New Type of Cortical Neuroplasticity After Nerve Repair in Brachial Plexus Lesions

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**Background:** In brachial plexus avulsion, a recent technique connects the ending of the disrupted musculocutaneous nerve to the side of the intact phrenic nerve to regain elbow flexion. This requires the phrenic nerve to perform a new double function: independent control of breathing and elbow flexion. Neuroplastic changes associated with acquisition of double nerve functions have not yet been investigated.

**Objective:** To evaluate neuroplastic changes associated with acquisition of double nerve functions in a monofunctional nerve (phrenic nerve).

**Design:** Clinical and functional magnetic resonance imaging investigations during arm movements, forced inspiration, and motor control tasks.

**Setting:** Investigations at the Medical University of Vienna, Vienna, Austria.

**Participants:** Three healthy control subjects, 2 patients with phrenic nerve end-to-side coaptation, and 1 control patient with C7 end-to-end coaptation (same clinical presentation but phrenic nerve unchanged).

**Results:** Clinical documentation showed that both patients with phrenic nerve end-to-side coaptation were able to control the diaphragm and the biceps independently via the same phrenic nerve. In contrast to all controls, both patients with phrenic nerve end-to-side coaptation activated the cortical diaphragm areas with flexion of the diseased arm.

**Conclusion:** Our functional magnetic resonance imaging data indicate that the patient’s cortical diaphragm areas reorganize in such a way that independent control of breathing and elbow flexion is possible with the same neuronal population.

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 PATIENTS

The control patient was a right-handed boy aged 6 years at the time of a traumatic left complete brachial plexus lesion. He had end-to-end coaptation of (1) contralateral root C7 to (2) the musculocutaneous nerve 5 months after trauma. Left elbow flexion was possible against light resistance at the time of fMRI (6.5 years after surgery).

Patient 1 was a right-handed woman aged 29 years at the time of a traumatic right complete brachial plexus lesion. She had end-to-side coaptation of (1) the ipsilateral phrenic nerve to (2) the musculocutaneous nerve 5 months after trauma. Right elbow flexion was possible against medium resistance at the time of fMRI (2.5 years after surgery).

Patient 2 was a right-handed man aged 43 years at the time of a traumatic left complete brachial plexus lesion. He had end-to-side coaptation of (1) the ipsilateral phrenic nerve to (2) the musculocutaneous nerve 5 months after trauma. Left elbow flexion was possible against medium resistance at the time of fMRI (7 years after surgery). A general case description including preliminary data analysis is included in the article by Beisteiner et al.8

In both patients with end-to-side nerve repair, the nerve fiber transfer from the phrenic nerve to the musculocutaneous nerve was done using 2 sural nerve grafts coapted end to side to the phrenic nerve and end to end to the musculocutaneous nerve. Every patient provided fully informed consent with a protocol approved by the local ethics committee.

CLINICAL DOCUMENTATION

In the control patient with C7 end-to-end coaptation, chest radiography documented a normal bilateral diaphragm innervation with deep inspiration (Figure 1). Electromyography of the affected biceps muscle demonstrated independence of muscle innervation and breathing (Figure 2B).

In patient 1 with phrenic nerve end-to-side coaptation, video recording showed a lack of biceps contractions with deep inspiration or coughing and no change of breathing patterns with elbow flexion. Chest radiography documented bilateral diaphragm innervation with deep inspiration and no elevated diaphragm (Figure 1). Electromyography of the affected biceps muscle demonstrated independence of muscle innervation and breathing.

In patient 2 with phrenic nerve end-to-side coaptation, video recording and fluoroscopy of the thorax showed a lack of biceps contractions with deep inspiration or coughing and a lack of diaphragm innervation with elbow flexion. Chest radiography documented an elevated but innervated diaphragm on the affected side (Figure 1). Electromyography of the affected biceps muscle demonstrated independence of muscle innervation and breathing (Figure 2A). During forced inspiration and coughing, spikes of motor activation appeared in very few parts of the electromyographic recordings.

