# Pathways of Sensory Recovery after Face Transplantation

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**Background:** Severely disfiguring facial injuries have a devastating impact on the patient's quality of life. The advent of facial allotransplantation has allowed optimal anatomical reconstruction to be achieved; however, the need for lifelong immunosuppression and unpredictable functional outcomes preclude it from routine acceptance in clinical practice. Evidence from published reports on the first four face transplant recipients indicates improved and accelerated return of sensation to the facial allograft despite suboptimal repair of the sensory nerves.

**Methods:** The authors performed a comparative analysis of the sensory outcomes following face transplantation with the sensory recovery achieved after conventional nerve repair, autologous face and scalp replantation, and vascularized free tissue transfer.

**Results:** Sensory recovery following face transplantation, even when the sensory nerves were not repaired, was comparable to the outcome of microsurgical repair of the peripheral branches of the trigeminal nerve and innervated free flaps.

**Conclusions:** Nearly normal sensory recovery can be expected following facial allotransplantation with or without repair of the sensory nerves. The mechanisms responsible for this surprising outcome include preservation of normal density of the receptors within the facial allograft, regeneration from the recipient bed and allograft margins, transmission of the sensory inputs through afferent fibers contained in the facial nerve, nervi nervorum of the facial nerve, or trigeminofacial communicating rami. Furthermore, immunosuppressive therapy with tacrolimus contributes to the accelerated nerve regeneration. The minimum requirements for quantitative sensory testing and timing of the follow-up assessments are outlined to facilitate comparison of sensory outcomes after face transplantation. (*Plast. Reconstr. Surg.* 127: 1875, 2011.)

In recent years, composite tissue allotransplantation has offered a unique opportunity for optimal restoration of facial anatomy and function in patients presenting with massive and disfiguring facial defects. Return of normal function is a critical determinant of transplant success and is essential to justify a favorable risk-to-benefit balance in view of the long-term side effects of immunosuppression and concerns about integration and psychological acceptance of the donor face. It should be further emphasized that recovery of fine facial movements is fundamental for sphincterial control, prevention of ectropion and drooling, and facilitation of normal speech; whereas normal sensation is critical for interaction with the environment, initiation of defense mechanisms, and deriving pleasure and satisfaction from the external stimuli. The motor and sensory pathways of the human face interact closely, and these interactions are essential for normal facial functions. Although the recovery of facial motor function has been studied extensively, the mechanisms of sensory return are not well established because of the lack of standard methods of assessments of facial sensory recovery after trauma. The available reports on the first four face transplant patients confirm a steady and consistent improvement of sensation, despite suboptimal repair of the sensory nerves.

*From the Dermatology and Plastic Surgery Institute, Cleveland Clinic.*
*Received for publication September 27, 2010; accepted November 8, 2010.*

DOI: 10.1097/PRS.0b013e31820e90c3

**Disclosure:** *The authors have no financial interest to declare in relation to the content of this article. This work has been supported with institutional funds.*

To fulfill the existing gap in the literature, the focus of this review is to present different mechanisms and pathways of sensory recovery and factors that contribute to optimal sensory outcomes after face transplantation. Understanding of sensory recovery pathways in the setting of face transplantation should be of value to all physicians involved in counseling and care of potential candidates for facial transplantation.

## MATERIALS AND METHODS

### Search Strategy and Selection Criteria

We considered the following clinical conditions that could bring insight to the mechanisms of facial sensory recovery: (1) repair of the severed peripheral branches of the trigeminal nerve, (2) autologous vascularized tissue transfers commonly used in head and neck reconstruction, and (3) autologous scalp and face replantation. Access to the International Registry on Hand and Composite Tissue Transplantation was obtained. A comprehensive PubMed and Ovid MEDLINE search was performed in the English literature for peer-reviewed articles published between 1940 and 2010. The keywords used in the search are listed in Table 1. Articles relevant to the topic were selected from the reference list of the reviewed articles as well. In addition, a Google search was performed using "face transplantation" and "allotransplantation" as key words.

### Statistical Analysis

To compare the sensory outcomes in different clinical conditions, the sensory return was graded using the Medical Research Council Scale as modified by Mackinnon and Dellon[1] based on the evaluation of light touch, pain, and two-point discrimination (Table 2). The Wilcoxon sum of ranks test was used to detect significant differences in the sensory recovery of innervated and noninnervated free flaps, innervated and noninnervated free fasciocutaneous flaps, and innervated and noninnervated free radial forearm flaps.

**Table 2. Medical Research Council Scale as Modified by Mackinnon and Dellon***

| Score | Interpretation |
|---|---|
| S0 | No recovery |
| S1 | Recovery of deep cutaneous pain |
| S2 | Return of some superficial pain/tactile sensation |
| S2+ | Return of some superficial pain/tactile sensation with overreaction |
| S3 | Return of some superficial pain/tactile sensation without overreaction and the presence of static two-point discrimination >15 mm |
| S3+ | As per S3 with good localization of stimulus, static two-point discrimination = 7–15 mm |
| S4 | As per S3+, static two-point discrimination = 2–6 mm |

*Mackinnon SE, Dellon AL. *Surgery of the Peripheral Nerve.* 1st ed. New York: Thieme Medical Publishers; 1988.

## RESULTS

### Sensory Recovery after Repair of Peripheral Branches of the Trigeminal Nerve

Thirteen publications summarizing assessment of neurosensory outcomes following repair of the peripheral branches of the trigeminal nerve were relevant to the study. These reports addressed the outcomes after repair of the inferior alveolar, lingual, infraorbital, and mental nerves that were damaged during orthognathic surgery or facial trauma. The population of patients in most of the studies was not uniform for either the type of nerve repaired or the type of procedure used for nerve repair. These procedures included external neurolysis, internal neurolysis, and nerve repair using either direct neurorrhaphy or interpositional nerve grafting. The presented outcomes were not based on the method of nerve repair. Although all reports used quantitative sensory testing as a method of sensory assessment, the outcomes were mainly expressed as a "degree of improvement" in the global sensation in contrast to the expected quantitative results. Only four studies, presenting detailed results of objective neurosensory tests, were available following repair of a completely transected nerve (Table 3).[2–5] The Medical Research Council Scale could be applied

**Table 1. Key Words Used for Literature Search**

| Clinical Scenario | Key Words |
|---|---|
| Nerve repair | "Trigeminal nerve," "supraorbital nerve," "infraorbital nerve," "mental nerve," "lingual nerve," "inferior alveolar nerve plus nerve repair," "microsurgery," "neurorrhaphy" |
| Autologous vascularized tissue transfer | "Innervated," "noninnervated free flaps plus sensory reinnervation," "sensory recovery plus facial," "orofacial," "oral" "oropharyngeal reconstruction" |
| Scalp and face replantation | "Scalp replantation," "scalp avulsion plus sensory recovery" |
| Face transplantation | "Face transplantation," "face allotransplantation plus sensory recovery" |

**Table 3. Sensory Recovery following Repair of the Sensory Nerves of the Face**

| Reference | No. of Cases | Age (yr) | Injured Nerve | Procedure | Surgical Delay (mo) | MRC Scale Score | Follow-Up (mo) |
|---|---|---|---|---|---|---|---|
| Robinson and Smith, 1996[2] | 13 | 31 | Lingual | Direct suture | 16 | S3+ | 17 |
| Robinson et al., 2000[3] | 53 | 30 | Lingual | Direct suture | 15 | S3+ | 12 |
| Hillerup and Stoltze, 2007[4] | 67 | 30 | Lingual | Direct suture | 8.5 | NA | 13 |
| Tay et al., 2008[5] | 3 | 27 | Inferior alveolar | Direct suture | 0 | S4 | 12 |

MRC, Medical Research Council; NA, not applicable.

to three series. These clinical studies confirmed that after an average of 14 months, direct repair of facial sensory nerves results in a functional sensory recovery ranging between S3+ and S4 on the Medical Research Council Scale.

