Sequelae after Facial Palsy

Clinical, Anatomical and Electrophysiological Studies

DAVID JENSSON
Dissertation presented at Uppsala University to be publicly examined in Skoog salen, Ingång 78-79, Akademiska sjukhuset, Uppsala, Saturday, 30 November 2019 at 09:00 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in English. Faculty examiner: Associate Professor Sinikka Suominen (Department of Plastic Surgery, Töölö Hospital, Helsinki University, Helsinki University Hospital).

Abstract

Background: Sequelae after peripheral facial palsy, which among others include synkinesis, non-functional smile and/or lower lip asymmetry, may be devastating for the patient. Bell’s palsy is the most common form of peripheral facial palsy.

Aim: The aim was to study a) frequency and potential predictive factors of synkinesis in Bell’s palsy b) new surgical treatment options after facial nerve injury c) coactivation between muscles innervated by the facial nerve and the most common donor nerves in smile reanimation d) anatomical features of the lower lip depressors.

Methods: I: Frequency, severity and early predictors of synkinesis development were studied in 829 Bell’s palsy patients. II and IV: Anatomical technical feasibility of intra-facial nerve transfers was analyzed. V: Anatomical features of lower lip depressor muscles were studied and a literature review for lower lip depressor myectomies was performed. III: Coactivation of muscles innervated by cranial nerves during voluntary facial movements was measured with electromyography.

Results: I: In Bell’s palsy, synkinesis frequency was 21.3% at 12-months and Sunnybrook composite score at one month was found to be a good predictor for synkinesis. II and IV: A tension-free oculo-zygomatic and platysma-marginal mandibular nerve transfer was anatomically feasible. Full recovery of the lower lip after platysma-marginal mandibular nerve transfer was found in a clinical case. III: The masseter muscle had a narrower coactivation pattern compared to the tongue. Bite induced a strong coactivation in the zygomaticus major muscle. V: The width of the depressor labii inferioris was 20 ± 4 mm and the distance from the midline to the lateral muscle border was 32 ± 4 mm. For the depressor anguli oris muscle, the corresponding measurements were 14 ± 3 mm and 54 ± 4 mm. The mean recurrence rate after lower lip myectomy reported in the literature is 21%.

Conclusion: I: Synkinesis in Bell’s palsy was 21%. Sunnybrook composite score at one month is a good predictor for synkinesis. II: Oculo-zygomatic nerve transfer may be a suitable technique to reduce eye synkinesis and achieve a stronger smile. III: The narrow coactivation pattern in the masseter muscle may be advantageous for spontaneous smile development. IV: The platysma motor nerve transfer is a feasible procedure and can lead to full recovery in lower lip paralysis. V: Knowledge of the width of the depressor muscles is of importance to ensure complete resection in lower lip myectomy.

Keywords: Facial palsy, Marginal mandibular paralysis, Smile reconstruction, Synkinesis

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urn:nbn:se:uu:diva-394136 (http://urn.kb.se/resolve?urn:nbn:se:uu:diva-394136)
For my beautiful wife and kids,
Þórdís, Jökull, Fannar and Ágústa Líllý
This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


V. Kildal V,* Jensson D,* Weninger W, Meng S, Tzou CH, Rodriguez-Lorenzo A. Anatomical features in lower lip depressor muscles for optimization of myectomies in marginal mandibular nerve palsy. Submitted for publication.

* Denotes equal contribution
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## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>EMG</td>
<td>Electromyography</td>
</tr>
<tr>
<td>AU</td>
<td>Arbitrary Units</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>AUC</td>
<td>Area Under the Curve</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>P</td>
<td>Probability</td>
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<td>n</td>
<td>Number</td>
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<tr>
<td>fMRI</td>
<td>Functional Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>DLI</td>
<td>Depressor Labii Inferioris</td>
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<tr>
<td>DAO</td>
<td>Depressor Anguli Oris</td>
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Introduction

The facial nerve innervates the mimic muscles that are responsible for voluntary and involuntary facial expressions. Its peripheral part emerges from the facial nucleus in the pons and travels in the temporal bone to exit the skull base through the stylomastoid foramen. The nerve runs anteriorly in the parotid gland, gradually becomes more superficial, and divides into its five terminal branches (temporal, zygomatic, buccal, marginal mandibular and cervical). The temporal and zygomatic branches innervate the muscles around the forehead and eye, the buccal and marginal mandibular branches innervate the midface, mouth and lower lip, while the cervical branch innervates the platysma muscle of the neck.

