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Retrospective study of the functional recovery of men compared with that of women with long-term facial paralysis

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Abstract

Sex is likely to play an important part in reanimation of the face after paralysis, with women being superior in terms of resistance to neural injury and regeneration. Our aim was to evaluate the influence of the sex of the patient on the recovery of facial paralysis after surgical reanimation by comparing the degree of restored movement between men and women with long-standing paralysis that was reanimated by transfer of the hypoglossal nerve or cross-face nerve grafting. Between 1999 and 2010 we operated on 174 patients with facial paralysis. Of these we studied 26 cases (19 women and 7 men) with complete long-standing paralysis reanimated with either cross-face nerve grafting ($n = 14$) or transfer of the hemihypoglossal nerve ($n = 12$). The degree of movement restored was recorded in each case. Statistical analysis showed that in cases with long-standing paralysis women had significantly more movement restored than men for both cross-face nerve grafting ($p = 0.02$) and hypoglossal transposition ($p = 0.04$). We conclude that, after a neural injury, women tend to maintain the viability of the facial musculature longer than men, which suggests that they are more resistant to both denervation and the development of muscular atrophy. Whether this phenomenon can be explained by neural or muscular processes, or both, warrants further studies.

Keywords: Facial paralysis; Gender; Cross-face nerve graft; Nerve transfer

Introduction

Facial paralysis is a challenging topic in reconstructive surgery, and during past decades different operations have been described to treat it.[1–3] However, some basic concepts related to degeneration and regeneration of nerves, and muscular denervation and atrophy, must be considered. It has been established elsewhere that the cut-off point for the development of irreversible muscular atrophy is denervation of more than 2 years. For short-term paralysis (<2 years), therefore, because there is still viable facial musculature, options for dynamic reanimation include cross-face nerve grafting, the "baby sitter" procedure,[4] and transfers from the masseteric, hypoglossal, C7 root or accessory nerve.[5,6] However, if the time since injury is longer than 2 years, irreversible muscle atrophy will have developed and so, to recover movement, a new muscle unit must be transferred and reinnervated either by the opposite facial nerve by cross-face nerve graft or by a non-facial motor nerve (such as the masseteric or hypoglossal nerve) on the same side.[7,8]

Throughout our experience in reanimation of facial paralysis we have noted that in cases of long-term palsy, women can recover movement without the need for a new muscular unit.[9] After careful evaluation, therefore, we have used techniques indicated for short-term paralysis (such as transfer of a nerve or cross-face nerve grafting) in women after prolonged denervation, and found that tone and movement recovered in most of them. However, this has not been the case for men.

The aim of the present study was to describe our clinical observation that women (but not men) with facial paralysis of more than 2 years' duration, are capable of recovering

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facial tone and movement with techniques traditionally indicated for short-term palsy. This suggests that recovery after reanimation may be sex-related.

Patients and methods

Patients

We retrospectively reviewed the charts of all the patients who had had reanimation procedures for facial paralysis between 1999 and 2011. To make our study group as homogeneous as possible, we compared restoration of movement after prolonged denervation only among patients with longstanding unilateral secondary paralysis (more than 2 years) who had been treated with cross-face nerve grafting or transfer of the hypoglossal nerve. Exclusion criteria were the presence of preoperative movement, tone, or electromyographic (EMG) activity (which would mean incomplete paralysis), or any patient who had previously had a reanimation procedure of any kind (static or dynamic).

Patients were classified according to sex, and we recorded age, aetiology of the paralysis, the time that it had lasted, restoration of movement, and follow-up in all cases. Restoration was defined as symmetry at rest and excursion of the commissure of $\geq 75\%$ on the healthy side (equivalent to grades II–III on the House–Brackmann scale). All patients were evaluated preoperatively by physical examination, standard photographs and video, EMG, and FACIAL CLIMA, an automatic optical system for the capture of facial movements.[10] Postoperatively patients were evaluated by the senior author at 3, 6, and 12 months, and then once a year. At each visit he assessed commissural excursion on the reanimated side.

Rehabilitation protocol

All patients were asked to start training one month postoperatively. Smiling in front of a mirror for 10 min/day was recommended. Patients treated by hemihypoglossal nerve transfer were instructed to move the reconstructed side initially by pressing the tongue against the front teeth and then, once movement has been restored, to attempt to smile independently of the movement of the tongue. It is important to emphasise that we did not notice differences in the adherence to the protocol between men and women.

