Does use of a myoelectric prosthesis prevent cortical reorganization and phantom limb pain?

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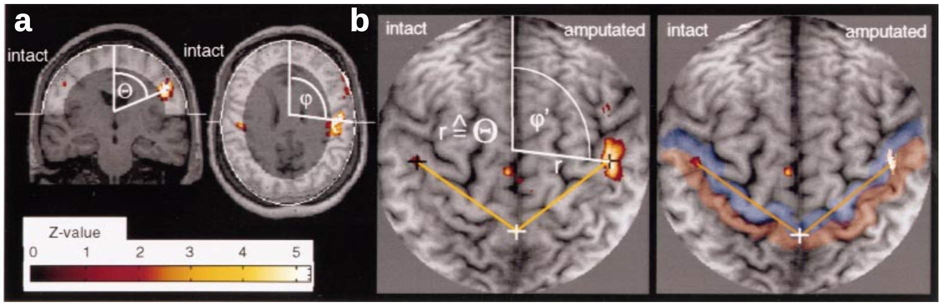
Injury, stimulation or training can induce changes in the homuncular organization of primary somatosensory (S1) and motor cortex (M1)[1–6]. Phantom limb pain was identified as a perceptual correlate of this cortical reorganization[2,7]. Using functional magnetic resonance imaging (fMRI), we found that enhanced use of a myoelectric prosthesis in upper extremity amputees was associated with reduced phantom limb pain and reduced cortical reorganization. Extensive use of a myoelectric prosthesis might have beneficial effects on phantom limb pain.

Fourteen unilateral upper-limb amputees whose amputation occurred 3–53 years before the investigation were examined with fMRI while they moved the lip. A 1.5-Tesla Siemens Scanner was used for echo planar imaging (EPI, matrix 96 × 128; field of view 250 mm; TE 59 ms; scan time 7 s) of the whole brain in 36 3-mm thick transverse slices spaced at 1 mm. Forty-eight measurements (six each, alternating four times during movement and rest) were acquired. Additionally, a T1-weighted anatomical 3D-dataset was evaluated (192 sagittal slices, thickness 1.5 mm; matrix 224 × 256, field of view 250 mm; TR 9.7 ms). Correction for movement artifact, coregistration of functional and structural images, smoothing with a 4 mm Gaussian filter and statistical analysis (z-value cut-off limit, uncorrected, $p \leq 0.01$; additional extension threshold, $p \leq 0.05$) was carried out using SPM96 (Wellcome Center of Cognitive Neuroscience). Cortical reorganization was assessed by comparing the location and the extent of the cortical representation of the lip movements in the precentral (M1) and postcentral (S1) gyri of the two hemispheres. A projection method transformed the three-dimensional image onto a two-dimensional circle (Fig. 1). The following fMRI parameters were evaluated: difference of location of activation maxima and center of gravity in the precentral and postcentral gyrus of both hemispheres and number and intensity of activated voxels. The subjects completed a phantom and stump pain version of the West Haven-Yale Multidimensional Pain Inventory (MPI), a comprehensive phantom- and stump-phenomena interview, as well as a prosthesis questionnaire that assessed in detail the amount and intensity of prosthesis use[2]. A research assistant uninformed of the experimental hypothesis subsequently interviewed patients to explore onset of phantom limb pain and prosthesis use as well as reasons for discontinuation of prosthesis use.

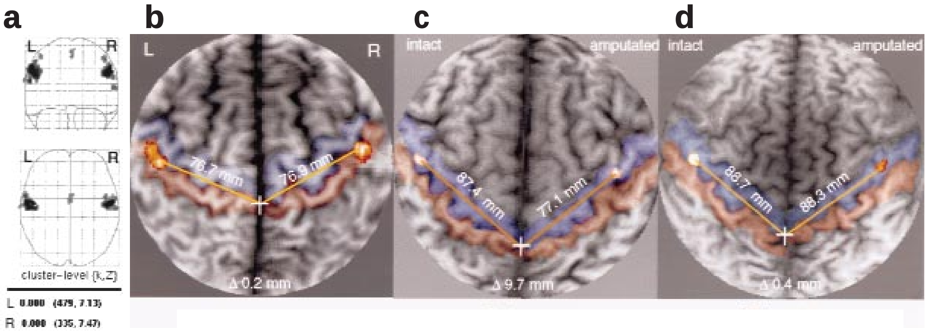
In the hemisphere contralateral to the amputation in the seven amputees with phantom limb pain, activation maxima during lip movement were displaced toward the hand area by 10.67 ± 7.33 mm (s.d.) in S1 and 5.84 ± 3.57 mm in M1 (Table 1 and Fig. 2). In pain-free amputees, the lip location was symmetrical (mean displacement M1:M = 0.35 ± 0.43 mm; S1: M = 0.13 ± 0.33 mm); M1 group difference, $t_{6.18} = 4.04$; $p < 0.01$; S1, $t_{6.03} = 3.79$, $p < 0.01$). Phantom limb pain and displacement of the contralateral lip activation maxima were correlated $r = 0.73$ ($p < 0.005$) for M1 and $r = 0.69$ ($p < 0.01$) for S1. All other measures of cortical reorganization (center of gravity, number of activated voxels) showed similar correlations with phantom limb pain ($r \geq 0.48$) and were positively correlated among each other ($r \geq 0.43$).