Central versus peripheral facial palsy

A central lesion, most often caused by brain hemorrhage or stroke, will result in a contralateral paralysis of the lower face. The upper face, however, remains unaffected. This is explained by the fact that the upper face, in contrast to the lower, has bilateral cortical innervation. The typical clinical appearance of a peripheral facial nerve lesion from the facial nucleus and distally (lower motor neuron lesion) is weakness or paralysis of both the upper and lower ipsilateral face.

Causes of peripheral facial palsy

Acute idiopathic peripheral facial palsy, so-called Bell’s palsy, is the most common form of unilateral peripheral facial palsy, accounting for approximately 53% of peripheral facial palsies. The incidence of Bell’s palsy is around 30 patients per 100,000 per year. About 70% of Bell’s palsy patients recover completely. In 30%, however, recovery is incomplete: persistent facial asymmetry including muscle weakness, muscle contracture and/or involuntary facial movements, also named synkinesis, occurs. Other causes of peripheral facial disorders are, in decreasing order of incidence, trauma (14%), tumor (9%), herpes zoster (6%), congenital/birth/neonatal (5%), infection (excluding herpes zoster) (4%) and other palsies (9%).[1-3]
Grading of facial palsy

The severity of facial palsy and its sequelae is clinically graded by the use of subjective scoring systems. The two most widely used are the House-Brackmann and Sunnybrook facial grading systems. House-Brackmann is a gross grading scale that grades facial function as I to VI, in which normal function is grade I and the most severe dysfunction with no movement grade VI.[4] The regionally-weighted Sunnybrook system separately scores symmetry at rest, facial movement and synkinesis in different regions of the face. It is graded from 0 to 100 where 0 is no movement and 100 normal function. Synkinesis is scored from 0 to 3 for each of the five standard facial expressions where 0 is no synkinesis and 15 the most severe.[5] Newer instruments utilizing digital photographs and videos have been developed in an attempt to better evaluate changes and improve objectivity after facial palsy treatment.[6-8] The electronic, clinician-graded facial function scale (eFACE), recently developed to improve reporting outcomes after facial reanimation, uses graphical user-interface and a visual analogue scale to grade 15 facial features critical for facial function giving a score from 0-100. Some of its major benefits are that its digital nature and graphic outputs allow easy comparison and sharing of data. The eFACE grading system has been shown to have high intrarater and interrater reliability and has been well received by facial nerve experts.[9-11]

Classification of facial nerve injuries

A facial nerve injury can be classified into five degrees of severity. Neuropraxia is the mildest form, with the inability to transmit the nerve impulse over a region of compression. In this type of injury, axonal degeneration is absent and nerve function will recover within 3 weeks. Axonotmesis, a second-degree injury, means that the axons undergo Wallerian degeneration. This injury recovers over a period of 3 months. Neurotmesis, a third-degree injury, results in axonal and endoneural destruction. This leads to delayed recovery beginning at 2-4 months and with a high risk for aberrant regeneration and synkinesis. Sunderland’s first to third-degree nerve injuries occur with any etiology, including Bell’s palsy. Fourth and fifth-degree facial nerve injuries include destruction of the perineurium around the nerve fascicles and complete disruption of the nerve respectively. These latter two forms are usually caused by trauma or transection from surgery.[12]
Sequelae after peripheral facial palsy

In facial palsy, the mimic muscles are paralyzed and the ability to effectively express emotion is dramatically decreased. This is a devastating condition for patients.[13] Initially, they present with a flaccid face, widening of the eye and flattening of the nasolabial fold (Fig. 1a). With no or incomplete recovery, the patient often presents a myriad of reconstructive challenges. These include the inability to close the eye, marked facial asymmetry as well as difficulties with eating and speech. Over time, incomplete recovery causes facial muscle contractures to develop, resulting in a smaller contracted eye, deepening of the nasolabial fold and pulled up corner of the mouth.

Figure 1a. Peripheral facial palsy in the acute stage. Note the widening of the eye, flattening of the nasolabial fold and the dropping of the corner of the mouth.
Synkinesis

Facial synkinesis is another troublesome sequela following incomplete recovery after facial palsy. Synkinesis is defined as involuntary movement in one region of the face produced during voluntary movement in another region (Fig. 1b). If the facial nerve suffers neurotmesis, a third-degree injury or higher injury, synkinesis can develop, which is usually seen around 3 to 6 months after onset of facial palsy. The prevailing theory for synkinesis development is that injured axons undergo aberrant regeneration resulting in innervation of facial muscles other than those originally innervated.[12] Different methods have been proposed to evaluate the severity of nerve injury and predict synkinesis development. They include subjective grading systems as well as electrophysiological findings.[14-18] Synkinesis is routinely treated with chemodenervation (botulinum toxin injections) in combination with physiotherapy.[19-21] A drawback with chemodenervation is that the effect only lasts for 3 to 4 months. To achieve permanent relief, different surgical neurectomy and/or myectomy techniques have been described.[22-24]
Smile