Statistical analysis

The significance of differences between quantitative variables was assessed using the Mann–Whitney *U* test, and the differences in restoration of movement between the sexes using Fisher's exact test. We used the Statistical Package for the Social Sciences (version 17.0, SPSS Inc, Chicago, IL) for all statistical tests, and probabilities of less than 0.05 were accepted as significant.

Results

Between 1999 and 2011, 174 patients had their facial paralyses reanimated in our department. The operations included cross-face nerve grafts, nerve transpositions (hypoglossal and masseteric), and microvascular gracilis transplants innervated by the opposite facial nerve by cross-face grafting or grafting to the ipsilateral masseteric nerve. We included 26 patients with complete long-standing paralysis in the present study, 19 women and 7 men. Their details are summarised in Table 1. The senior author (BH) operated on all cases, and there were no complications. Needle EMG showed no activity in amplitude or conduction velocity, which confirmed complete paralysis in all patients. Groups were comparable for age, time of injury, and follow-up (Table 1).

Comparison of the restoration of movement showed significant differences, with women achieving higher rates of recovery (Table 2). To study the possible influence of age and duration of paralysis in recovery, we compared the mean value of both these variables in women who recovered and those who did not and in men who recovered and those

Table 2
Recovery of movement in patients whose facial paralysis had lasted more than 2 years. Significantly more women than men had recovered some movement. Data are number of patients.

Operation	Women ($n = 19$)	Men ($n = 7$)	p value
Cross-face nerve graft			
No recovered	8/10	0/4	0.02
Transposition of hypoglossal nerve			
No recovered	9/9	1/3	0.04

Table 1
Details of patients and outcomes. There were no significant differences between men and women for any variable. Data are mean (SD) unless otherwise stated.

Operation and other variables	Women ($n = 19$)	Men ($n = 7$)	p value
No with cross-face nerve graft >2 years	10	4	
Age (years)	42 (6)	44 (5)	0.83
Time (months since paralysis)	34 (8)	32 (6)	0.72
Duration of follow-up (months)	29 (8)	29 (7)	0.78
No with transposed hypoglossal nerve >2 years	9	3	
Age (years)	41 (8)	38 (5)	0.71
Time (months since paralysis)	42 (12)	30 (3)	0.09
Duration of follow-up (months)	33 (12)	38 (19)	0.57

Fig. 1. Case 3: a 37 year-old woman who had an operation on her brainstem in 2002 that resulted in paralysis of the left VII, IX, X, and XI cranial nerves. In December 2006 she consulted us about reanimation. She presented with an inability to lift her left eyebrow, no commissural excursion, and deviation of the right nasal tip. We treated this with transfer of the hemihypoglossal nerve to an ipsilateral zygomatic branch. At follow-up she was satisfied with the results obtained. Preoperative appearance: at rest (A) and smiling (B). Two years postoperatively: at rest (C) and smiling (D).
Source: All photographs published with the permission of the patient.

who did not, and they did not differ significantly. Once we started to realise that men with longstanding paralysis did not recover, we stopped using these techniques for them. It would have been unethical to continue submitting our male patients to a procedure that we knew did not work properly. Instead they were reanimated using other techniques (Fig. 1).

Discussion

Whenever a nerve is injured its normal morphology and function are severely altered. In the proximal stump the neuron switches from a "signalling mode" to a "growing mode", while there is Wallerian degeneration in the distal stump with breakdown of myelin and proliferation of Schwann cells.[11] Under ideal circumstances, the rate of axonal growth is 1 mm/day,[12] but the final success of a nerve's regeneration is highly dependent on what happens in the interstump zone.

Prolonged denervation of the distal segment results in fibrosis, and muscles that are denervated for a year develop non-functional motor end plates and this leads to irreversible atrophy.[13–15] Even though our treatment protocol follows these premises, clinical observation and experimental evidence of sexual dimorphism in functional recovery has led us to use some procedures that are indicated for short-term paralysis beyond their recommended time in women. It is important to emphasise that this was not decided in a straightforward manner but indicates the gradual evolution of our clinical observations.

At first, we attempted to extend the indication for hemihypoglossal nerve transfer for a few months beyond the current recommendations, so women with paralysis of 2.5–3 years' duration had the operation, leading to a remarkable recovery of movement and tone. We then extended the indication for hemihypoglossal nerve transfer to women with more prolonged denervation (up to 5 years in some cases) and, once we realised that it actually worked and that the patients

were satisfied with the results, we attempted to do the same with cross-face nerve grafting. At this point, even though we found that some women recovered tone and movement, the results were suboptimal and patients usually ended up needing further operations to achieve adequate reanimation. We no longer did cross-face nerve grafting.

