations in the outcome of muscle activity or functional characteristics of these muscles such as their thickness and contraction force. These changes may thus be investigated both as regards the outcome of long-term changes in muscle activity, by measuring maximal bite force, and as regards muscle cross-section, by measuring ultrasound muscle thickness.

Functional appliances and stability of treatment in relation to the masticatory musculature

In the treatment of Class II malocclusion children, relapse of overjet, overbite, mandibular incisor inclination, and sagittal molar relationship are often observed, but do not always compromise an otherwise successful correction of the Class II malocclusion (Fidler *et al.*, 1995). Long-term stability following Class II malocclusion treatment is the fundamental key to a successful orthodontic treatment outcome, and of prime concern for patients and orthodontists alike. A large amount of variability is seen between patients as regards post-treatment changes, implying that in some patients the results are

stable while in others this is not the case. Relapse tendencies are observed in some patients, although their extent and clinical significance are variable (Fidler *et al.*, 1995; Herzberg, 1973). Relapse, however, following orthodontic treatment, both functional and otherwise, cannot be predicted at an individual level (Bondemark *et al.*, 2007).

Several factors have been proposed to try and explain relapse and the variability seen in the stability of treatment results following treatment with functional appliances in Class II division 1 malocclusion children. A major factor contributing to stability is thought to be the growth pattern of the patients (Ormiston *et al.*, 2005). After the orthopedic intervention period, maxillary and mandibular growth patterns seem to strive to catch up with their early patterns (Dermaut & Aelbers, 1996). A favorable growth pattern, in addition to correct diagnosis, treatment, and retention protocols in motivated patients probably increases the likelihood of stable long-term treatment results (Lerstøl *et al.*, 2010). Prediction of relapse and/or stability after orthodontic treatment seems to be difficult as the dentition constantly changes throughout life, with or without orthodontic treatment (Bondevik, 1998). Besides growth, forces derived from the surrounding orofacial tissues are believed to promote stability (Melrose and Millet, 1998). When dentoalveolar changes are in harmony with the tongue and facial muscles, the result is thought to be more stable (Nanda *et al.*, 1993).

Good occlusal intercuspitation following Class II malocclusion treatment has been reported to be necessary in order to prevent skeletal and dentoalveolar relapse (Pancherz, 1991; Wieslander, 1993). Nanda *et al.* (1993) suggest good occlusion and cuspal interdigitation, a constant intercanine width, and no proclination of the lower incisors as some of the most important factors for long-term stability following orthodontic treatment. Intercuspitation, as a proposed factor affecting stability, would come into play when the teeth are in occlusion, and dental occlusion has been proposed to be an important factor in the equilibrium theory of tooth position (Proffit, 1978). However, occlusal contacts as such may not be sufficient in order to maintain good occlusal interdigitation following treatment. What may be more important in this respect are the forces derived from the masticatory musculature and the soft tissues, which may play an important role in conserving the intermaxillary occlusal position by the delivery of occlusal forces. This suggests that masticatory muscle characteristics may play a role in stability and the relapse potential following functional appliance treatment.

Comments

Another factor that may therefore influence the stability of treatment results following functional appliance therapy in Class II malocclusion growing children is the functional capacity of the masticatory muscles. These muscles, which are directly involved in the mode of action of functional appliance treatment, may also play a role in determining the post-treatment effects once the functional appliance is discontinued.

AIMS

The general aim of the present thesis was to evaluate the short-term antero-posterior effects on Class II division 1 malocclusion in growing children using functional appliances, and to investigate whether the functional capacity of the masticatory musculature can be used as a predictive variable in determining the treatment and post-treatment effects following functional appliance treatment.

The specific aims of the four papers included in the present thesis were:

- To evaluate, using meta-analysis methodology based on published cephalometric data, short-term antero-posterior skeletal and dentoalveolar effects on Class II division 1 malocclusion in growing patients following treatment with functional appliances. (Paper I)
- To investigate the effects of twin-block appliance treatment on masseter muscle thickness measured with ultrasound imaging. (Paper II)
- To investigate the effects during and after functional appliance treatment on maximal molar bite force. (Papers III and IV)
- To investigate the predictive value of pre-treatment masseter muscle thickness in determining treatment effects of twin-block appliances in Class II division 1 malocclusion children. (Paper II)
- To investigate the predictive value of pre-treatment maximal molar bite force in determining treatment effects of functional appliances in Class II division 1 malocclusion children. (Paper III)
- To investigate the predictive value of pre-treatment maximal molar bite force in determining post-treatment changes and relapse potential, following functional appliance treatment in Class II division 1 malocclusion children. (Paper IV)

MATERIAL AND METHODS

The present thesis was based on one study using meta-analysis methodology (Paper I) and three clinical investigations (Papers II-IV). Paper II involved patients from one patient sample, while Papers III and IV involved patients from another common patient sample.

Material and Methods – *Meta-Analysis* (Paper I)

Search strategy

To identify orthodontic articles reporting on the treatment of Class II division 1 malocclusion in growing children with functional appliances or headgear, a literature search was performed using the following databases (up until May 2006): PubMed; Ovid (including OLDMEDLINE); Cochrane Library; other databases (Web of Science, Google Scholar Beta, Embase, Extenza, African Journals Online, Bandolier, Evidence-Based Medicine, Latin American and Caribbean Center on Health Sciences Information, Bibliografia Brasileira de Odontologia, ChinaInfo database).

Terms used in the search were *functional appliances, headgear or extraoral traction, and Class II*, combined with *clinical trial or randomized controlled trial*. No date limits or language limits were set. A further search, for the sake of verification that all articles had been located, was carried out using *activator, bionator, twin-block*, and names of specific functional appliances as opposed to simply functional appliances. The search was expanded by searching references of articles consulted. Full-text sources available on the Internet for the *American Journal of Orthodontics and Dentofacial Orthopedics*, the *European Journal of Orthodontics*, and the *Angle Orthodontist* were also searched to validate that the search had identified all relevant articles (Mavropoulos and Kiliaridis, 2003).

Selection criteria

Articles were selected for inclusion and analysis if the following criteria were met:

- human studies;
- pertained to removable functional appliance and/or headgear appliance use in the treatment of Class II malocclusion;
- sample size mentioned (minimum of 10 patients; case reports or case series were excluded);
- treatment carried out on growing patients with age ranges mentioned;
- duration of treatment mentioned (with a minimum duration of 9 months, to avoid erroneous annualized values);
- in the form of prospective clinical trials;
- availability of a suitable control group (untreated Class II individuals);

- measurable pre-treatment and post-treatment cephalometric values, as well as changes during treatment, for SNA, SNB, ANB, and overjet mentioned;
- sufficient data available for statistical calculations.

In the case of more than one publication about the same patient group, the most informative and relevant article was included. For studies stating one or more but not all of the desired cephalometric variables (SNA, SNB, ANB, overjet), the corresponding author was contacted, and values for these variables were also obtained from the raw data. A quality analysis was also carried out according to the methods described by Petrén et al. (2003). Studies were described as being of low, medium, or high quality. Only those falling into the medium- and high-quality categories were included for analysis.

Data collection

The data provided in the included studies were divided into different patient groups, which were patients treated with activators, patients treated with twin-block appliances, patients treated with headgear, patients treated with combination appliances (including both functional and headgear components), and untreated Class II control groups. No distinction was made between different types of activators or headgear appliances. Herbst appliances were excluded as these tend to be fixed and would bias the results with regard to compliance. Fränkel appliances were also excluded since they may differ from other functional appliances in their mode of action (Fränkel, 1969; Lubit, 1983; Bishara and Ziaja, 1989; Turner, 1991; Janson *et al.*, 2003). From the identified studies, the changes referring to the maxillary position relative to the cranial base (expressed by the SNA angle), the mandibular position relative to the cranial base (expressed by the SNB angle), the intermaxillary relationship (expressed by the ANB angle), and overjet were analyzed. Treatment time between studies varied and therefore data were annualized in order to standardize this variation.

Data analysis

Data were entered into the meta-analysis program of the Cochrane Collaboration's Review Manager Software (RevMan 4.2.8, released July 8, 2005), and all statistical evaluations were carried out using this program.

Descriptive statistics were calculated for the different variables (SNA, SNB, ANB, overjet) in the different groups (activators, twin-block, headgear, and combination appliances) including arithmetic mean and standard deviation. Using the random effects model of meta-analysis, forest plots were drawn and significance tests carried out (calculating *p*-values). Heterogeneity tests were also performed.

Material (Papers II, III, IV)

Patient sample (Paper II)

The sample of this study was made up of a treatment and a control group. The size of each group was chosen by performing a power analysis based on the results of a pilot study, and was calculated to be 22.

Treatment group

The first 22 consecutive patients from the 28 patient samples of Mills and McCulloch (1998) made up the treatment group. The criteria for case selection for the treatment group were the following:

- presence of a skeletal Class II relationship ($ANB \geq 5^\circ$);
- Class II malocclusion in which the esthetic appearance of the patient improved when the mandible was postured forward;
- full cusp Class II molar relationship on one side and $\geq \frac{1}{2}$ cusp Class II molar relationship on the opposite site;
- overjet ≥ 6 mm.

This group of 22 children included 8 boys and 14 girls, and were between the ages of 8 and 12 at the start of treatment (mean age 9 years 5 months). These children were treated with a twin-block appliance. The patients were instructed to wear their appliances full-time, except for meal times and for brushing.

The initial wax construction bite was taken with the mandible protracted approximately 6 mm and opened vertically by about 5 mm. In patients with slight asymmetries of the mandible, the construction bite was taken with the upper and lower midlines coincident. As treatment progressed, when 3 to 4mm of overjet reduction had been achieved, 1.5 to 2.0 mm of acrylic was added onto the distal inclines of the lower appliance bite shelves to maintain sufficient activation.