One major concern in patients with facial palsy is the inability to produce a functional smile. However, several techniques for smile reconstruction are available. Prior to 12 to 18 months, the affected muscles may be re-innervated by cross-facial nerve graft or nerve transfer.[25] After this period, the neuro-muscular endplates have degenerated, which demands both nerve and muscle transfer for dynamic reconstruction. The goal of smile reconstruction is not only to overcome weak commissure excursion, but also to achieve spontaneous smile.

Lower lip

The marginal mandibular branch of the facial nerve innervates the muscles of the lower lip. The depressor labii inferioris and depressor anguli oris muscles function as lip depressors, pulling the lower lip and corner of the mouth down and laterally. Lower lip asymmetry, in marginal mandibular branch paralysis, results from elevation of the paralyzed lower lip, while the depressor muscles on the non-affected side pull the lip down.[26] This can be particularly eye-catching in patients with active lower lip depressor function during smile. Surgical treatment includes symmetrization procedures with deanimation through myectomy or neurectomy on the non-affected side or dynamic reconstruction with nerve or muscle transfer to the paralyzed lower lip.[27-31]
Rationale for this thesis

To study sequelae after facial nerve palsy, surgical treatment options and neuromotizers in smile regeneration.

a. To study the development of synkinesis in Bell’s palsy.
b. To study peripheral cranial nerve coactivation to try and explain spontaneous smile development after smile reanimation with a non-facial donor nerve.
c. To find new treatment options after facial nerve injury and sequelae after facial palsy with intrafacial nerve transfers.
d. To study anatomical features of lower lip depressors to improve results of myectomy in marginal mandibular branch paralysis.
Aims

Study I
To assess the development of clinical synkinesis in Bell’s palsy with data from the Scandinavian Bell’s palsy trial. Synkinesis frequency, severity and gender aspects were studied. Early predictors for the risk of synkinesis were also analyzed.

Study II
To explore the anatomical and technical feasibility of selective intra-facial nerve transfer between branches innervating the orbicularis oculi and zygomaticus major muscles in the treatment of facial synkinesis.

Study III
To study potential mechanisms for spontaneous smile development. The correlation between voluntary facial muscle movements and simultaneous electromyographic (EMG) co-activation activity were studied in muscles innervated by the masseter, hypoglossal and spinal accessory nerves. The association between voluntary movements in the latter muscles and simultaneous co-activation in facial muscles was also assessed.

Study IV
To investigate the anatomical and technical feasibility for nerve transfer of the platysma motor nerve to the marginal mandibular nerve to restore lower lip function in marginal mandibular branch paralysis.
Study V

To study the anatomy of the depressor labii inferioris and depressor anguli oris muscles with regard to their width and to conduct a literature review on lower lip myectomy with focus on surgical technique and recurrence rates.
Ethical considerations

Study I Synkinesis in Bell’s palsy in a randomized controlled trial
Data were drawn from the Scandinavian Bell’s palsy trial. This trial was approved by regional ethics review boards (Dnr 2000/99432). Written informed consent was obtained from all patients. The study was conducted in accordance with the CONSORT guidelines for randomized clinical trials and registered with ClinicalTrials.gov (identifier: NCT00510263). Evaluation of synkinesis was a secondary endpoint in the pre-specified analysis plan.

Study III Cranial Nerve Coactivation and Implication for Nerve Transfers to the Facial Nerve
The study was approved by the Regional Ethic Review Board in Uppsala (Dnr 2014/165). Written consent was obtained from all participants in the study. Studies I and III were performed in accordance with the Declaration of Helsinki and good clinical practice guidelines.

Studies II, IV and V are anatomical cadaver studies conducted at the Center of Anatomy, Medical University of Vienna, Austria. The studies were carried out according to local ethical regulations applicable in 2015. According to these regulations, approval from the regional ethic review board was not required, since dissections were supervised by a medical specialist in anatomy. All body donors had signed a contract with the Medical University of Vienna in which it was stated that their bodies would be used in pre- and postgraduate teaching and for medical research. In study IV, written consent for publication was obtained from the patient in the clinical case presented.
Materials and methods