In parallel, we found that men with prolonged denervation recovered neither tone nor movement with either technique and in consequence we opted for other techniques. The fact that our female and not our male patients with denervation of more than 2 years' duration have been able to recover tone, or movement, or both, with these operations suggests that some form of sexual dimorphism exists in the development of muscle atrophy after denervation and on the surgical rehabilitation of a paralysed face.

During regeneration of nerves, motor end plates become deprived of input and remain viable for a period that, in facial paralysis, has been established at 2 years.[7,8] Beyond this limit there is irreversible muscle atrophy. In the present study we have provided clinical evidence that women tend to retain function for longer than men, but the biological explanation of this phenomenon has not yet been investigated. Studies in rats have thrown some light on the issue, but the results have not been reproduced in humans so far. We cannot know for certain if the differences observed are the result of more effective nerve regeneration in women, greater resistance to irreversible atrophy at the neuromuscular junction, or both. Further studies are needed to elucidate the underlying cause.

Evidence that supports the fact that women recover from neural injury faster than men is abundant.[16–20] Regeneration or degeneration of nerves depend greatly on the interaction between the proximal and distal stump. It is likely that female nerves "defend" better from injury and regenerate faster because of more effective cell support in the distal segment.[21] The finding that macrophage activity is more effective in women supports this idea, as it is essential for the removal of axonal debris, axonal elongation, and remyelination.[22] But what makes female nerves superior in terms of regeneration? Sex hormones might be the key.

Regeneration of nerves is influenced by several factors, of which gonadal hormones might be crucial. Of particular interest is the role of progesterone. Several studies have shown that progesterone is ubiquitous in the central and peripheral nervous systems; it stimulates axonal growth and accelerates the myelinating process directly. Interestingly, in female rodents, progesterone concentrations in peripheral nerves are higher and cause greater proliferation of Schwann cells than in men,[23] which suggests that remyelination after neural injury is a sex-related process. Terzis and Noah noticed a trend towards earlier onset in female patients in a clinical series of free muscle transplantation for reconstruction after facial paralysis.[24] Two years postoperatively male patients showed a significantly lower rate of motor unit potential. Forootan et al. reported the case of a 21-year-old woman with long standing facial paralysis who recovered tone and movement after cross-face nerve grafting alone.[25]

Do female patients regenerate nerves more effectively or do they have a higher resistance to injury to begin with? In our experience, in cases of prolonged denervation, women have a greater capacity to recover tone and movement without the need for a new muscular unit. Consequently, after careful and individualised evaluation, we have used techniques that were originally described for the treatment of short-standing paralysis for patients with longstanding disease, and achieved significantly better functional and aesthetic results in women. The concept of sexual dimorphism in reanimation after facial paralysis has already been published by our team, and we think that this is further supported by the statistical work conducted in the present study.[17]

It is true that examination of biopsy specimens would have been the most reliable way of showing that women are more resistant to denervation and the development of muscular atrophy. However, we think that our results illustrate this phenomenon indirectly from a clinical point of view. It has traditionally been suggested that 2 years of denervation causes patients with facial paralysis to develop irreversible muscle atrophy. This is why reanimation is best undertaken in such patients by adding a new muscular unit (free muscle transfer). The finding that women (and not men) with long-standing complete paralysis were able to recover movement without the need of a new muscle indicates that some form of sexual dimorphism exists in the rehabilitation of facial palsy.

The main drawbacks of the present study are that it is retrospective and the sample is small. However, designing and conducting a prospective, randomised trial would not be easy. Throughout our experience we have carefully and individually selected our patients with long-standing complete paralysis to have reanimation with cross-face nerve graft or hemihypoglossal transfer, making randomisation practically impossible. As far as sample size is concerned, the main point of our finding is that it precludes us from recruiting any more men. Clinical observation and statistical data show us that men with long-term paralysis do not recover adequately after either operation, and in consequence we cannot continue to try to reanimate the faces of these patients with techniques that we know are ineffective.

Finally, how should our results be interpreted? The main purpose of our work is to communicate our finding that, in cases of long-term facial paralysis, women and not men are capable of recovering facial tone and movement with techniques traditionally indicated for short-term palsy, and this suggests that irreversible muscle atrophy secondary to prolonged denervation is a sex-related process. It is important to emphasise that this is not a work about surgical techniques, but a comparison of the sexes. Our aim is not to provide recommendations on nerve transfer or cross-face nerve grafting in patients with prolonged denervation, but to inform about the dichotomy between the sexes that we have systematically observed throughout our experience. The biological processes underlying this remain unknown, and must be thoroughly studied.

Conflict of interest

None declared.

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