The basic design of the twin-block appliance used in this study is illustrated and described in Mills and McCulloch (1998). One particularity of the twin-block appliance used was that the maxillary incisors were not engaged in the appliance (no maxillary labial bow was included), while an acrylic labial bow was added to the lower incisors. (Figure 1)

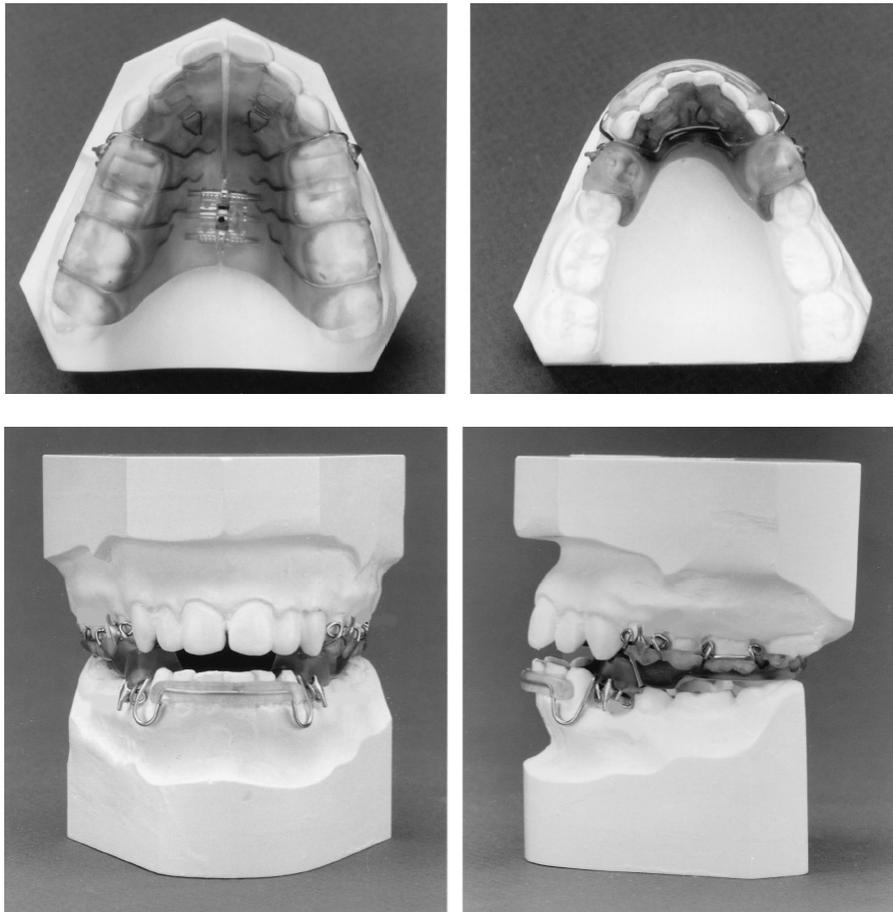


Figure 1: Modified twin-block appliance showing the occlusal views of the upper and lower components with an acrylic labial bow to improve retention of the mandibular appliance, while no labial bow is present on the maxillary appliance. The maxillary appliance has an expansion screw incorporated. (taken from Mills and McCulloch, 1998)

Control group

Twenty-two growing children, between the ages of 8 and 12 (mean age 9 years 9 months) without immediate need for orthodontic treatment, served as control subjects. This included 12 boys and 10 girls, of whom 8 had a Class I molar relationship, while the remaining 14 had a Class II molar relationship. These children were observed longitudinally.

Patient sample (Papers III and IV)

This sample of children was derived from a larger sample of Class II division 1 malocclusion children mentioned in Kjellberg *et al.* (1995). Twenty-five children in the mixed dentition and with a Class II division 1 malocclusion (17 male, 8 female), between the ages of 9 and 13 at the start of the

study (mean age 10 years 6 months) made up the patient sample in Study III. Twenty-eight children in the mixed dentition and with a Class II division 1 malocclusion (16 male, 12 female), between the ages of 8 and 14 at the start of the study (mean age 10 years 6 months) made up the patient sample in Study IV.

Children were chosen according to the following criteria:

- presence of a skeletal Class II relationship ($ANB > 4^\circ$);
- retrognathic mandible ($SNB \leq 78^\circ$);
- full cusp Class II molar relationship on one side and $\geq \frac{1}{2}$ cusp Class II molar relationship on the opposite site;
- overjet $\geq 6\text{mm}$;
- no transverse discrepancies;
- no signs of condylar lesions.

These children were treated with a bow activator according to Schwarz (Graber and Neumann, 1977), and instructed to wear the appliance for a minimum of 12 hours per day. The bow activator according to Schwarz is a modification of the activator originally described by Andresen and Häupl (1945). The Schwarz bow activator is horizontally divided and the two parts are joined together with an elastic bow (0.9 mm blue elgiloy; Rocky Mountain Orthodontics, Denver, Colorado, USA), which allows small transverse movements of the mandible. The mode of action of the activator according to Schwarz is similar to that of the Andresen activator. (Figure 2)

The initial wax construction bite was taken with the mandible protracted approximately half of the individual's maximal protrusion, but did not proceed to an edge to edge position. The mandible was lowered as little as possible from occlusal contact.

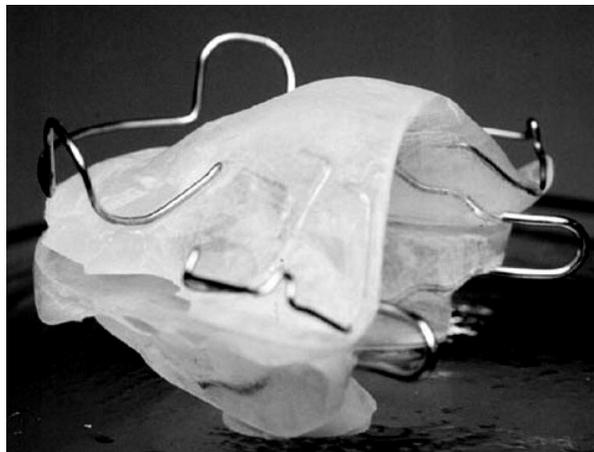


Figure 2: Bow activator according to Schwarz: the labial bow, the clasps on the first maxillary molars, and the elastic bow joining together the maxillary and mandibular parts are shown.

Methods (Papers II, III, IV)

Cephalometric analyses

(Paper II)

Lateral cephalograms were taken of all children in centric occlusion and with the head fixed in a cephalostat. The same machine was used for all children. Radiographs were traced and digitized using the Dentofacial Planner software program (Dentofacial Software, Toronto, ON, Canada). Details of the cephalometric analyses used here are illustrated and described in Mills and McCulloch (2000). A standard Jarabak analysis as well as a custom analysis was generated for each case. The custom analysis used Sella-Nasion as a reference line for superimposition. The specific cephalometric measurements examined are illustrated in Paper II.

The anterior cranial base structures were traced in detail, and a superimposition on the best fit of the anterior cranial base, cribriform plate, and inner contours of the anterior cranium as well as the Sella Turcica structures was carried out to ensure that the choice of the points for the Sella and Nasion on the T2 cephalograms were on the same line as for the T1 cephalogram. In addition, a vertical reference plane was constructed through Sella Turcica perpendicular to the palatal plane. A series of horizontal measurements were then made from various landmarks perpendicular to this vertical reference plane.

(Papers III and IV)

Lateral cephalograms were taken of all children in centric occlusion and with the head fixed in a cephalostat. The same machine was used for all children and the magnification adjusted to zero. The radiographs obtained were analysed using a computerized cephalometric analysis (PC-DIG version 5.1 data system; Dr John McWilliam, Karolinska Institute, Stockholm, Sweden). The landmarks drawn on acetate sheets were digitized twice on the same occasion. The mean values between the two measurements were used in the study. The reference points and lines used are shown in Papers III and IV. The superimposition of the lateral cephalograms was performed according to the structural method described by Björk and Skieller (1983).

Dental cast measurements (Papers III and IV)

Dental casts were taken to measure overjet, overbite, and molar relationships. The molar relationship was recorded as a percentage of the Angle Class II relationship, an Angle Class I relationship of molars denoted by 0%, and a full Angle Class II relationship denoted by 100% (Staudt and Kiliaridis, 2010). Dental developmental stage was also recorded in Paper IV, using the classification according to Thilander *et al.* (2001).

Ultrasound imaging (Paper II)

Muscle thickness was measured by ultrasonography, the details of which are described in Kiliaridis and Kälebo (1991), modified by Raadsheer *et al.* (1994). The same technique was used both for the treatment group and the control group. In brief, ultrasound measurements were obtained by means of a real-time scanner (Pie Medical Scanner 480, 7.5 MHz linear array transducer; Pie Medical Imaging, Maastricht, The Netherlands). The participants were seated in an upright position, with their heads in a natural position. The masseter muscle was scanned bilaterally on a level halfway between the zygomatic arch and gonial angle. The scan plane was orientated perpendicular to the anterior border of the muscle and perpendicular to the surface of the underlying ramus. The recordings were made during two conditions, relaxed and contracted. The first was obtained by asking the participants to maintain slight interocclusal contacts, the second by asking them to clench maximally in the intercuspal position. Under all recording conditions, light pressure was applied so as to avoid compression of the soft tissues and muscle, thus avoiding erroneous measurements. All recordings were repeated twice, and the final thickness was obtained from the mean of the repeated measurements. Muscle thickness was registered to the nearest 0.1 mm.

Bite force and finger force measurements (Papers III and IV)

Maximum voluntary molar bite force (measured in Newtons) was determined using a bite force recorder (a metal bite fork with a plastic coating to prevent enamel chipping, connected to a strain gauge) as described by Helkimo *et al.* (1975), which was custom-made at the University of Gothenburg, Sweden. When the fork was loaded, the bite force was recorded graphically (Speedomax recorder, Leeds and Northrup, London, UK). The thickness of the fork was 6.9 mm for the metal part and 4 mm for the plastic coating, which decreased slightly during biting pressure. The subject was seated upright in a dental chair, and the bite fork was placed between the first molars on each side. The subject was instructed to bite as hard as possible, without inflicting pain. All recordings were made twice in each position. In order to obtain as high bite force levels as possible, the subjects were encouraged to 'do their best'. The highest value recorded was used as the maximum force level.

Maximal finger force, as an indicator of general muscle force (Kiliaridis *et al.*, 1993), was similarly recorded with the bite fork placed between the thumb and index fingers of both left and right hands and recorded twice for each hand. The higher of the two values was used for each child.

Experimental design (Papers II, III, IV)

(Paper II)

The treatment group children were treated with a twin-block appliance for 9–17 months (mean of 13.1 months), until a Class I molar relationship was achieved. Lateral cephalometric radiographs, ultrasonographic imaging of the masseter muscle to measure the cross-sectional thickness, and body stature (height) and weight measurement of the treatment group were performed both before starting treatment (T1) and after the completion of this phase of treatment (T2).

The control group children were followed-up (observed) for 11 to 17 months (mean of 13.5 months). The control group had ultrasonographic masseter muscle thickness recordings at the beginning (T1) and end (T2) of the observation period.

(Paper III)

The children were first seen 1-2 years (mean 1.4 ± 0.2 years) prior to the commencement of treatment and observed for this time interval without any treatment being carried out. They were then treated with a Schwarz activator for a period of 1–2 years (mean 1.7 ± 0.5 years). At the initial registration (T0), before (T1) and after (T2) treatment, body stature (height) measurements, maximal molar bite force measurements, finger force measurements, lateral cephalometric radiographs, and impressions for dental casts were taken. The observation period T0–T1 served as the control for the same patients that underwent activator treatment from T1 to T2.

(Paper IV)

The children were treated with a Schwarz activator for a period of approximately 1 to 2 years (mean 1.6 ± 0.4 years). They were subsequently followed-up for at least 1 year after the completion of treatment (mean 2.2 ± 0.9 years) without any further treatment during this period. Before treatment (T1), after treatment (T2), and after the post-treatment follow-up period (T3), body stature (height) measurements, maximal molar bite force measurements, maximal finger force measurements, lateral cephalometric radiographs, and impressions for dental casts were taken.

