

Orofacial dysfunctions in children and
adolescents with myotonic dystrophy type
- evaluation and intervention

by

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To the memory of my brother Janne

ABSTRACT

Myotonic dystrophy type 1 (DM1) is a slowly progressive neuromuscular disease. The overall aim of this thesis was primarily to describe the characteristics, prevalence, and development of orofacial functions in a group of children and adolescents with DM1 and secondly to investigate the effect of lip strengthening exercises.

In total, the study population consisted of 66 individuals with DM1, five with Möbius syndrome, six with facioscapulohumeral muscular dystrophy and 106 healthy controls. Fifty-six of the patients (30 males, 26 females; median age 13 years [2–21 years]) with DM1 and 56 of the healthy age and gender matched controls were enrolled in Study I. Thirty-five patients and 31 controls were assessed twice with approximately 3–4-year intervals (Study II). Facial expression, intelligibility, oral motor performance, and lip force, were assessed by a speech-language pathologist and the families answered questions about eating and saliva control in a questionnaire. Eight individuals (7–17 years) from the same study group participated in an intervention study (Study IV). After baseline measurements, four participants began 16 weeks of treatment while the others acted as controls. Thereafter, those who had started as controls began treatment and the other had no training. Lip exercises were carried out five days a week. Follow-ups were conducted every fourth week. Assessments were performed with both quantitative and qualitative methods. These methods were developed and validated in a previous methodology study. Lip mobility was measured with 3D video analysis and lip strength with a lip force meter. Fifty healthy adults and 23 adults with diagnoses affecting the facial muscles participated in the methodology study (Study III).

All patients with DM1 had impaired facial expression. Intelligibility was considerably reduced in 30 patients (60 %), excluding 6 patients without speech. The majority had moderate or severe impairment of lip motility (76 %), tongue motility (52 %), and lip force (69 %). Deviant production of bilabial and dental consonants was common. Families reported problems with drooling (37 %) and eating (52 %). Oral motor dysfunction was most prominent in congenital DM1, and males were more affected than females. Intelligibility, eating and drinking ability, and saliva control improved during childhood in some patients. Facial expression deteriorated significantly, especially in patients with childhood DM1, but the progressive weakening of the orofacial muscles also manifested as reduced intelligibility and increased drooling. The measuring instruments were found to be reliable as well as clinically relevant and could therefore be used for evaluation of treatment as a complement to qualitative assessments. Seven of

eight participants in the intervention study improved lip strength but not lip function.

Orofacial dysfunctions such as impaired facial expression, speech, eating and drooling are common in children and adolescents with DM1. Both improved and deteriorated orofacial functions could be seen in this group of patients at follow-up. The progression of muscle weakness in DM1 is clearly expressed in the deterioration of facial expression. Children and adolescents with DM1 can improve lip strength. However, improved lip strength will not automatically lead to improved lip function.

Key words: myotonic dystrophy type 1, children, facial expression, dysarthria, dysphagia, drooling, lip force, lip mobility, 3D motion analysis, oral screen.

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LIST OF PUBLICATIONS

This thesis is based on the following publications, referred to in the text by their Roman numerals:

- I Sjögreen L, Engvall M, Ekström AB, Lohmander A, Kiliaridis S, Tulinius M. Orofacial Dysfunction in Children and Adolescents with Myotonic Dystrophy. *Developmental Medicine and Child Neurology*. 2007 Jan; 49(1):18-22.
- II Sjögreen L, Engvall M, Kiliaridis S, Tulinius M, Lohmander A. Development of Orofacial Functions in Young Individuals with Myotonic Dystrophy: a Retrospective Study. *Journal of Medical Speech Language Pathology*. 2008;18: 33–41.
- III Sjögreen L, Lohmander A, Kiliaridis S. Exploration of quantitative methods for evaluation of lip function (submitted).
- IV Sjögreen L, Tulinius M, Kiliaridis S, Lohmander A. The effect of lip strengthening exercises in children and adolescents with myotonic dystrophy type 1 (submitted).

INTRODUCTION AND BACKGROUND

Impaired muscle strength and muscle function can cause dysfunction such as sucking and feeding difficulties, impaired facial expression, dysarthria, dysphagia, and drooling if the orofacial muscles are involved. Orofacial dysfunction is common in patients with neurological impairments, neuromuscular diseases and genetic syndromes, and often has a great impact on quality of life for the individual *as well as* the whole family. Oral motor impairment in children interferes with the development of speech and feeding. Myotonic dystrophy type 1 (DM1) is a neuromuscular disease with weak and hypotonic orofacial muscles as characteristic symptoms. Despite this, information in the literature on orofacial dysfunction in children and adolescents with DM1 is rare, and no published study has investigated this area in depth.

Myotonic dystrophy type 1

DM1 is caused by an expansion of a CTG-repeat sequence (trinucleotide expansion) on chromosome 19q13. The number of CTG repeats broadly correlates with the overall severity of the disease (Marchini et al., 2000). The inheritance pattern is autosomal dominant. Disease onset typically occurs earlier in the child than the parent, a phenomenon called “anticipation”. In general, the earlier the symptoms occur, the more severe the clinical symptoms of the disease will be. DM1 can be divided into four subtypes according to age at onset (Koch et al., 1991):

- Mild DM1 – onset occurs in late adulthood.
- Classical or adult DM1 – onset occurs during adolescence or early adulthood.
- Childhood DM1 – development in the first year of life is normal; symptoms begin appearing by age 10.
- Congenital DM1 – symptoms are present from birth.

As in other countries, the prevalence of DM1 in Sweden varies between geographic areas. In Sweden, the prevalence of congenital myotonic dystrophy is estimated to be 1:20,000 inhabitants (Darin & Tulinius, 2000). DM1 is a neuromuscular disease with muscle weakness and myotonia (delayed muscle relaxation) as cardinal symptoms. Muscles in the face, jaw, neck, hands, and feet are generally most affected. Muscle fibres are reduced in number and size, and the immaturity of the muscle fibres in congenital DM1 suggests a failure in

muscle development rather than active muscle degeneration (Farkas-Bargeton et al., 1988). Muscle weakness is slowly progressive (Harper, 2004). Respiratory insufficiency and sucking difficulties are common in newborns with DM1 due to severe hypotonia (De Die-Smulders, 2004; Hageman, Gabreels et al. 1993; Harper, 2004). Muscle tone and muscle strength improve during the first years of life (De Die-Smulders, 2004; Roig et al., 1994). It is still unclear at what age improvement in muscle strength turns to deterioration in children with congenital DM1, but around puberty has been suggested (Hageman et al., 1993). Clinical symptoms of myotonia in the hands, jaws, and tongue become successively more common as the children grow older (Kroksmark et al., 2005). Although orofacial muscles are generally severely affected in congenital and childhood DM1, research concerning consequences for sucking, chewing and swallowing, and speech development is limited, with no published study describing the developmental changes of orofacial functions.

DM1 is a multisystemic disease, and skeletal muscle is only one of the systems it affects. Other systems commonly affected are the heart, smooth muscle, brain, peripheral nerves, endocrine regulation, and skin. Children with congenital DM1 have a developmental delay, which is also true for many children with the childhood-onset type (De Die-Smulders, 2004; Hageman et al., 1993; Steyaert et al., 2000; Steyaert et al., 1997). Most individuals with congenital or childhood DM1 have learning disabilities of varying degree and the prevalence of neuropsychiatric disorders is higher in these patients than in the general population (Ekström et al., 2008; Goossens et al., 2000; Steyaert et al., 1997). Cognitive deficits also occur in classical DM1 (Winblad, et al., 2005). Another sign of central nervous system involvement is excessive tiredness (Hilton-Jones, 2004).

Multidisciplinary survey

In 1999–2001, all children and adolescents (n=50) with a confirmed diagnosis of DM1 living in western and southern Sweden (3 million inhabitants) were invited by their paediatric neurologist to participate in a multidisciplinary study; 42 (84 %) accepted. A paediatric neurologist and a physiotherapist met the patients, made a clinical medical examination, took the medical history, and reviewed the records. The patients were then divided into four subgroups by the paediatric neurologist: severe congenital DM1, mild congenital DM1, childhood DM1, and classical DM1. A patient with congenital DM1 was classified as having the severe or mild form depending on whether or not they had had a life-threatening condition at birth (Kroksmark et al., 2005). The diagnostic criteria for childhood DM1 were symptoms appearing between 1 and 10 years of age and an uneventful prenatal and postnatal history. In classical DM1, the symptoms occurred at 10 years of age or later (Koch et al., 1991).

The physiotherapist investigated skeletal deformities and assessed motor function and muscle strength (Kroksmark et al., 2005). A geneticist made a genetic analysis of blood samples. A paediatric dentist together with a speech-language pathologist assessed odontological aspects, orofacial functions, and oral motor behaviour (Engvall et al., 2007; Sjögreen et al., 2007). An orthodontist was consulted for the morphologic analysis.

Four years later (2003) the same patients were invited to participate in a follow-up. This time the multidisciplinary team was expanded to include an ophthalmologist, a psychologist, and a neuropsychiatrist (Ekström et al., 2008; Ekström et al., 2009; Engvall et al., 2009; Sjögreen et al., 2008). Seventeen new patients were enrolled in the study. Three of them had been identified at the first assessment but did not participate and the others were either newly diagnosed with DM1 or had moved into the area. One patient from the first assessment had moved away from the area. Thus, in 2003 there were 63 known children and adolescents with DM1 in western and southern Sweden and 58 (92 %) agreed to take part in the multidisciplinary survey.

