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TITLE:

2 Structured Motor Rehabilitation After Selective Nerve Transfers

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Nerve injury, selective nerve transfers, rehabilitation, physiotherapy, occupational therapy, motor re-education, biofeedback

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SHORT ABSTRACT:

Here, we present a protocol for the motor rehabilitation of patients with severe nerve injuries and selective nerve transfer surgery. It aims at restoring the motor function proposing several stages in patient education, early-stage therapy after surgery and interventions for rehabilitation after successful re-innervation of the nerve's target.

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LONG ABSTRACT:

After severe nerve injuries, selective nerve transfers provide an opportunity to restore motor and sensory function. Functional recovery depends both on the successful re-innervation of the targets in the periphery and on the motor re-learning process entailing cortical plasticity. While there is an increasing number of methods to improve rehabilitation, their routine implementation in a clinical setting remains a challenge due to their complexity and long duration. Therefore, recommendations for rehabilitation strategies are presented with the aim of guiding medical doctors and therapists through the long-lasting rehabilitation process and providing step-by-step instructions for supporting motor re-learning.

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Directly after nerve transfer surgery, no motor function is present, and therapy should focus on

promoting activity in the sensory-motor cortex areas of the paralyzed body part. After about two to six months (depending on the severity and modality of injury, the distance of nerve regeneration and many other factors), the first motor activity can be detected via electromyography (EMG). Within this phase of rehabilitation, multimodal feedback is used to relearn the motor function. This is especially critical after nerve transfers, as muscle activation patterns change due to the altered neural connection. Finally, muscle strength should be sufficient to overcome gravity/resistance of antagonistic muscles and joint stiffness, and more functional tasks can be implemented in rehabilitation.

INTRODUCTION:

Selective nerve transfers provide an opportunity for restoring the motor function after nerve injuries when recovery by the use of neurolysis, nerve repair, or nerve grafting cannot be expected^{1,2}. Possible indications for nerve transfers are severe distal nerve injuries, avulsion-type injuries, the lack of available nerve roots for grafting, the extensive scarring at the injury site and delayed reconstruction^{3,4}. Following motor nerve injury, reconstruction is time-critical as degeneration of muscle tissue and motor end plates only allow for the successful muscle reinnervation within 1-2 years after injury^{5,6}. Here, nerve transfers provide the advantage of a relatively short re-innervation time after surgery, as they allow nerve coaptation close to the target. This procedure, also known as neurotization, involves the surgical redirection of an intact nerve (donor nerve) to the distal part of the recipient nerve. As this connection is distal to the damaged site of the recipient nerve, it allows bypassing the injured nerve segment⁷.

As neural pathways are altered after nerve transfer surgery, patients cannot be treated with standard post-operative therapy protocols otherwise used after direct nerve repair^{8,9}. While donor axons grow into the new target, they take over a function they did not have before while cortically still being connected to their original function. As an example, the Oberlin ulnar nerve transfer is used to restore elbow flexion after irreparable damage to the upper trunk or nerve roots C5 and C6¹. As shown in **Figure 1**, it involves transferring one or more ulnar nerve fascicles to the musculocutaneous motor branch of the biceps muscle¹⁰. However, after the successful reinnervation, these fascicles of the ulnar nerve are cortically still connected to their previous function of finger flexion and/or ulnar abduction and flexion of the wrist. On a functional level this implies that at the beginning of the rehabilitation, the patient needs to focus on the previous nerve function (hand closing) in order to activate and strengthen the recipient muscle (biceps contraction). This approach is also known as "donor activation focused rehabilitation approach"⁹.

[Insert Figure 1 here]

While comprehension of this concept is the foundation of successful rehabilitation, re-learning of new motor patterns can be challenging for patients and clinicians. This is due to the long duration of rehabilitation, the complexity of nerve regeneration and re-innervation and the limited amount of directly observable muscular activity during early re-innervation⁸. Apart from the changes in the peripheral nervous system, there is an increasing awareness among surgeons and therapists for the relevance of changes in the central nervous system (CNS), i.e., reorganization of the hand motor and sensory cortical areas occurring as a consequence to

denervation¹¹. When neural input to the CNS is deprived, the associated cortical area diminishes to a certain extent at the expense of adjacent areas¹². Restoration of function, therefore, depends on the central recovery of its representation in the brain. Within the last years, the use of biofeedback methods⁸ and approaches to support cortical re-organization¹³⁻¹⁵ has led to extended possibilities in rehabilitation after nerve transfers. However, due to the complexity of post-surgical therapy, it is important to provide the right interventions at the right time¹³.

Therefore, the aim of this structured protocol for rehabilitation after selective nerve transfers is to provide a feasible and holistic approach to support motor recovery. It is based on current recommendations and the authors' experience with incorporating it in a clinical setting. The protocol is meant to guide medical doctors, occupational and physical therapists as well as other health professionals through the long-lasting rehabilitation process.