Study I
Data were drawn from the Scandinavian Bell’s palsy trial, a randomized, double-blinded, placebo-controlled multicenter trial that was carried out in Sweden and Finland during May 2001 through September 2007. The trial included 829 patients diagnosed with Bell’s palsy. Patients were aged 18–75 years. Three hundred and forty one women (41%) and 488 men (59%) were included within 72 hours after onset of Bell’s palsy. The mean age was 42 ± 15 years for females and 43 ± 14 for males. Four treatment arms were investigated: prednisolone+valacyclovir, prednisolone+placebo, valacyclovir+placebo and placebo+placebo. The study design was factorial. Four hundred and sixteen patients were treated with prednisolone (60 mg daily for 5 days, then tapering 10 mg per day) while 413 did not receive the steroid. Follow-up visits were scheduled at days 11–17 and at 1, 2, 3, 6 and 12 months. Facial function was assessed using the House-Brackmann and Sunnybrook facial grading systems. We defined a synkinesis Sunnybrook score of < 6 as mild and ≥6 as moderate to severe synkinesis. The House-Brackmann system does not separately measure synkinesis and was not included in this analysis.

Study II
Ten fresh adult cadavers (18 hemifaces) were dissected. Measurements included number of nerve branches to the orbicularis oculi and zygomaticus major muscles as well as the maximum length of nerve dissection. The reach and possible coaptation of the most caudal nerve branch innervating the orbicularis oculi to the most cranial branch innervating the zygomaticus major muscle was assessed. Histomorphometric analysis of the nerve branches was performed.
Study III

Ten healthy individuals aged 22 to 44 years (median 32.5 years), 3 females and 7 males, volunteered to participate in this study. EMG recordings were made with routine clinical equipment (Keypoint®). Needle electrodes were inserted into the respective muscle and adjusted to record sharp motor unit potentials (Fig. 2). Seven different voluntary facial muscle movements were initially performed with simultaneous EMG recording of masseter, trapezius and tongue muscles. Five different movements of muscles innervated by the trigeminal, hypoglossal and spinal accessory nerves were then investigated with simultaneous EMG recording of coactivation in the frontalis, zygomaticus and platysma muscles (surface electrode).

Figure 2. Left: EMG needle electrodes in the masseter, tongue and trapezius muscles. Right: EMG needle electrodes in the frontalis, zygomaticus major and platysma muscles.[32] Shown with permission from Wolters Kluwer Health, Inc.

The motor units and interference patterns of muscle activity during the different movements were evaluated by the sound and signals on the oscilloscope. The signals were saved and printouts made of the maximal interference patterns. Muscle activity was classified into four degrees of activity with respect to the interference pattern. EMG results are presented in arbitrary units (AU) and standard error of the mean. Activity of 1 AU or higher was considered as co-activation.
Study IV

Ten adult fresh cadavers (19 hemifaces) were dissected. Measurements included the number of marginal mandibular nerve branches and platysma motor nerve branches, the maximum length of the platysma motor nerve from the parotid gland, and the distance from the anterior border of the parotid gland to the facial artery (Fig. 3). The platysma motor nerve reach for direct coaptation to the marginal mandibular nerve at the level of the crossing with the facial artery was assessed. We performed histomorphometric analysis of the marginal mandibular nerve and platysma motor nerve branches.

Figure 3. Cadaver dissection of the branches of the right facial nerve after retraction of the facial skin flap.[33] Shown with permission from Wolters Kluwer Health, Inc.

Study V

Ten fresh adult hemifaces were dissected. Measurements included the widths of depressor labii inferioris and depressor anguli oris muscles, the distance
from the mandibular midline to the lateral borders of the muscles, and the intra-oral distance from the lateral canine to the lateral border of the depressor anguli oris muscle (Fig. 4). A Pubmed search was conducted for ‘marginal mandibular paralysis’ within the disciplines ‘medicine’ and ‘anatomy & physiology’. Articles mentioning lower lip depressor myectomy were selected for further scrutiny. Three articles described lip depressor myectomy in detail and could be analyzed for surgical technique and recurrence rates.

Figure 4. Cadaver dissection with markings of the borders of the lower lip muscles
Statistical analysis

Study I
Results for continuous variables are given as mean values with standard deviations (SD). Results are presented with number of observations and percentages and area under the curve (AUC) values (95% CI). P-values <0.05 were considered significant.

Patients with synkinesis at 6 months and who had a 12-month follow-up were analyzed. Their mean synkinesis score at 6 months was compared with the score at 12 months. The paired t-test was used.

Potential prognostic factors for synkinesis at 12 months were analyzed by univariate logistic regression analysis. Statistically significant predictors were then analyzed for their independent predictive values using multivariate logistic regression. Receiver operating characteristic curves were constructed to evaluate the diagnostic performance of the logistic regression models.