As an evaluation of post-treatment stability, patients were separated into two groups, namely stable and unstable. Stability was judged by evaluating dentoalveolar changes. Cases with a shift towards a Class II molar relationship (at least one molar was shifted $\frac{1}{4}$ cusp width towards a Class II molar relationship) and with an increase in overjet (≥ 0.5 mm) post-treatment were judged as unstable, whereas cases where no post-treatment relapse in overjet or molar relationship occurred were judged as stable. Cases where the molars were towards a Class III relationship after treatment and shifted to a

Class I relationship after follow-up were judged as stable despite a shift in molar Class, since a Class I molar relationship was the final result.

Statistical methods (Papers II, III, IV)

All statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) version 15.0 (SPSS Inc, Chicago, IL, USA). Apart from the statistical tests detailed below, descriptive statistics were also calculated for cephalometric, dental, ultrasonographic masseter muscle thickness, and maximal bite and finger force measurements.

Statistical hypothesis tests

Cephalometric and dentoalveolar changes during the different time periods (pre-treatment, during treatment, post-treatment follow-up) were evaluated using paired *t*-tests. Masseter muscle thickness (Paper II), as well as bite force and finger force (Papers III and IV) changes were also evaluated using paired *t*-tests. Significance was set at the $p < 0.05$ level.

Unpaired *t*-tests were used in Paper IV when comparing the stable and unstable group of patients. Differences were looked at as regards maximal molar bite force, body stature, body stature changes, age, dental developmental stage, dental and cephalometric variables, and dental and cephalometric changes.

Correlation analyses

Univariate and multivariate linear regression analysis were carried out to determine associations between pre-treatment masseter muscle thickness (Paper II) or pre-treatment maximal molar bite force (Paper III and IV) with cephalometric or dentoalveolar changes during treatment (Papers II and III) or post-treatment (Paper IV). Multivariate regression analyses also included factors such as sex, age, body stature, weight, and pre-treatment cephalometric or dental measurements as independent variables. Correlations were considered statistically significant at $p < 0.05$.

Error of the method

Errors of measurement can be either random or systematic (Houston, 1983). Both types of error were examined separately in the present thesis.

Random errors were evaluated using Dahlberg's formula (Dahlberg, 1940) comparing duplicate recordings. This was used to determine the random error for masseter muscle thickness, maximal molar bite force, cephalometric, and dental cast measurements. In using Dahlberg's formula ($\sqrt{\sum d^2/2n}$), $\sum d^2$

denotes the sum of the squared differences between pairs of recordings, while n denotes the number of duplicate measurements.

Systematic errors were evaluated using paired t -tests (Houston, 1983) comparing duplicate recordings. Again, this was carried out for masseter muscle thickness, maximal molar bite force, cephalometric, and dental cast measurements.

Lateral cephalometric radiograph measurements (Papers II, III, and IV)

In Paper II, repeated cephalometric measurements were taken for 10 patients from the treatment group, on two different occasions, approximately a year apart. The random error in locating landmarks and measuring the variables on lateral cephalograms was determined to be 1.0 mm for linear measurements and 1.1 degrees for angular measurements. Using the same repeated measurements for detection of the systematic error, there was no statistically significant difference, at the 5% level, between the first and second measurements.

In Papers III and IV, the random error for the cephalometric variables was calculated by performing duplicate determinations on 15 randomly selected cephalometric radiographs, with a 2 week interval between the measurements. For linear measurements, the error of the method did not exceed 0.7 mm, and for angular measurements, this did not exceed 0.9 degrees except for the incisal angular measurements, where the error varied from 1.0 to 1.5 degrees. Using the same repeated measurements for detection of the systematic error, there was no statistically significant difference, at the 5% level, between the first and second measurements.

Dental cast measurements (Papers III and IV)

The random error for the dental cast measurements was calculated by performing duplicate determinations on 15 randomly selected dental casts. For linear measurements, the error of the method was 0.3mm both for overjet and overbite. For the molar relationship measurements, the error of the method was 8% (where 100% represents a full cusp width). Using the same repeated measurements for detection of the systematic error, there was no statistically significant difference, at the 5% level, between the first and second measurements.

Ultrasound masseter muscle thickness measurements (Paper II)

To account for any random error, including possible biologic variation, the error of the method for the ultrasound technique was calculated by repeated measurements of 20 patients from the control group, on two separate occasions, 2 weeks apart. This was found to not exceed 0.3 mm. Using the same repeated measurements for detection of the systematic error, there was no statistically significant difference, at the 5% level, between the first and second measurements.

To further test the reliability of the ultrasound measurements, and the systematic error, a third group was included in the study. This group consisted of adult individuals, where all growth had been completed. Fifteen adults (aged between 21 and 35), nine of which were women and six men, with no need of orthodontic treatment made up this group. They were observed for 2 years. Ultrasound thickness measurements of the masseter muscle were taken before and after the observation period. In adult individuals of this age, no changes in muscle thickness would be expected (Newton *et al.*, 1993). The rationale for the inclusion of this group was to account for a possible learning curve of the operator, as well as modification and adaptation in the details of the measuring procedure. By learning curve, what is implied is that with time there may be a change in the way measurements are taken, because of experience. The adult group showed no statistically significant differences (an average increase of 0.05 mm) in the masseter thickness measurements during the observation period, indicating that the method was reliable over this period.

Maximal molar bite force measurements (Papers III and IV)

The random error for maximal molar bite force measurements was studied by repeated measurements of 20 randomly selected patients on two separate occasions, 2 to 4 weeks apart, and found to be 69 N. Using the same repeated measurements for detection of the systematic error, there was no statistically significant difference, at the 5% level, between the first and second measurements.

COMMENTS ON MATERIAL AND METHODS

Comments on material and methods – Meta-Analysis (Paper I)

Search strategy

The literature search in this investigation was executed in various databases, resulting in a higher number of included articles than if only one database had been used. It should be borne in mind, however, that there are limitations to the literature search. These limitations include the fact that some studies may not be included in the databases searched and others may not have been published (introducing publication bias). Medline is nevertheless regarded as a powerful and relatively accurate tool in retrieving orthodontic literature (Mavropoulos and Kiliaridis, 2003).

The literature search and selection of studies was only done by one author in the present thesis. This would have been more reliable if the search had been carried out independently by two authors, and any disagreements resolved by discussion.

Data collection and analysis

An accumulation of data from existing studies implies that the sample size will increase dramatically, and hence even small skeletal changes will be statistically significant. However, statistically significant changes do not necessarily correspond to noticeable therapeutic effects. Changes seen in the data from studies are often small but statistically significant, which has also been suggested by Proffit and Tulloch (2002). Thus, too much weight should not be placed on statistically significant changes but rather on clinically significant ones. A cutoff value for clinical significance was set at 1 degree for angular measurements and 1 mm for linear measurements, as it is often described to be the error in lateral cephalogram measurements (Aelbers and Dermaut, 1996). In this respect, the control group was necessary, providing a comparison consisting of untreated growing Class II individuals displaying changes due to natural growth alone.

The variation in treatment success amongst studies and amongst patients is undoubtedly affected in part by patient compliance. Uniformity was desired with regard to compliance. Thus, trials using appliances fixed to the dental hard tissues were excluded. Other factors contributing to variability amongst studies include patient age, patient maturity, growth pattern, severity and aetiology of the initial condition, treatment timing, soft tissue characteristics, and amount of force applied. Data collection reveals that studies differ in areas such as age, sample size, control groups, and appliances. Data were, however, grouped as best as possible, weighting studies according to number of patients and annualizing mean changes. In the inclusion criteria, the treatment duration minimum was set at 9

months since any treatment time less than that would mean that the methodological error is likely to increase and would give an overestimation when annualized.

The random effects model of meta-analysis was thus used. The random-effects model assumes that there is no common treatment effect for all included studies but rather that the variation of the effects across studies follows a particular distribution. In a random-effects model it is believed that the included studies represent a random sample from a larger population of studies addressing the question of interest, and therefore this model considers both within- and between-study variability.

Comments on material

Sample size

Sample sizes in the individual papers were limited. One must thus be cautious when interpreting the findings obtained. Associations or differences could be present but may not be detectable due to the limitations of the sample sizes, introducing type II error (or so-called false negative).

Patient sample (Papers III and IV)

The patients included in Papers III (n=25) and IV (n=28) are derived from the same patient sample, as mentioned previously. The number of patients included in the two studies, however, is not the same due to the absence or presence of the recordings in the different time periods examined. In Paper III, recordings at the T0 (1-2 years prior to the beginning of treatment), T1 (before treatment), and T2 (after treatment) time periods were required whereas in Paper IV, recordings from the T1 (before treatment), T2 (after treatment), and T3 (after post-treatment follow-up) periods were required. Not all of the patients from the total sample had T0 recordings and so could not be included in Paper III, and similarly not all patients had T3 recordings and so could not be included in Paper IV. The number of patients which are common to both Papers III and Papers IV is seventeen.

Control group (Paper IV)

Paper IV was an association study looking at correlations, and attempting to compare patients who showed stable treatment outcomes to those who did not. The stable group of patients served as the control for the unstable group of patients, thus, the inclusion of an untreated sample of children serving as a control group was not necessary.

Compliance

The question of compliance with regard to the wear of functional appliances is always an issue when carrying out human studies. It may be assumed that all children that were included in the present

investigation, both with thicker or thinner masseter muscles, and both with a weaker or stronger maximal molar bite forces, all faced the issue of compliance and so comparisons can be made without taking this factor into account. The twin-block appliance, in contrast to other removable functional appliances, is worn full-time, allowing a greater amount of time where favorable dentoalveolar and skeletal changes can take place.

Comments on methods

Masseter muscle thickness and maximal molar bite force measurements (Papers II, III, and IV)

The thickness of the bite fork used (6.9 mm for the metal part and 4 mm for the plastic coating, adding up to approximately 11 mm) is because bite force levels increase when clenching is performed with increased jaw opening until about 15-20mm of interincisal distance (corresponding to about 11 mm of intermolar distance), then decrease with further opening, probably corresponding to the optimum length of the jaw elevator muscle sarcomeres (Bakke, 2006).

Masseter muscle thickness or maximal molar bite force measurements are both associated with a random error, but this is somewhat larger for maximal molar bite force measurements. The coefficient of reliability, expressed by $1 - Se^2 / Sd^2$, where Se is the random error while Sd is the standard deviation, gives us a comparative means of evaluating random error (Houston, 1983). This was found to be approximately 0.94 for ultrasound masseter muscle thickness measurements and 0.52 for maximal molar bite force measurements, showing the differences in reliability. The importance of variance due to random error is that it increases the total variance of the measurements. A large variance may obscure existing true differences (type II error). However, if despite the large random error statistically significant differences are detected, this substantiates the findings.

Cephalometric analyses (Papers II, III, and IV)

The cephalometric analyses used in Papers II and III, which investigate masticatory functional capacity and functional appliance treatment outcomes, are not similar, and a direct comparison of the results of these two studies is therefore not possible. The reason for the dissimilarities in the cephalometric analyses carried out was that the tracings and analyses were done in two different universities, each using the analysis which is habitually used by the respective institution. Ideally, a similar cephalometric analysis would have been more beneficial as far as being able to compare and contrast results. The individual results from each paper nevertheless add in different ways to conclusions arrived at, and complement each other.