## Sensory Recovery after Free Tissue Transfer

Of 20 reviewed studies, 13 described noninnervated flaps, including radial forearm, lateral thigh, anterolateral thigh, latissimus dorsi, trapezius, rectus abdominis musculocutaneous, fibula osteocutaneous, jejunal, and gastroomental flaps (Table 4).[6–18] In contrast, seven studies reported results of innervated free flaps, including radial forearm, anterolateral thigh, and rectus abdominis musculocutaneous flaps (Table 5).[7,8,12,13,17,19,20] For scoring, the Medical Research Council Scale was applicable to 11 series of patients in the noninnervated flap group and six series of patients in the innervated flap group. Considering the median Medical Research Council Scale values in

**Table 4. Sensory Recovery following Reconstruction of Defects in the Head and Neck Region with Noninnervated Free Flaps**

| Reference | Free Flap | No. of Cases | Average Age (yr) | Indication, Site | Radiotherapy | MRC Scale Score | Average Follow-Up (mo) |
|---|---|---|---|---|---|---|---|
| Lähteenmäki et al., 1989[6] | Dorsalis pedis flap | 1 | 31 | ND, face | ND | S3 | 36 |
| | Latissimus dorsi flap | 2 | 40 | ND, face | ND | S2 | 39 |
| | Trapezius flap | 1 | 25 | ND, face | ND | S0 | 28 |
| Boyd et al., 1994[7] | Radial forearm flap | 10 | 56 | Cancer, oral cavity | 10 | S2 | 14 |
| Katou et al., 1995[8] | Radial forearm flap | 9 | 62 | Cancer, oral cavity | ND | NA | 25 |
| Close et al., 1995[9] | Radial forearm flap | 4 | 62 | Cancer, oral cavity | 3 | S3+ | 18 |
| | Lateral thigh flap | 4 | 53 | Cancer, oral cavity | 3 | S3+ | 7 |
| Shindo et al., 1995[10] | Radial forearm flap | 9 | ND | Cancer, orofacial | 8 | S3 | 10 |
| | Fibula osteocutaneous flap | 9 | ND | Cancer, orofacial | ND | S2 | 13 |
| Vriens et al., 1996[11] | Radial forearm flap | 40 | 60 | Cancer, oral cavity | 28 | S3+ | 38 |
| Kimata et al., 1999[12] | Anterolateral thigh flap | 6 | 58 | Cancer, oral cavity | ND | S1 | 12 |
| | Rectus abdominis musculocutaneous flap | 10 | 57 | Cancer, oral cavity | ND | S1 | 27 |
| Yu, 2004[13] | Anterolateral thigh flap | 5 | 60 | Cancer, tongue | 5 | S1 | 15 |
| Avery et al., 2006[14] | Subfascial radial forearm flap | 20 | 68 | Cancer, oral cavity | ND | S3 | ≥6 |
| | Suprafascial radial forearm flap | 20 | 58 | Cancer, oral cavity | ND | S3 | ≥6 |
| Kerawala et al., 2006[15] | Osteofascial radial forearm flap | 12 | 65 | ND, mandible | 7 | S2 | 38 |
| | Radial forearm flap | 38 | | ND, oral cavity | 17 | S3 | |
| Shibahara et al., 2006[16] | Radial forearm flap | 30 | 60 | Cancer, oral cavity | 0% | NA | 50 |
| Kim et al., 2008[17] | Radial forearm flap | 12 | 55 | Cancer, oral and oropharyngeal | ND | S2 | 6 |
| Sabesan et al., 2008[18] | Radial forearm flap | 24 | 57 | Cancer, oral cavity | 28 | S3 | 12 |
| | Jejunal flap | 10 | | Cancer, lateral pharyngeal wall | | S3 | |
| | Gastroomental flap | 6 | | Cancer, tongue base | | S2 | |

ND, not determined; NA, not available.

**Table 5. Sensory Recovery following Reconstruction of Defects in the Head and Neck Region with Innervated Free Flaps**

| Reference | Free Flap | Nerves Repaired | No. of Cases | Average Age (yr) | Indication, Site | Radiotherapy | MRC Scale Score | Average Follow-Up (mo) |
|---|---|---|---|---|---|---|---|---|
| Boyd et al.,1994[7] | Radial forearm | Lateral antebrachial cutaneous, lingual | 8 | 55 | Cancer, oral cavity | 8 | S4 | 11 |
| Katou et al., 1995[8] | Radial forearm | Lateral antebrachial cutaneous, lingual | 4 | 34 | Cancer, oral cavity | ND | NA | 13 |
| Santamaria et al., 1999[19] | Radial forearm | Lateral antebrachial cutaneous, lingual ($n = 16$), inferior alveolar ($n = 6$), posterior auricular ($n = 3$), cervical plexus ($n = 2$), hypoglossal ($n = 1$) | 28 | 45 | Cancer, tongue | 9 | S4 | 18 |
| Kimata et al., 1999[12] | Anterolateral thigh | Lateral antebrachial cutaneous nerve of the thigh, lingual | 8 | 63 | Cancer, oral cavity | ND | S3+ | 18 |
| | Rectus abdominis musculocutaneous | 2 anterior cutaneous branches of the intercostal, lingual | 5 | 60 | Cancer, oral cavity | ND | S3+ | 14 |
| Kuriakose et al., 2001[20] | Radial forearm | Antebrachial cutaneous, lingual | 17 | 51 | Cancer, oral cavity | 8 | S3+ | 23 |
| Yu, 2004[13] | Anterolateral thigh | Lateral femoral cutaneous, lingual | 6 | 62 | Cancer, tongue | 6 | S4 | 16 |
| Kim et al., 2008[17] | Radial forearm | Antebrachial cutaneous, lingual ($n = 14$), cervical plexus branch ($n = 1$) | 15 | 55 | Cancer, oral and oropharyngeal | ND | S3+ | 6 |

ND, not determined.

these series, in noninnervated flaps, sensory recovery was graded S2+ at a mean follow-up of 33 months. In contrast, coaptation of sensory nerves of the flaps with sensory nerves at the recipient site improved significantly ($p = 0.0004$) the quality of sensation, and functional sensation (S3+) was achieved at a mean follow-up of 15 months. A similar outcome was observed when innervated and noninnervated fasciocutaneous flaps ($p = 0.002$) or innervated and noninnervated radial forearm flaps ($p = 0.013$) were used for reconstruction.