Prosthesis use was quantified by multiplying type of prosthesis with wearing time and average usage (Table 1). This procedure yielded one group (MP) that was composed of patients with a myoelectric prosthesis who reported extensive wearing time (≥ 8 h/day) and usage (≥ 50 on a visual analogue scale (VAS) ranging from 0–100) and a second group (NMP) who had either no prosthesis or a cosmetic prosthesis or wore myoelectric prostheses for minimal times (< 8 h/day) and/or usage (< 50 VAS). The NMP group showed an average phantom limb pain intensity of 2.33 ± 1.53, whereas the MP group reported an intensity of 0 ± 0. Type of prosthesis alone did not matter ($F_{2,13} = 0.51$, n.s). The MP group showed a symmetrical lip representation in S1 (average shift, 0 ± 0) compared to an average shift of 8.39 ± 7.81 mm in the NMP group ($t_8 = 3.22$, $p < 0.01$). Reorganization of M1 was 0.32 ± 0.41 mm in the MP and 4.64 ± 3.91 mm in the NMP group ($t_{8.32} = 3.29$, $p < 0.01$). Prosthesis use was significantly negatively correlated with reorganization in S1 ($r = -0.55$, $p < 0.05$) and M1 ($r = -0.53$, $p < 0.05$) and with phantom limb pain ($r = -0.49$, $p < 0.05$). When the effect of cortical reor-



Fitting a shell to an individual cortex   Evaluation of COG localization   Evaluation of AM localization

Fig. 1. Procedure used to determine fMRI displacement in M1 and S1. **(a)** After overlaying the functional and anatomical datasets, an ellipsoid, 2-cm shell of thickness (light gray shaded area) was fitted to the cortical surface. For each point of the ellipsoid, a vector from the center of the brain to the surface of the ellipsoid was calculated. The angles θ and φ define the location of each point on the shell. **(b)** Two-dimensional plane derived from the ellipsoid shell. The point of interest is defined by the two variables r and φ' with $r = \theta$ denoting the distance from the center and $\varphi' = \varphi$ denoting the polar angle referenced to the center. Center of gravity was computed from all activated voxels in the pre- or postcentral gyrus exceeding statistical and extent thresholds of $p \leq 0.01$ and $p \leq 0.05$, respectively. On each hemisphere, distance from the intersection of the interhemispheric fissure and central sulcus to the center of gravity of activation was measured (yellow line). Distances were subsequently compared to determine cortical reorganization. Right, activation maxima (highest activated voxel labeled separately for each hemisphere) in the precentral (blue) and postcentral (red) gyrus were compared between the hemispheres.



SPM maps of 10 controls

ISOVIEW projection of SPM96 normalized brains of 10 controls

Pain, no myoelectric prosthesis, patient #5

No pain, frequent use of myoelectric prosthesis, patient #6

Fig. 2. Lip representation in controls and upper limb amputated patients. **(a)** Normalized SPM96 glass brain (overlay of 10 subjects in an overview through the whole brain) of ten right-handed control subjects during repetitive lip pursing (cut-off level, $p \leq 0.0001$; extent threshold, $p \leq 0.05$). Group ordinates of activation maxima were 58, –14, 40 in the right and –52, –8, 36 in the left M1/S1. **(b)** Activation maxima of the normalized data of 10 controls. Side differences for the group data amounted to 0.2 mm in M1 and 1.4 mm in S1. For individuals, the average difference between the left and right activation maxima was 2.36 ± 1.31 mm for M1 and 3.88 ± 3.78 mm for SI. **(c)** Projection of one patient with phantom limb pain (3.5) without myoelectric prosthesis. This patient showed 9.7 mm displacement in M1 and 12.8 mm in S1. **(d)** Patient extensively using myoelectric prosthesis with no phantom pain had no measurable displacement of activation maxima during lip movement in M1 and S1.