Measurements from the Condylion, used in Papers III and IV to measure mandibular unit length for example, may be judged as unreliable as this point is sometimes difficult to locate accurately on a

lateral cephalogram. This difficulty was somewhat overcome by looking at T1 and T2 cephalograms from the same patient when tracing, to obtain a more certain outline of the condyle. In addition, wooden ear rods with plastic covers were used, as opposed to metal ear rods, so as to avoid obscuring of the condylar structures. Moreover, the presence of a large random error normally increases type II error and the chance of failing to detect an effect that is there. Thus, if a difference is found, this is backed up statistically.

Skeletal maturation judgment according to the cervical vertebral maturation method of Baccetti *et al.* (2005) was attempted, but was not possible to judge on all radiographs as the cervical vertebrae C2, C3, and C4 were not always entirely visible due to the lead shield (apron or thyroid collar) worn by the children. Landmarks in the neck region are at risk of being hidden by the lead shield, especially from the second cervical vertebra and below, as has been asserted by Wiechmann *et al.* (2007). It was thus decided to use changes in body stature to account for developmental and growth changes during the treatment and post-treatment periods.

Comments on statistical methods

Regression analyses (Papers II, III, and IV)

Both age and gender can influence maximal molar bite force measurements (Koc *et al.*, 2010) and possibly masseter muscle thickness measurement using ultrasound imaging (Serra *et al.*, 2008). It would therefore have been advantageous to study a larger and more homogeneous sample of patients. This was somewhat overcome by including age and gender as confounding variables in the multiple regression analyses, thereby addressing these differences.

RESULTS

Evaluation of treatment effects – *Meta-Analysis* (Paper I)

Treatment effects are shown with the help of forest plots. Forest plots represent the effect of activators (Figure 3) and twin-block appliances (Figure 4) on the SNA, SNB, ANB angles, and overjet (OJ). Shown for every study is the weighted mean difference (WMD) between the treatment and control groups based on the random effects meta-analysis model, as well as the 95% confidence interval (95% CI) for each variable. The diamonds represent the overall WMD and 95% CI. Values for heterogeneity and *p*-values (for statistical significance) are shown below each forest plot.

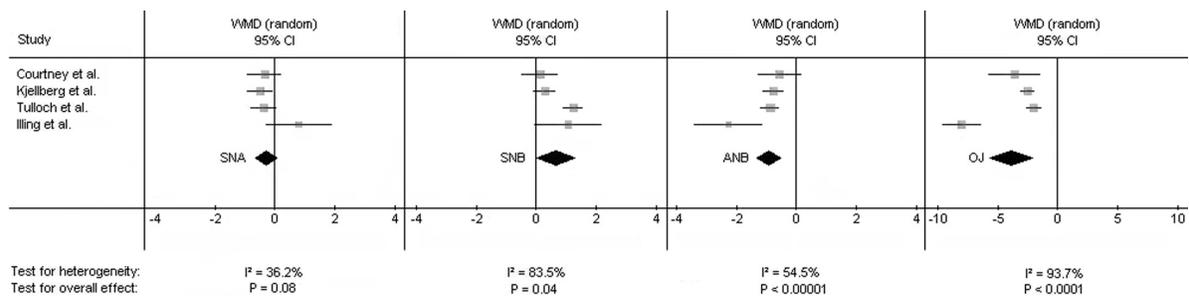


Figure 3: Forest plots representing the effect of activator type appliances on SNA, SNB, ANB, and OJ

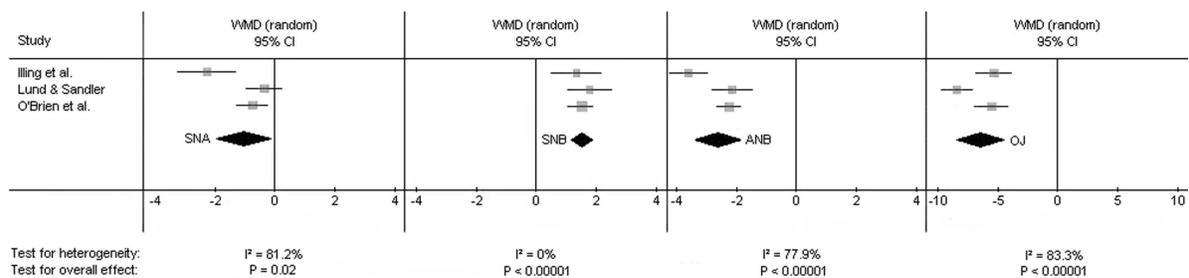


Figure 4: Forest plots representing the effect of twin-block appliances on SNA, SNB, ANB, and OJ

In summary (Table 1), functional appliances (activators and twin-block) improve the sagittal intermaxillary relationship (ANB angle) mainly by their effect on the mandibular position (SNB angle) in relation to the anterior cranial base and show an important dentoalveolar effect by overjet reduction. Twin-block appliances also show an effect on maxillary position (SNA angle).

Table 1: Summary of meta-analysis results showing the annualized mean change and 95% Confidence Intervals (95% CI) for the different appliance groups when compared to controls

Appliance	SNA		SNB		ANB		Overjet	
	Mean Change	95% CI	Mean Change	95% CI	Mean Change	95% CI	Mean Change	95% CI
Activator	-0.31	-0.65, -0.04	0.66	0.03, 1.29	-0.92	-1.31, -0.52	-3.88	-5.65, -2.11
Twin block	-1.03	-1.94, -0.13	1.53	1.18, 1.87	-2.61	-3.39, -1.83	-6.45	-8.46, -4.44

* Changes in the SNA, SNB, and ANB categories are changes in degrees, while in the overjet category, the changes are in millimeters. Mean change values in bold denote statistical significance (*P* < .05).

Masticatory muscle changes during and after functional appliance treatment

Changes in masseter muscle thickness during treatment (Paper II) (Figure 5)

Ultrasonography revealed that masseter muscle thickness in the treated subjects (n=22) was 0.4 mm (± 0.7 mm) thinner at the end of treatment (T2) than it was pre-treatment (T1) ($p = 0.02$), decreasing from an average 10.7 mm (± 1.2 mm) pre-treatment muscle thickness to an average 10.3 mm (± 1.4 mm) muscle thickness after treatment. In the control group (n=22), however, an augmentation in masseter muscle thickness of 0.6 mm (± 0.2 mm) was seen over a similar time period ($p < 0.001$), increasing from an average 10.9 mm (± 1.1 mm) muscle thickness before (T1) to an average 11.5 mm (± 1.2 mm) muscle thickness after (T2) the observation period.

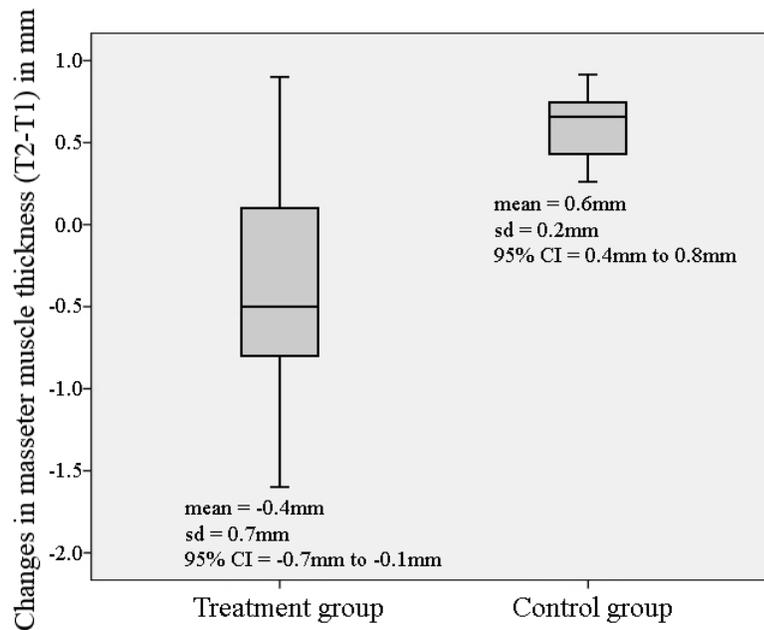


Figure 5: Box plots showing changes in masseter muscle thickness between the initial and the post-treatment or post-observation measurements, respectively. The lower border of the box represents the lower quartile, the upper border the upper quartile, and the line within the box the median. Whiskers represent maximum and minimum values.

Changes in maximal molar bite force during treatment (Paper III) (Figure 6)

Maximal molar bite force in the patient sample (n=25) was 34.2 N (± 78.4 N) less at the end of treatment (T2) than it was pre-treatment (T1) ($p=0.039$), decreasing from an average of 532.0 N (± 124.9 N) maximal molar bite force to an average of 497.8 N (± 101.6 N) maximal molar bite force. During the observation period before treatment (T0 to T1), maximal molar bite force increased by 53.2 N (± 99.4 N) ($p=0.017$) from a T0 maximal molar bite force of 478.8 N (± 121.8 N) to a T1 maximal molar bite force value of 532.0 N (± 124.9 N). Finger force on the other hand increased from T0 to T1 ($p=0.014$) and continued to increase form T1 to T2 ($p=0.002$).

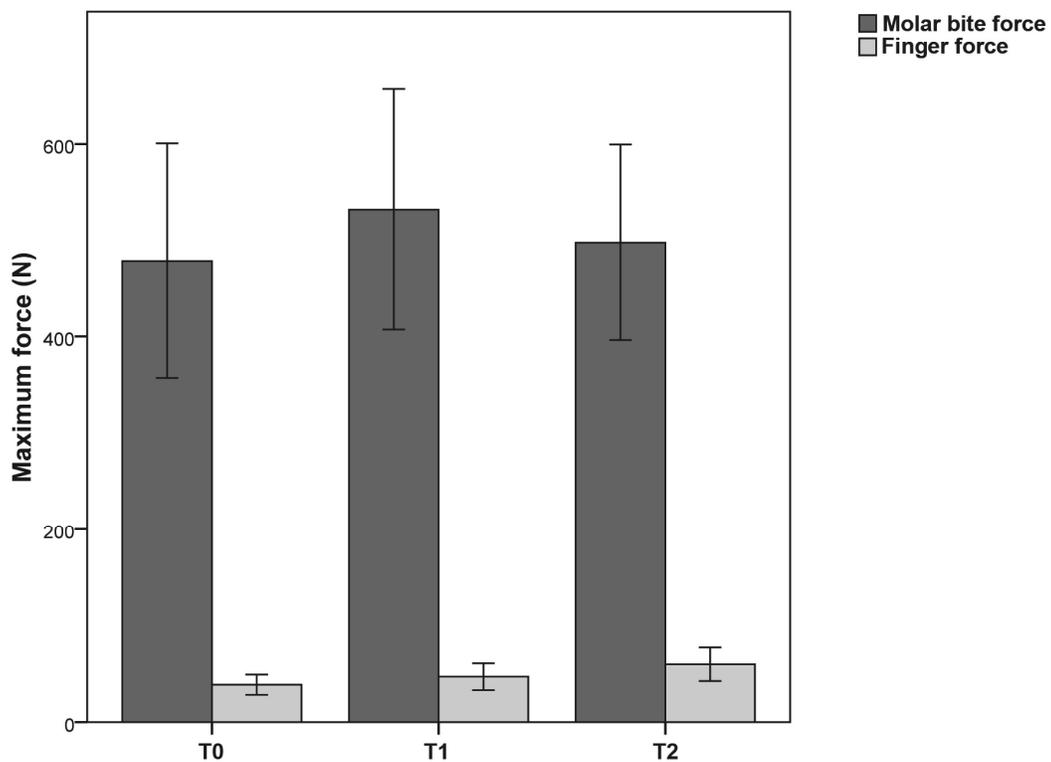


Figure 6: Maximal molar bite force and finger force measurements of the patient sample. Bars represent means while whiskers represent standard deviations for each time period (T0, T1, and T2).