### Sensory Recovery after Scalp and Face Replantation

We reviewed 11 publications presenting results of sensory recovery following replantation of scalp and forehead in 34 patients (Table 6).[21–31] However, the Medical Research Council Scale could not be applied to any of these reports, as the assessment methods was not specified or did not include all three basic determinants (i.e., touch, pain, and two-point discrimination) required by the Medical Research Council Scale.

In these series, sensory nerves were repaired in seven of 34 patients and the two-point discrimination was assessed at 15 mm at 2-year follow-up. In the remaining 27 patients, despite the fact that no nerve repair was performed, four patients had full or nearly full recovery of sensation, seven patients recovered light touch, and seven patients reported protective sensation. "Acceptable" sensibility was reported in six patients. In the remaining three patients, the two-point discrimination threshold was higher than normal: 37.6 versus 23.2 mm for the parietal scalp and 27.6 versus 22.3 mm and for the occipital scalp.

### Sensory Recovery after Facial Transplantation

The results of sensory recovery were published for four face transplant recipients. Relevant patient data are detailed in Table 7.[32–37] Sensory nerves were repaired directly in only one patient.[32,33] In one patient, repair of the sensory nerves was technically difficult because of the shortness of the recipient's nerve stumps: the repair of the infraorbital nerves required fibrin glue and the mental nerves were not repaired.[35] In two patients, repair of sensory nerves of the allograft (infraorbital nerves) was not feasible because of trauma-related nerve damage.[34,36]

The first face transplant patient[32,33] (Fig. 1) followed an early sensory reeducation and cortical

**Table 6. Sensory Recovery following Scalp Replantation**

| Reference | No. of Cases | Mean Age (yr) | Site | Nerve Repair | Outcome Measure | Outcome | Follow-Up (mo) |
|---|---|---|---|---|---|---|---|
| Cheng et al., 1996[21] | 7 | 26 | Scalp, ear, forehead | 7 | 2-PD | 15 mm | 24 |
| Ueda et al., 2000[22] | 1 | 55 | Right parietal and occipital scalp; right forehead skin; part of the right cheek and the right ear | No | Semmes-Weinstein test | 2.44 | 36 |
| Nahai et al., 1985[23] | 6 | 31 | Scalp, ear, forehead | No | ND | Protective sensibility | ND |
| Yin et al., 2008[24] | 1 | 35 | Scalp, forehead, right eyebrow | No | ND | Protective sensibility, no function frontalis | 36 |
| Cho et al., 2000[25] | 5 | 25 | Scalp | No | 2-PD | Supraorbital, 13.5 mm; forehead, 24 mm; parietal scalp, 39 mm; occipital scalp, 29.5 mm | 42 |
| Chen and Wan, 1996[26] | 4 | 24 | Scalp | No | ND | Light touch | 6–12 ($n = 2$) ND ($n = 2$) |
| Chou et al., 1992[27] | 2 | 39 | Scalp, forehead | No | ND | Light touch (forehead), deep pain (vertex) | 6 |
| Fogdestam and Lilja, 1986[28] | 1 | 9 | Scalp, forehead | No | ND | Recovery of sensibility | 6 |
| Zhou et al.[29] | 1 | 33 | Scalp, forehead, eyebrows | No | ND | Full recovery of sensation | 6 |
| Topalan and Ermis, 2001[30] | 1 | 15 | Scalp | No | ND | Light touch | 6 |
| Sabapathy et al., 2006[31] | 5 | 24 | Scalp, forehead | No | ND | Acceptable recovery of sensation | 6–9 |

2-PD, two-point discrimination; ND, not determined.

reintegration protocol. The initial signs of sensory recovery were recorded at 2 weeks for thermal stimuli. At 10 weeks, sensory return was present at the lateral part of the upper lip and lateral area of the chin on both sides of the graft. At 14 weeks, sensory recovery was found over the entire facial graft, including the tip of the nose, and response to painful stimuli was registered as well. After 6 months, pressure thresholds were normal in the upper half of the graft, whereas in the lower half, the patient reported diminished light touch. Heat and cold sensation was nearly normal at 4 months and normal at 6 months.

In the second transplant patient[34] (Fig. 2), sensory discrimination was restored at 3 months, whereas heat and cold sensations were recorded over the entire graft at 8 months following transplantation.

The third patient[35] (Fig. 3) had return of thermal and mechanical sensation 3 months after transplantation and improvement of the sensory thresholds at 12 months.

The fourth patient[36,37] (Fig. 4) started sensory reeducation 48 hours after surgery, once per day for the first 6 weeks, then 3 times per week during follow-up. She recovered pain discrimination over a period of 5 months, and at 6 months the sensation returned to the entire transplanted face, with an average two-point discrimination of 7 mm (S3+) (Fig. 5).

## Factors Contributing to Sensory Recovery

### Recipient and Donor Characteristics

Clinical studies of vascularized autologous tissue transfer have shown that several factors can affect sensory recovery in the facial region. Anatomical location of the recipient site plays an important role, because sensory recovery within the orofacial region is better as opposed to trunk and lower extremity reconstruction.[15,38,39] Several studies have shown that sensory upgrading (improved two-point discrimination compared with the donor site) can occur when flaps harvested from regions of lower innervation density are transferred to the orofacial regions. This has been explained by wider cortical representation of the human face.[7]

Scarring of the recipient bed delays and hinders nerve regeneration.[40,41] Composition of the flaps could either facilitate or delay sensory return. Presence of a skin component within the flap has been associated with improved sensory return, whereas muscle or bone components have been found to create a barrier for potential neurotiza-

**Table 7. Summarized Clinical Data of the Four Face Transplant Patients with Documented Long-Term Follow-Up**

| Recipient | | | | Repaired Nerves | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Age (yr), Sex | Tissue Loss (Cause) | Status before Transplantation | Donor Age, Sex | Motor Nerves | Sensory Nerves | Postoperative Sensory Reeducation | Outcome Measure | Follow-Up, Function | MRC Scale Score |
| 38, F[32,33] | Distal nose, full-thickness upper and lower lips, chin, adjacent parts of right and left cheek (dog bite) | Preserved integrity of the proximal stumps of the zygomatic and levator anguli oris muscles; mouth opening 19 mm, surgical delay 6 mo; no previous reconstruction | 46, F | Facial nerve: mandibular branch (left side) end to end; right side unrepaired because of scar | Mental nerves: right and left sides end to end<br>Infraorbital nerve: right and left sides end to end | Yes | Pressure thresholds (Semmes-Weinstein test)<br>Heat and cold sensation (method not reported) | 2.5 mo, lateral part upper lip, lateral mental area; 3.5 mo, whole skin surface including tip of nose; 4 mo, heat and cold sensation almost normal (normal at 6 mo) | NA |
| 30, M[34] | Extensive skin and soft-tissue loss in the right buccal division, upper lip, total nose, front wall of the right maxillary sinus, lateral right orbital wall, infraorbital wall, right zygomatic bone, and large portion of right parotid gland (bear attack) | Severe cicatricial contracture deformity; first reconstruction radial forearm free flap, waited 17 mo before definitive reconstruction | 25, male | Facial nerve: repair reported not satisfactory | Infraorbital nerve: not repaired | ND | Pressure thresholds (Semmes-Weinstein test)<br>Heat and cold sensation (method not reported) | 3 mo, sensory discrimination; 8 mo, heat and cold sensation | NA |
| 29, M[35] | Massive plexiform neurofibroma middle and lower part of face | Complete facial paralysis (right side), partial paralysis (left side); immediate reconstruction | ND | Facial nerve: both nerves sutured and glued | Infraorbital nerve: both nerves sutured and glued<br>Mental nerve: not repaired but just placed in front of the foramen | ND | Not reported | 3 mo, sensory reinnervation of skin for thermal, mechanical sensation; 4 mo, pain sensation; 12 mo, improvement in sensory thresholds | NA |
| 45, F[36,37] | Absence of nose, nasal lining, and underlying bone; contracted remnants of upper lip; loss of orbicularis oris and orbicularis oculi muscle functions; distorted and scarred lower eyelids (close-range shotgun blast) | 23 previous reconstructive procedures; surgical delay to face transplantation, 51 mo | ND | Facial nerve; interpositional nerve graft from donor vagus nerve (right side); interpositional nerve graft from donor hypoglossal (left side) | Infraorbital nerve; not available for repair | Yes | Pressure thresholds (Pressure-Specified Sensory Device; Sensory Management Services, LLC, Baltimore, Md.)<br>Two-point discrimination (Disk-Criminator; Kom Kare Company, Middletown, Ohio)<br>Temperature (Hot and Cold Discrimination Kit; TRIRICE, Oak Park, Mich.) | 5 mo, sensation to pinprick; 6 mo, sensory discrimination over entire flap | S3+ |


