Nerve transfers for brachial plexus injuries: grading of volitional control

Socolovsky, M.; Barillaro, K.; Bonilla, G.; Masi, G. di; Malessy, M.

JNS

CLINICAL ARTICLE

J Neurosurg 138:1419–1425, 2023

Nerve transfers for brachial plexus injuries: grading of volitional control

Mariano Socolovsky, MD, PhD,[1] Karina Barillaro, BSN,[1] Gonzalo Bonilla, MD,[1] Gilda Di Masi, MD,[1] and Martijn Malessy, MD, PhD[2]

[1]Department of Neurosurgery, University of Buenos Aires School of Medicine, Buenos Aires, Argentina; and [2]Department of Neurosurgery, Leiden University Medical Center, Leiden, The Netherlands

OBJECTIVE After brachial plexus injuries (BPIs), nerve transfers are used to restore lost muscle function. Brain plasticity underlies the process of regaining volitional control, which encompasses disconnection of the original donor nerve–related programs and reconnection to acceptor nerve programs. To the authors' knowledge, the levels of disconnection and reconnection have never been studied systematically. In this study, the authors developed a novel 4-point plasticity grading scale (PGS) and assessed the degree of volitional control achieved, identifying clinical correlations with this score.

METHODS Patients with BPI who underwent a phrenic, spinal accessory, median, and/or ulnar fascicle nerve transfer to restore biceps and deltoid function were asked to maximally contract their target muscle as follows: 1) by using only the donor nerve program, and 2) by activating the target muscle while consciously trying to avoid using the donor nerve, with assessment each time of the Medical Research Council (MRC) scale grade for muscle strength. The authors' PGS was used to rate the level of volitional control achieved. PGS grade 1 represented the lowest independent volitional control, with MRC grade 4 obtained in response to the donor command and MRC grade 0 in response to the acceptor command (minimum brain plasticity), whereas PGS grade 4 was no noticeable contraction in response to the donor command and MRC grade 4 in response to the acceptor command (maximum brain plasticity).

RESULTS In total, 153 patients were studied. For biceps restoration, the phrenic nerve was used as a donor in 44 patients, the spinal accessory nerve in 40 patients, and the median and/or ulnar fascicles in 44 patients. A triceps branch was used to restore deltoid function in 25 patients. The level of volitional control achieved was PGS grade 1 in 1 patient (0.6%), grade 2 in 21 patients (13.7%), grade 3 in 103 patients (67.3%), and grade 4 in 28 patients (18.3%). The median PGS grade did not differ significantly between the four donor nerves. No correlations were observed between age, time from BPI to surgery, duration of follow-up, or compliance with rehabilitation and PGS grade.

CONCLUSIONS Just around 20% of the authors' patients developed a complete disconnection of the donor program along with complete independent control over the reinnervated muscle. Incomplete disconnection was present in the vast majority of the patients, and the level of disconnection and control was poor in approximately 15% of patients. Brain plasticity underlies patient ability to regain volitional control after a nerve transfer, but this capacity is limited.

https://thejns.org/doi/abs/10.3171/2022.7.JNS22887

KEYWORDS brachial plexus injury; nerve transfer; brain plasticity; peripheral nerve

Nerve transfers are widely used after severe brachial plexus (BP) injuries (BPIs) to reinnervate muscle function. Nerve transfers are employed when roots are avulsed from the spinal cord or when a large gap exists between the proximal and distal stumps. An extraplexual to intraplexual transfer involves a donor nerve from outside, but in the vicinity of the BP and, by definition, still in continuity with the CNS. The donor nerve is transected, transposed, and coaptated to an acceptor BP nerve. In an intraplexual transfer, intact dispensable BP fascicles are used as donors. Many different donor-acceptor nerve transfer combinations have been introduced over more than 100 years.[1–3]

Prior to transfer, any donor nerve is connected to a CNS motor program for skilled movements, a learned series of functions stored in the brain, which responds to a specific command to execute a function, enabling the patient to activate a determined muscle. For instance, the phrenic nerve responds to a program call for respiration to move the diaphragm. When the phrenic nerve is transferred and

ABBREVIATIONS BP = brachial plexus; BPI = BP injury; KW-ANOVA = Kruskal-Wallis one-way analysis of variance; MCN = musculocutaneous nerve; MRC = Medical Research Council; PGS = plasticity grading scale; RQS = Rehabilitation Quality Scale; SA = spinal accessory.

SUBMITTED April 15, 2022. **ACCEPTED** July 15, 2022.

INCLUDE WHEN CITING Published online September 16, 2022; DOI: 10.3171/2022.7.JNS22887.

connected to the musculocutaneous nerve (MCN) to obtain elbow flexion, the central respiratory program of the donor nerve is now connected to the MCN, which was originally intended to reinnervate elbow flexion.