This structured protocol for motor rehabilitation was evaluated in a feasibility study⁸ in five patients with brachial plexus injuries as shown in **Table 1**. All of them received several nerve transfers (some in combination with nerve grafts) to restore upper extremity function. Therefore, for the sake of clarity, when describing specific interventions in this protocol, they refer to the upper limb. In detail, we take the Oberlin ulnar nerve transfer¹⁰ as an example, which was performed in patients 1-3. For this, we refer to parts of the ulnar nerve as being the donor nerve and the musculocutaneous nerve being the recipient nerve. Thus, the biceps and brachialis muscles are the recipient muscles being re-innervated by parts of the ulnar nerve. Functionally, this means that following a donor activation focused approach⁹, movements associated with ulnar nerve activity (such as hand closing or ulnar abduction of the wrist) are used for the activation of the biceps muscle directly after re-innervation. However, exercises based on this approach can be performed in other body parts as well. If special considerations are necessary to implement this in other body parts (e.g., the lower extremity), this is pointed out within the protocol.

Independent from the body part affected, therapy sessions should not exceed 30 min as muscles become easily fatigued shortly after re-innervation⁸ and successful training requires a patient's full commitment and focus.

PROTOCOL:

The study was approved by the local research ethics committee (number: 1009/2014) and carried out in accordance with the Declaration of Helsinki. All patients provided written informed consent to participate in this study.

1. Patient education

1.1. Despite any given previous information to the patient, use the first post-surgical consultation/ therapy session to thoroughly explain the type of injury, as well as, the performed surgery in detail.

133 1.1.1. Visualize the nerve transfers, that were performed, on a scheme or print-out from an anatomy figure.

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136 1.1.2. Explain how the altered neural pathway initially requires thinking of a nerve's original movement pattern.

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1.2. Give the patient a rough rehabilitation plan and an idea of what outcomes might be realisticat what point in time.

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1.3. If the patient suffers from the negative consequences of the injury on a psychological level^{16,17} or needs support in coping with stress or pain, contact a psychologist.

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1.4. Ask the patient to explain the impact of the nerve transfers in their own words to find out how they understood the concept.

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1.4.1. If necessary, repeat certain explanations and answer open questions.

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1.4.1. If the rehabilitation institution has a leaflet with the most important facts, hand this over to the patient (see **Supplementary File** for an example).

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153 1.5. Discuss a home program with the patient.

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1.5.1. Explain that a high frequency of training is important for good outcomes, and thus home exercises are an integral part of rehabilitation.

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1.5.2. Discuss with the patient how he/she thinks this can be best approached. Thus, empower the patient to assume responsibility for his/her own rehabilitation.

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161 1.5.3. Hand out the discussed home exercise program in a written form. Make sure it only contains exercises that were previously performed within a therapy session.

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1.5.4. In order to preserve adherence over time, regularly ask the patient how he/she feels about the home program and discuss how it should be altered to be feasible and meaningful to the patient.

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2. Enhancing cortical re-presentation of the denervated body part

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NOTE: The following rehabilitation techniques promote activation of the denervated motor and sensory cortical areas to regain cortical representation of the paralyzed body part. During this phase no active muscle contraction is possible.

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174 2.1. Follow an approach for the lateralization training (left/right discrimination) as described by
 175 Mosely et al¹⁸.

- 2.1.1. Prepare cards showing left and right extremities in a random order (upper extremity, if the upper extremity is affected and lower extremity for lower extremity nerve injuries). Show them to the patient in a random order.
- 180
 181 2.1.2. Ask the patient if a left or a right extremity is shown. While speed of approximately 2 s/card
 182 is normal¹⁸, give the patient at least 15 s to answer, if needed.
- 184 2.1.3. Give the patient feedback, and if necessary, time to understand why the answer was
 185 wrong.
- 2.1.4. Do this for 5 to 10 min to avoid fatigue. Ask the patient to do this at home as well, twice a
 day for 5-10 min.
- 2.2. Instruct the patient to imagine movements of the paralyzed body part, although no motoroutput is expected.
- 193 2.2.1. Make sure that the patient is in a calm environment without any distraction.

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- 2.2.2. Ask the patient which movements of the paralyzed extremity are easy to imagine.
- 197 2.2.3. Instruct the patient to imagine these movements for about 5 min with the exact timing198 depending on the patient's ability to fully concentrate on these imagined movements.
- 2.2.4. Within the treatment process, instruct the patient to imagine more complex motions aswell.
- 203 2.2.5. As a home exercise, ask the patient to imagine these movements 5 to 10 min, twice a day.
- 205 2.3. Use the mirror therapy to create the illusion of active movement of the paralyzed part 19,20.
- 207 2.3.1. Place a standing mirror or a mirror box in front of the therapist and the patient. Place it on a desk for the upper extremity or on the floor for the lower extremity.
- 2.3.2. Explain that mirror therapy works by making use of the reflection of the sound side to
 create the image of the simultaneous movement of the sound side and denervated extremity^{19,21}.
 Shortly demonstrate this with the therapist's own upper or lower extremity.
- 2.3.3. Place the mirror medially in front of the patient in a way that he/she sees the reflection of the sound side exactly where the injured extremity is expected. Make sure that the whole injured extremity is covered by the mirror (box), i.e., it cannot be seen by the patient.
- 2.3.4. Ask him/her which movements he/she can easily imagine. Instruct the patient to perform
 these movements with the sound side while looking at the mirror. Start with slow movements.

2.3.5. Instruct the patient to move both sides for 5 to 10 min. Explain, that the injured side will
 not move, but that it is still important to generate the illusion of simultaneous movement of both
 sides.

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2.3.6. Within the treatment process, encourage the patient to also perform movements that
 he/she cannot imagine easily to gradually increase the difficulty.