Changes in maximal molar bite force during post-treatment follow-up (Paper IV) (Figure 7)

Maximal molar bite force in the patient sample (n=28) was seen to increase during the post-treatment follow-up period by 39.7 N (± 71.8 N) ($p=0.039$), from a maximal molar bite force value of 477.6 N (± 98.7 N) after treatment (T2) to 517.3 N (± 86.6 N) after the post-treatment follow-up (T3). During treatment, the maximal molar bite force had decreased by 47.7 N (± 116.9 N) ($p=0.030$), from a pre-treatment (T1) value of 525.3 N (± 117.8 N) to a post-treatment (T2) value of 477.6 N (± 98.7 N). Finger force on the other hand, increased progressively throughout the treatment ($p=0.021$) and post-treatment ($p=0.011$) periods.

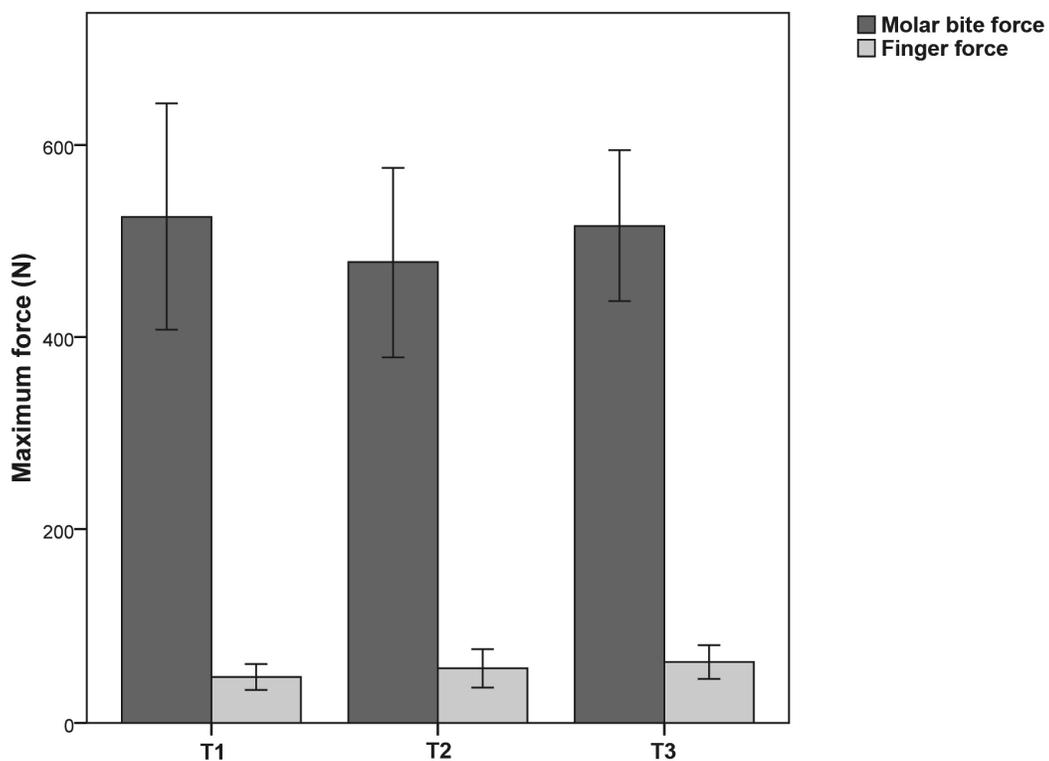


Figure 7: Maximal molar bite force and finger force measurements of the patient sample. Bars represent means while whiskers represent standard deviations for each time period (T1, T2, and T3).

Associations between masticatory muscles and treatment or post-treatment results

Association between pre-treatment masseter muscle thickness and treatment results (Paper II)

A statistically significant relationship was observed in relevance to proclination of mandibular incisors in relation to the mandibular plane. Namely, individuals with thinner muscles pre-treatment, showed a significantly more pronounced proclination of mandibular incisors (Figure 8). Likewise, it was found that the gonial angle was also associated with mandibular incisor proclination, where a larger pre-treatment gonial angle was correlated with a larger proclination of mandibular incisors (Figure 9).

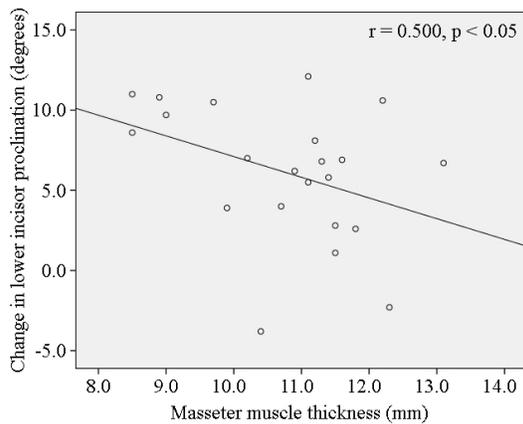


Figure 8: Scatter diagram showing mandibular incisor tipping during twin-block treatment in relation to initial masseter muscle thickness. Mandibular incisors proclination was measured with reference to the mandibular plane (Go–Gn).

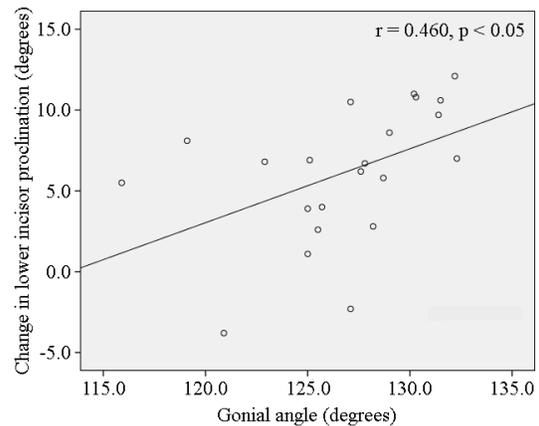


Figure 9: Scatter diagram showing mandibular incisor tipping during twin-block treatment in relation to the pre-treatment gonial angle measurement. Mandibular incisors proclination was measured with reference to the mandibular plane (Go–Gn).

Additionally, individuals with thinner masseter muscles also showed more of a distalisation of maxillary molars ($r=0.453$; $p=0.034$) and posterior displacement of the cephalometric A point ($r=0.674$; $p=0.001$) with reference to the vertical reference plane. Those with thicker masseter muscle showed a more pronounced increase in the posterior facial height (Sella–Gonion) ($r=0.577$; $p=0.005$), condyle-ramus height (Condylion–Gonion) ($r=0.464$; $p=0.029$), and mandibular unit length (Condylion–Gnathion) ($r=0.426$; $p=0.048$).

When multiple regressions were carried out, sex was another variable that was related to treatment results. When adding sex as a variable in the regression analyses, it was still found that individuals with thinner pre-treatment masseter muscles showed greater proclination of mandibular incisors ($r=0.537$; $p=0.039$) and posterior displacement of the cephalometric A point with reference to the vertical reference plane ($r=0.666$; $p=0.004$), while those with thicker pre-treatment masseter muscles showed a more pronounced increase in the posterior facial height ($r=0.580$; $p=0.020$).

Association between pre-treatment molar bite force and treatment results (Paper III) (Tables 2-5)

Table 2: Changes in overjet in relation to age, gender, maximal molar bite force and pre-treatment overjet

Variables	Coefficient beta	Significance
Age (T1)	0.780	0.030
Gender	-0.388	0.392
Maximal molar bite force (T1)	0.005	0.005
Overjet (T1)	-0.419	0.020

b_0 , constant; b_1 , b_2 , and b_3 , regression coefficients; R , correlation coefficient; R^2 , percentage of explained variance.
 $b_0 = -12.774$.
 Significance of the model: $R = 0.84$, $R^2 = 71$ per cent, $P < 0.001$.

Multiple regression analysis: $Y = b_0 + b_1\text{age} + b_2\text{gender} + b_3\text{maximal molar bite force} + b_4\text{overjet}$; dependent variable (Y): change in overjet during treatment (T2-T1); independent variables: age at T1 (y), gender (1 = male and 2 = female), maximal molar bite force at T1 (N), overjet at T1 (mm).

Table 4: Changes in the ANB angle in relation to age, gender, and maximal molar bite force

Variables	Coefficient Beta	Significance
Age (T1)	0.820	0.030
Gender	1.021	0.058
Maximal molar bite force (T1)	0.002	0.042

b_0 , constant; b_1 , b_2 , and b_3 , regression coefficients; R , correlation coefficient; R^2 , percentage of explained variance.
 $b_0 = -13.166$.
 Significance of the model: $R = 0.59$, $R^2 = 35$ per cent, $P = 0.039$.

Multiple regression analysis: $Y = b_0 + b_1\text{age} + b_2\text{gender} + b_3\text{maximal molar bite force}$; dependent variable (Y): change in SNA angle during treatment (T2-T1); independent variables: age at T1 (y), gender (1 = male and 2 = female), maximal molar bite force at T1 (N), overjet at T1 (mm).

Table 3: Changes in molar relationships in relation to age, gender, maximal molar bite force, and pre-treatment molar relationships

Variables	Coefficient Beta	Significance
Age (T1)	9.898	0.118
Gender	-9.245	0.414
Maximal molar bite force (T1)	0.077	0.045
Molar Relationship (T1)	-0.950	<0.001

b_0 , constant; b_1 , b_2 , and b_3 , regression coefficients; R , correlation coefficient; R^2 , percentage of explained variance.
 $b_0 = -113.554$.
 Significance of the model: $R = 0.79$, $R^2 = 62$ per cent, $P = 0.001$.

Multiple regression analysis: $Y = b_0 + b_1\text{age} + b_2\text{gender} + b_3\text{maximal molar bite force} + b_4\text{molar relationship}$; dependent variable (Y): change in molar relationship during treatment (T2-T1); independent variables: age at T1 (y), gender (1 = male and 2 = female), maximal molar bite force at T1 (N), overjet at T1 (mm).