ganization was removed by partial correlation, the relationship between phantom limb pain and prosthesis use became nonsignificant ($r = -0.17$), suggesting that pain reduction associated with prosthesis use is mediated by cortical reorganization. The interview revealed that phantom limb pain was experienced within the first two weeks after amputation. Prosthesis use began between 3 months and 16 years after the amputation. Reasons given for discontinuation (typically in the first months after amputation) were preference for the intact arm and/or impracticability of the prosthesis, but never phantom limb or stump pain. All except one patient each in the MP and NMP groups complained of phantom limb pain immediately after the amputation (Table 1). Reduction in phantom limb pain over time was significantly positively correlated with extensive myoelectric prosthesis use ($r_{13} = 0.64, p < 0.01$).

This study showed that frequent and extensive use of a myoelectric prosthesis is correlated negatively with cortical reorganization and phantom limb pain and positively with the reduction in phantom limb pain over time. This suggests that the ongoing stimulation, muscular training of the stump and visual feedback[8] from the prosthesis might have a beneficial effect on both cortical reorganization and phantom limb pain. The converse, that increased phantom limb pain might have motivated patients to decrease prosthesis use, is unlikely because no patient reported increased phantom limb pain with prosthesis use or gave stump or phantom limb pain as reason for discontinuing prosthesis use. Our data are in accordance with animal experiments suggesting that behaviorally relevant tactile stimulation expands the cortical representation of the stimulated body region[5,6]. Our data strongly suggest that extended use of a myoelectric prosthesis might reduce both cortical reorganization and phantom limb pain, a still relatively treatment-resistant disorder[9].

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Table 1. Demographic and clinical data of the amputees in the study grouped according to prosthesis use.

	No extensive myoelectric prosthesis use										Extensive myoelectric prosthesis use					
Subject	7	9	8	14	5	1	3	10	4	Mean ± s.d.	2	6	11	13	12	Mean ± s.d.
Amputated hand[1]	nd	nd	nd	nd	d	d	nd	d	d	—	d	d	d	d	d	—
Age	28	56	31	62	78	35	31	63	58	49.11 ± 18.10	26	32	60	35	66	43.8 ± 17.94
Years since amputation	3	30	7	48	53	19	11	3	27	22.33 ± 18.71	9	7	7	3	15	5.4 ± 3.29
Prosthetic type[2]	2	2	1	1	1	0	0	0	0	—	2	2	2	2	2	—
Time wearing prosthetic[3]	8	4	16	16	3	0	0	0	0	5.22 ± 6.66	16	16	12	16	16	15.2 ± 1.79
Prosthetic usage[4]	42	9	61	38	25	0	0	0	0	19.44 ± 23.00	100	100	100	71	58	85.8 ± 19.98
Phantom limb pain[5]	3	4	4	0	2	0	2	3	4	2.33 ± 1.53	0	0	0	0	0	0 ± 0
Stump pain[6]	0	0	4	0	1	0	0	1	0	0.57 ± 1.21	0	0	0	0	0.7	0.13 ± 0.3
Initial phantom pain[5]	5	6	5	0	2	4	2	3	4	3.33 ± 1.79	6	3.5	0	4.8	4.8	3.82 ± 2.31
M1 displacement-AM[7]	0	7	7	0	10	1	2	7	9	4.64 ± 3.91	0.2	0.4	0	0	1	0.32 ± 0.41
S1 displacement-AM[7]	0	9	24	0	13	1	13	7	9	8.39 ± 7.81	0	0	0	0	0	0 ± 0

[1]d, dominant; nd, nondominant hand. [2]no prosthesis, 0; cosmetic prosthesis, 1; myoelectric prosthesis, 2. [3]not at all, 0; all the time, 16. [4]usage of prosthesis in VAS (usage 0–100% in daily living, homemaking and work outside home). [5]Phantom limb pain intensity based on the MPI Pain Intensity Scale (range, 0–6). [6]Stump pain intensity based on the MPI Pain Intensity Scale (range, 0–6). [7]Displacement of activation maxima (AM) of the contralateral lip representation in M1 and S1.