Following a nerve transfer, CNS changes occur that are essential to obtaining volitional control of the target muscle. This process is called neuroplasticity.[4–15] Optimally, the level of volitional control ultimately achieved over the target muscle should be at the same level that existed prior to the transfer. Initially, however, activation of the target muscle is almost invariably tied to movement of the muscle(s) initially innervated by the donor. Therefore, a change in central control is required that entails disconnecting the donor nerve's ties to its original area in the CNS and reconnecting it to the area of the brain regulating the motor function of the new target muscle. If this transition/neuroplasticity process is incomplete, then the patient's volitional control over their restored muscle functions will also be incomplete. For instance, the functional outcome following a transfer of the hypoglossal nerve to the MCN is limited because the restoration of volitional control is poor. Voluntary flexion of the elbow can be initiated only when the tongue is pushed against the hard palate, and flexion is lost as soon as the patient starts to speak. Moreover, involuntary biceps contraction will occur during tongue movements associated with eating. Following this transfer, disconnection of the hypoglossal nerve from its CNS roots is insufficient. Consequently, the hypoglossal nerve is no longer used as a donor during BP nerve reconstructive surgery.[16,17]

To our knowledge, this process of disconnecting the donor nerve from its CNS links and reconnecting it to the CNS areas that regulate acceptor muscle function has not been systematically examined to date. We have developed a 4-point scale to rate the level of neuroplasticity that occurs and, hence, the extent of volitional control that is achieved following nerve transfers. In the present study, we have used this scale to assess the extent to which donor nerves are disconnected from their original CNS links and rediverted to areas linked to the muscles targeted for restoration. Specifically, we used the neuroplasticity scale to assess the following: 1) the levels of donor program disconnection and acceptor program reconnection achieved after nerve transfers; 2) differences in disconnection between different nerve donors; and 3) whether the degrees of disconnection and reconnection correlate with patient age, the time interval between trauma and surgery, the duration of follow-up (time between surgery and the moment our final plasticity scoring was performed), or the degree of patient compliance with rehabilitation.

Methods

Consecutive patients who underwent surgery in the Peripheral Nerve Unit of the Department of Neurosurgery, University of Buenos Aires School of Medicine, between January 1, 2002, and December 31, 2018, following BPI were reviewed if they required nerve transfer for either biceps or deltoid muscle restoration. The following donor and acceptor nerve combinations were used to achieve biceps restoration: 1) phrenic nerve to either the anterior division of the upper trunk or lateral cord or the MCN or the biceps branch; 2) spinal accessory (SA) nerve to the MCN; or 3) median and/or ulnar fascicles to the MCN. Only one nerve transfer was studied per patient. To restore deltoid function, a transfer of a triceps branch to the axillary nerve was performed. Patient inclusion in our analysis began when their target muscle contraction strength reached grade 4 on the Medical Research Council (MRC) scale in the end stage of recovery. However, follow-up and outcomes did not end at that inclusion point, but at the moment when our final plasticity scoring was performed at final follow-up. Patients were excluded for the following criteria: 1) additional spinal nerve root grafting was performed to obtain the same function; 2) the interval of time between the trauma and nerve transfer was more than 12 months, to eliminate the potential for any bias caused by a delayed surgery; or 3) root avulsion was not the cause of the neurological deficit that required a nerve transfer, and root stretching associated with a neuroma-in-continuity was found.

All patient evaluations followed a predetermined two-step examination protocol. In step 1, patients were asked to maximally activate their target muscle by using only the donor nerve program. To activate the donor nerve program, patients were asked to respond to commands related to the involved donor nerve. Thus, they responded to the phrenic nerve by maximal inspiration, to the SA nerve by shrugging their shoulder, to the median and/or ulnar fascicles by flexing their wrist and/or fingers, and to deltoid restoration of the triceps branch by extending their elbow. For example, if the phrenic nerve was used, biceps muscle contraction was assessed during sustained inspiration.

In step 2, patients were asked to maximally activate the target muscle while consciously trying to avoid using any donor nerve muscle. For example, if the patients had had a phrenic nerve transfer, they were asked to flex their elbow at the end of expiration and avoid breathing in. Likewise, if the SA nerve was the donor, the patients were asked not to shrug, and if motor fascicles of the ulnar/median nerves had been used as donors, the patients were instructed not to move their forearm or hand muscles. Each time, the MRC scale strength grade was rated for both the donor and target muscles.

To score outcomes in a way to determine the relative levels of donor nerve disconnection with its original CNS area and reconnection to CNS areas linked to target muscle function, we developed a 4-point plasticity grading scale (PGS). Patients were assigned a PGS grade of 1 when MRC score 4 contraction of the target muscle only was obtainable during step 1, when the donor nerve was maximally activated (in response to the "donor muscle command"; see above), with no response documented during step 2 when activation of the donor muscle was discouraged (the "target muscle command"). For example, a PGS score of 1 was assigned when the patient's biceps muscle achieved an MRC score of 4 for strength during deep inspiration (via activation of the phrenic nerve), and a minimum score (MRC score 0) when the patient was not breathing while just trying to flex the elbow. Meanwhile, whereas an MRC score of 4 was achieved for the target muscle in step 2 (with the target muscle command) for PGS grades 2–4,

TABLE 1. PGS for nerve transfers

Grade	Target Muscle Contraction↔Motor Program Activation	MRC Grade of Target Muscle Contraction	
		Donor Command	Acceptor Command
1	Exclusively donor (no plasticity)	4	0
2	Via donor & acceptor (poor plasticity)	2, 3, or 4	4
3	Subtle via donor, predominantly via acceptor (good plasticity)	1	4
4	Exclusively acceptor (excellent plasticity)	0	4

the donor muscle only exhibited MRC grades of 2-, 3-, or 4-level strength with the donor command for a PGS grade 2; only subtle contraction (MRC grade 1) with the donor command for PGS grade 3; and no noticeable contraction (MRS grade 0) with the donor muscle command for PGS grade 4. These definitions are summarized in Table 1.