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228 2.3.7. As a home exercise, ask the patient to perform/imagine these movements 5 to 10 min, twice a day.

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NOTE: Together with the other exercises to enhance cortical reorganization, this accounts for about 20 min of the home program, twice a day. Ask the patient if this is feasible. Otherwise, choose one or two of these interventions based on the patient's preferences and reduce the training time to a manageable amount.

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2.4. As there is no active motion expected within the first months after surgery, make sure that
the range of motion (ROM) is preserved in all joints.

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239 2.4.1. Let the patient actively move all joints.

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2.4.2. Instruct the patient to perform this every day by him/herself.

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2.4.3. Additionally, in paralyzed hands or ankles use splints or orthoses to stabilize the joints in a position that avoids contractures of joints, ligaments, and tendons (as the intrinsic plus position for the hand²²). If necessary, fabricate a hand splint or make sure that the patients get a well-fitted device. In patients with an unstable shoulder and/or no elbow flexion use a sling¹⁵.

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2.4.4. Depending on the patient's needs, include exercises for body symmetry, trunk stability, and posture. Especially, if hand function is severely impaired, include training of one-handed activities and provide the patient with assistive devices.

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3. Motor activation using a donor side approach

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3.1. Start this part of the rehabilitation as soon as the first volitional contraction of the reinnervated muscle can be detected, which can usually be expected within 3-5 months after surgery (see **Table 2**).

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3.1.1. Set up a system for surface EMG biofeedback by unpacking it on a table, plugging in all cables and pressing the power button. This can be a stand-alone device, or one connected to a computer. If a computer is used, connect the device with the computer and start the appropriate software.

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3.1.2. Prepare the patient's skin to reduce impedance²³. Do so by carefully shaving the respective body part and/or by gently removing dead skin cells with a peeling gel and/or a wet paper towel.

Shortly explain the functionality of the system to the patient.

3.1.3. Ask the patient to think of movements that the donor nerves were originally responsible for (e.g., hand closing if the ulnar nerve was used) and palpate the recipient muscle.

3.1.4. Place a surface EMG electrode on the exact position, where muscle contraction can be palpated. While surface EMG may be detected with wet and dry electrodes, in this experiment dry electrodes are preferred for testing as these can be easily moved on the skin to alter electrode position. Even if no movement can be palpated, check for the EMG activity regularly within the first 3-6 months after surgery.

NOTE: The re-innervation can be confirmed, if the signal amplitude during activation is repeatedly 2-3 times higher than background noise during relaxation⁸.

3.1.5. If this cannot be confirmed, slightly change the position of the electrode and try other motor commands related to the donor nerve (e.g., ulnar abduction or flexion of the wrist, if the ulnar nerve was used as a donor). Otherwise, continue with the interventions for cortical activation and test again after a few weeks.

3.2. Train the activation of the newly re-innervated muscles with sEMG biofeedback.

3.2.1. As the first step of muscle activation training, educate the patient on the function of sEMG biofeedback and explain the principles of the donor activation approach.

3.2.2. Switch on the biofeedback system and place the surface EMG electrode on the patient's skin above the muscle to display the patient's muscle activation.

3.2.3. Make sure that the patient is comfortably seated and instruct the patient to think of movement patterns related to the donor nerve while picking up sEMG signals from the recipient muscle. If a system with the possibility to adjust signal gains is used, set it up in a way that the signal amplitude is high enough to be easily observed. In the beginning, this usually requires a high amplification.

3.2.4. As soon as the patient can repeatably activate the muscle, ask him/her to fully relax after muscle activation, which corresponds to EMG amplitudes close to zero. Full relaxation is often hard to achieve for the patient and can take some time. Ask the patient to repeatedly activate the muscle and fully relax it.

3.2.5. Try different movement cues and electrode positions in order to find the highest amplitude. After finding a good combination, maintain it the rest of the session.

3.2.6. Provide the patient with a structured home exercise program including the amount of training per week (10-20 min of concentrated training per day is recommended) and exact instructions of what to train. If it is possible for the patient to use a device for sEMG biofeedback

at home, encourage this⁸. Update the home exercise program regularly.

3.2.7. As soon as the patient feels confident with the sEMG setup, introduce motor commands including both the activation of the donor nerve and the actual function of the recipient muscle. For a patient with an Oberlin's ulnar nerve transfer to the biceps muscle, this means thinking of

314 hand closing and elbow flexion at the same time.

CAUTION: In patients where a nerve branch from an antagonistic muscle was transferred, do only focus on the donor nerve function and omit this step.

3.2.8. Train muscle activation with and without sEMG biofeedback until muscle strength is sufficient to overcome gravity or resistance of antagonistic muscles. Additionally, repeat the interventions for activation of the motor cortex.

4. Re-learning the original movement pattern

4.1. As soon as the muscle is strong enough to overcome gravity or the resistance of antagonistic muscles and joint stiffness, focus therapy on re-learning the original movement pattern of the recipient nerve. This means that a patient after an Oberlin's ulnar nerve transfer finally needs to learn how to flex the elbow without any movement of the hand and conversely, move the hand without flexion of the elbow.

4.2. Encourage the patient to slightly activate the recipient muscle without the movement in the muscles originally innervated by the donor nerve.

4.3. Support this by using sEMG biofeedback with two channels. Place one bipolar electrode on the skin above the re-innervated muscle and put the other one on the skin above the original donor nerve muscle. This allows the patient to simultaneously see the activation of both muscles. Encourage the patient to activate the recipient muscle and ensure that the donor muscle is relaxed with a low EMG signal amplitude.