Characteristic orofacial features

Impaired facial expression due to weak and hypotonic facial muscles is a characteristic feature of DM1 and is often combined with a special mouth shape, sometimes called tented lips (Figure 1) (Hageman et al., 1993; Harper, 2004). The mouth is typically triangular shaped (like a tent), with the upper lip retracted and the lower lip rotated outward, and often held open. Studies have shown that craniofacial development of many individuals with DM1 is characteristic with a more vertical cranial growth, narrower maxillary arches, and deeper palatal depth than healthy controls and that malocclusion, especially frontal open bite and cross bite, is common (Kiliaridis et al., 1989; Staley et al., 1992).



Figure 1. The mouth of a child with DM1

Feeding problems

Children with congenital DM1 generally have profound sucking problems as newborns due to neonatal hypotonia. Many infants need life-sustaining interventions in the neonatal period such as assisted respiration and tube feeding (Kroksmark et al., 2005). Excessive amniotic fluid (polyhydramnios) during pregnancy caused by poor foetal swallowing is often noted (De Die-Smulders, 2004; Hageman et al., 1993; Harper, 2004; Kroksmark et al., 2005). Delayed stomach emptying can be a major contributor to feeding difficulties in infants with DM1 (Bodensteiner & Grunow, 1984; Horowitz et al., 1987).

Dysphagia

The oral phase of swallowing could be affected by impaired lip, tongue, masticatory muscles and malocclusion. Bolus control, chewing efficiency and ability to bite off may also be impaired. The pharyngeal and oesophageal phases of swallowing have been studied with videofluoroscopy and manometry and in electrophysiological examinations of adult patients with DM (DM is used when DM type, 1 or 2, was not specified in the referred studies) (Bosma & Brodie, 1969; Costantini et al., 1996; Ertekin et al., 2001; Hillarp et al., 1994; Marcon et al., 1998; Mari et al., 1997). Abnormalities consistent with DM were nasal reflux caused by velopharyngeal insufficiency, diminished pharyngeal contraction, and poor or absent peristaltic activity in striated *and* smooth oesophageal muscles. According to Hillarp et al. (1994) and Marcon et al. (1998), symptoms were often subclinical. Gastroesophageal reflux and gastrointestinal dysfunction are common in children and adults with DM1 (Costantini et al., 1996; Horowitz et al., 1987).

Dysarthria

Speech characteristics of children and adolescents with DM1 have not been described in detail in the literature, but some studies include adult patients with DM. Adults often develop flaccid dysarthria with indistinct articulation and hypernasal speech due to weak and hypotonic orofacial muscles. Myotonia of the tongue may also contribute to speech impairment (Holmberg et al., 1996; Maassen et al., 1995; Salomonson et al., 1988; Weinberg et al., 1968). A case report of a 27-year-old man with DM was one of the first descriptions in the literature of some of the speech and swallowing abnormalities associated with the disease (Weinberg et al., 1968). The abnormalities listed were a “myopathic” facial appearance, deviant smile, speech impairment, inadequate oral diadochokinetic performance, compensatory motions during speech, abnormal swallowing motions and atypical resting postures. Speech impairment was characterised by hypernasality, reduced speaking rate, and articulatory deterioration. According to Salomonson et al. (1988) and Hillarp et al. (1994), hypernasality due to velopharyngeal impairment could be the first sign of DM. Maassen et al. (1995) made a quantitative assessment of speech in 15 mildly affected patients

with an adult-onset form of DM and 15 controls who were matched with according to age, gender, educational level and with a history free of speech or hearing related problems. The mean age of the patients was 36 years with normal hearing and no intellectual impairment or known neuropsychological dysfunction. Spontaneous speech was assessed by a speech pathologist and found to be normal in ten patients with slight signs of imprecise articulation in five. All patients were perfectly intelligible. The overall performance of patients with DM1 was poorer concerning duration and rate of consonant articulation. These findings were interpreted as an effect of myotonia. Holmberg et al. (1996) studied the prevalence of dysarthria in 23 adult patients with DM with a mean age of 40 years. Nine were assessed to have dysarthria of varying degrees, of which all had a hypernasal resonatory problem and six had articulatory difficulties. The authors noted a relation between degree of motor disability and dysarthria. They concluded that neither patient age nor disease duration seemed to be reliable predictors of dysarthria and suggested that there are different types of DM: with dysarthria and without dysarthria.

Lip strengthening exercises in DM1

Although muscle weakness and wasting is the primary cause behind dysphagia, dysarthria and drooling in many patients with DM1, there is little evidence for or against the effect of oral motor strengthening exercises in this group of patients. Moderate-intensity strength training can be recommended in DM1 without an increased risk of damage to the muscles but it remains to be shown if the training can improve strength and motor function (Bar-Or, 1996; Cup et al., 2007; van der Kooi et al., 2005; Voet et al., 2010).

There are some fundamental questions concerning lip strength and lip function in DM1 that still need to be elucidated. Can lip exercises increase lip strength in individuals with DM1? Can increased lip strength improve functions such as sucking, chewing, swallowing, speech, facial expression and saliva control? Can improvements in lip strength postpone the progression of these dysfunctions? These are basic questions in an area that needs more attention concerning both therapy methods and research, which with a greater knowledge of motor learning, motor function and motor strength should eventually provide the clinicians with improved tools and techniques for effective treatment (Clark, 2008).

No intervention studies investigating the effect of lip strengthening exercises in individuals with DM1 have been found in the literature and it was therefore assumed that this type of research is very rare or absent.

Methods for assessment of orofacial functions

Qualitative assessments

Speech assessment

Speech production can be assessed on the basis of spontaneous speech or by the repetition, naming, or reading of single words or sentences (Kent et al., 1994). Evaluations of speech are based on perceptual or acoustic analysis (Weismer et al., 2001). Overall intelligibility can be investigated and each subsystem of speech production – respiration, phonation, resonance, and articulation – assessed (Kent et al., 1994; Love, 2000). In a textbook (Love, 2000), Love recommends speech intelligibility as an excellent measure to rate change in speech, as it encompasses all aspects of speech and is easily understood by both expert and lay person alike. Intelligibility of spontaneous speech can be evaluated on a rating scale, and when intelligibility of single words or sentences is tested, the number or percentage of intelligible words is calculated (Kent et al., 1994; Kent et al., 1989; Love, 2000; Whitehill, 2002; Yorkston & Beukelman, 1980). Measurements of intelligibility give valuable information about oral communication competence and are therefore recommended in research and clinical work (Kent et al., 1994). The reliability of the assessment should be determined (Kent et al., 1994; Whitehill, 2002). Kent et al., (1994) confirm that intelligibility measurements are adequate for single-observation assessment of oral competence in children, but there is no consensus among clinicians and researchers as to how intelligibility should be measured and assessed. One reason for this could be that the intelligibility assessment procedure is dependent on its purpose (Kent et al., 1994).

An articulation test could be used in order to study how a certain oral sensorimotor or structural deficit affects the ability to produce speech and speech sounds, for instance when investigating how velopharyngeal impairment or weak lips influence speech. In Sweden, an articulation and nasality test named SVANTE (Lohmander et al., 2005) is used for this purpose.

Oral motor assessment

Different aspects of oral motor function should be addressed in an oral motor assessment and certain muscle groups examined (Bakke et al., 2007; Kenny et al., 1989). The muscle groups included are the mimic muscles, the tongue, the jaw muscles, and the velopharyngeal muscles. Observed dysfunctions should also be noted such as drooling, dry mouth, oral habits, tooth grinding (daytime), pathological reflexes, affected voice or breathing, mouth breathing and involuntary movements (Figure 2).

Oral motor assessment

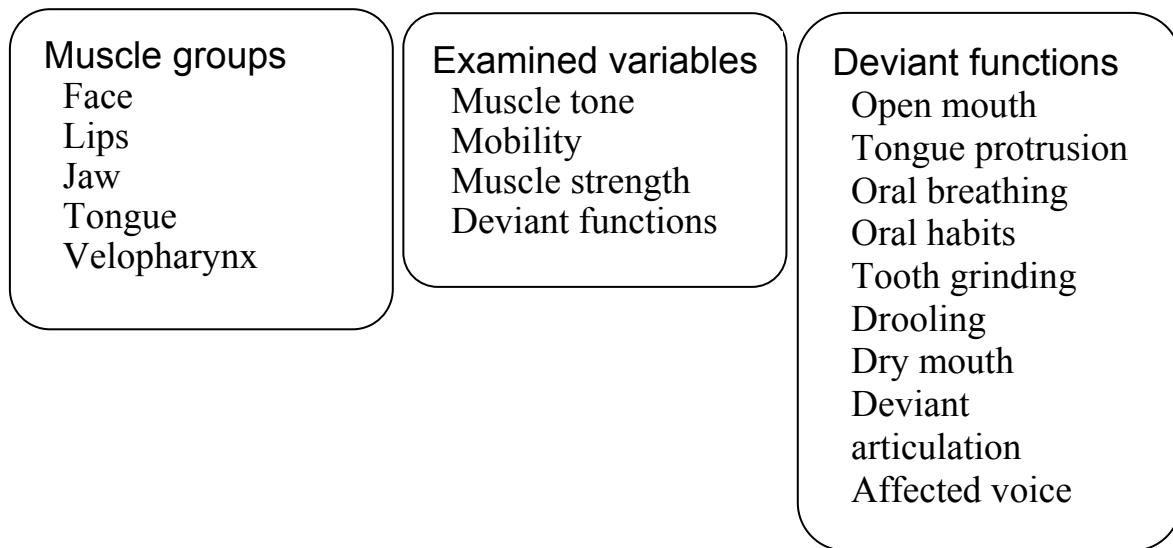


Figure 2. Muscle groups, variables, and deviant functions that are investigated in an oral motor examination (Bakke et al., 2007; Kenny et al., 1989)

Observing the patient at rest gives the opportunity to evaluate muscle tone and rest position of the orofacial muscles and also the body posture and head position. A common way to arrange a rest position is to show the patient a picture to look at for a short while. The strength of the orofacial muscles can be assessed perceptually by having the patient activate the muscles against resistance provided by the examiner. In order to assess the range of movement of the orofacial muscles the patient is asked to perform maximal contractions. Simple and complex diadochokinetic tasks are often used to investigate other aspects of mobility such as coordination, dissociation and timing (Ackermann et al., 1995; Kenny et al., 1989).