Studies II, III, IV, and V
Descriptive statistics were used with mean values and corresponding standard deviations (± SD) or standard error of the mean.
Summary of results

Study I
Synkinesis frequency was 21.3% in the 743 Bell’s palsy patients who had a 12-month follow-up. The condition was moderate to severe in 6.6%. There was no gender difference. Patients with synkinesis at 6 months had a synkinesis score of 4.1 (±2.8 SD), which increased to 4.7 (±3.2) (P = 0.047) at 12 months (n = 93) (Fig. 5).

Figure 5. Mean Sunnybrook synkinesis score (triangles), voluntary movement score (squares) and composite score (diamonds) in 93 Bell’s palsy patients with synkinesis present at 6 months who attended the 12-month follow-up. Bars show standard error of the mean. Shown with permission from John Wiley and Sons.
Sunnybrook composite score at 1 month was the best predictor for synkinesis development with receiver operating characteristics and area under the curve (AUC) 0.87. The risk for synkinesis increased with a lower Sunnybrook composite score at one month (Fig. 6). Furthermore, symmetry of voluntary movement had a higher predictive value for synkinesis than resting symmetry with AUC 0.87 and 0.77 respectively. Gentle eye closure and open-mouth smile were the only independent significant predictive items (AUC 0.86).

![Figure 6. Predicted probabilities for the presence of synkinesis at 12 months according to the 1-month Sunnybrook composite score.][34] Shown with permission from John Wiley and Sons.

### Study II

The average number of facial nerve branches to the orbicularis oculi muscle was 3.1 (±SD 1.0) and to the zygomaticus major muscle 4.7 (±SD 1.2). The average maximum length of the most caudal orbicularis oculi nerve branches was 28.3 (±SD 7.3) mm and for the most cranial zygomaticus major nerve branches 23.8 (±SD 6.5) mm. Transection and tension-free coaptation was possible in all cases but one (Fig. 7). Histomorphometric analysis of the coaptated nerves demonstrated an average of 5173 (±SD 2293) myelinated fibers per mm² from the orbicularis oculi branch and 5256 (±SD 1774) for the zygomaticus major branch.
Study III

Smile coactivated the masseter and tongue muscles equally. During the seven mimic movements, the masseter muscle had fewer EMG-measured coactivations compared with the tongue (2/7 vs. 5/7). The trapezius muscle demonstrated no coactivation during the seven mimic movements (Fig. 8).

![Figure 8](image_url)
Movements of the masseter, tongue and trapezius muscles induced EMG-recorded co-activation in the facial muscles. Bite resulted in the strongest co-activation of the zygomaticus major muscle (Fig. 9).

![Figure 9. EMG-registered co-activation in the frontalis, zygomaticus major and platysma muscles during movement of the masseter, tongue and trapezius muscles. Presented as medium arbitrary units (0 = no activity, 1 = low activity, 2 = moderate activity, 3 = strong activity) with standard error of the mean.[32] Shown with permission from Wolters Kluwer Health, Inc.]

**Study IV**

The location of the marginal mandibular nerve and platysma motor nerve was consistent in all dissections. The average number of sub-branches was 1.5 ± 0.8 for the marginal mandibular nerve and 1.2 ± 0.4 for the platysma motor nerve. The average maximum length of dissection of the platysma motor nerve from the anterior border of the parotid gland to its branching inside the platysma was 46.5 ± 13.4 mm. The average distance of the marginal mandibular nerve from the anterior border of the parotid gland to the crossing over the facial artery was 30.7 ± 7.9 mm. In all cadavers, tension-free coaptation with the marginal mandibular nerve was possible at the level of crossing with the facial artery. Histomorphometric analysis demonstrated that the marginal mandibular nerve contained an average of 3866 ± 1434 myelinated fibers per mm² and the platysma motor nerve contained 5025 ± 2352 myelinated fibers per mm². Our clinical case demonstrated a full clinical recovery of lower lip depressor function by platysma motor nerve transfer to the marginal mandibular nerve. Furthermore, no clinically relevant donor-site morbidity was observed after denervation of the platysma muscle.
Study V

The average width of the depressor labii inferioris muscle was 20 ± 4 mm and for the depressor anguli oris muscle 14 ± 3 mm. The distance from the mandibular midline to the lateral border of the depressor labii inferioris muscle was 32 ± 4 mm and 54 ± 4 mm for the depressor anguli oris muscle. The literature review revealed a mean recurrence rate of 21% after lower lip depressor myectomies (Table 1).