**Fig. 1.** (*Above, left*) Drawing depicting the first face transplant patient. The outline of the allograft is shown. (*Above, right*) Different tissue components of the allograft are highlighted. (*Below*) Schematic representation of the details of sensory and motor nerve repair. *IoN*, infraorbital nerve; *FN*, facial nerve; *MN*, mental nerve; *DAO*, depressor anguli oris; *LLS*, levator labii superioris; *LLSAN*, levator labii superioris alaeque nasi; *N*, nasalis; *OOr*, orbicularis oris; *QLI*, quadratus labii inferioris; *R*, risorius; *ZMj*, zygomaticus major; *ZMi*, zygomaticus minor. (Reprinted with permission from the Cleveland Clinic Center for Medical Art & Photography © 2010. All rights reserved.)

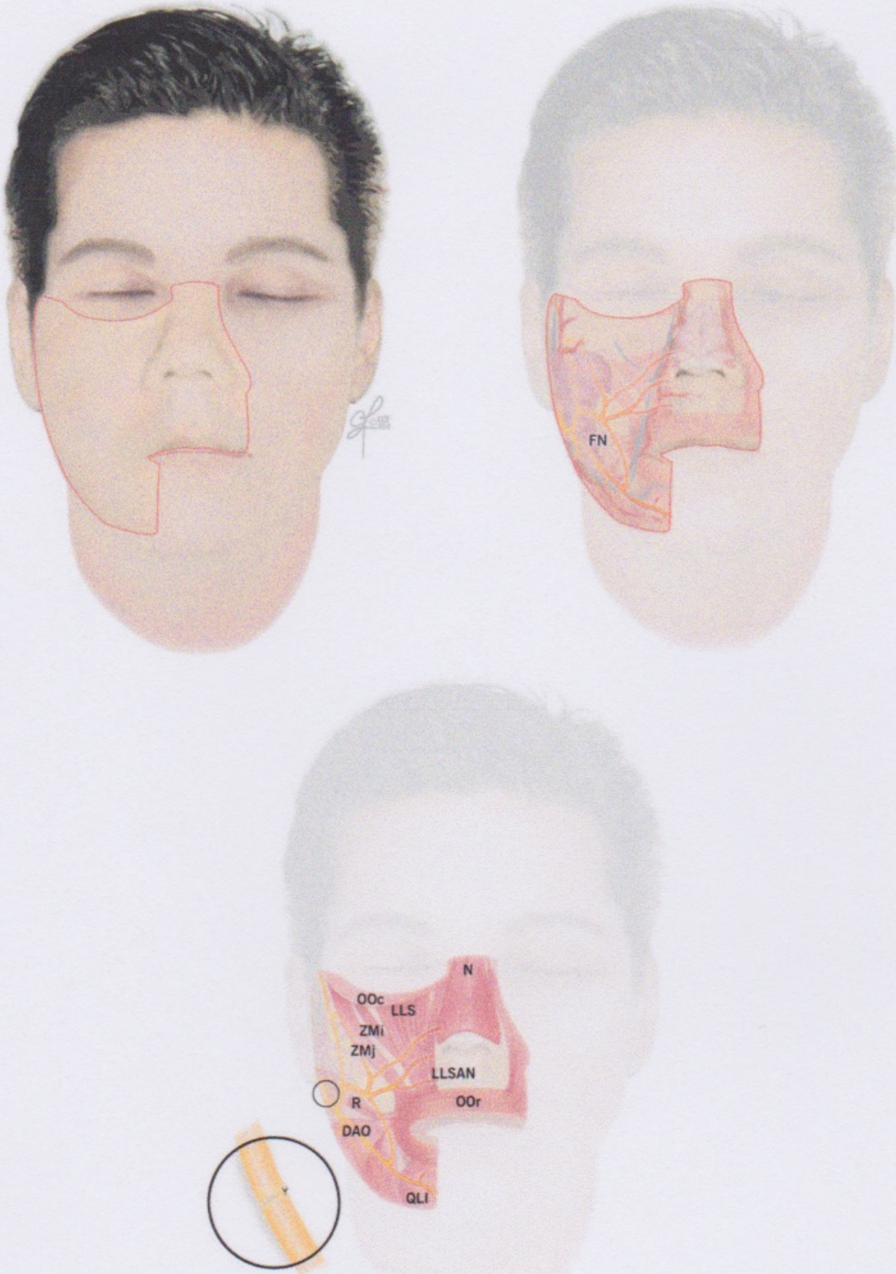


**Fig. 2.** (*Above, left*) Drawing depicting the second face transplant patient. The outline of the allograft is shown. (*Above, right*) Different tissue components of the allograft are highlighted. (*Below*) Schematic representation of the details of sensory and motor nerve repair. *FN*, facial nerve; *DAO*, depressor anguli oris; *LLS*, levator labii superioris; *LLSAN*, levator labii superioris alaeque nasi; *N*, nasalis; *OOc*, orbicularis oculi; *OOr*, orbicularis oris; *QLI*, quadratus labii inferioris; *R*, risorius; *ZMj*, zygomaticus major; *ZMi*, zygomaticus minor. (Reprinted with permission from the Cleveland Clinic Center for Medical Art & Photography © 2010. All rights reserved.)


**Fig. 3.** (*Above, lef*) Drawing depicting the third face transplant patient. The outline of the allograft is shown. (*Above, right*) Different tissue components of the allograft are highlighted. (*Below*) Schematic representation of the details of sensory and motor nerve repair. *IoN*, infraorbital nerve; *FN*, facial nerve; *DAO*, depressor anguli oris; *LLS*, levator labii superioris; *LLSAN*, levator labii superioris alaeque nasi; *N*, nasalis; *OOc*, orbicularis oculi; *OOr*, orbicularis oris; *QLI*, quadratus labii inferioris; *R*, risorius; *ZMj*, zygomaticus major; *ZMi*, zygomaticus minor. (Reprinted with permission from the Cleveland Clinic Center for Medical Art & Photography © 2010. All rights reserved.)