If the patient is unable to imitate or perform voluntary activities on command due to their young age, learning disability or neuropsychiatric disorder the oral motor assessment is built on observation. This could be done in a standardised way if certain foods and food equipments are used as in SOMA (Schedule for Oral Motor Assessment) (Reilly et al., 1995; Skuse et al., 1995).

Evans-Morris and Dunn-Klein (2000) have described the typical oral motor development of healthy children. Norms for certain age groups are often suggested for the specific tasks included in standardised protocols for oral motor assessment.

ORIS – a protocol for oral motor assessment (Holmberg & Bergström, 1996) – was published in 1996 and has since been used by many speech-language pathologists in Sweden as their clinical tool for evaluating oral motor performance. The test procedure is standardised, and the test variables are defined. Norms for children age 3–6 years are given. The validity and reliability of ORIS are however unknown.

Self-reports on eating and drinking ability and saliva control

Parental observations and self-reports concerning daily activities such as eating and drinking and saliva control contribute important information to the overall picture of orofacial function and are generally collected through structured interviews and questionnaires. If defined rating scales or visual analogue scales (VAS) are included in the questionnaire, the possibility to compare results within and between patients is facilitated. The defined scales for rating the frequency and severity of drooling recommended by the Consortium on Drooling (Scully et al., 2009) have been adapted by many clinicians and researchers.

Quantitative assessments

Numerous technical solutions have been developed to measure the strength of orofacial muscles, and some are available on the market. Bite force has been measured using surface electromyography (EMG), acoustic myography (AMG), an occlusal force gauge, and an electronic dynamometer (Guimaraes et al., 2007; Ortug, 2002; Tortopidis et al., 1998). There are also instruments for measuring maximal force and endurance in tongue (Lazarus et al., 2000) and lips (Barlow & Abbs, 1983; Chu et al., 2010; Hägg et al., 2008; Ingervall & Eliasson, 1982; Jung et al., 2003; Thiele, 1996; Trotman et al., 2007; Williams et al., 1988).

Different interactive systems for video-computer analyses of facial expressions have been developed during the last 20 years. The most recent systems generally present a 3D analysis which has proven to be the most accurate way to present facial mobility. Tongue mobility can be registered using ultrasonography (Bressmann et al., 2005) or electropalatography (Gibbon et al., 2007; Hardcastle, 1972; Murdoch et al., 2004).

Reliability of study results

Grading scales are often used for rating the severity of oral motor dysfunction. However, insufficient reliability of subjective grading scales is a recognised problem. Many clinicians and researchers working in the field of oral motor assessment and mimic muscle evaluation have underlined the need for objective, reliable and sensitive outcome measures as a supplement to more subjective assessments (Chee & Nedzelski, 2000; Felicio & Ferreira, 2008; Linstrom et al.,

2002). The reliability of the results from any studies needs to be estimated, either by estimating inter- or intra-examiner agreement or the error of methods. To use control groups and reference groups are additional ways to ensure the reliability and validity of the study results.

AIMS

The overall aim of this thesis was primarily to describe the characteristics, prevalence, and development of orofacial functions in a group of children and adolescents with DM1 and secondly to investigate the effect of lip strengthening exercises.

Specific aims

- To describe the characteristics and prevalence of oral motor dysfunction in a cohort of children and adolescents with DM1 and to compare different aspects of oral motor function with type of DM1 and gender (Study I).
- To explore changes in facial expression, intelligibility, eating and drinking ability and saliva control in young individuals with DM1 from a retrospective perspective *and* to investigate whether improvement or deterioration of orofacial functions could be related to gender, DM1 subgroup, or age (Study II).
- To explore quantitative methods for assessment of lip mobility and lip force and compare these with qualitative methods describing different aspects of lip function *and* to investigate the diagnostic value of these measurements (Study III).
- To investigate if regular training with an oral screen could strengthen the lip muscles in children and adolescents with DM1 *and* to analyse if improved lip strength could have an immediate effect on lip functions such as lip mobility, eating and drinking ability, saliva control, and lip articulation (Study IV).

METHODS

Study population

In total, 66 individuals with DM1, five with Möbius syndrome, six with facio-scapulohumeral muscular dystrophy (FSHD) and 106 controls participated in Study I–IV (Table 1, Figure 3). Fifty-six young individuals with DM1 and 56 healthy age and gender matched controls participated in study I, a cross-sectional survey. Thirty-five of these patients (age >2 years) and 31 of the matched controls, all of whom had been assessed approximately 3–4 years earlier were selected for study II, a retrospective investigation. The 56 individuals in study I comprised 89 percent (56/63) of all children and adolescents with a verified diagnosis of DM1 according to the multidisciplinary survey in the western and southern regions of Sweden. Seven patients withdrew: five declined to participate, and two only agreed to be examined by the paediatric neurologist and the physiotherapist. Most patients (84 %) had a developmental delay or learning disability. The control group was recruited from the Public Dental Service Clinic at the Department of Odontology, University of Gothenburg.

Seventy-three adults were enrolled in the methodological study (study III) - 50 healthy controls and 23 with diagnoses affecting the facial muscles (Table 1). Diagnoses were Myotonic dystrophy type 1 (DM1), Möbius syndrome and Facioscapulohumeral muscular dystrophy (FSHD). The participants were recruited via the Neuromuscular Center at Sahlgrenska University Hospital, Gothenburg, and the Swedish Möbius Syndrome Association or via personal (healthy adults). The diagnosis groups were selected for the study on the basis that they represented different types and degrees of facial impairment (Harper, 2004; Möbius, 2008; Padberg et al., 1991).

A letter inviting school-aged children with DM1 to participate in an intervention study was sent out to 18 families via the local habilitation team. Eight accepted the invitation, five with congenital DM1 and three with childhood DM1 (Table 1). Another four replied stating they would have liked to participate but were unable due to health conditions or other reasons. Six did not reply and no reminding letter was sent out.

All participants signed informed consent forms before inclusion in the projects and the studies were approved by the Ethics Committees of the Medical Faculties at the Universities of Gothenburg and Lund.

Table 1. Study populations in Study I–IV. Distribution on subgroups and age (mean age [range]). DM1 = Myotonic dystrophy type 1. FSHD = Facioscapulo-humeral muscular dystrophy.

Subgroup	Study I		Study II		Study III		Study IV	
	No	Age	No	Age	No	Age	No	Age
Congenital DM1, severe (n=18)	18	9 (2–21)	9	11 (6–17)	1	19	1	19
Congenital DM1, mild (n=18)	18	13 (3–18)	13	9 (3–15)	2	19 (18–19)	4	11 (7–19)
Childhood DM1 (n=19)	18	13 (8–20)	13	9 (5–17)			3	13 (11–15)
Classical DM1 (n=11)	2	17 (16–17)			9	48 (31–62)		
Möbius syndrome (n=5)					5	29 (21–36)		
FSHD (n=6)					6	40 (17–55)		
Healthy controls (n=106)	56	13 (2–23)	31	10 (2–17)	50	47 (25–67)		
Total	112		66		73		8	

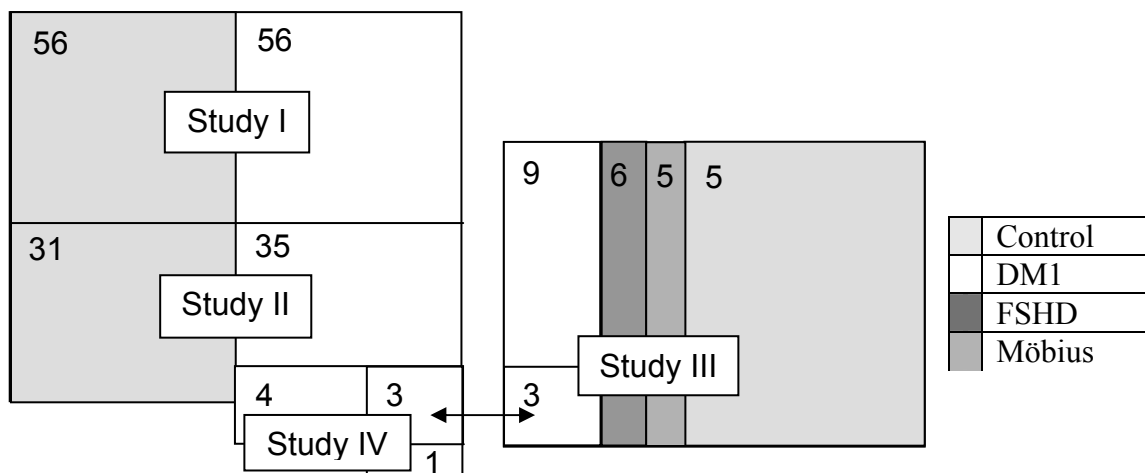


Figure 3. Distribution and overlapping of the study groups participating in Study I–IV. DM1 = Myotonic dystrophy type 1. FSHD = Facioscapulo-humeral muscular dystrophy.