Table 1. Data on surgical myectomies

<table>
<thead>
<tr>
<th>Article</th>
<th>Recurrence rate (n)</th>
<th>Muscles resected</th>
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<tr>
<td>Hussain et al (2004)</td>
<td>17 % (7/42)</td>
<td>DLI</td>
</tr>
<tr>
<td>Chen &amp; Tang (2007)</td>
<td>24 % (8/33)</td>
<td>DLI + DAO</td>
</tr>
<tr>
<td>Lindsay et al (2011)</td>
<td>33 % (1/3)</td>
<td>DLI</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>21% (16/78)</strong></td>
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Discussion

Synkinesis
The overall incidence of synkinesis in the present Bell’s palsy study was 21.3% at 12 months. In 6.6% of patients, synkinesis was considered moderate to severe. Furthermore, the condition increased between 6 and 12 months. When analyzing predictive factors, the Sunnybrook composite score at one month was a good predictor for the development of synkinesis.

The incidence of synkinesis in our study accords with previous findings of 8 to 30% in Bell’s palsy.[14, 20, 36] The Sunnybrook facial system includes grading of synkinesis severity (0-15). We defined moderate to severe synkinesis as a Sunnybrook synkinesis score of ≥6. With a yearly incidence of Bell’s palsy of approximately 30 cases per 100,000 individuals, it can be estimated that the number of patients with moderate to severe synkinesis is 2 per 100,000 per year. These patients will need prolonged healthcare with physiotherapy, botulinum toxin injections and/or surgery.

The mainstay treatment for synkinesis is chemodenervation (botulinum toxin injections) in combination with physiotherapy.[19, 37] Botulinum toxin is a neurotoxin, inhibiting presynaptic release of acetylcholine and resulting in a temporary chemical denervation of the muscle. The effect of botulinum toxin is, however, not permanent with partial recurrence of muscle movement due to compensatory axonal sprouting.[38] Patients therefore require repeated treatment every 3-4 months.

The most common form of facial synkinesis is oculo-oral or oro-ocular synkinesis.[39] Oro-ocular synkinesis refers to involuntary contraction of the eye during smile. In moderate to severe oro-ocular synkinesis, weak commissure excursion is often present. This may be due to the aberrant regeneration of facial nerve fibers and its treatment remains a challenge. In theory, redirecting nerve fibers with intra-facial nerve transfer may reduce synkinetic eye movement and achieve a more symmetrical smile.
We found that nerve transfer of a caudal nerve branch from the eye to the most cranial nerve branch innervating the zygomatic major muscle was an anatomically feasible procedure. These two nerve branches had similar size and myelinated fiber counts allowing for a good match nerve repair.

Qin-kai Zhai et al. reported excellent outcomes in 23 of 26 patients suffering zygomatic and marginal mandibular nerve injuries reconstructed by intra-facial nerve transfer of a buccal or cervical nerve branch. In this study, intra-facial nerve transfer was not shown to be complicated by post-operative synkinesis.[40] A recent study on modified selective neurectomy showed significant improvements in synkinesis as well as symmetry of the nasolabial fold and mouth.[41] Furthermore, selective neurectomy of nerve branches to the eye has been shown to reduce ocular synkinesis.[24] However, long-term follow up on these patients revealed recurrent synkinesis requiring renewed botulinum toxin treatment.[42] This reinnervation of the orbicularis oculi muscle can potentially be avoided by nerve transfer, routing the sprouting axons to a new target muscle. Thus, combining the effect of selective neurectomy and nerve transfer is potentially a new treatment method for oro-ocular synkinesis.

Reanimation and development of spontaneous smile

In long-standing facial paralysis affecting the smile, the neuromuscular endplates undergo degeneration rendering the muscles non-functional. If addressed before 12 to 18 months, the muscles can be re-innervated by a cross-facial nerve graft or ipsilateral nerve transfer from a non-facial donor nerve such as the hypoglossal nerve or a branch from the trigeminal nerve (masseter nerve).[25, 43-48] After 18 months, however, reconstruction of the smile requires a new muscle. Local muscle flaps, such as the temporalis muscle flap or the masseter muscle flap, can be used.[49-51] However, limited commissure excursion and spontaneity have been a drawback with these techniques.[52] Free muscle flap with a nerve transfer has therefore become a more common treatment option in smile reconstruction. The gracilis muscle is the most commonly used free muscle flap in smile reanimation.[53-57] Other muscles used as free flaps in facial reanimation include the latissimus dorsi,[53, 58, 59] pectoralis minor,[60, 61] biceps femoris,[62] rectus abdominis[63] and abductor hallucis[64] muscles.