Table 5: Changes in the SNB angle in relation to age, gender, and maximal molar bite force

Variables	Coefficient Beta	Significance
Age (T1)	-0.628	0.074
Gender	-1.045	0.043
Maximal molar bite force (T1)	-0.004	0.041

b_0 , constant; b_1 , b_2 , and b_3 , regression coefficients; R , correlation coefficient; R^2 , percentage of explained variance.
 $b_0 = 10.953$.
 Significance of the model: $R = 0.57$, $R^2 = 33$ per cent, $P = 0.05$.

Multiple regression analysis: $Y = b_0 + b_1\text{age} + b_2\text{gender} + b_3\text{maximal molar bite force}$; dependent variable (Y): change in SNB angle during treatment (T2-T1); independent variables: age at T1 (y), gender (1 = male and 2 = female), maximal molar bite force at T1 (N), overjet at T1 (mm).

Multiple linear regression analyses showed statistically significant correlations for changes in overjet, molar relationships, ANB, and SNB angles. A larger overjet reduction and greater improvement in the molar relationship from Class II to Class I during treatment, as measured on the dental casts, were associated with a lower initial maximal molar bite force. A greater reduction in the ANB angle and a greater augmentation in the SNB angle during treatment were also associated with a lower initial maximal molar bite force.

With respect to the other variables in the multiple regression analyses, a younger age was associated with a larger decrease in overjet and a larger decrease in the ANB angle during treatment, while the male gender was associated with a larger increase in the SNB angle during treatment. Finally,

children with a larger overjet pre-treatment showed a larger decrease in overjet during treatment and similarly children with a more pronounced Class II molar relationship pre-treatment showed a greater change in molar relationship towards a Class I molar relationship during treatment.

As a further analysis, not performed in the published paper pertaining to Class II children treated with activators, pre-treatment maximal molar bite force was looked at in relation to the compensation of incisor inclination (combination of mandibular incisor proclination and maxillary incisor retroclination) during treatment but no association was found. However, an association was found for the pre-treatment gonial angle and the compensation of incisor inclination in that children with more obtuse gonial angles pre-treatment showed more incisor compensation ($r=0.446$; $p=0.037$).

Differences in pre-treatment maximal molar bite force and dentofacial characteristics of stable and unstable groups (Paper IV)

When cases were divided into stable or unstable, referring to their post-treatment dentoalveolar changes, the stable group consisted of 15 patients, while the unstable group consisted of 13 patients. The unstable group revealed a mean increase in overjet of 1.4 mm (± 0.9 mm; min 0.5mm, max 3.0mm), and a worsening of the molar sagittal relationship towards a Class II situation of 18.3% (± 10.4 %; min 12.5%, max 50%). No differences were found between the two groups as regards sex, age, treatment duration, body stature, post-treatment occlusion.

Independent sample *t*-tests revealed that initial maximal molar bite force was statistically significantly different between the two groups. Cases judged as stable showed a higher pre-treatment maximal molar bite force than those judged as unstable (Figure 10). In addition, when looking at the children who had maximal molar bite force values which were higher or lower than one standard deviation from the mean, the three children who were above one standard deviation were all in the stable group of patients whereas from the five children who were below one standard deviation, three were in the unstable group while two were in the stable group.

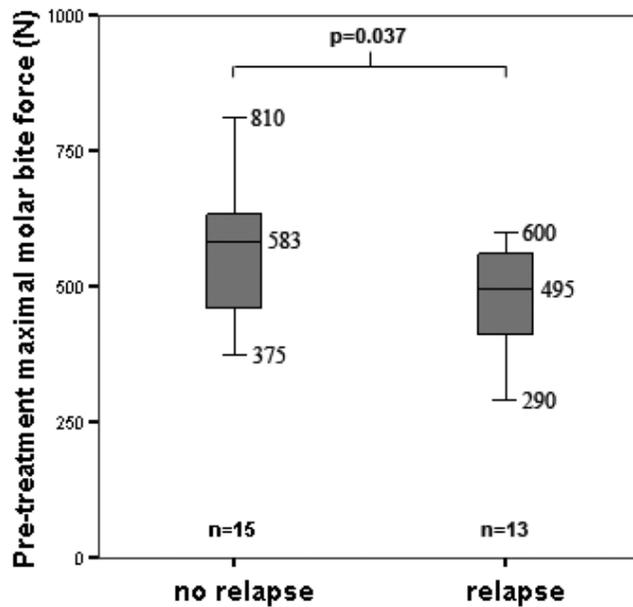


Figure 10: Box plots of pre-treatment maximal molar bite force in the stable (no relapse) and unstable (relapse) groups. The boxes in the box plots display the lower quartile, median, and upper quartile. The whiskers display the smallest observation (minimum) and largest observation (maximum). The sample size in each group is indicated by n. The p-value for the independent sample t-test comparing pre-treatment maximal molar bite force values in the two groups is also shown.

When comparing initial dentoalveolar and cephalometric characteristics, only the gonial angle showed a statistically significant difference ($p=0.035$), where the unstable group presented a larger gonial angle pre-treatment ($125.2^{\circ} \pm 3.9^{\circ}$) than the stable group ($121.8^{\circ} \pm 4.7^{\circ}$). No correlations were found between the initial intermaxillary situation and post-treatment stability or with treatment changes and stability.

GENERAL DISCUSSION

Functional appliances and treatment results

Using meta-analysis methodology, results show that functional appliances (activators and twin-block appliances) improve the sagittal intermaxillary relationship, based on a reduction in the ANB angle. This is mainly by their effect on mandibular position in relation to the anterior cranial base, as seen by an increase in the SNB angle. Twin-block appliances also show a significant effect on the position of the maxilla in relation to the anterior cranial base, namely by a decrease in the SNA angle. In addition, with the use of both activators and twin-block appliances, an important dentoalveolar effect takes place, seen by a decrease in overjet.

The differences which were found for the two groups of functional appliances, namely activators and twin-block appliances could be due, to a large extent, to the amount of hours per day that the patients are instructed to wear their appliances. Normally, patients are instructed to wear activators for approximately 12-14 hours per day, whereas patients are instructed to wear twin-block appliances for up to 24 hours per day (O'Brien *et al.*, 2003b).

Not all individuals respond similarly to functional appliance treatment, and considerable variation is present among children. Given a certain amount of mandibular advancement, the forces applied through the functional appliance by the soft tissues vary greatly (Noro *et al.*, 1994; Katsavrias and Halazonetis, 1999) and it has been speculated that these differences are due to variation in the masticatory muscle induced myotatic reflexes or in the soft tissue viscoelasticity (Kiliaridis, 1998). This is perhaps one of the reasons behind the high heterogeneity observed in the outcomes of functional appliance treatment.

Appliances that have a supposed orthopedic effect may cause changes, but whether these changes are maintained long term and to what extent is a further critical question. Dermaut and Aelbers (1996) concluded that on a long-term basis, the few studies that provide scientific data report that orthopedic changes induced by Class II therapy are only temporary. They further state that this does not, however, hold true for dentoalveolar changes that were generally found to be more stable. Data on long-term changes during functional appliance treatment, coming from investigations using prospective controlled study designs, are lacking. These studies, if undertaken, will allow a meta-analysis to be carried out combining data from different studies in order to reach a consensus conclusion based on a larger patient sample.

Masseter muscle thickness and maximal molar bite force changes during treatment

Treatment of Class II division 1 growing children with functional appliances was found to reduce masseter muscle thickness and maximal molar bite force respectively. This decrease is in contrast to the findings seen in growing patients followed up without treatment, where an increase in masseter muscle thickness and an increase in maximal molar bite force are observed. These findings in untreated individuals are in line with the findings of Raadsheer *et al.* (1996). In their cross-sectional study in growing individuals, an increase in masseter muscle thickness was found with age. The increase in masseter muscle thickness with age seen in growing individuals without treatment is in all probability the result of normal growth and explains the increase in bite force during the growth period (Kiliaridis *et al.*, 1993; Braun *et al.*, 1996). This increase in masseter muscle thickness and maximal molar bite force with age seen in untreated controls may be associated with a general increase in muscle force during this growth period (Asmussen, 1973). Finger force was used in the present investigation as an indicator of general muscular force in the body, and this was found to increase with age.

The decrease in masseter muscle thickness and maximal molar bite force observed during Class II functional appliance treatment, when one would expect an increase in growing children of similar ages, could be due to mild atrophy of the masticatory muscles. This may be attributable to a prolonged decreased functional activity of these muscles, as observed in previous animal experiments and clinical electromyographic studies. Sessle *et al.* (1990) and Yamin-Lacouture *et al.* (1997) in their investigations using chronically implanted electrodes in non-human primates wearing functional appliances inducing progressive mandibular protrusion, report a decrease in postural and swallowing electromyographic activity of the masseter muscle during the first six weeks of functional appliance wear, followed by a gradual return to normal levels during the following six weeks. In growing children, Pancherz and Anehus-Pancherz (1980) and Pancherz and Anehus-Pancherz (1982) measured masseter muscle electromyographic activity during maximal biting and chewing before and upon insertion of the Herbst appliance, as well as three months into treatment, and six months into treatment when the appliance was removed. They detected an initial decrease in activity but this increased again gradually until appliance removal after six months of treatment. Some patients however, continued to show a decreased electromyographic activity even at three months after appliance insertion. Ingervall and Bitsanis (1986) found an initial decrease in electromyographic activity in the masseter muscle during maximal biting and chewing in growing children treated with functional appliances, which continued to remain low for chewing muscle activity throughout the six months of treatment. Our findings may suggest that the prolonged use of functional appliances can lead to a prolonged reduction in muscle activity which may lead to mild atrophy of the masticatory muscles, resulting in a reduction in masseter muscle thickness and maximum molar bite force.

A decrease in masticatory muscle activity, at least during the initial period of functional appliance wear may be due to occlusal instability. A stable occlusion has been shown to be a prerequisite for maximal muscle activity (Ingervall and Egermark-Eriksson, 1979; Ingervall *et al.*, 1979; Bakke and Møller, 1980). During the course of functional appliance treatment occlusal instability may be present which can lead to a decreased activity of the masticatory muscles. Once functional appliance treatment is completed and appliance wear discontinued, occlusal stability is attained which can re-establish a more normal muscular activity.

Apart from occlusal instability, a decrease in masticatory muscle activity may be due to the splint effect, such as that seen in patients wearing occlusal splints which are thought to be muscle relaxation splints. Dahlström and Haraldson (1986) found a decrease in masseter muscle activity during maximal biting upon insertion of a bite plate. Shi and Wang (1991) also found a decrease in the electromyographic activity of the masseter muscle, during maximum clenching, six weeks after splint wear in patients with temporomandibular disorders. Greco *et al.* (1999), using needle electromyography at rest and maximal closure, measured a decrease in masseter muscle activity in patients wearing a Hawley bite plate or a superior repositioning splint after two weeks of wear. The reason for the decrease in muscle activity upon the insertion of a splint or bite plate has been proposed to be that there are less occlusal contacts, and most of these are anterior. This leads to an altered tactile sensation by the periodontal receptors and less proprioceptive input, hence decreased muscle activity (Greco *et al.*, 1999).