**Fig. 4.** (*Above, left*) Drawing depicting the fourth face transplant patient. The outline of the allograft is shown. (*Above, right*) Different tissue components of the allograft are highlighted. (*Below*) Schematic representation of the details of sensory and motor nerve repair. *FN*, facial nerve; *DAO*, depressor anguli oris; *LLS*, levator labii superioris; *LLSAN*, levator labii superioris alaeque nasi; *N*, nasalis; *OOc*, orbicularis oculi; *OOr*, orbicularis oris; *R*, risorius; *ZMj*, zygomaticus major; *ZMi*, zygomaticus minor. (Reprinted with permission from the Cleveland Clinic Center for Medical Art & Photography © 2010. All rights reserved.)

tion coming from the recipient bed.[42] Thickness of the flap could impair sensory return, even in the absence of muscular or bony components.[38] In thin flaps such as the noninnervated radial forearm flap used for orofacial reconstruction, remarkable spontaneous return of sensation has been observed[15]; however, significantly better results have been recorded for innervated versus noninnervated flaps.[7] In noninnervated vascularized tissue transfers, reinnervation seems to occur

**Fig. 5.** Drawings depicting the first U.S. face transplant recipient. Progressive recovery of tactile and calorimetric sensation evaluation over the face at 1 month (*above, left*), 3 months (*above, right*), 6 months (*below, left*), and 12 months (*below, right*) after transplantation. *Violet*, absent sensation; *pink*, recovered sensation. (Reprinted with permission from the Cleveland Clinic Center for Medical Art & Photography © 2010. All rights reserved.)

by ingrowth of the nerves from the recipient bed and from the flap's margins and along the neural sheaths within transferred tissues.[33,41]

### Immunosuppressive Therapy with Tacrolimus

The immunosuppressive protocol with tacrolimus confers a potential advantage for nerve regeneration, as observed in limb allografts. It was reported that tacrolimus increased the rate of axonal regeneration in a dose-dependent manner[43] and influenced collateral sprouting of peripheral nerve fibers.[44] It was also confirmed that tacrolimus doubles the number of regenerating axons after nerve injury, increases the number of myelinated axons by 40 percent, and significantly augments myelin thickness.[45] In addition, tacrolimus reduces by half the time needed for neuronal recovery after repair of nerve lesions.[46,47]

The immunosuppressive treatment protocol used in the first successful hand transplantation included tacrolimus, which facilitated median and ulnar nerve regeneration and promoted sensory and motor recovery.[48] The rate of nerve regeneration as indicated by an advancing Tinel sign was faster than expected, and it was estimated to progress at approximately 2 to 3 mm/day.[49]

## Pathways of Sensory Recovery

### Trigeminofacial Communications

Afferent fibers found in the communicating rami between trigeminal and facial nerves appear to contribute to the deep sensibility or proprioception of the face[50] (Fig. 6, *2*). The impulses conveying cutaneous sensation, which travel with the trigeminal nerve, contribute to the appreciation of facial movements.[51] Therefore, there is a close relationship between the two systems. In the absence of impulses from the trigeminal nerve, the afferents of the facial nerve could contribute to the return of perception of position and deep pressure sensation and thus may directly play a role in transmission of superficial touch and pain sensation.

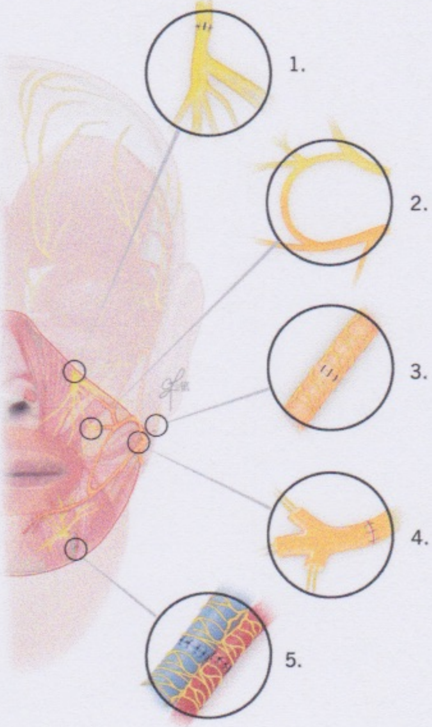


**Fig. 6.** Pathways of sensory recovery in face transplantation are summarized. (*1*) Direct sensory nerve growth through microsurgical nerve repair. (*2*) Trigeminofacial communications. (*3*) Nervi nervorum of the facial nerve. (*4*) Somatic afferents of the facial nerve. (*5*) Adrenergic plexus of the vascular pedicle. (Reprinted with permission from the Cleveland Clinic Center for Medical Art & Photography © 2010. All rights reserved.)

### Nervi Nervorum of the Facial Nerve

The third neural pathway that may contribute to sensory recovery of the face is represented by nervi nervorum (Fig. 6, *3*). All cranial nerves are richly innervated by their own nerves, known as nervi nervorum, which are derived from the nerve trunk fibers and are known to have nociceptive function.[52] It was confirmed that stimulation of the nervi nervorum of the facial nerve trunk can be transmitted to the trigeminocervical complex.[53] However, whether these nerves can mediate somatic or referred pain has to be confirmed.

### Somatic Afferents of the Facial Nerve

The facial nerve contains somatic fibers, collecting the sensation of the external auditory meatus and posterior surface of the ear. Distal to the level where these components have left the nerve trunk, the sensory fibers are sparse. However, a sensory component within the facial nerve is still present, which is mediating deep facial sensation such as pressure, pressure pain, and muscle sense (Fig. 6, *4*). The presence of this component explains preservation of deep facial sensation after trigeminal neurectomy.[54,55] This was confirmed in physiologic studies using a cat model.[56] In the same model, the existence of purely sensory fibers was confirmed in three major peripheral facial nerve branches.[57]

The pattern of sensory recovery in noninnervated free flaps occurs usually from the periphery to the center,[7,58–60] whereas in innervated flaps the reverse occurs, with reinnervation proceeding along the distribution of the sensory nerve.[61] In face transplants, the observed direction of sensory return was from the periphery to the central portion of the allograft, and it paralleled the direction of facial nerve regeneration. Therefore, this directionality may be consequent to sensory reinnervation along the somatic afferents of the facial nerve as well.

### Adrenergic Plexus of the Vascular Pedicle

The adrenergic fibers present in the skin innervate the erector pili muscles and form an extensive network around the vessels. After transfer of free vascularized tissues, there is an ingrowth of the adrenergic fibers from the graft margins, from the wound bed, and along the artery and the vein, forming a rich neural plexus around the vascular pedicle of the flap (Fig. 6, *5*). The number of single nerve fibers invading the flap around the margins decreases over time, whereas more nerves have been observed around the arteries and arterioles.[62] The restoration of sympathetic innervations of the skin contributes to restoration of thermal regulation mechanisms of the graft.