In our study, we found that smile coactivated the masseter and tongue muscles equally. The tongue was coactivated during 5 of 7 facial mimic movements whereas the masseter muscle was only coactivated during smile and forehead wrinkle. The trapezius muscle (innervated by the spinal accessory nerve) had no coactivation during facial mimic movements. During contraction of the masseter, tongue and trapezius muscle, the masseter muscle (bite) resulted in
the strongest coactivation of the zygomaticus major muscle (smile). Coactivation during smile and the narrow coactivation pattern (2 of 7 mimic movements) of the masseter muscle indicate that the masseter nerve may be the preferred donor nerve to develop a spontaneous smile in smile reanimation. An additional interesting finding was that the zygomaticus major muscle demonstrated strong coactivation during bite.

In theory, coactivation may be a prerequisite for spontaneous smile development after nerve transfer in smile reanimation, but it is not clear if coactivation is a peripheral or a central phenomenon. Schaverien et al. demonstrated that activation of the masseter muscle occurs during normal smile production in about half of the population.[65] The authors speculate that this may be a contributory factor to the high frequency of patients with a spontaneous smile after masseter nerve transfer in smile reanimation.

Historically, innervation of the free muscle flap in smile reanimation via cross-facial nerve graft from the contralateral facial nerve has been the gold standard. It has been argued that development of a spontaneous smile after cross-facial nerve graft is more reliable than after a nerve transfer procedure. However, the traditional cross-facial nerve graft technique, requires a two-step approach and long re-innervation time. Furthermore, the need for two anastomoses will result in considerably lower neuronal count, often leading to a weaker contraction and less excursion of the oral commissure compared to a nerve transfer.[54] In contrast, nerve transfers provide a source of axons close to the target muscle by direct nerve anastomosis, which thus avoids nerve grafts and makes re-innervation both faster and more predictable. The most common donor nerves used for nerve transfer in smile restoration are the masseter nerve[66], hypoglossal nerve[67, 68] and spinal accessory nerve,[69] as well as branches from the cervical plexus.[70]

The mechanism for the development of a spontaneous smile after nerve transfer is not fully understood, but is in part thought to be associated with cortical plasticity through central relearning.[71, 72] Spontaneous smile has been reported in 56-59% of patients following smile reanimation surgery with masseter nerve transfer.[66, 72] Another factor that may predispose patients to achieve spontaneous smile is coactivation induced by the non-facial donor nerve during voluntary smile.[65] Lenz et al. reported that 94% of patients with the presence of preoperative coactivation of the masseter muscle during smile developed synchronous smile after a free gracilis flap and a masseter nerve transfer. Patients with no preoperative coactivation in the masseter muscle upon smiling showed 0% synchronicity during smile.[73] In a study using the spinal accessory nerve as donor nerve in smile reconstruction with a free muscle flap, 33% of patients had spontaneous smile movement with the presence of dominant involuntary movement and 12% had spontaneous smile
movement with little or no involuntary movement.[69] To our knowledge, there are no reports on the development of synchronous or spontaneous smile after hypoglossal nerve transfer. Unfortunately, the lack of a standardized protocol for reporting outcomes after reanimation surgery, makes the interpretation and comparison of results difficult.[74] Hopefully, experts in the field of facial reanimation will agree on a comprehensive reporting system for post-operative evaluation in the future.

Lower lip
Iatrogenic injury to the marginal mandibular branch of the facial nerve may occur during surgery for benign and malignant disorders in the submandibular region. The nerve branch is particularly vulnerable where it crosses the facial vessels.[75, 76] If nerve injury is detected intra-operatively, direct nerve repair or grafting is performed.

In cases of marginal mandibular nerve injury with delayed discovery or a long nerve gap, direct coaptation or nerve graft may not be possible. In these patients, an alternative method is to innervate the distal part of the marginal mandibular branch. The platysma motor nerve innervates the platysma muscle of the neck. Through its insertion around the corner of the mouth and lower lip, the platysma muscle has a synergistic function with the muscles innervated by the marginal mandibular nerve, functioning as a depressor of the lower face.[22]

We found that nerve transfer of the platysma motor nerve to the marginal mandibular nerve was an anatomically feasible procedure. The dissection of the platysma motor nerve was consistent in all cadavers. Furthermore, the length of the nerve was suitable for tension-free coaptation and with a large source of axons to the marginal mandibular nerve. Our findings, in addition to the synergistic effect of the platysma motor nerve, make such a transfer a good alternative for re-innervating the marginal mandibular nerve in selected patients. This was demonstrated in our clinical case report in which a large part of the marginal mandibular nerve had to be sacrificed during surgery for a malignant tumor. No post-operative morbidity related to the denervation of the platysma muscle was observed in our patient. This is in line with previous findings after platysma motor nerve transfer in reconstruction of the brachial plexus and isolated spinal accessory nerve injuries. [77, 78]