Procedure

Different ways of assessing oral motor function, facial expression and speech were applied in the study. The methods for collecting self-reported information concerning eating and drinking ability and saliva control were similar in all four studies. All assessments (except force measurements) were video recorded and some speech examinations were both video and audio recorded. A dental nurse administrated the measuring instruments that were used in study III and IV. Most examinations were carried out at a dental clinic. All evaluations were made by a speech-language pathologist (the author). Two other speech-language pathologists not involved in the study performed evaluations to study inter-rater agreement.

To study inter- and intra-observer agreement in the assessment of *facial expression, speech and oral motor performance* according to ORIS, randomly chosen videotape recordings of patients with DM1 and their controls were evaluated by another speech-language pathologist not involved in the study and re-evaluated by the first observer (Study I and II).

An evaluation of *rest position and lip mobility in an open mouth smile and a lip pucker* was independently performed by two speech-language pathologists according to SFGS allowing calculation of inter-rater agreement (Study III). In case of disagreement they watched the video recording together and made a consensus decision used as the result.

Lip articulation of bilabial consonants was independently evaluated by two speech-language pathologists from audio files (Study III). They made a narrow transcription using the international phonetic alphabet with extensions for disordered speech (IPA, 1999, 2005). When disagreement arose, the final decision was made by a third speech-language pathologist.

In the intervention study, *lip articulation* was independently evaluated by two speech-language pathologists from video recordings made at first baseline, after treatment and after maintenance. They decided whether or not the bilabial or labiodental consonants were correctly produced and described existing compensatory strategies as labiodental, labiolingual, dental, or other. When disagreement arose, a consensus decision was made.

A one-group single-treatment counterbalanced design was used for the evaluation of the effect of lip strengthening exercises (Hegde, 1994) (Study III). Baseline measurements were made once a week during three weeks and after this the participants were randomly divided into two groups. One group started exercising for 16 weeks immediately after baseline and thereafter had a 16-week

period of maintenance. The other group acted as controls and started with 16 weeks maintenance and ended with 16 weeks exercising. Follow-up examinations were done every fourth week. The assessments carried out during baseline and after the treatment and maintenance periods were done at the clinic but the less extensive examinations made in between could be done at school or in the patient's home. The training instruction was to exercise with an oral screen 16 minutes, five days a week. The programme included 3 minutes active training with the oral screen twice a day and 10 minutes passive use of the oral screen inside closed lips. The exercises were performed at school or at home and a log book was used to keep record of the training.

In study I and II the results from children and adolescents with DM1 were compared to results from healthy controls that were matched for age and gender. Normative data describing lip function in healthy adults were collected in study III. The following qualitative and quantitative methods and instruments were used for data collection.

Qualitative assessments

Resting position of lips, jaw and tongue

The resting position was observed and recorded while the participant watched a picture for one minute (Study I and II). The degree of mouth opening and the tongue position at rest was evaluated on a four-point scale (Table 2).

Lip and tongue mobility

Lip function was evaluated in eight tasks and tongue mobility in four according to ORIS, a Swedish standardised protocol for examination of oral motor function (Holmberg & Bergström, 1996) (Study I). The range of lip and tongue movement was evaluated on a four-point grading scale with ratings from normal to severely affected (Table 2).

Facial expression

In study I and II, spontaneous facial expression was evaluated on a four-point grading scale using the definitions suggested in ORIS (Table 2). In the methodological study the voluntary mobility of the facial muscles were tested and described on five-point scales according to the Sunnybrook Facial Grading System (SFGS) (Ross et al., 1996) (Table 2). The facial expressions finally chosen for analysis were lip pucker and open mouth smile. These expressions have proven to be the best reproducible in earlier studies (Houstis & Kiliaridis, 2009; Johnston et al., 2003; Miyakawa et al., 2006).

Table 2. Variables and grading scales for assessment of oral motor function and speech.

	<i>Study</i>
<i>Resting position of the lips (ORIS)</i>	I
0: Closed mouth or changing between closed and half-open	
1: Half-open mouth	
2: Half-open to wide-open mouth	
3: Wide-open mouth	
<i>Resting position of the tongue (ORIS)</i>	I
0: Tongue is inside the teeth	
1: Tongue is sometimes outside the teeth	
2: Tongue is outside the teeth more than half of the time	
3: Tongue is constantly outside the teeth	
<i>Lip function and Tongue motility (ORIS)</i>	I
0: Normal range of movement and coordination for age	
1: Slightly reduced range of movement and/or slightly reduced coordination	
2: Clearly impaired range of movement or coordination, position/target is reached with effort	
3: Severely affected range of movement and coordination, position/target is not reached	
<i>Spontaneous facial expression (ORIS)</i>	I, II
0: Normal function	
1: Mild deviation	
2: Moderate deviation	
3: Severe deviation	
<i>Intelligibility of spontaneous speech</i>	I, II
0: Speech is fully understood	
1: Speech is largely understood, repetitions and verifications are occasionally needed	
2: There is an ongoing need for repetitions and verifications, listener effort is required	
3: Only a few words/phrases recognisable, alternative and complementary methods of communication are require	
<i>Voluntary movement of facial muscles (SFGS)</i>	III
1: Unable to initiate movement	
2: Initiates slight movement	
3: Initiates movement with mid excursion	
4: Movement almost complete	
5: Movement complete	

Speech

In order to detect specific articulation deficits in the survey of orofacial dysfunctions in children and adolescents with DM1 (Study I) a single word repetition test was included in the test protocol. The test was part of ORIS and contained short familiar words beginning with bilabial, labiodental, dental and velar consonants. It was assessed whether the consonants were correctly pronounced or not. The intelligibility of spontaneous speech was rated on a four-point scale. Each score was defined (Table 2). SVANTE, a Swedish articulation and nasality test (Lohmander et al., 2005), was included in study III and IV. In study III the articulation of bilabial consonants in different word positions were evaluated from audio recordings using narrow phonetic transcription (IPA, 2005). In study IV, a visual evaluation of lip articulation was made from video recordings of test items (single words and sentences) with bilabial and labiodental consonants.

Parental report on eating and drinking ability and saliva control

A questionnaire (Andersson-Norinder, 1996) with questions about eating and drinking ability and saliva control was used in all studies. The participant or the parents answered yes/no questions and rated the severity of drooling (Table 3).

Table 3. Variables and grading scales for eating/drinking ability and saliva control.

	<i>Study</i>
<i>Eating and drinking ability</i>	I, II, III, IV
Q1: Has difficulty in getting food off a spoon with the lips	
Q2: Takes a long time to swallow bites of food	
Q3: Food and liquids leak out of the corners of the mouth	
Q4: Food gets stuck in the gums	
Q5: Swallows large pieces of food without chewing	
Q6: Chokes on food	
Q7: Coughs when receiving liquids	
Q8: Presses tongue forward when swallowing	
Q9: Food/liquid goes up the nose	
<i>Saliva control</i>	I, II, III, IV
0: no drooling	
1: mild drooling, on lips only	
2: moderate drooling, saliva on the chin	
3: severe drooling, saliva on the clothes	
<i>Difficulties with eating and drinking</i>	III, IV
0: not at all	
1: not really	
2: somewhat	
3: very much	

Quantitative assessments

Lip force

Lip force was measured with a calibrated lip force meter (LF100, Detektor AB, Gothenburg, Sweden) in Study I, III, and IV. A prefabricated oral screen (Ulmer model, Dentarum, Pforzheim, Germany) was attached to a handle by a string, and the handle was connected to the measuring instrument (Figure 4). The oral screen (Figure 5) is available in two sizes, and the smaller one was used for children younger than 7 years (figure 3). The patients were seated during the test. The oral screen was placed inside the lips and the patients were told to try their best to keep it there while the examiner pulled the handle. A water level on the handle helped the examiner pull in a horizontal direction. The instrument saved the highest value (Newton) measured during a 10-second period. The best of three values was saved as result. In the intervention study the lip force meter was connected to a computer with software especially designed for this study installed, making it possible to measure lip force endurance. Endurance of the lip muscles was evaluated by testing how many seconds the patient could keep the oral screen inside the lips against a resistance equal to 50 percent of the achieved maximum lip force.



Figure 4. Lip force meter.

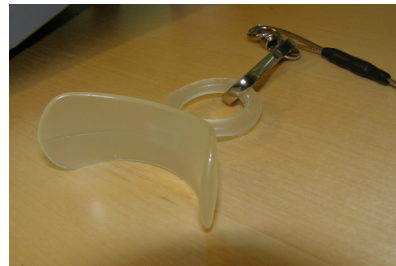


Figure 5. Oral screen.

Grip force

Grip force was used as a control variable in the intervention study and measured with a grip force meter (Grippit, Detektor AB, Gothenburg, Sweden) (Figure 6). The best of three values obtained (Newton) was saved.



Figure 6. Grip force meter.

3D motion analysis

A 3D analysis of lip mobility was included in study III and IV which gave information about the range and the direction of voluntary movements. The analysis was performed with a video-computer interactive system for automatic tracking of facial movements (SmartEye Pro 3.7 - MME (Mimic Muscle Evaluation), SmartEye AB, Göteborg, Sweden). Two calibrated video cameras (Sony XC-HR50) with IR lightings were used for the recordings. Video recordings were made during rest position (30 seconds), whilst the participant carried out a maximal retraction of the lips in an open mouth smile and a maximal contraction of the lips in a lip pucker. The tasks were repeated twice with a short break in-between. Individual landmark profiles were manually plotted with the mouse on photographs taken in different poses (Figure 7) and the positions of the landmarks were then automatically tracked when the video was running in tracking mode. The program had a built-in correction to allow for any head movements accompanying the facial movements. During tracking (Figure 8), a log file was generated by the computer which registered the horizontal, vertical and anterior-posterior position of the oral commissures in relation to origin (the 3D position). Information that could be extracted from the 3D position of the oral commissures were mouth width, mouth width asymmetry, mouth width change in a lip pucker and in an open mouth smile, and the resultant of the combined 3D oral commissure displacement in these expressions.