## DISCUSSION

Face transplantation is a novel experimental procedure and as such it is still reserved for a highly selected population of patients who have exhausted all conventional means of reconstruction and are left with severe facial disfigurement. Therefore, the first reported face transplantations have been performed in the setting of distorted facial anatomy and function. The functional outcome of these first cases will have an important impact on the future development of this complex procedure. In three of four cases with long-term follow-up, repair of the sensory nerves was less than optimal or could not be performed because of the severity of original trauma or disease. Because many candidates for face transplantation present with extensive facial injury where damage of the recipient nerves is irreversible, it was our aim to estimate how sensory recovery will progress under these unfavorable conditions and how this will impact the final functional outcome.

Based on the results of our comparative analysis, we can conclude that, in the absence of extensive soft-tissue injury, simple repair of facial sensory nerves leads to restoration of nearly normal sensation. After tissue avulsion or extensive trauma, despite repair of the sensory nerves, the outcomes are suboptimal, although some sensory return can be expected (e.g., face and scalp replantation). When tissues other than facial tissues are transferred to the facial region from different anatomical sites of the body, good functional sensory recovery can be achieved only when the sensory nerves of the transferred flaps are connected to the sensory nerves of the recipient site. Interestingly, face transplantation is the only clinical condition where, in the absence of sensory nerve repair, good functional outcome is achieved despite severe trauma causing soft-tissue and sensory nerve damage.

An important issue that emerged from the comprehensive review of the literature is an evident lack of universal methods of neurosensory assessment and an urgent need for establishment of guidelines that will help with comparative analysis of the sensory recovery data. This applies to the reported cases of face transplantation, where documentation of sensory recovery is either marginal or overlooked.

We found that the Medical Research Council Scale as modified by Mackinnon and Dellon[1] provided an objective and simple method that allows for assessment and comparative analysis of results from different centers.[63] Therefore, to facilitate comparison of results of sensory recovery, we propose that investigators working with face transplant patients will routinely assess the following measures: pressure thresholds,[64,65] pain thresholds, and two-point discrimination. The follow-up visits for quantitative sensory testing should be scheduled at least once per month for the first 6 months, every 3 months during the first year, and every 6 months thereafter or until a plateau of sensory recovery is reached. Finally, because inclusion of a sensory training program during postoperative care has proved to affect significantly the outcomes following orthognathic surgery[66] and toe-to-hand transfer,[67] sensory rehabilitation protocols should be included in the postoperative management of face transplant patients, and the details of results should be disclosed. Establishment of unified standards of sensory assessment will aid in the functional evaluation of future cases of face transplantation.

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## REFERENCES

1. Mackinnon SE, Dellon AL. *Surgery of the Peripheral Nerve.* 1st ed. New York: Thieme Medical Publishers; 1988.
2. Robinson PP, Smith KG. A study on the efficacy of late lingual nerve repair. *Br J Oral Maxillofac Surg.* 1996;34:96–103.
3. Robinson PP, Loescher AR, Smith KG. A prospective, quantitative study on the clinical outcome of lingual nerve repair. *Br J Oral Maxillofac Surg.* 2000;38:255–263.
4. Hillerup S, Stoltze K. Lingual nerve injury: II. Observations on sensory recovery after micro-neurosurgical reconstruction. *Int J Oral Maxillofac Surg.* 2007;36:1139–1145.
5. Tay AB, Poon CY, Teh LY. Immediate repair of transected inferior alveolar nerves in sagittal split osteotomies. *J Oral Maxillofac Surg.* 2008;66:2476–2481.
6. Lähteenmäki T, Waris T, Asko-Seljavaara S, Sundell B. Recovery of sensation in free flaps. *Scand J Plast Reconstr Surg Hand Surg.* 1989;23:217–222.
7. Boyd B, Mulholland S, Gullane P, et al. Reinnervated lateral antebrachial cutaneous neurosome flaps in oral reconstruction: Are we making sense? *Plast Reconstr Surg.* 1994;93:1350–1359; discussion 1360–1362.
8. Katou F, Shirai N, Kamakura S, et al. Intraoral reconstruction with innervated forearm flap: A comparison of sensibility and reinnervation in innervated versus noninnervated forearm flap. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1995; 80:638–644.
9. Close LG, Truelson JM, Milledge RA, Schweitzer C. Sensory recovery in noninnervated flaps used for oral cavity and