Another hypothesis, not able however to entirely explain the reduction in masseter muscle thickness and maximal molar bite force, may be the stretching of the masticatory muscles. In this case, a consequent adaptation of the length of the muscles is expected to take place, as had been shown by Carlson and Schneiderman (1983) in monkeys and Bresin *et al.* (2000) in rats. For this reason, we believe that the initial stretching of the muscle is not a decisive factor since even though in theory the apparent thickness of the muscle can be influenced, this hypothesis does not explain the decrease in maximal molar bite force. Masticatory muscles are thought to adapt to a new functional length with concomitant changes in muscle structure (Lewis *et al.*, 2001).

Concerning the decrease in maximal molar bite force during functional appliance treatment, a further explanation could be given based purely on geometry, namely by the diverging of the force application following mesialisation of the mandibular molars. In other words, if the maxillomandibular hinge is assumed to be at the temporomandibular joint (condyle), then the location where the bite force is measured (at the level of the first molars) is further away from the hinge after treatment due to the mesialisation of mandibular molars and hence the maximal bite force will be smaller. This is related to the concept of mechanical advantage (Charalampidou *et al.*, 2008). This third-order lever effect in which forces decrease in proportion to the distance to the fulcrum (condyle) has also been proposed by

MacDonald and Hannam (1984), and may transmit less proprioceptive input and hence decrease maximal molar bite force. However, masseter muscle thickness remains unchanged as this has no connection with where maximal force measurements are taken in relation to the condyle and so this argument does not hold true for and explain the changes in muscle thickness and hence neither fully for maximal molar bite force.

Maximal molar bite force changes during post-treatment follow-up

Maximal molar bite force in Class II malocclusion children having undergone treatment with a functional appliance was found to increase during post-treatment follow-up. This increase in maximal molar bite force is in all probability the result of normal growth, and may be associated with a general increase in muscle force throughout the body, evaluated in this investigation by measuring finger force. During functional appliance treatment, maximal molar bite force decreases possibly due to mild muscular atrophy because of the prolonged decrease in functional activity of masticatory muscles, related to occlusal instability. This decreased functional activity may show a certain amount of recovery after the interruption of functional appliances, resulting in an increase in the maximal molar bite force post-treatment in these patients. The bite force, in the present investigation, did not seem to exceed pre-treatment levels during the follow-up period, and this could be due to the length of the follow-up implying that had the follow-up been longer, perhaps the bite force would have had more time to catch-up to pre-treatment levels and further go on to exceed them. Another possible reason is the fact that at a higher bite force, pain is more easily experienced (Farella *et al.*, 2010) and thus the children who could have achieved a higher maximal molar bite force did not bite to their maximum effect due to the sensation of pain.

Masticatory muscle characteristics and dentoalveolar and skeletal effects during treatment

The masticatory muscles are thought to play a pivotal role not only in contributing to the aetiology of malocclusions and the application of treatment mechanics, but also on the potential success of treatment outcomes (Hunt, 2010). The initial condition of the masticatory musculature and its functional capacity may influence dentoalveolar and skeletal treatment effects in Class II division 1 malocclusion growing children treated with functional appliances.

Pertinent findings

When looking at masseter muscle thickness in relation to changes during twin-block treatment in growing children, those with thinner pre-treatment muscles showed greater mandibular incisor proclination in relation to the mandibular plane, distalisation of maxillary molars, and posterior

displacement of the cephalometric A point during treatment. When looking at maximal molar bite force in relation to changes during activator treatment in growing children, those with a weaker maximal molar bite force showed a greater change in overjet and molar relationship from Class II to Class I. Those with a weaker maximal molar bite force also showed a greater change in the ANB and SNB angles.

On the other hand, children with thicker pre-treatment muscles seem to develop a greater posterior facial height, condyle-ramus height, and mandibular unit length during treatment. This finding is perhaps attributable to muscular stimulation on the gonial angle of the mandible. In the present study, the gonial angle was found to be negatively correlated to maximal molar bite force. It has been put forward that the size and shape of the gonial process being a site of muscle attachment, is dictated by the relative development and organization of the muscles, as they provide a major mechanical stimulus for bone formation (Atchley and Hall, 1991; Mavropoulos *et al.*, 2004). Our findings show that individuals with a more obtuse gonial angle tend to show greater proclination of mandibular incisors with reference to the mandibular plane during treatment with a twin-block appliance, and greater compensation of incisor inclination (combination of mandibular incisor proclination and maxillary incisor retroclination) during treatment with an activator. This association with the gonial angle and incisor compensation actually demonstrates the relationship between the masticatory muscle capacity and the dentoalveolar response. Individuals with a larger gonial angle suggest that the gonial process has not been subject to large mechanical muscular stimulation because of a weaker masseter muscle and lower contraction forces. The volume of the masseter muscle has been inversely correlated with the gonial angle (Benington *et al.*, 1999), meaning that those with a more obtuse gonial angle have a smaller masseter muscle volume. Likewise, individuals with a lower bite force have been found to have on average a more obtuse gonial angle than individuals with a higher bite force (Ingervall and Helkimo, 1978; Ingervall and Minder, 1997).

When comparing the findings from children treated with a twin-block appliance and those treated with an activator, the differences found concerning the gonial angle and incisor compensation may be due to the differences in the appliance. The twin-block appliance was constructed without the inclusion of a maxillary labial bow and so perhaps the majority of the incisor compensation taking place was related to mandibular incisor proclination. Conversely, with the activator, both mandibular and maxillary incisors were actively engaged in the appliance and so were implicated in the compensation mechanism. In the children treated with activators, considering only the mandibular or maxillary incisors separately failed to display importance, perhaps because the difference by itself was not sufficient, but the combination of the two revealed a statistically significant association.

In a study looking into the predictors of mandibular change induced by functional appliances in Class II patients, it was found that the gonial angle could be used as an indicator which dictates whether a treatment will be favorable (increase in total mandibular length), concluding that patients with an

obtuse gonial angle are expected to respond less favorably (Franchi and Baccetti, 2006). Perhaps in extrapolating their data, one can say that patients showing less mandibular change would be expected to show more dentoalveolar change in order to achieve a Class I molar occlusion post-treatment.

The findings from the two different studies looking at differences in functional appliance treatment effects in relation to the masticatory muscle functional capacity are not identical. The differences as regards the appliance, the patient sample, the method used to measure the masticatory muscle functional capacity, and the experimental design, may be responsible for this. Firstly, the initial characteristics of the two patient samples were different, as was the duration of treatment. Another obvious difference is the daily wear of the appliance which is supposed to be 24 hours when wearing the twin-block appliance but only about half of this (12-14 hours) when wearing activators. The design of the appliance is also different, in that the twin-block appliance is divided into a maxillary and mandibular part allowing more functional movements whereas the activator, despite being divided into two parts is joined together with an elastic bow. The absence of a maxillary labial bow in the twin-block appliance is a further dissimilarity. Masseter muscle thickness measurements in comparison to maximal molar bite force measurements are also a further difference. The former investigates the thickness of a particular muscle and is associated with less measurement error while the second measures the force outcome of muscle activity resulting from all of the jaw elevator muscles and is also associated with a larger measurement error. Finally study design was different in that the children treated with a twin-block appliance all achieved a Class I molar relationship at the end of treatment whereas the children treated with an activator showed an improvement in dental relationships but only thirteen children reached a Class I molar relationship. Children which had a more severe Class II malocclusion before treatment (larger overjet and full Class II molar relationship on both sides) showed a larger change during treatment. Activation was also different in that the twin-block appliances were re-activated by the addition of acrylic after a certain amount of overjet reduction, whereas activation was one-step with the activators.

The findings from the two aforementioned samples were not identical, but can be considered as complementary, both adding to the larger picture. A smaller masticatory muscle functional capacity is thus associated with greater mandibular incisor proclination, distalisation of maxillary molars, posterior displacement of the cephalometric A point, change in overjet and molar relationships, change in ANB and SNB angles, as well as less increase in posterior facial height, condyle-ramus height, and mandibular unit length during treatment. Preliminary results of a prospective longitudinal study looking into both masseter muscle thickness and maximal molar bite force in relation to Class II functional appliance treatment, show comparable findings.

Mandibular incisor proclination and shifting of the occlusion

Functional appliances have been criticized for their tendency to procline mandibular incisors and retrocline maxillary incisors (Björk, 1951; Trayfoot and Richardson, 1968; Vargervik and Harvold, 1985; Macey-Dare and Nixon, 1999). An increase in mandibular incisor proclination translates to the mesialisation of the whole mandibular dental arch, while maxillary incisor retroclination translates to the distalisation of the entire maxillary arch. A larger dentoalveolar movement may imply a smaller skeletal effect in achieving Class I dental relationships. O'Brien *et al.* (2003b), in a multicenter randomized controlled trial, found the average percentage of skeletal change contributing to the reduction in overjet to be 27%, with variation between individuals, the remaining amount being dentoalveolar. They further go on to reason that this variation in apparent skeletal change may be because of other factors, probably reflecting individual growth variation as opposed to growth modification because of appliance wear. Previous studies using the twin-block appliance display a large variation in mandibular incisor proclination among the treated subjects. Mills and McCulloch (1998) detected a $5.2^\circ (\pm 3.9^\circ)$ proclination of mandibular incisors, while Lund and Sandler (1998) found an $8.2^\circ (\pm 7.1^\circ)$ proclination following twin-block treatment in Class II growing individuals. Variation of the proclination of mandibular incisors has previously been proposed to be attributable to many factors, such as the construction bite, the initial overjet, and the thickness of the mandibular symphysis (Aki *et al.*, 1994). The results of the present investigation suggest that part of the variation may also be able to be explained by the functional capacity of masticatory muscles.

Thin pre-treatment masseter muscles were observed to be correlated with a greater proclination of mandibular incisors, in relation to the mandibular plane, during twin-block treatment. Masseter muscles are in the group of jaw elevator muscles, which would consequently not be directly involved in the sagittal muscle tension evident when the mandible is protruded forward with the use of functional appliances. Masseter muscles are therefore more important as regards vertical forces. It can be hypothesized that children with thinner masseter muscles will probably generate less vertical intermaxillary forces, and as a consequence when shifting the occlusion from Class II to Class I, resistance to dentoalveolar effects will be less. Thicker masticatory muscles may increase the anchorage of the mandibular dentition because of the exertion of larger masticatory vertical forces. Forces created from occlusal contact, even though very large, are of a very short duration. In healthy patients without parafunctions, the teeth come into occlusion during mastication and swallowing, which only make up a total duration of tooth contacts of a few minutes per day; Sheppard and Markus (1962) for example found a total of 11.7 minutes. Despite their short duration, vertical occlusal forces seem to be important as regards the shifting of the occlusion. This raises some questions concerning the equilibrium theory with respect to forces in a vertical direction. A similar explanation, namely that of less resistance to shifting of the occlusion, can be given for the position of the first maxillary molar and point A with

respect to the vertical reference plane. The headgear-like effect of functional appliances (Jakobsson, 1967; Pancherz, 1984; Vargervik and Harvold, 1985; Jakobsson and Paulin, 1990) on the maxillary molars and the maxillary skeleton was more visible in individuals with thinner muscles, while those with thicker muscles show a larger resistance to this effect. No relationship was found between masseter muscle thickness and maxillary incisor retroclination perhaps due to the fact that the maxillary incisors were not engaged in the twin-block appliance. In the children treated with activators, no relationship were detected between maximal molar bite force and changes in mandibular and/or maxillary incisor inclination, and this could possibly be due to the large error of the method associated with bite force measurements. However when both maxillary and mandibular dental compensation was taken into account by adding the proclination of mandibular and retroclination of maxillary incisors, then a correlation was found in relation to the masticatory muscle capacity, as indirectly observed by the gonial angle. Those with a more obtuse gonial angle showed a larger amount of incisor compensation.