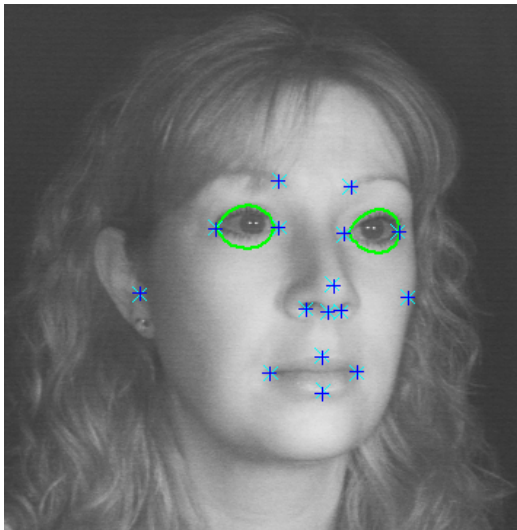


Figure 7. Individual landmark settings

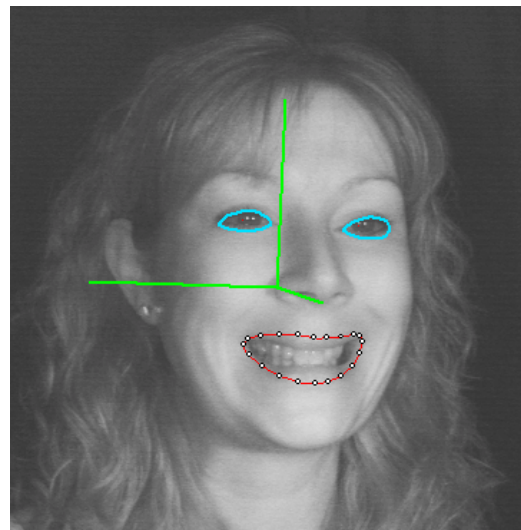


Figure 8. Tracking mode

Statistical analyses

Data was analysed with SPSS for Windows, version 14.0 and 15.0. Nonparametric tests were used for statistical analysis of categorical data. Crosstabulations and correlations were made with Kendall's tau_b. The Wilcoxon Signed-Rank Test (two related samples), the Mann-Whitney U Test (two unrelated samples), and the Kruskal-Wallis Test (more than two independent samples) were chosen for comparisons between groups.

Parametric tests were applied in the methodological study where continuous data were analysed and normal distribution assumed. Pearson's correlation coefficients were used, and means of unrelated pair of groups were compared with Student's t-test. Comparisons between more than two groups were performed with two-way ANOVA. The sensitivity and specificity of cut-off values for lip mobility and lip force were analysed.

Estimation of error of methods

Inter-observer and intra-observer reliability (Table 5)

- Approximately 30 percent of the videotape recordings from the *ORIS examination* at assessment A and B were randomly chosen to study inter-observer agreement. Fifteen percent of the videotape recordings from assessment A, and 30 percent from assessment B were reassessed by the first observer.
- Inter-observer agreement of the assessments of facial expression using the *Sunnybrook Facial Grading System (SFGS)* was tested on the videotape recordings from all participants (n=73) in the methodological study. The final results were based on consensus agreement.
- Audio files containing test sentences from *SVANTE, Swedish Articulation and Nasality Test* were used for the estimation of inter-transcriber agreement. Three sentences from each of the 73 participants in the methodological study were assessed. Test items were presented in a random order. Twenty-five percent of the sentences were presented twice on the listener file, in order to calculate consistency of transcriptions.
- In the intervention study, three video recordings containing 51 test items each (single words and sentences) were included in the estimation of inter-observer agreement.

Table 5. Results from the reliability testing: Inter-observer and intra-observer percentage agreement point-by-point.

Assessment	Study	Inter-observer agreement, %	Intra-observer agreement, %
ORIS	Study I	84.3 (mean)	90.7 (mean)
ORIS	Study II, A	71.7 (mean)	78.4 (mean)
	Study II, B	82.4 (mean)	97.5 (mean)
SVANTE	Study III	97	100; 95
SFGS	Study III	82	-
SVANTE	Study IV	95	-

Intra-individual variation

Thirty percent of the study group with healthy adults in Study III was randomly selected for the estimation of intra-individual variation in mouth width. The results from two different videotape recordings from the same individual were compared and the standard deviation of the intra-individual variation was found to be 1.1 mm for mouth width in an open mouth smile and 1.4 mm in a lip pucker.

The intra-individual variability in lip force was tested on 12 healthy adults on two occasions with at least 24 hours between measurements. The mean standard deviation between the first and the second measurement was 3.2 Newton.

The baseline measurements of eight children and adolescents with DM1 in the intervention study contributed with information about intra-individual variation within a period of three weeks concerning lip force, lip mobility, and lip articulation, eating and drinking ability, and saliva control in this group of patients. Intra-individual variations were most prominent concerning lip articulation (Table 6). The parental reports also showed some variation during baseline; four individuals varied between “not at all” and “not really” when they were asked if they had any difficulties with eating and drinking and two individuals varied between no and mild drooling.

Table 6. Median (min – max) variation between three baseline measurements from eight children and adolescents with myotonic dystrophy type 1 who participated in an intervention study. Data were obtained once a week during a three week period.

Assessed variable	Median	Min-Max
Mouth width in a lip pucker	2.2 mm	0.4 – 3.9 mm
Mouth width in an open mouth smile	2.0 mm	1.4 – 10.6 mm
Maximal lip force	3 Newton	0 – 7.0 Newton
Maximal grip force	23 Newton	1 – 40 Newton
Percentage correct articulation of bilabial consonants*	18 %	0 – 44 %
Percentage correct articulation of labiodental consonants*	10.5 %	0 – 13 %

*Only four individuals who had deviant lip articulation were included in this calculation.

Measuring error

The accuracy of the analyses generated by the 3D analysis of lip mobility in Study III was analysed in the group of healthy adults. Video tape recordings from 30 percent of the participants in this group were randomly chosen to estimate the measuring error. Firstly, the original examiner redid the landmark profiles to ensure intra-individual reliability. Secondly, to scrutinize inter-individual reliability another examiner made new landmark profiles on the same video tape recordings. Calibrations were performed before examination and the procedure was done according to a written manual. Standard deviations for inter-individual reliability were 1.3 mm for mouth width at rest, 1.8 mm for mouth width in an open mouth smile, and 2.0 mm in a lip pucker. The intra-individual variation test showed a standard deviation of 1.1 mm for mouth width in an open mouth smile and 1.4 mm for mouth width in a lip pucker.

RESULTS

Orofacial function in children and adolescents with myotonic dystrophy type 1

Characteristics and prevalence of oral motor dysfunction

Facial expression

The cross sectional study of 56 individuals (2–21 years of age) with DM1 showed that facial expression was impaired in all subjects with DM1 compared to none in the control group. Nearly half the group was severely affected. Patients with congenital DM1 had more impaired facial expression than patients with childhood DM1, and males were more affected than females. The facial expression deteriorated in some patients and no one showed any improvement during the 4–year follow up (study II). Changes concerning facial expression were significant.

Speech

The intelligibility was evaluated in 50 patients with DM1. Twelve percent were assessed to have fully intelligible speech, 28 percent mildly reduced, 42 percent moderately reduced, and 18 percent severely reduced intelligibility. Patients with congenital DM1 were most affected. Intelligibility was improved in four patients and deteriorated in eight. Improvements were only found in children younger than 15 years however, and there was no clear association between changed intelligibility and age and no correlation to gender or DM1 subgroup.

Deviant production of consonants was found in one-third of the patients. The most common articulation errors were interdental articulation of dentals and production of bilabials with the tongue between the lips (labiolingual) or with the lower lip against the upper teeth (labiodental).

Resting position

Open mouth posture was a frequent finding in patients with DM1, and some held their tongue in a low and forward resting position (between the front teeth) most of the time.

Tongue mobility and lip function

Approximately half the group of children and adolescents with DM1 had a major impairment of tongue mobility. The tongue was significantly more impaired in patients with congenital DM1 compared to patients with childhood DM1 and males were more affected than females. Patients with the classical

form of DM1 had no oral motor impairments or only mild oral motor impairments. A major impairment of lip function was found in more than two thirds of patients and was more severe in patients with congenital DM1 than in patients with childhood DM1. Lip function was most affected in males.

Some of the healthy children and adolescents had half-open mouth at rest, and two occasionally held their tongue between their teeth. Otherwise there were no orofacial dysfunctions in this group reported by the parents or detected during assessment.

Lip force

The maximal lip force of all study groups included in this thesis is presented in figure 9. The majority of the children and adolescents with DM1 who were able to participate in the task of measuring maximal lip force had weak lip muscles (lip force <8 Newton, which was the cut-off score for the controls) (Figure 10). Mean (SD) maximal lip force of the children and adolescents with DM1 was 7 (± 3.5) Newton and for the controls 21 (± 7.8) Newton. Lip force correlated significantly with age in the control group ($r = 0.442$, $p = 0.005$) but not in the DM1 group ($r = 0.289$, $p = 0.074$).