4.3.1. Let the patient know that signal separation is usually easier with slight muscle activation and that unwanted co-contraction of both muscles is common at the beginning of training.

4.3.2. Using the same sEMG setup, ask the patient to activate the donor muscle without the activation of the re-innervated muscle and monitor for desirable/undesirable strategies resulting in better/worse separation of signals. Encourage strategies that support signal separation.

4.3.3. If both signals can be separated with slight muscle contractions, ask the patient to perform stronger contractions.

4.4. As soon as good signal separation while using sEMG biofeedback can be observed, ask the patient to perform separated "donor" and "recipient" movements without feedback.

4.5. As this phase is cognitively demanding and repetition is of great importance for motor relearning, make sure that the patient has a suitable home exercise program. Again, encourage the use of sEMG biofeedback devices at home, if possible.

use of sEMG biofeedback devices at home, if possible.

4.6. With increased motor function, encourage the patient to do more complex tasks including increased muscle force or improved precision. Also start "classic" strengthening exercises, if necessary.

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4.7. Finally, focus on activities of daily living and those needed in the patient's home, work environment and when performing sport exercise.

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4.8. In lower limb nerve transfers, start gait training with the focus on avoiding undesired compensatory movements.

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4.8.1. Ask the patient to walk along a corridor and analyze the gait based on the principles of observational gait analysis^{24,25}.

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4.8.2. Define deviations from the physiological gait pattern and analyze them with respect to the origin (e.g., which muscle might be weak) and the connection between each other (e.g., how hip kinematics affects knee kinematics and vice versa). If necessary, for clarification, conduct additional tests (e.g., for muscle strength or joint mobility).

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4.8.3. Develop a treatment plan based on your findings^{24,25}.

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4.8.4. Evaluate the interventions while the patient is doing them, as well as the therapy progressover time. If necessary, conduct another gait analysis and/or change interventions.

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4.9. See the patient three, six and twelve months after discharge from rehabilitation to find out about the long-term therapy success and patient satisfaction. If necessary and requested by the patient provide further training sessions.

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4.10. Evaluate, if the functional goal, that was discussed with the patient before surgery/at the beginning of rehabilitation could be reached.

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NOTE: For some patients, this might be fully functional recovery, while for others the return of minimal function might be enough.

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4.10.1. Ask the patient, if he/she is satisfied with the rehabilitation outcome and make clear that this is very subjective and is not necessarily reflected by any scores in outcome assessment instruments.

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4.10.2. If the patient is unsatisfied with the outcome, inform the patient about further (surgical) strategies to enhance function.

REPRESENTATIVE RESULTS:

The described rehabilitation protocol was implemented in a clinical setting at the Medical University of Vienna and its feasibility was assessed in a previous study⁸.

As reported in our previous publication⁸, five patients participated in the trial to evaluate the feasibility and outcomes of such a program for motor rehabilitation after complex peripheral nerve injuries. Patient characteristics including injury and performed surgical reconstruction can be found in **Table 1**. All of the included patients suffered severe brachial plexus injuries. Thus, motor recovery without surgical intervention was deemed unlikely and direct nerve suture was not possible in any of the cases. The performed nerve transfers were chosen depending on the intact anatomy, and where possible, nerve transfers from agonistic muscles were performed. This was done to reduce the cognitive load during motor re-learning.

In order to evaluate the motor outcomes, the patients' muscle strength was evaluated prior to reconstructive surgery and after discharge from rehabilitation using the British Medical Research Council (BMRC) scale²⁶.

The results presented in **Table 2** show that all patients had an improved shoulder and elbow function after rehabilitation, allowing them to flex the arm against gravity. This is in line with earlier research, reporting that a majority of patients regain useful shoulder and elbow function after selective nerve transfers and rehabiliation^{3,27,28}. However, two of the patients with an Oberlin's ulnar nerve transfer included in this study, regained full elbow flexion strength (M5), which is better than described by Bertelli and Ghizoni (2004)²⁹ who used the same surgical method. However, Ray et al. (2011)²⁸ could also show full recovery of elbow function in some of the patients treated in their center. Therefore, the presented motor outcomes are similar or slightly better than those described in the literature. This indicates that this protocol contributes to good outcomes in proximal muscles, where re-innervation of the muscles is likely.

However, in more distal parts of the body, the full function could not be regained for all patients, which is in line with other research^{3,30}. While we believe that motor re-education using a structured training protocol may facilitate motor rehabilitation by the central recovery of the hand's representation in the brain, it has limited influence on the peripheral processes needed for the re-innervation of muscles after nerve transfer surgery. Thus, the authors propose the use of this protocol, if peripheral nerve re-innervation is expected, but do not believe it to promote nerve regeneration at the peripheral level.