Children with a lower pre-treatment maximal molar bite force were however more likely to attain a larger overjet reduction and improvement in the molar relationship from Class II to Class I during activator treatment, even when factors such as gender and age were taken into consideration. The treatment effects on the intermaxillary dentoalveolar relationships (overjet and molar Class) are more apparent in individuals with a weaker maximal bite force, while those with a stronger maximal bite force show a larger resistance to this effect. If one can relate maximal molar bite force to masticatory muscle thickness, thick muscles may increase the anchorage of the mandibular dentition due to the exertion of larger masticatory forces. The headgear-like effect of functional appliances may also be responsible for some of the intermaxillary changes, which may be more pronounced in those with a weaker maximal molar bite force, perhaps suggesting that it is easier to 'jump' the occlusion in those with a weaker maximal molar bite force.

The effects of functional appliances on mandibular position in relation to the anterior cranial base (namely the increase in the SNB angle) as well as the intermaxillary relationships (reduction in the ANB angle) are more apparent in individuals with a weaker maximal molar bite force, while those with a stronger maximal molar bite force show a larger resistance to this effect. The explanation for this could be similar to that mentioned previously, namely that thicker muscles, and hence a stronger maximal molar bite force, make it more difficult to jump the bite and thus less changes are seen in the ANB and SNB angles during treatment with functional appliances.

Another factor related to masticatory muscle characteristics and perhaps to treatment effects may be the quality of the mandibular alveolar bone. The mandibular trabecular bone is subject to physiological remodeling throughout life, and can be influenced by masticatory demands (White, 2002). Jonasson and Kiliaridis (2004) have found that masseter muscle thickness is a significant determinant of mandibular alveolar bone mass. In rats, lower bone density has been associated with faster orthodontic

tooth movement than in those with significantly higher bone density (Bridges *et al.*, 1988). If one assumes that children with lower bite forces or thinner masseter muscles exhibit lower bone density, then that is perhaps another reason as to why more dentoalveolar changes are present during functional appliance treatment in those with weaker or thinner muscles.

Masticatory functional capacity and post-treatment stability

In the present investigation, post-treatment response in Class II division 1 malocclusion growing patients treated with functional appliances varied. Some children showed relapse, while others showed a more stable post-treatment result. Bite force may be associated with the sagittal stability of functional appliance treatment, whereby children with a lower pre-treatment maximal molar bite force may be more prone to sagittal dentoalveolar relapse, namely an increase in overjet and a shift of the molar relationship towards a Class II relationship.

Additionally, the children who had maximal molar bite force values which were above one standard deviation from the mean were all considered to be stable, while those who had maximal molar bite force values which were below one standard deviation from the mean were either stable or unstable. Individuals with strong masticatory muscles have been found to have a more homogeneous facial morphology than those with weak masticatory muscles (Ingervall and Helkimo, 1978). This, in combination with the present results, may imply that individuals with stronger masticatory muscles can be expected to show more stable results while individuals with weaker masticatory muscles may show more heterogeneous results as regards stability.

As was the case during treatment where the exertion of weaker masticatory forces was proposed to decrease the anchorage of the mandibular dentition, suggesting that it is easier to 'jump' the occlusion in those with a weaker bite force, the same may apply to stability. Weaker masticatory forces were associated with a less stable dentoalveolar sagittal result. The reason for this difference may be that in those with a weaker bite force, the occlusion jumps back towards a more Class II relationship easier. This may be explained by the eruption pattern of teeth following different jaw rotations, namely that those with a forward rotation of the jaws show a resulting forward eruption path of the molars and a forward shift of the lower dental arch, as opposed to a more vertical or backward eruption path in those exhibiting a backward rotation (Björk and Skieller, 1972). Hence, children with a stronger maximal molar bite force may show more anterior rotation and forward eruption of the lower molars and hence a better chance for dentoalveolar stability and conservation of the molar relationships. Pancherz (1977) found that Class II patients who relapse following functional appliance treatment had more posterior jaw rotation than those who were stable, showing more anterior jaw rotation. Bone density may also be important, as mentioned in relation to the functional appliance treatment effects. Assuming that

children with lower bite forces have lower bone density, then these children would be more prone to greater tooth movements and hence dentoalveolar changes leading to relapse during the post-treatment follow-up period.

It is also interesting to note that the group of patients who showed a more unstable result post-treatment tended to have not only a weaker bite force pre-treatment, but also a more obtuse gonial angle pre-treatment. This finding can perhaps be explained, similarly to the findings where a more obtuse gonial angle is associated with greater changes in incisor proclination during treatment, by the muscular stimulation on the gonial angle of the mandible, this being a site of muscle attachment. In patients with a more obtuse gonial angle, the gonial process may not been subject to as much mechanical muscular stimulation due to lower contraction forces, and thus less anchorage of the mandibular dentition is present, allowing easier shifting and relapse of the occlusion.

Our findings are in line with the results of Pancherz & Anehus (1978) who took temporal and masseter electromyographic recordings during chewing at the time of the follow-up examination, on patients who had been treated with activators ten to twenty years previously. They found that the electromyographic activity seemed to be less on average in patients who showed relapse than in those where the treatment was considered stable.

A certain number of patients relapsed during the follow-up period after functional appliance treatment, which would be expected in any patient sample. Relapse is frequently seen in patients following active orthodontic treatment. All occlusal traits change gradually over time (Al Yami *et al.*, 1999). Changes obtained during the active treatment period of a successful functional appliance therapy tend to relapse toward the initial malocclusion in the post-treatment years (DeVincenzo, 1991). It is not possible however, to identify if post-treatment changes are the result of pure relapse following orthodontic treatment alone, or the result of physiological changes in the dentition and surrounding tissues that normally take place whether or not treatment has been carried out (Bondemark *et al.*, 2007). Mandibular growth seems to be important both during and after active treatment. It has thus been proposed that significant long-term changes in the occlusal relationships can be achieved with functional appliance therapy only when the functional treatment includes the growth spurt (Faltin *et al.*, 2003). Other authors suggest that stability is dependent on the age when treatment was carried out, by arguing that if Class II treatment is delayed, the treatment results, namely with the Herbst appliance, tend to be more stable (Pancherz, 1997). In the present patient sample, by looking at height changes and dental stage, we did not find that growth stage influenced stability. This may have been due to the small sample size, the relatively small age range of the patients, or the short follow-up period.

Besides growth, variation in post-treatment stability following Class II malocclusion treatment may depend on several factors, such as malocclusion severity, intercuspidation, molar change and overjet reduction. Pancherz and Hansen (1986) noticed that a greater molar change during treatment is

more prone to relapse. Correspondingly, Drage and Hunt (1990) found a small correlation between the amount of overjet corrected during functional appliance therapy and relapse. Janson *et al.* (2004), on the other hand, found that initial Class II malocclusion severity and initial molar relationship did not present any correlation with relapse of molar relationship and overjet. They observed, however, that if there was a greater molar change during treatment, this was less stable. In the present study, no such correlations were found between the initial intermaxillary situation and post-treatment stability or with treatment changes and stability. This may have been due again to the small size of the patient sample investigated, or the short length of the post-treatment follow-up period.

It has been suggested that good clinical intercuspidation is necessary to prevent skeletal and dentoalveolar relapse (Pancherz, 1991; Wieslander, 1993; Nanda *et al.*, 1993). This, however, was not found in the present study when comparing relapse in patients who finished treatment in a Class I versus a 25%-50% Class II molar relationship. This is in accordance with Fidler *et al.* (1995) who evaluated patients with successful occlusal results (good intercuspidation and incisor occlusion) and found that despite this, there were significant changes seen post-treatment. Ferguson (2010) emphasizes that post-treatment ideal sagittal molar intercuspidation does not guarantee post-treatment stability.

Clinical significance of the findings

Masseter muscle thickness and maximal molar bite force are perhaps capable of suggesting what the outcomes and relapse potential of functional appliance treatment may be. Because of the fact that orthodontists treating patients with functional appliances usually do not have access to an ultrasound machine to measure masseter muscle thickness or to a bite force gauge in order to measure maximal molar bite force, a clinical recommendation can be made according to the finding concerning the gonial angle in relation to incisor compensation, as well as to stability. The gonial angle, serving as a site of attachment of the masseter muscle, and hence the mandibular morphology, provides a good indication as to the cross-sectional thickness and the force of the masseter muscle. Firstly, this angle can be measured cephalometrically and used as an indication of expected incisor compensation. In other words, patients presenting with an obtuse gonial angle may prepare the treating orthodontist to anticipate a greater degree of incisor compensation during functional appliance treatment, than patients presenting with a more acute gonial angle. Moreover, the gonial angle can also be used as an indication of expected stability, preparing the treating orthodontist to expect a larger probability for post-treatment relapse following functional appliance treatment in children with a more obtuse gonial angle.

CONCLUSIONS

Functional appliances used in the treatment of Class II division 1 malocclusion growing children may bring about an improvement of the sagittal intermaxillary relationship and decrease in overjet, mainly by acting on the mandibular position in relation to the anterior cranial base. Some appliances, namely twin-block appliances, also seem to act on the maxillary position in relation to the anterior cranial base. During and following this treatment, an adaptation of the masticatory muscles is observed. During treatment, a decrease in masseter muscle thickness and in maximal molar bite force is found, possibly indicating mild atrophy of the masticatory muscles due to their decreased functional activity. After the functional appliances are discontinued, a certain amount of muscle recovery occurs, seen by an increase in maximal molar bite force.

The initial condition of the masticatory muscles, represented by masseter muscle thickness or by maximal molar bite force, may be one of the factors that influence treatment and post-treatment outcomes. Children with thinner pre-treatment masseter muscles treated with twin-block appliances, show a greater proclination of mandibular incisors, distalisation of maxillary molars and posterior displacement of the cephalometric A point during treatment, as well as a less pronounced increase in posterior facial height, condyle-ramus height, and mandibular unit length. Likewise, children with weaker maximal molar bite force pre-treatment, treated with activators, show greater improvement in dentoalveolar sagittal relationships, as well as greater changes in the SNB and ANB angles. Following activator treatment, children who show dentoalveolar sagittal relapse are more likely to have a lower maximal molar bite force pre-treatment. Children with an obtuse gonial angle are also more likely to show greater incisor compensation during treatment, as well as a greater risk of relapse during post-treatment follow-up.

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