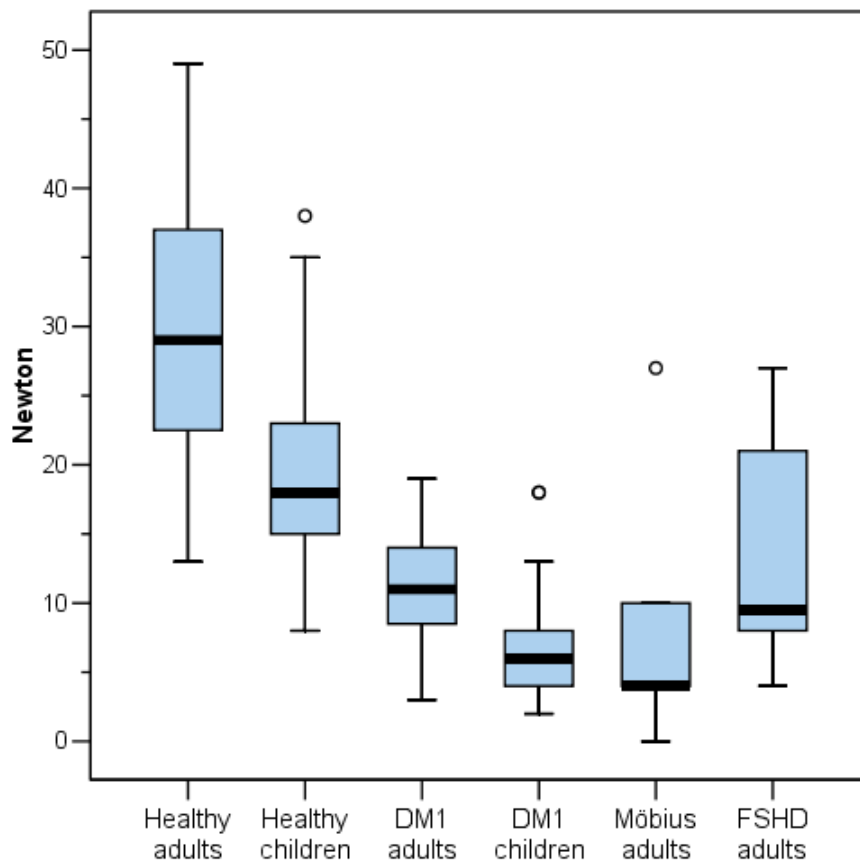


Figure 9. Maximal lip force in different subgroups enrolled in the study.

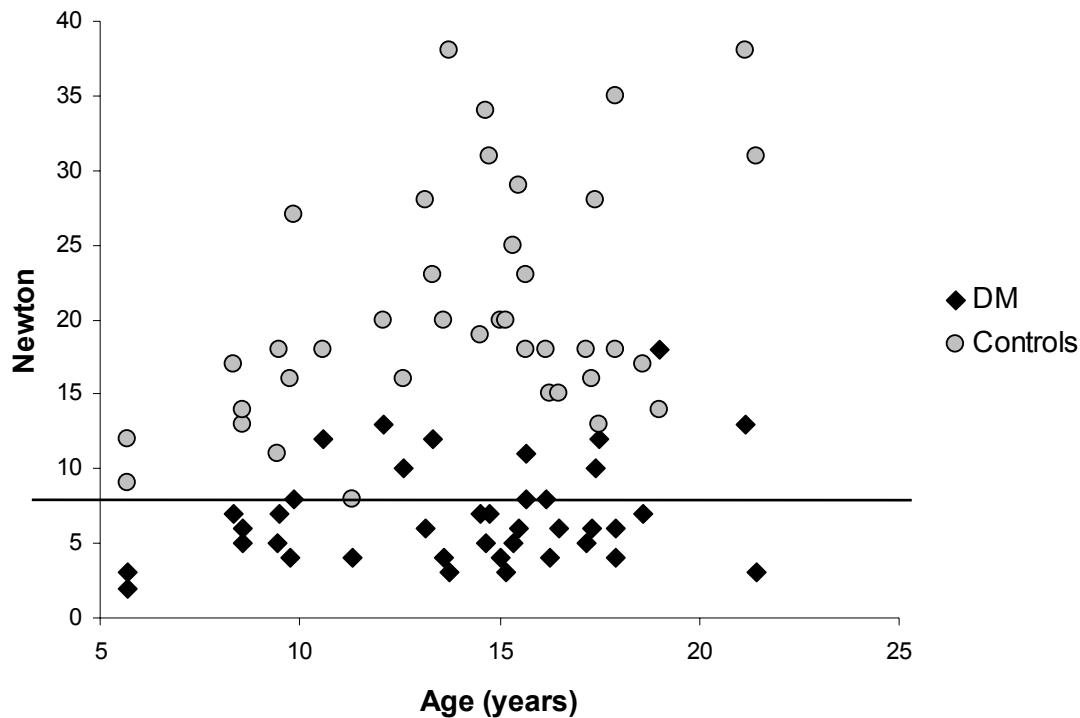


Figure 10. Maximal lip force in 39 patients (5–21 years) with DM1 and their age and gender matched controls who participated in a cross sectional case-control study (Study I).

Eating and drinking ability

Fifty percent of the group of children and adolescents with DM1 were reported to have some difficulties with eating and drinking, with 15 percent having severe difficulties. Five percent of the healthy children and adolescents reported minor problems. Most patients could chew ordinary food, some children and adolescents needed mashed foods, one 5 year-old child was still primarily bottle fed, and two children had a gastrostomy for nutritional support. Eating and drinking competence had improved in some patients and worsened in others during the time between the assessments. Eating and drinking ability improved *and* deteriorated equally in all age groups.

Saliva control

Drooling was reported in one third of the children and adolescents with DM1 and drooling was most common in congenital DM1. Drooling was generally rated to be mild or moderate. Only one child reported severe problems with drooling. The problem with saliva control was evenly spread between gender and age groups. All patients with moderate and severe drooling had lip dysfunction and weak lips. Drooling was improved in four children under the age of 10 during the follow-up period. The correlation between age and improved drooling was significant. Deteriorated saliva control was noted in 20 percent of the patients.

Improvements and deteriorations of orofacial functions

Altogether, 13 out of 35 individuals with DM1 showed improvement in one or more orofacial dysfunction after the 4-year follow-up. The median age (at the second assessment) for patients with improved functions (9:10 years) was lower than the median age for the whole group (13:9 years). One or more orofacial function had deteriorated in 22 patients. A combination of improved and deteriorated functions was observed in 8 patients and 8 patients showed no changes.

The effect of lip strengthening exercises

Maximal lip force and endurance increased in seven individuals compared to the baseline measurements. Maximal grip force improved in one, decreased in two, and varied within or close to baseline in five. Two individuals in the group who started with treatment improved maximal lip force after treatment and the improvement lasted for 12-16 weeks during the following period without training. The other two in this group reached peak performance during treatment. In the group who started with maintenance, three individuals improved maximal lip force before treatment and in one case the maximal lip force was improved further after treatment.

Increased lip force could not be related to changes in lip mobility, lip articulation, eating and drinking ability or drooling. Four individuals had deviant lip articulation, one never used the lips for speech production and the other three alternated between correct and incorrect lip articulation during the same session. The number of correctly produced bilabial and labiodental consonants varied greatly between the assessments with no single explanation for the variations.

Quantitative methods for assessment of lip mobility and lip force

Diagnostic value of quantitative measurements

Cut-off values for lip force and lip mobility were proposed for the identification of adults with lip dysfunction (Table 7) and the diagnostic value of these thresholds was evaluated. If individuals with impaired facial expression according to the SFGS assessment were compared to individuals without facial impairment the specificity for the proposed thresholds for lip mobility was high (89-97 %) but lower for sensitivity (61-67 %). When individuals with mild facial impairment (SFGS-score 4/4 or 4/5) were excluded from the group with impairments the sensitivity increased (73-83 %) and the specificity remained high (88-94 %). Measuring mouth width asymmetry could not differentiate between individuals with mild facial asymmetry and those evaluated to have symmetric function. When comparing individuals with or without facial impairment the

sensitivity for the proposed cut-off values for maximal lip force was 87 percent and the specificity 91 percent.

Table 7. Proposed cut-off values for lip mobility and lip force for identification of adults with lip dysfunction. Mouth width change = the difference in distance between the oral commissures at rest compared to maximal contraction. Oral commissure resultant = the combined 3D (horizontal, vertical and anterior-posterior) oral commissure displacement.

	Cut-off value
Open mouth smile	Mouth width change < 9 mm
	Oral commissure resultant < 8mm
Lip pucker	Mouth width change < 11 mm
	Oral commissure resultant < 12 mm
Lip force	Maximal lip force < 12 Newton

Correlations between results from qualitative and quantitative assessments

In the methodology study, mouth width change in an open mouth smile and in a lip pucker correlated significantly with the results from the subjective evaluations of facial expression (SFGS). It was also found that mouth with change in a lip pucker correlated significantly with maximal lip force. Compared to the rest of the group, lip mobility and maximal lip force were significantly reduced in adults who reported drooling and/or difficulties with eating and drinking. Two adults had deviant production of bilabials and they had results below cut-off on both maximal lip force and lip mobility.

DISCUSSION

Orofacial function in children and adolescents with myotonic dystrophy type 1

Characteristics and prevalence of oral motor dysfunction

In this thesis it was found that most children and adolescents with DM1 have orofacial dysfunction manifested as impaired facial expression, speech with reduced intelligibility, eating and drinking difficulties, and drooling. Different aspects of oral motor behaviour such as muscle strength, muscle tone at rest, lip and tongue motility and sound production were affected.

The high prevalence of impaired facial expression found in this study group agrees with the findings of other studies of young individuals with DM1 (De Die-Smulders, 2004; Hageman et al., 1993; Harper, 2004). If facial expression is impaired, the ability to express emotions and expectations will be limited. Winblad et al., (2006) found in a study of patients with classical DM1 that recognition of facial emotions was impaired compared with controls and this deficit was correlated to personality dimensions associated with sociability. It would be interesting to study whether there might be a correlation between lack of facial muscle feedback in patients with DM1 and impaired ability to recognise facial emotions.