FIGURE AND TABLE LEGENDS:

Figure 1: Schematic illustration of the functional principle of an ulnar to musculocutaneous nerve transfer. (A) In a healthy person, there is a clear separation between activity in the motor cortex for functions of different nerves/joints as here the musculocutaneous nerve (red) and the ulnar nerve (blue). (B) After an injury of the musculocutaneous nerve, the biceps muscle cannot be activated, while the uninjured ulnar nerve (in blue) still functions. (C). After the Oberlin's nerve transfer and re-innervation, fascicles of the ulnar nerve control the biceps muscles as well as all

other muscles anatomically innervated by the ulnar nerve. Before cortical reorganization occurs, both muscles are activated together as there is no cortical separation between these nerve fibers (in blue). (**D**) With successful rehabilitation, the patient has learned to use certain cortical axons for "normal" ulnar nerve functions (in blue), while others (in purple) are now controlling the biceps muscle. This allows independent movement of both muscle groups.

Figure 2: Different surfaces can be used to support regaining of sensibility. Usually, the patient first gets the chance to touch these with both hands first, while he/she might afterward try to recognize the different surfaces without vision using the hand with limited sensibility.

Figure 3: A box filled with rice for sensory re-education of the hand. In therapy, the patient might put his/her hand with reduced sensitivity carefully in this box and slowly move the hand. To focus the patient's attention, the therapist can put some small objects (e.g., wooden blocks or paper clips) in this box and ask to find them without visual control.

Table 1: Patient characteristics. Please note the following abbreviations: BP, brachial plexus; MCN, musculocutaneous nerve; OBPL, obstetrical brachial plexus lesion; OP, operation; XI, spinal accessory nerve. This table is adapted from Sturma et al. (2018)⁸.

Table 2: Motor outcomes of the rehabilitation protocol. There was no functional impairment of the muscles not included in the table. In all patients, shoulder and elbow function were impaired at baseline and improved to follow-up. Additionally, the time between surgery and first volitional sEMG activity, as well as the number of therapy sessions for each patient are presented. This table is adapted from Sturma et al. (2018)⁸.

DISCUSSION:

Recently, nerve transfers have been increasingly used to restore function after severe proximal nerve injuries with promising outcomes^{1,4,31,32}. However, while there is a consensus that structured training programs are necessary to promote beneficial neuroplastic changes³³⁻³⁵, there is no structured protocol available to describe motor rehabilitation approaches after nerve transfers step-by-step. Therefore, the aim of the presented protocol was to provide detailed instructions for post-surgical rehabilitation to embrace cortical changes and enhance surgical outcomes. In contrast to other protocols^{9,36}, visualization of muscular activity via surface EMG biofeedback is a key element in the presented protocol.

Within therapy, patient education is a critical step as the patient needs to understand the rather complex surgical procedure and be educated on activities improving the health status in order to be actively involved in the long rehabilitation process^{8,13,37}. There is broad agreement that repetition is fundamental and daily home exercises are needed to reinforce a well-established cortical representation of the hand^{8,34,38,39}. Apart from pure patient information, the authors strongly recommend a patient-centered approach for rehabilitation. This additionally involves treating the patient as a unique person, the involvement of the patient in care, good clinician-patient communication and empowering the patient. In medical rehabilitation, this approach positively influences patient satisfaction and outcomes⁴⁰. Regarding the motor rehabilitation

itself, it is recommended to start interventions before re-innervation of the muscles and to follow a donor activation focused approach⁹. To ensure that muscular activity is detected as early as possible, EMG biofeedback devices can be used. While the authors are aware that EMG biofeedback devices are not yet clinical standard, their use is highly recommended as they allow to start early active motor rehabilitation and provide valuable feedback on newly re-innervated muscles⁸.

The principles described within this protocol can be applied for different types of nerve transfers, although modifications within the protocol might be necessary. While motor re-learning is relatively easy if synergistic muscles/nerves were used, the use of antagonistic muscles/nerves requires a longer rehabilitation time and the use of biofeedback might be of even greater importance^{3,8}. Especially in those cases where a higher amount of repetitions is needed, future protocols might also include serious games to maintain patient motivation⁴¹.

As the timing of nerve regeneration and the amount of recovery hugely depends on the injury and surgical interventions, there is no strict timeline for rehabilitation. Instead, the therapist is asked to proceed depending on the signs of motor recovery as stated in the protocol. In the same way, it is important to note that the success of nerve transfer surgery is based on many factors including type and severity of the injury, the surgeon's skills, and expertise as well as the patient's age, health status, cognition and motivation^{8,13,42,43}. While rehabilitation is a main pillar for regaining function after severe nerve injuries, even the best program for motor re-education cannot improve function, if there are inadequate peripheral nerve regeneration and muscle reinnervation. Thus, the authors strongly recommend seeing the patients regularly together within a multidisciplinary team to be able to discuss if recovery goes as expected or if any additional medical interventions are necessary. However, especially after severe injuries such as C8 and Th1 nerve root avulsions, realistic outcomes might not include full recovery of extremity function^{3,30}. In these cases, the clinical team needs to communicate this to the patient as soon as a realistic prognosis can be stated (approximately one year after the nerve transfers). At this point, further possibilities in rehabilitation, assistive devices or surgical interventions (as tendon transfers) need to be discussed. In cases, where absolutely no hand function returns, replacing the functionless limb with a prosthetic device can be considered as an option as well^{44,45}. This is, however, only recommended as a last resort and after in-depth physical and psychological assessment⁴⁶.