oropharyngeal reconstruction. *Arch Otolaryngol Head Neck Surg.* 1995;121:967–972.
10. Shindo ML, Sinha UK, Rice DH. Sensory recovery in noninnervated free flaps for head and neck reconstruction. *Laryngoscope* 1995;105:1290–1293.
11. Vriens JP, Acosta R, Soutar DS, Webster MH. Recovery of sensation in the radial forearm free flap in oral reconstruction. *Plast Reconstr Surg.* 1996;98:649–656.
12. Kimata Y, Uchiyama K, Ebihara S, et al. Comparison of innervated and noninnervated free flaps in oral reconstruction. *Plast Reconstr Surg.* 1999;104:1307–1313.
13. Yu P. Reinnervated anterolateral thigh flap for tongue reconstruction. *Head Neck* 2004;26:1038–1044.
14. Avery CM, Iqbal M, Hayter JP. Recovery of sensation in the skin of non-innervated radial flaps after subfascial and suprafascial dissection. *Br J Oral Maxillofac Surg.* 2006;44:213–216.
15. Kerawala CJ, Newlands C, Martin I. Spontaneous sensory recovery in non-innervated radial forearm flaps used for head and neck reconstruction. *Int J Oral Maxillofac Surg.* 2006;35:714–717.
16. Shibahara T, Mohammed AF, Katakura A, Nomura T. Long-term results of free radial forearm flap used for oral reconstruction: Functional and histological evaluation. *J Oral Maxillofac Surg.* 2006;64:1255–1260.
17. Kim JH, Rho YS, Ahn HY, Chung CH. Comparison of sensory recovery and morphologic change between sensate and nonsensate flaps in oral cavity and oropharyngeal reconstruction. *Head Neck* 2008;30:1099–1104.
18. Sabesan T, Ramchandani PL, Ilankovan V. Sensory recovery of noninnervated free flap in oral and oropharyngeal reconstruction. *Int J Oral Maxillofac Surg.* 2008;37:819–823.
19. Santamaria E, Wei FC, Chen IH, Chuang DC. Sensation recovery on innervated radial forearm flap for hemiglossectomy reconstruction by using different recipient nerves. *Plast Reconstr Surg.* 1999;103:450–457.
20. Kuriakose MA, Loree TR, Spies A, Myers S, Hicks WL Jr. Sensate radial forearm free flaps in tongue reconstruction. *Arch Otolaryngol Head Neck Surg.* 2001;127:1463–1466.
21. Cheng K, Zhou S, Jiang K, et al. Microsurgical replantation of the avulsed scalp: Report of 20 cases. *Plast Reconstr Surg.* 1996;97:1099–1106; discussion 1107–1108.
22. Ueda K, Nomatsi T, Omiya Y, Tajima S. Replanted scalp recovers normal sensation without nerve anastomosis. *Plast Reconstr Surg.* 2000;106:1651–1652.
23. Nahai F, Hester TR, Jurkiewicz MJ. Microsurgical replantation of the scalp. *J Trauma* 1985;25:897–902.
24. Yin JW, Matsuo JM, Hsieh CH, Yeh MC, Liao WC, Jeng SF. Replantation of total avulsed scalp with microsurgery: Experience of eight cases and literature review. *J Trauma* 2008;64:796–802.
25. Cho BC, Lee DH, Park JW, Byun JS, Baik BS. Replantation of avulsed scalps and secondary aesthetic correction. *Ann Plast Surg.* 2000;44:361–366.
26. Chen IC, Wan HL. Microsurgical replantation of avulsed scalps. *J Reconstr Microsurg.* 1996;12:105–112.
27. Chou CK, Lin SD, Yang CC, Lai CS, Lin GT. Microsurgical replantation of avulsed scalp: Two cases report. *Gaoxiong Yi Xue Ke Xue Za Zhi* 1992;8:285–289.
28. Fogdestam I, Lilja J. Microsurgical replantation of a total scalp avulsion: Case report. *Scand J Plast Reconstr Surg.* 1986;20:319–322.
29. Zhou S, Chang TS, Guan WX, et al. Microsurgical replantation of the avulsed scalp: Report of six cases. *J Reconstr Microsurg.* 1993;9:121–125; discussion 125–129.
30. Topalan M, Ermis I. Replantation and triple expansion of a three-piece total scalp avulsion: Six-year follow-up. *Ann Plast Surg.* 2001;46:167–169.
31. Sabapathy SR, Venkatramani H, Bharathi RR, D'Silva J. Technical considerations in replantation of total scalp avulsions. *J Plast Reconstr Aesthet Surg.* 2006;59:2–10.
32. Devauchelle B, Badet L, Lengelé B, et al. First human face allograft: Early report. *Lancet* 2006;368:203–209.
33. Dubernard JM, Lengelé B, Morelon E, et al. Outcomes 18 months after the first human partial face transplantation. *N Engl J Med.* 2007;357:2451–2460.
34. Guo S, Han Y, Zhang X, et al. Human facial allotransplantation: A 2-year follow-up study. *Lancet* 2008;372:631–638.
35. Lantieri L, Meningaud JP, Grimbert P, et al. Repair of the lower and middle parts of the face by composite tissue allotransplantation in a patient with massive plexiform neurofibroma: A 1-year follow-up study. *Lancet* 2008;372:639–645.
36. Siemionow M, Papay F, Alam D, et al. Near-total human face transplantation for a severely disfigured patient in the USA. *Lancet* 2009;374:203–209.
37. Siemionow MZ, Papay F, Djohan R, et al. First U.S. near-total human face transplantation: A paradigm shift for massive complex injuries. *Plast Reconstr Surg.* 2010;125:111–122.
38. Lähteenmäki T, Waris T, Asko-Seljavaara S, Astrand K, Sundell B, Järvilehto T. The return of sensitivity to cold, warmth and pain from excessive heat in free microvascular flaps. *Scand J Plast Reconstr Surg Hand Surg.* 1991;25:143–150.
39. Santanelli F, Tenna S, Pace A, Scuderi N. Free flap reconstruction of the sole of the foot with or without sensory nerve coaptation. *Plast Reconstr Surg.* 2002;109:2314–2322; discussion 2323–2324.
40. Hermanson A, Dalsgaard CJ, Arnander C, Lindblom U. Sensibility and cutaneous reinnervation in free flaps. *Plast Reconstr Surg.* 1987;79:422–427.
41. Turkof E, Jurecka W, Sikos G, Piza-Katzer H. Sensory recovery in myocutaneous, noninnervated free flaps: A morphologic, immunohistochemical, and electron microscopic study. *Plast Reconstr Surg.* 1993;92:238–247.
42. Sönmez A, Bayramiçli M, Sönmez B, Numanoğlu A. Reconstruction of the weight-bearing surface of the foot with nonneurosensory free flaps. *Plast Reconstr Surg.* 2003;111:2230–2336.
43. Wang MS, Zeleny-Pooley M, Gold BG. Comparative dose-dependence study of FK506 and cyclosporin A on the rate of axonal regeneration in the rat sciatic nerve. *J Pharmacol Exp Ther.* 1997;282:1084–1093.
44. Udina E, Voda J, Gold BG, Navarro X. Comparative dose-dependence study of FK506 on transected mouse sciatic nerve repaired by allograft or xenograft. *J Peripher Nerv Syst.* 2003;8:145–154.
45. Sulaiman OA, Voda J, Gold BG, Gordon T. FK506 increases peripheral nerve regeneration after chronic axotomy but not after chronic schwann cell denervation. *Exp Neurol.* 2002;175:127–137.
46. Sosa I, Reyes O, Kuffler DP. Immunosuppressants: Neuroprotection and promoting neurological recovery following peripheral nerve and spinal cord lesions. *Exp Neurol.* 2005;195:7–15.
47. Gold BG. FK506 and the role of the immunophilin FKBP-52 in nerve regeneration. *Drug Metab Rev.* 1999;31:649–663.
48. Dubernard JM, Owen E, Herzberg G, et al. Human hand allograft: Report on first 6 months. *Lancet* 1999;353:1315–1320.
49. Bain JR. Peripheral nerve and neuromuscular allotransplantation: Current status. *Microsurgery* 2000;20:384–388.

50. Baumel JJ. Trigeminal-facial nerve communications: Their function in facial muscle innervation and reinnervation. *Arch Otolaryngol.* 1974;99:34–44.
51. Trulsson M, Johansson RS. Orofacial mechanoreceptors in humans: Encoding characteristics and responses during natural orofacial behaviors. *Behav Brain Res.* 2002;135:27–33.
52. Thomas PK. The anatomical substratum of pain: Evidence derived from morphometric studies on peripheral nerve. *Can J Neurol Sci.* 2004;31:398–403.
53. Han DG. Pain around the ear in Bell's palsy is referred pain of facial nerve origin: The role of nervi nervorum. *Med Hypotheses* 2010;74:235–236.
54. Carmichael EA, Woolard HH. Some observations on the fifth and seventh cranial nerves. *Brain* 1933;56:109–125.
55. Ley A, Guitart JM. Clinical observations on sensory effects of trigeminal dorsal root section. *J Neurol Neurosurg Psychiatry* 1971;34:260–264.
56. Davis LE. The deep sensibility of the face. *Arch Neurol Psychiatry* 1923;9:283–305.
57. Thomander L, Arvidsson J, Aldskogius H. Distribution of sensory ganglion cells innervating facial muscles in the cat: An anatomical study with the horseradish peroxidase technique. *Acta Otolaryngol.* 1982;94:81–92.
58. Tindholdt TT, Tønseth KA. Spontaneous reinnervation of deep inferior epigastric artery perforator flaps after secondary breast reconstruction. *Scand J Plast Reconstr Surg Hand Surg.* 2008;42:28–31.
59. Place MJ, Song T, Hardesty RA, Hendricks DL. Sensory reinnervation of autologous tissue TRAM flaps after breast reconstruction. *Ann Plast Surg.* 1997;38:19–22.
60. Blondeel PN, Demuynck M, Mete D, et al. Sensory nerve repair in perforator flaps for autologous breast reconstruction: Sensational or senseless? *Br J Plast Surg.* 1999;52:37–44.
61. Schultes G, Gaggl A, Kärcher H. Neuronal anastomosis of the cutaneous ramus of the intercostal nerve to achieve sensibility in the latissimus dorsi transplant. *J Oral Maxillofac Surg.* 2000;58:36–39.
62. Lähteenmäki T. The regeneration of adrenergic nerves in a free microvascular groin flap in the rat. *Scand J Plast Reconstr Surg.* 1986;20:183–188.
63. Dodson TB, Kaban LB. Recommendations for management of trigeminal nerve defects based on a critical appraisal of the literature. *J Oral Maxillofac Surg.* 1997;55:1380–1386; discussion 1387.
64. Bell-Krotoski J, Tomancik E. The repeatability of testing with Semmes-Weinstein monofilaments. *J Hand Surg Am.* 1987;12:155–161.
65. Dellon AL, Andonian E, DeJesus RA. Measuring sensibility of the trigeminal nerve. *Plast Reconstr Surg.* 2007;120:1546–1550.
66. Essick GK, Phillips C, Kim SH, Zuniga J. Sensory retraining following orthognathic surgery: Effect on threshold measures of sensory function. *J Oral Rehabil.* 2009;36:415–426.
67. Graham B, Dellon AL. Sensory recovery in innervated free-tissue transfers. *J Reconstr Microsurg.* 1995;11:157–166.