The aetiology of communication disorders in young individuals with DM1 is often complex, with a mixture of language impairment, pragmatic difficulties and dysarthria. Ideally, all of these aspects of communication should have been assessed in depth. The number of examinations had to be limited, however, and therefore a general evaluation of intelligibility was chosen. Although the degree of intelligibility does not describe the aetiology or body dysfunction that causes the impairment, it gives valuable information about how speech functions in daily life and whether the patient needs augmentative or alternative ways of communication to be able to take part in activities that require communicative skills. The primary cause of reduced intelligibility was clinically considered to be flaccid dysarthria in this group of patients, but cognitive and neuropsychiatric difficulties also influenced oral communication.

Speech difficulties caused by myotonia of the tongue were a common complaint among parents with DM1, however the same symptom was not detected among the children and adolescents. Further studies are needed to explain different

aspects of speech production in patients with DM1 such as respiration, phonation, resonance, and articulation.

The intervention study offered unique information concerning the individual variations in lip articulation in children and adolescents with DM1 as this aspect of speech production was assessed three times to establish baseline and then every fourth week during approximately 9 months. An interesting finding was that the production of bilabial consonants could vary significantly from one assessment to the other and even during the same assessment. Both correct and deviant articulation of the same consonant was mixed in a seemingly random distribution. None of the participants with dysarthria seemed to be aware of their articulation errors as they never made any attempt to correct themselves during speech assessment or during spontaneous communication.

Based on the families' reports, half of the patients with DM1 had some kind of difficulty concerning eating and drinking, and about 15 percent were severely affected. Most problems were associated with the oral preparatory phase of swallowing such as difficulty in getting food off the spoon with the lips and leakage of food and liquids from the mouth. A few patients also reported coughing and choking during meals and nasal reflux, which are signs of impairment of the pharyngeal phase of swallowing. Hillarp et al. (1994) and Marcon et al. (1998) found that adult patients with DM1 often had subclinical symptoms of dysphagia - swallowing dysfunction could therefore have been more severe than was reported by the families. Swallowing cannot be evaluated by clinical observation alone, and was not assessed in the present studies. Neither was an association of reported difficulties in eating and drinking with gastrointestinal disturbances, respiratory problems or malocclusion investigated.

Drooling in individuals with DM1 is not a recognised problem in the literature, and yet a third of the children and adolescents in this study group had difficulties with saliva control.

The tongue was generally less affected than the facial muscles and could compensate for impaired lip function to some extent. Besides their tongue, the children sometimes used their teeth, chin muscles, and hands to compensate for impaired lip closure during speech, sucking, swallowing and chewing. Measurements of lip force confirmed that the facial muscles in most patients were weak compared to controls.

It is well known that many of the symptoms associated with DM1 are more frequent and more severe in congenital DM1 than in childhood DM1 (Goossens et al., 2000; Hageman et al., 1993; Harper, 2004; Steyaert et al., 1997). This was also true for the different aspects of orofacial dysfunction explored in this study.

A significantly higher frequency of reduced intelligibility, impaired facial expression and oral motor dysfunction was found in males compared to females. A gender difference in the prevalence and symptoms of DM1 has not been noted in the literature before, However, this difference may partly be explained by the higher proportion of males with congenital DM1, especially in the severe congenital group.

Improvements and deteriorations in orofacial functions

In Study II, it was reported whether facial expression, intelligibility, eating and drinking ability and saliva control were improved, unchanged or deteriorated in the time between the assessments. The progressive nature of DM1 seems to be clearly expressed in the gradual weakening of the facial muscles. No one had improved facial expression, but deteriorations were common. Deteriorated facial expression was the only change between assessments A and B that was significant. Late development of speech and language is a common feature in congenital and childhood DM1 (De Die-Smulders, 2004; Hageman et al., 1993; Harper, 2004). That some children in study II had improved intelligibility at assessment B could therefore be a consequence of late maturation. Deteriorated intelligibility was more common than improvement, probably due to increased flaccid dysarthria caused by progressive muscle weakness. One third of the patients varied considerably between the two assessments concerning frequency and type of eating and drinking difficulties. Improvements were more common than deteriorations. Five patients no longer pressed their tongue forward when swallowing, and seven had normalised the time it took to swallow pieces of food. These findings indicate that they had achieved a more mature and effective pattern of swallowing as they grew older. Deteriorations generally manifested as prolonged times to swallow pieces of food and food leakage from the mouth. Patients with increased food leakage from the mouth (n=4) at assessment B also had deteriorated saliva control as a sign of worsened lip competence. Drooling is a symptom that is expected to decrease, as patients grow older, and this was seen in four patients in the study group. A study of drooling prevalence in children with cerebral palsy found that the degree of drooling decreased as the child's dental age increased (Tahmassebi & Curzon, 2003). This spontaneous improvement in saliva control was thought to be due to oral-motor maturity. In study II, 11 patients had deteriorated saliva control; seven of these had begun to drool in the time between the two assessments. This is interpreted as a clear sign of the progression of the disease. More severe drooling was related to poorer eating and drinking ability in some patients.

Some patients developed one orofacial dysfunction in the interval between the two assessments and improved in another, indicating that explanations for the

developmental changes that occur vary. General developmental delay is common in DM1 (Steyaert et al., 1997), thus late maturation of oral motor skills could be one of the explanations for improvement. That all the preschool children with DM1 in study I had moderately or severely impaired lip function and tongue mobility, and that the improvements were negatively correlated with age confirms this suggestion. Maturity also increases social awareness and could be a reason for improved saliva control and perhaps improved eating. In Sweden, all children with disabilities are offered special care by a team of different professionals. Most of the patients in this study group had received treatment from speech-language pathologists and physiotherapists and many received excellent dental care, thus improvement could also be an effect of therapy.

Deterioration of facial expression was more common in childhood DM1. This was not surprising as facial expression in most of the patients with congenital DM1 was severely impaired at the first assessment and could therefore not get worse. It was also not surprising that muscle function and strength in children with congenital DM1 improved in the first years of life and that at some point muscle weakness began to develop and motor functions became affected (Hageman et al., 1993; Kroksmark et al., 2005). With the exception of facial expression, orofacial functions improved in patients with congenital DM1 *and* patients with childhood DM1. No developmental pattern that was typical for either subgroup and no specific time point when deterioration began were discernable. This may have been possible with a larger study population and comparable age groups. There was no clear gender difference concerning improvement or deterioration of the orofacial functions assessed.

The frequent observations of different aspects of lip function in the intervention study increased insight into the considerable intra-individual variations in children and adolescents with DM1. The true reason behind these variations is not known but was suspected to be related to the level of alertness at the time of assessment. Children and adolescents with DM1 are often affected by daytime sleepiness (Harper, 2004; Hilton-Jones, 2004). Intra-individual variation is an important aspect to consider when planning and performing a longitudinal study involving this patient group as these variations influence the results.

Effect of lip strengthening exercises

It was shown in the intervention study that school-aged children and adolescents with DM1 could improve maximal lip strength and lip strength endurance through lip exercises with an oral screen. Training against resistance is known to cause adaptive changes in the muscles *and* in the nervous system (neural adaptation) as both contribute to increases in strength (Lee & Carroll, 2007).

Neural adaptation due to frequent assessments of lip force could possibly be the explanation for increased lip strength in two patients during the maintenance period before the treatment. Voet et al (2010) examined the safety and efficacy of strength training in people with muscle disease. In this intervention review they found one randomised trial including patients with DM (Lindeman et al., 1995). The participants were between 16 and 60 years of age and were performing limb exercises. It was concluded that the study showed neither positive nor negative effect of the strength training. The positive effect on lip strength found in the present intervention study could indicate that strength training is more efficient in growing children and adolescents with DM1 compared to adults. More evidence is needed before this assumption can be confirmed or ruled out.

The measurement of grip force was included as a control variable in the study protocol. Grip force improved in one participant and deteriorated in two. Otherwise, grip force variations were within or very close to baseline. Thus, the grip force results support the assumption that increased lip force was an effect of intervention. One of the participants had two viral infections during the treatment period, which were followed by a significant decrease in lip force and a lesser decrease in grip force. The reason for the more profound effect on lip force could be that not only impaired health but also the intermission of treatment influenced the results.

Difficulties with speech, eating and drinking varied considerably between assessments and these variations could not be related to changes in lip force. Articulation seemed to be sensitive to fatigue due to tiredness and sleepiness – symptoms that are common in individuals with DM1 (Hilton-Jones, 2004).

It was expected that stronger lips would result in a more effective contraction of the orbicularis muscle and a decrease in mouth width when performing a lip pucker. This was not a consistent finding however, and the changes in mouth width were close to the expected measurement error.

The positive training effect on lip force was not transferred to improvements in lip function. Automation of new motor routines such as improved articulation can probably not be expected without practice and feedback (Maas et al., 2008). An urgent subject for research would be to study if speech therapy in combination with exercises for improved strength could improve lip articulation in individuals with DM1 and dysarthria.

Exploration of methods for assessment of lip function

Two methods for quantitative analysis of lip function were explored - a system for 3D motion analysis of lip mobility and a lip force meter.

A prerequisite for assessments that are applied in studies with children and adolescents with DM1 would be that it should be suitable also for individuals with learning disability and neuropsychiatric impairment. A number of systems for 3D facial analysis have been developed during the last two decades (Coulson et al., 2002; Frey et al., 1999; Giovanoli et al., 2003; Gross et al., 1996; Mehta et al., 2008; Mishima et al., 2006; Wachtman et al., 2001; Weeden et al., 2001). Most systems require that reflexive markers are attached to the face and that the participant must be able to sit perfectly still. The 3D system for motion analysis of lip mobility that was explored in the methodological study and then used in the intervention study could compensate for any head movements accompanying the lip movements, and no markers had to be attached to the face. The examination was not invasive and took only a few minutes to perform. All participants tolerated the investigation well but the children with learning disability sometimes had difficulty following the verbal instructions as facial expressions should be performed on command.