While the focus of peripheral nerve surgery usually lies on the reconstruction of motor function, sensory nerve transfers are sometimes used to restore the sensation in the hand after severe median or ulnar nerve injury^{4,47}. Similar to motor nerve transfers, this creates altered sensory neural pathways and results in sensations that are felt as if they were originating from the previous innervation area of the donor nerve. Even if no sensory nerve transfers were performed, there can still be changed/reduced sensation either due to the injury itself²⁷ or due to donor-side morbidity⁴⁸. In these cases, timely re-education can help to improve the sensory function⁴⁹, and reduce unwanted hyper-sensitivity and pain that often occurs after such injuries. To ensure good motor and sensory function, the authors strongly recommend complementing motor reeducation with tailored therapy approaches to promote re-organization in the corresponding sensory cortex as well^{39,50,51}. Regarding sensory re-education, it is recommended to start

interventions before re-innervation of the skin^{49,52,53}. This can include substitution of sensation by other senses as vision⁵³ or auditory feedback⁵⁴, as well as making use of the overlap of sensory innervation areas^{27,52}. As soon as the patient has regained a certain amount of sensitivity, tactile gnosis and object recognition can be trained, while maintaining a high amount of sensory input³⁴. Typical materials that can be used for this, include self-made plates with different surfaces to be recognized with closed eyes (see **Figure 2**) or a box filled with beans/lentils/rice (see **Figure 3**).

However, in both sensory and motor re-education, there is only limited evidence regarding the choice of interventions needed to promote good recovery³⁴. This limits the validity of the proposed rehabilitation protocol, as for other protocols. While the described protocol was assessed within a feasibility study and motor outcomes were similar or slightly better than those reported in the literature⁸, this study was performed on a small sample size and without a control group. This makes it impossible to compare the outcomes, advantages, and disadvantages of this protocol with respect to previous ones. Further research needs to include controlled studies in order to compare the possible advantages of using surface EMG biofeedback to conventional approaches.

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DISCLOSURES:

The authors have nothing to disclose.

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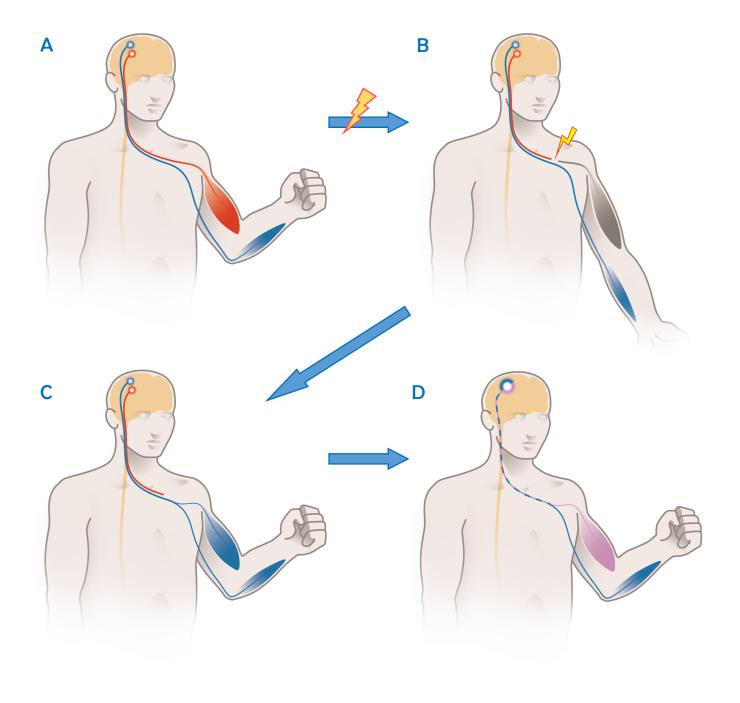
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Case nr.	Sex, Age (years)	Type of Accident	Type of Lesion
1	m, 68	Motorcycle accident	Polytrauma; Global brachial plexopathy
2	m, 56	Bicycle accident	Nerve root avulsion of C5-C6
3	m, 62	Bicycle accident	Extensive damage to superior trunk of the BP; traction injury of C7
4	f, 22	Car accident	Nerve root avulsion of C7; damage to C8 and T1
5	f, 43	Minor trauma years after OBPL	Traction injury of superior and medial trunk of the BP

Reconstructive surgeries for restoration of upper limb function

Nerve grafts to bridge defect of MCN; thoracodorsal nerve grafts to bridge defect of axillary nerve; nerve grafts for posterior trunk reconstruction; Oberlin's ulnar nerve transfer to MCN motor branch to the short head of the biceps

Oberlin's ulnar nerve transfer to MCN motor branch for restoration of biceps function; transfer of radial triceps motor branch to axillary nerve

XI-to-suprascapular nerve transfer; end-to-end transfer of phrenic nerve to C7; transfer of ulnar nerve fascicle to biceps motor branch of MCN; transfer of median nerve fascicle to brachialis motor branch of MCN; transfer of radial nerve fascicle to axillary nerve

Nerve grafts from C5 and C6 to MCN, median and radial nerve; nerve grafts from C8 to median, radial and ulnar nerve; nerve grafts from T1 to ulnar nerve

Nerve grafts to bridge defect of C5, C6 and C7 to restore elbow function and shoulder stability; transfer of median nerve fascicle to brachial motor branch of MCN