In long-standing marginal mandibular nerve paralysis, reconstruction of the paralyzed lip can be attempted through dynamic reconstruction or with symmetrization techniques. The reconstructive approach will often depend on the
patient’s age and expectations as well as the surgeons experience. Reanimation of the lower lip can be performed with local muscle transfers such as the platysma or anterior belly of the digastric muscle. Muscle transfers have been shown to result in improved symmetry of the lower lip but the dynamic results have been a matter of debate.[27] With the introduction of botulinum toxin in the field of facial paralysis, chemodenervation of the lower lip depressors on the non-affected side has become a popular treatment option in marginal mandibular nerve paralysis. In a study comparing muscle transfer of the anterior belly of the digastric muscle with botulinum toxin to the lower lip, both treatments resulted in high patient satisfaction. However, there was a trend toward patients being more likely to report dissatisfaction with the outcome in the anterior digastric muscle transfer group and 42% of them reported a worsening of drooling.[29]

One major drawback with botulinum toxin treatment is that patients require repeated injections every 3-4 months. Patients who are satisfied with botulinum toxin treatment, but seek a more permanent solution, can be offered surgical neurectomy of the marginal mandibular branch. This procedure requires an extended facelift incision for selective neurectomy of the nerve branches to the depressor muscles of the lip.[79] Another option is to do myectomy of the lower lip depressors. In lower lip depressor myectomy, the depressor labii inferioris with or without the depressor anguli oris, is resected through a intraoral approach leaving no visible scar. The reasons for the high recurrence of lower lip depressor function reported in the literature after lower lip myectomy are not clear. Insufficient resection of the muscle length as well as difficulty in outlining the borders of the depressor muscles during surgery have been suggested as possible explanations.[80, 81] Our anatomical findings on the width of the depressor anguli oris and the depressor labi inferioris may guide surgeons in their estimation of muscle width resection during lower lip myectomy.
Future perspectives

We are currently exploring the activation patterns of the facial, masseter, hypoglossal and spinal accessory nerves in the motor cortex via functional magnetic resonance imaging (fMRI). The process of reorganization in the brain as a response to injury is called cortical plasticity. This reorganization, which can be visualized through brain imaging, is believed to contribute to the development of a spontaneous smile after nerve transfer. Two fMRI studies have analyzed the relationship between areas of cortical activation during smile and jaw-clenching. One of the studies that used finger-tapping as control showed that these two cortical areas were distinct with minimal overlapping.[82] The other study, which used visual input as baseline control, revealed significant overlapping and a similar pattern of brain activity for smile and jaw-clenching tasks. These authors concluded that the hypothesis of brain plasticity between the facial nerve area and masseter nerve area is supported by the broad cortical overlap in the representation of facial and masseter muscles.[83] In the study of Garmi et al.,[71] 5 patients who had developed a spontaneous smile after a lengthening temporal myoplasty were compared to 5 healthy controls. The cortical area in the brain associated with smile was enlarged postoperatively and merged with the cortical area associated with jaw-clenching. This further supports that cortical plasticity plays a part in the development of a spontaneous smile after nerve transfer. The aim of our study is to analyze the spatial arrangement of activation areas and possible areas of coactivation during movements representing activation of one of the four cranial nerves to be studied.
Conclusion

I Synkinesis is seen in 21% of patients after Bell’s palsy with deterioration between 6 and 12 months. The frequency of patients suffering from moderate-to-severe synkinesis is 7%. This group of patients will need treatment with a multidisciplinary approach. The Sunnybrook composite score at one month is a good predictor for synkinesis development.

II Nerve transfer of the most caudal nerve branch innervating the orbicularis oculi muscle to a cranial nerve branch innervating the zygomaticus major muscle is an anatomically-feasible procedure. In theory, this procedure may decrease oro-ocular synkinesis and provide a stronger, more symmetrical smile in selected patients.

III The masseter and tongue muscles coactivate during smile. The masseter muscle has a narrower coactivation pattern compared to the tongue. This may be advantageous for spontaneous smile development after nerve transfer in smile reanimation.

IV Using platysma motor nerve transfer to reconstruct the marginal mandibular nerve function is an anatomically-feasible procedure. Due to the synergistic function of the two nerves, full recovery of the lower lip depressors can be achieved which was demonstrated in a clinical case.

V The high recurrence rates after lower lip myectomy may be explained by inadequate resection of muscle fibers. The results in the presented study help to ensure full resection of the lower lip depressor muscles.
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References


A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title “Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine”.)