The measurement error of the 3D analysis of lip mobility was estimated and found to be within acceptable limits. The individual landmark profile was to a great extent manually plotted and this was thought to be the main reason for the measuring error. In a more recent version of the tracking system, the landmark profiles are generated by the computer in order to reduce the effect of measurement error. Schimmel et al (2010) found in a bench study of the same system, that it was possible to measure geometrical distances with high precision and facial distances with good accuracy and precision. New and better technical solutions and the development of userfriendly methods for quantitative measurements of facial movements will eventually make systems for 3D facial analysis suitable for clinical use.

The lip force meter could be used for all participants older than 5 years (Study I, III and IV). The possibility to measure not only maximal lip force but also lip force endurance was an addition to the measuring procedure in Study IV. It was considered an advantage that the lip force meter measured the same muscle activity and the same muscles that were exercised with the oral screen. However, this measuring device could not be used for measuring lip force during speech. According to Clark (2003), not only muscle strength and endurance but also power (the ability to produce force at a high speed) are important aspects of motor strength that are closely related to speech production.

There is no consensus on what type of measuring instrument would have been optimal for measuring lip force during speech. One of the technical problems that needs to be solved is how to inhibit the measuring instrument from interfering with speech production.

Diagnostic value of quantitative measurements

In Study III normative data on quantitative measurements of lip mobility and lip force were compared to results from qualitative assessments of facial expressions. This comparison resulted in proposed cut-off values for identifying individuals with impaired facial expression. When the diagnostic value of the proposed cut-off values was tested, it was found that they could be used to identify individuals with moderate or severe impairment. This first attempt to propose cut-off values for impaired lip mobility and lip force in adults needs to be challenged in further studies.

Correlations between results from qualitative and quantitative assessments

The combination of quantitative and qualitative methods for evaluation of lip function made it possible to investigate the relationship between lip contraction, lip force, eating ability and saliva control. Impaired lip pucker and weak lips were found in all or nearly all of the individuals with deviant production of bilabials, drooling and eating difficulties (Study I, III and IV). One individual (Study III) demonstrated that it is possible to have normal speech despite very weak lips and facial paresis. The ability to compensate for impaired oral motor function and strength could be expected to be dependent on individual prerequisites such as the presence of comorbidity, orofacial morphology, self awareness and access to speech therapy.

Methodological limitations

Some factors may have influenced the results in this thesis. It was difficult for the youngest children and those with severe communication disorders and cognitive deficits to take part in the test procedure and follow the examiner's instructions. These participants were excluded from some assessments which may have affected the results of lip function and tongue motility in study I. In study II, only variables that could be assessed in almost all patients were included. Although inter-observer agreement was good, there is still a risk that some of the developmental changes observed in study II are a consequence of imprecise assessments. Many individuals with DM1 are fragile and easily fatigued and therefore temporary fluctuations in general health and alertness are likely to

have influenced the results in all studies included in this thesis. Cognitive deficits are common in the classical type of DM1 (Winblad et al., 2005), and this could have had an impact on how the questionnaires were answered in some cases.

Clinical implications and future research

Children with DM1 should be given an early referral to a speech-language pathologist with special knowledge on neuromuscular diseases for support on optimal development of feeding and communication, and to get advice on compensatory strategies when intelligibility is reduced. The speech-language pathologist should follow the oral motor development of children and adolescents with DM1 and be aware that a deterioration of orofacial functions can begin early in life but also that improvements may occur throughout childhood and adolescence. The primary cause for flaccid dysarthria in DM1 is muscle weakness (Love, 2000) and it was shown in Study III that there is a strong correlation between lip force and lip function. If weak lips are contributing to speech impairment or dysphagia, lip strengthening exercises could be included in an intervention programme if they are combined with exercises that enhance the functional use of the achieved strength such as speech therapy and dysphagia treatment. A pre-fabricated oral screen is an easy to use tool suitable for strengthening lip exercises. When the outcome of treatment is evaluated the intra-individual variations have to be taken into account. Lip function is best assessed with a combination of qualitative and quantitative methods.

Speech-language pathologists should also keep in mind that facial weakness and speech problems are helpful clinical signs for recognising DM1 (De Die-Smulders, 2004). There is a need for further and deeper investigations into the different aspects of motor speech, language and communication disorders in congenital and childhood DM1. More clinical research is needed in order to find out the best treatment strategies for improving speech and communication, saliva control and difficulties related to sucking, chewing and swallowing in this patient group. Further research including multidisciplinary aspects is also required for the understanding of the progressive course of DM1 during childhood and adolescence.

CONCLUSIONS

Orofacial dysfunction – defined as impaired facial expression, reduced intelligibility, eating and drinking difficulties and drooling – were common features in congenital and childhood DM1 compared to healthy peers. Orofacial functions and oral motor performance were more affected in patients with congenital DM1 than in those with childhood DM1, and males were generally more affected than females.

Intelligibility, eating and drinking ability, and saliva control could improve during childhood in patients with DM1. Deteriorated facial expression, intelligibility, and saliva control were interpreted as signs of the progressive weakness and wasting of the orofacial muscles. Deterioration of orofacial functions often began before puberty in both congenital and childhood DM1.

Maximal lip force and lip force endurance could improve in children and adolescents with DM1. Improved lip strength alone could not be expected to have an effect on lip articulation, saliva control, or eating and drinking ability in this group.

The system for automated analysis of lip mobility that was tested, provided a possibility to register the 3D position of the oral commissures, and the lip force meter the maximal lip strength and endurance. The measurements were reliable and could be a supplement to qualitative methods for quantitative descriptions of facial impairment *and* for evaluation of eventual progress due to training. The methods were noninvasive and could be used in different patient groups.

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SUMMARY IN SWEDISH

(Svensk sammanfattning)

Dystrofia myotonika typ 1 (DM1) är en fortskridande neuromuskulär sjukdom. Det övergripande syftet med denna avhandling var att som första steg kartlägga förekomst och utveckling av orofaciala funktioner hos en grupp barn och ungdomar med DM1 och som andra steg att utvärdera effekten av styrketräning av läppmuskulaturen.

Hela undersökningsgruppen bestod av 66 personer med DM1, fem med Möbius syndrom, sex med facioscapulohumeral muskeldystrofi och 106 friska kontroller. Femtiosex personer (30 pojkar, 26 flickor; medianålder 13 år [2–21 år]) och 56 friska kontroller matchade till ålder och kön deltog i Studie I. Deltagarna representerade fyra undergrupper av DM1: svår medfödd (n=18), mild medfödd (n=18), barndomsdebuterande (n=18), och klassisk (n=2). Trettiofem av patienterna i undersökningsgruppen och 31 kontroller undersöktes vid två tillfällen med cirka 3–4 års mellanrum. Mimik, talförståelighet, oralmotorisk förmåga och läppkraft bedömdes av logoped och familjerna besvarade frågor om ät- och drickförmåga samt salivkontroll. Åtta barn och ungdomar (7–17 år) ur denna patientgrupp deltog senare i en behandlingsstudie (Studie IV). Efter genomförda baslinjemätningar påbörjade fyra deltagare 16 veckors träning medan övriga fungerade som kontrollgrupp. Därefter påbörjades träning med de fyra som startat som kontroller medan de som fått träning nu hade en period utan träning. Styrketräning av läpparna genomfördes 16 min/dag, fem dagar i veckan med uppföljning var fjärde vecka. Vid utvärderingen användes kvalitativa och kvantitativa undersökningsmetoder som först utvärderats i en metodstudie. Läpprörlighet mättes med datorbaserad 3D videoanalys och läppstyrka med läppkraftmätare. I metodstudien (Studie III) ingick 50 friska vuxna och 23 vuxna med diagnoser som medför påverkan på mimisk muskulatur.

Samtliga med DM1 hade påverkan på mimiken. Talförståeligheten var påtagligt reducerad hos 30 patienter (60 %), efter exkludering av sex patienter som saknade tal. Majoriteten hade måttlig till svår nedsättning av läppfunktion (76 %), tungrörlighet (52 %) och läppkraft (69 %). Avvikande produktion av bilabiala och dentala konsonanter var vanligt. Familjerna rapporterade problem med ät- och drickförmåga (52 %) och dregling (37 %). Oralmotorisk dysfunktion var mest uttalad hos personer med medfödd DM1 och pojkar var mer drabbade än flickor. Förståelighet, ät- och drickförmåga samt salivkontroll förbättrades under barndomen för några patienter. Det skedde en signifikant försämring av mimiken, särskilt hos patienter med den barndomsdebuterande formen av DM1, men försvagningen manifesterades också som nedsatt förståelighet och ökad dregling. De undersökningsinstrument som utvärderades bedömdes vara tillför-

litliga och kliniskt relevanta och kunde därför användas för utvärdering av behandling som ett komplement till kvalitativa metoder. Sju av åtta som ingick i behandlingsstudien fick starkare läppar men inte förbättrad läppfunktion.

Orofaciala funktionsnedsättningar i form av avvikande mimik, talsvårigheter, ät-svårigheter och dregling är vanligt förekommande hos barn och ungdomar med DM1. Både förbättring och försämring av dessa funktioner kan ses under uppväxten. Försämring av mimiken är ett tydligt tecken på fortskridande muskelsvaghet. Barn och ungdomar med DM1 kan få starkare läppar genom träning. Starkare läppar leder dock inte automatiskt till förbättrad läppfunktion.