Case nr.	Upper limb function including BMRC grades at baseline	Upper limb function including BMRC grades at follow-up	ltrancfor curgory and	No. of Therapy Sessions in total (30 min each)	
	Deltoid muscle: 0	Deltoid muscle: 2			
	Elbow flexion: 0	Elbow flexion: 3		25	
1	Triceps muscle: 0 No active hand function	Triceps muscle: 2 Wrist extension: 1	5 months		
		Finger extension: 2			
2	Elbow flexion: 1	Elbow flexion: 5	4 months	22	
2	Deltoid muscle: 2-	Deltoid muscle: 5	4 111011(113	22	
	Elbow flexion: 0	Elbow flexion: 5			
	Deltoid muscle: 0	Deltoid muscle: 4			
3	Triceps muscle: 3	Triceps muscle: 5	3 months	30	
	Wrist extension: 3+	Wrist extension: 5			
	Finger flexion: 3+	Finger flexion: 5			
	Elbow flexion: 0	Elbow flexion: 3+			
	Triceps muscle: 0	Triceps muscle: 2			
4	No active hand function	Wrist flexion: 3	5 months	20	
		Finger flexion (ulnar FDP			
		part): 3			
5	Elbow flexion: 0	Elbow flexion: 3			
	Deltoid muscle: 2	Deltoid muscle: 2	4 months	18	
	Triceps muscle: 3+	Triceps muscle: 4			
Mean (±SD)			4.2 ± 0.75 months	23 ± 4.20	

Name of Material/ Equipment Company

Otto bock Healthcare,

EMG electrodes Duderstadt, Germany

Reflex Pain

Management Therapy

Folding Mirror Therapy Box (Arm/F Store

Otto bock Healthcare,

Myoboy Duderstadt, Germany

Recognise[TM] Flash Cards noigroup

Catalogue Number

electrodes 13E202 = 50

Myoboy

Comments/Description

The EMG electrodes used in this study were bipolar and included a ground and a 50 Hz filter. They were used with the Moby.

This box was used for mirror therapy.

This EMG Biofeedback device that can be used as stand alone device or with a computer. While this device was used in the presented pilot study, other (cheaper) devices for sEMG biofeedback training are available as well.

If no self-made cards for left-right discrimination are used, these can be purchased from noigroup.com. There, a mobile app for training is available as well.



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Point-to-point reply to the editorial comments

1. The editor has formatted the manuscript to match the journal's style. Please retain the same.

Thank you for that. We have not knowingly changed anything. However, as we have added a few more references, we hope that these were integrated in the right way.

2. Please address all specific comments marked in the manuscript.

Please find our answers to your comments in the manuscript. Some comments suggested to delete a few words/sentences. Thus, when doing so, your comment itself was deleted as well.

3. For the second part of the protocol section, please either provide some representative results or remove it from the protocol section. However, these details can be discussed in the discussion. In the second case please reword the title to match the protocol section.

As we have unfortunately not obtained pre- and post-surgical results for these patients, we have deleted the whole protocol describing the sensory re-education. Instead, we discuss the importance of implementing sensory training alongside motor training in the discussion section of the revised manuscript.

4. Once done, please ensure that the highlighted section of the protocol is no more than 2.75 pages including headings and spacings.

Without the sensory part, the highlighted part of the manuscript is shorter than 2.75 pages.

5. Please proofread the manuscript well for any grammar or spelling issues before submitting.

We have proofread the manuscript and corrected all issues we could find.

6. Our UK ALA has been updated recently. Please resign the attached ALA. You can attach the newer ALA version to your editorial manager account. Thank You.

The new version is uploaded alongside the revised manuscript.

REHABILITATION LEAFLET

for patients receiving nerve transfers to restore upper extremity function







REHABILITATION LEAFLET

for patients receiving nerve transfers to restore upper extremity function

You have been diagnosed with a peripheral nerve injury and have undergone nerve transfer surgery in order to treat this condition. This leaflet has been written to help you learn more about this condition and to explain how rehabilitation may be structured to facilitate functional recovery. It might be used by your surgeon/therapist while explaining your further treatment plan. However, due to the general nature of this leaflet, it cannot cover all specific details that may be relevant for you. Please speak to your surgeon and/ or therapist if you have any questions about your condition and care.

What are peripheral nerves? What is a nerve injury?

Your peripheral nerves are cord-like structures of tissue formed from a collection of nerve fibres. A single nerve can consist of thousands of fibres. These fibres link your brain to the rest of your body. For a muscle to work, information must travel from the brain along a nerve to the muscle. Peripheral nerves are fragile and easily damaged. A nerve injury can affect your brain's ability to communicate with your muscles and organs. Thus, when nerve fibres are injured, the muscles linked to that nerve are weakened, even though the injury is not in the muscle itself. Additionally, you may have a loss of sensation or feel tingling sensations.

What treatment options are available after nerve injuries?

The treatment of choice depends hugely on how your nerve was injured, the severity of injury and the time elapsed since the injury. If you suffered multiple nerve injuries, a combination of the techniques listed may be applied. Please speak to your surgeon, if you want a more detailed explanation on the surgical techniques and why he/she decided to do the nerve transfers.