FUNCTIONAL MRI

Investigations included 4 tasks: (1) elbow flexion of the diseased arm; (2) elbow flexion of the healthy arm; (3) forced abdominal inspiration; and (4) foot flexion on the side of the diseased arm.

Patient 1 with phrenic nerve end-to-side coaptation performed tasks 1 through 4, patient 2 with phrenic nerve end-to-side coaptation and the healthy control subjects performed tasks 1 and 2, and the control patient with C7 end-to-end coaptation performed tasks 1 through 3. Repetitive investigations were performed with 3-T MRI and 7-T MRI (blood oxygen level–dependent gradient echo–echo planar imaging; 34 slices; 128 x 128 matrix; 230 x 230 x 3-mm field of view; generalized autocalibrating partially parallel acquisition factor 2; and repetition time 2500 milliseconds; for 3-T MRI: echo time 35 milliseconds, bandwidth 2220 Hz; for 7-T MRI: echo time 22 milliseconds, bandwidth 1396 Hz). Between 5 and 10 identical runs (blocked design; 4 rest and 3 activation phases; 20
seconds/phase) were performed per task per patient. At least 2 different MRI investigations were performed per patient on different days. The healthy control subjects performed only 1 fMRI investigation at 3 T. Individual data analysis was performed with SPM8 software (Wellcome Trust Centre for Neuroimaging, London, England) (general linear model; uncorrected \( P < .001 \); technique adapted for pathological brains). 

**RESULTS**

Clinical documentation showed that both patients with phrenic nerve end-to-side coaptation were able to control the diaphragm and the biceps independently via the same phrenic nerve: breathing did not change with arm movements (documented by video recording), the affected biceps muscle was not activated with normal breathing (no regular biceps electromyographic activity), and both sides of the diaphragm were innervated during breathing and did not move with elbow flexion (chest radiography, fluoroscopy of the thorax).

The IMRI studies showed bilateral superior activations of the primary motor cortex with forced inspiration (Figure 3). In addition, lateralized midline activations were found in deeper slices. These activations correspond to earlier descriptions of diaphragm representations and normal breathing networks. In contrast to the control patient with C7 end-to-end coaptation, both patients with phrenic nerve end-to-side coaptation activated the diaphragm areas with flexion of the diseased arm. Flexion of the healthy arm and foot did not activate diaphragm areas. Figure 3 shows the significant activation of diaphragm areas with diseased arm flexion in comparison with healthy arm flexion. In addition, the primary arm areas were also activated (lateral from diaphragm areas). All patient findings could be replicated intraindividually and interindividually when repeating experiments on different days and at different magnetic field strengths (3 T, 7 T). Elbow flexion in the healthy control subjects only showed arm areas active—no activity was found in diaphragm areas even when lowering the threshold.

**COMMENT**

As demonstrated by the clinical investigations, the 2 patients with phrenic nerve end-to-side coaptation were able to move their diseased arm independently from their diaphragm via the same phrenic nerve. With respect to these tasks, they were clinically not distinguishable from the control patient with C7 end-to-end coaptation. However, distinction was possible with the IMRI data, which showed activation of diaphragm areas with breathing as well as diseased arm flexion in the patients with phrenic nerve end-to-side coaptation. As expected, there was no diaphragm area activation in the healthy control sub-

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**Figure 2.** Electromyographic (EMG) recordings of the biceps muscles of patient 2 with phrenic nerve end-to-side coaptation (A) and the control patient with C7 end-to-end coaptation (B) with simultaneous monitoring of respiration. Both patients demonstrate absence of muscle involvement during respiration and no correlation of EMG activity with breathing during forced biceps innervation. (Cyclic EMG activations correspond to electrocardiographic activity.)
We conclude that specific cortical neuroplasticity provides the neurophysiological basis for rehabilitation after peripheral end-to-side repair. Data from fMRI indicate effectiveness of this surgical procedure. Neurological practice should consider this option for therapeutic handling of complete plexus lesions.

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REFERENCES