# Discussion: Pathways of Sensory Recovery after Face Transplantation

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On December 9, 2008, the reconstructive transplant team at the Cleveland Clinic realized several decades of preparation and performed the first face transplantation in the United States. More importantly, the patient ended 4 years of failed partial reconstructions and was able to begin rehabilitating after complete restoration of her soft-tissue and bony defect. In this article, Siemionow et al. detail the sensory recovery achieved with this transplant despite the lack of a direct nerve repair. They compare this return of function with the outcomes reported in the literature for autologous reconstruction. Moreover, they highlight the outcomes in the reported cases of face transplantation, all of whom have had different sensory nerve reconstructions.

Their patient was a 45-year-old woman who had a composite defect of her midface after a shotgun injury. She had what is considered the state-of-the-art reconstruction using autologous flaps. Despite this, she continued to have functional limitations and remained disfigured. She underwent a composite facial allotransplantation, which was based on a Le Fort III template. Bilateral facial nerves were anastomosed using interpositional grafts, but the sensory branches of the trigeminal nerve could not be anastomosed.[1]

She received sensory reeducation 48 hours after surgery. At 5 months, she had pain perception and was able to discriminate 7 mm by 6 months. Progression of sensory nerve recovery was graded using the Medical Research Council Scale, which evaluates light touch, pain, and two-point discrimination. Based on their literature review, noninnervated reconstructions using autologous tissue did not approach the sensory return that was achieved with their transplant. In fact, these patients could at best feel only superficial pain and tactile sensation, with no true ability to discriminate two points. Moreover, the transplant recipient's recovery compared favorably and even exceeded the sensory return in patients who had repair of an injured trigeminal nerve, an innervated free flap, or even an innervated scalp replant.

The authors propose several possible mechanisms that may contribute to their findings. There may be sensory upgrading caused by placement on the face because of its higher cortical representation. This may not apply to a facial allograft. However, tacrolimus may have some beneficial effect on nerve regeneration and recovery. Because their sensory return paralleled the recovery of the facial nerve, the authors postulate that trigeminofacial nerve communications and the complex interplay between the facial nerve afferents and the trigeminal complex may contribute to their findings. In several animal models, facial motor nerve recovery has been shown to be dependent on an intact sensory system.[2,3] It would be interesting to compare the motor recovery of the transplant recipients who have had reconstruction of their sensory branches and received early sensory rehabilitation.

Each face transplant has been different. This is attributable to the nature and extent of the initial injury and the numerous reconstructive procedures performed before transplantation.[4–6] Consequently, many of these patients have not had their sensory nerves repaired. In the series presented, the only direct sensory nerve repair for the entire allograft was performed in the first transplant patient from France. However, the others have all shown remarkable return of sensation. Each group has reported pain and temperature sensation and return of light touch demonstrated by cutaneous pressure thresholds. Dr. Siemionow's group reports their outcomes based on the Medical Research Council Scale, a system that facilitates ready comparison between groups based

*From the Department of Plastic Surgery, University of Texas Southwestern Medical Center.*
*Received for publication December 13, 2010; accepted December 15, 2010.*

DOI: 10.1097/PRS.0b013e31820e88c9

**Disclosure:** *The author has no financial interest to declare in relation to the content of this Discussion or of the associated article.*

on established metrics. Given the intrinsic variability in the technical aspects of these operations, it is critical to adopt a grading system with fixed time points to advance the field.

Another factor limiting comparison and study of face transplant recipients is the differences in the postoperative protocols. For instance, the therapeutic range of tacrolimus, which has beneficial effects on nerve regeneration, varies between the groups. Differences in the maintenance immunosuppression and induction protocols may also affect acute rejection episodes, and this may limit overall graft function and delay rehabilitation. Face and hand transplant recipients, unlike solid organ transplant patients, have the ability to affect the functional outcome of their allograft. Consequently, an early and aggressive program may facilitate improved graft function. The Cleveland Clinic patient underwent aggressive speech therapy, range-of-motion exercises, and sensory reeducation as early as 48 hours after the transplantation. This contributed to her excellent return of function and acceptance of the graft. It would be instructional if the group could publish a detailed protocol for their rehabilitation program. Also, it would be interesting to follow changes in the functional magnetic resonance imaging scans with their program.

This is an exciting time for the field of reconstructive transplantation, with at least 10 face transplants in the world performed thus far. The authors have shown excellent recovery of sensory function to a greater extent and earlier than conventional reconstructive procedures. This in addition to the unmatched motor and cosmetic reconstruction argues for consideration of face transplantation earlier in the reconstructive algorithm of these disfigured patients. The morbidity of immunosuppression, however, continues to limit the widespread acceptance and use of face transplantation. Advances in the field will depend on the minimization of these drugs or the development of novel immunosuppressive agents.

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## REFERENCES

1. Siemionow M, Papay F, Alam D, et al. Near-total human face transplantation for a severely disfigured patient in the USA. *Lancet* 2009;374:203–209.
2. Pavlov SP, Grosheva M, Streppel M, et al. Manually-stimulated recovery of motor function after facial nerve injury requires intact sensory input. *Exp Neurol.* 2008;211:292–300.
3. Streppel M, Popratiloff A, Angelov DN, et al. Significance of trigeminal sensory input on regrowth of hypoglossal and facial motoneurons after hypoglossal facial anastomosis in rats. *Acta Otolaryngol.* 1998;118:790–796.
4. Lantieri L, Meningaud JP, Grimbert P, et al. Repair of the lower and middle parts of the face by composite tissue allotransplantation in a patient with massive plexiform neurofibroma: A 1-year follow-up study. *Lancet* 2008;372:639–645.
5. Guo S, Han Y, Zhang X, et al. Human facial allotransplantation: A 2-year follow-up study. *Lancet* 2008;372:631–638.
6. Dubernard JM, Lengelé B, Morelon E, et al. Outcomes 18 months after the first human partial face transplantation. *N Engl J Med.* 2007;357:2451–2460.