- In cases of mild injuries, spontaneous recovery may occur, and no surgical repair is needed. Usually, regular check-ups are needed to ensure that recovery continues to its maximum potential. Still, nerves recover slowly, and maximal recovery may take several months and even years. In these cases, usually physiotherapy is recommended to prevent stiffness and restore function.
- If a section of a nerve is cut completely or damaged beyond repair, the surgeon can remove the damaged section and reconnect healthy nerve ends. This is called nerve repair or direct nerve suture. Sometimes the surgeon needs to transplant a piece of nerve from another part of your body, if there is a gap to bridge. You would refer to this technique as a nerve graft. Both procedures can help your nerves to regrow.
- In cases of extensive and severe nerve injuries a so-called nerve transfer may be indicated. This means that your surgeon borrows another working nerve to restore the function that the injured nerve was responsible for. Sometimes this might be combined with transferring a muscle from another part of your body.
- After particularly severe nerve injuries, if the other surgical techniques do not lead to the desired result, or your condition has been untreated for a long time, your doctor may suggest surgery to restore function

to critical muscles by transferring tendons from one muscle to another. This can also be done years after the injury and primary treatment. Thus, this option might be considered, if your functional goal cannot be reached with nerve transfers and subsequent rehabilitation.

What is the prognosis after nerve transfer surgery?

Unfortunately, it is nearly impossible to give you a prognosis of the long-term outcome shortly after nerve transfer surgery. Many factors influence the outcome after nerve injuries and subsequent nerve transfers. This implies that other people you may meet (or read about) who had a nerve injury as well could have a completely different long-term outcome than you.

After the surgery, your nerve needs to "grow" into the new muscle (or skin), which takes a lot of time. Thus, it is completely normal that you will not have any gain in function in the first months after the surgery. Your clinical team will regularly check your muscle activity and let you know as soon as they see voluntary muscle activity. After that you will slowly gain more control over your muscle activation and there will be an increase in strength over time. Usually, sensory function improves over times as well. However, within the first year after nerve injury, it is not possible to predict if you will have a full functional

recovery or if impairments will remain after the rehabilitation process.

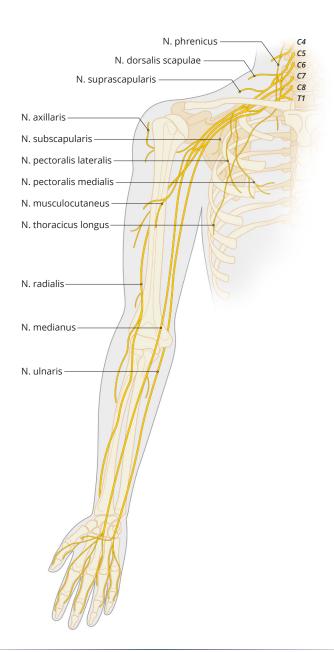
How do the nerve transfers affect my rehabilitation plan?

As the nerves take a while to "grow" into the new muscle after the nerve transfers, the first part of the rehabilitation plan is designed to guide you through the phase where you will not be able to actively move your arm/hand.

As soon as the nerve has reached its target, therapy will focus on activating the muscle that was previously paralyzed. Nerve transfers work by borrowing parts of an intact nerve. As these intact nerve fibres have been used to control a different muscle before they were transferred, you will be able to activate them by thinking about a movement their original muscle is usually responsible for. Your surgeon/therapist might use the following anatomy chart and table to explain the nerve transfers that were done and what this means for you. Within rehabilitation, the goal is to strengthen the previously paralyzed muscles and to support your brain in learning to use the transferred nerve fibres for their new function. Additionally, therapy will support you to get a better sensitivity and should help to reduce strange sensations and pain over time. Again, all of this will take a relatively long time. However, you can actively support this process by following the home exercise program that your therapist has discussed with you.

Nerves of the upper extremity

Your surgeon/therapist might use this to explain your injuries and the nerve transfers.



Your nerve transfers

Your surgeon/therapist might use this table to indicate your surgical treatment and its implications for rehabilitation.

Injured nerve	Transferred nerve to restore the injured nerve's function	What does that mean for you?

Additional surgical details/comments:				

Your home exercises

In order to maximise the outcome afte	r the nerve transfer surgery,	your active participation in
therapy and home exercises is needed	. This plan will be updated o	ver time.

Suggested reading

If you are interested in some scientific publications about the topic, you might want to have a look at:

- Novak CB. Rehabilitation Following Motor Nerve Transfers. Hand Clinics. 2008;24(4):417–423.
- Kahn LC, Moore AM. Donor Activation Focused Rehabilitation Approach: Maximizing Outcomes After Nerve Transfers. Hand Clin. 2016;32(2):263-277.
- Sturma A, Hruby LA, Prahm C, Mayer JA, Aszmann OC. Rehabilitation of Upper Extremity Nerve Injuries Using Surface EMG Biofeedback: Protocols for Clinical Application. Frontiers in neuroscience. 2018;12(906).

Additional notes

Contact details

Please get in touch with us, if you have any questions.

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Datum 2019-01-31 15:07

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I hope this information is useful, if you have any questions about this please do let me know, I would be happy to help.

Best wishes,

Charlotte Crawford-Sharpe Review Operations Assistant

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On Wed, 30 Jan 2019 at 09:39, <noreply@frontiersin.org> wrote:

Dear Sir or Madame,

I am currently preparing a manuscript for submission at the Journal of Visualized Experiments. Parts of this manuscript will refer to my previous Frontiers publication "Rehabilitation of Upper Extremity Nerve Injuries Using Surface EMG Biofeedback: Protocols for Clinical Application". Therefore, I would like to show and cite results from this publication (Table 3 and 4) within the JoVE manuscript.

May I ask you to grant me permission for including these results in the new manuscript with proper citation?

Yours sincerely,

Agnes Sturma