We also assessed patient compliance with the rehabilitation therapy by using our own 4-point Rehabilitation Quality Scale (RQS).[6,18–21] With this scale, any patient who failed to attend rehabilitation therapy at all or attended less than once a week was assigned an RQS score of 1; any patient who had rehabilitation therapy at a regular center more than once a week was assigned an RQS score of 2; any patient who exhibited good adherence to a rehabilitation program at a nonspecialized neurorehabilitation center with periodic assessments at a specialized neurorehabilitation center was assigned an RQS score of 3; and any patient who exhibited good adherence to a rehabilitation program at a specialized institution was assigned an RQS score of 4.

This study was performed in full accordance with the Declaration of Helsinki II and our institutional ethics committee. All eligible patients were asked to participate in our study protocol, which included a clinical examination. Written informed consent was obtained from each patient prior to their participation. Patient demographic characteristics, including sex, age, time from trauma to surgery, and the duration of follow-up, were recorded at the time of assessment.

Surgical Strategies and Techniques

General descriptions of the BP surgery and rehabilitation program have recently been published elsewhere.[6,22–24] For all nerve transfers, an end-to-end donor-acceptor coaptation was performed. Nerve transfers were used only when proximal roots for grafting were unavailable as assessed by preoperative MRI and intraoperative inspection. Postoperative evaluations were performed every 6 months by at least two of the authors.

Statistical Analysis

Primary intergroup comparisons performed were between patients with each of the four PGS grades (1–4) and between patients undergoing transfers using four different nerve donors (ulnar/median, triceps, phrenic, SA). After initial analysis suggested significant intergroup differences between the two lowest and two highest PGS grades (1–2 vs 3–4) and between patients for whom either the ulnar/median or triceps nerve was used as a donor and patients for whom either the phrenic or SA nerve was used, these two variables were recategorized into binary variables, with PGS grades reclassified as poor-fair (1–2) or good-excellent (3–4) plasticity, and donors were reclassified as intraplexual (ulnar/median or triceps) or extraplexual (phrenic or SA). Continuous variables (patient age, time interval from BPI to surgery, duration of follow-up, and level of compliance/RQS grade) were summarized as means ± SDs and minimum to maximum ranges and were subsequently tested for normality of distribution using the Shapiro-Wilk test. Since all four continuous variables were nonnormally distributed and were compared between donor nerve groups, the Mann-Whitney U-test and the Kruskal-Wallis one-way analysis of variance (KW-ANOVA) were used to compare medians and distributions, depending on whether two or more than two groups were being compared, respectively. Intergroup comparisons of categorical variables were performed using either Pearson chi-square analysis or Fisher's exact test, as indicated. All bivariable tests were two-tailed, with $p \leq 0.05$ set as the a priori criterion for statistical significance.

Multivariable analysis was also performed to identify predictors of the final PGS grade, again as a binary variable (poor-fair vs good-excellent) using hierarchical logistic regression, entering variables by forward entry in three blocks: block 1, patient age and sex; block 2, donor nerve; and block 3, time between injury and surgery (months), duration of follow-up (months), and level of compliance/RQS grade. For this multivariable analysis, age was entered first as a continuous variable and then as a binary variable (age ≤ 20 vs > 20 years), while the donor nerve was entered first as four nerves and then as the reclassified binary variable (intra- vs extraplexual). For multivariable analysis, any variable with a final $p \leq 0.100$ was retained in the final model. All analyses were performed in IBM SPSS software (version 28; IBM Corp.).

Results

In total, 153 patients with a traumatic BPI were included (141 males, 92.2%). The mean interval between trauma and surgery was 6 months (median 6.37, SD 3.03 months). The mean age was 28.22 ± 12.41 years (range 3–69 years). All of these demographic characteristics are shown in Table 2, with the age distribution summarized in Table 3.

For elbow flexion, the phrenic nerve was used as a donor in 44 patients, the SA nerve in 40 patients, and the median and/or ulnar fascicles in 44 patients. For abduction, the triceps branch was used in 25 patients.

TABLE 2. Demographic characteristics of BPI patients (n = 153)

Variable	Mean	SD	Range
Age, yrs	28.22	12.41	3–69
Male sex	92.2%		
Time to op, mos	6.37	3.03	1–12
Follow-up, mos	53.93	35.13	12–182
PGS grade	3.05	0.65	1–4
RQS score	3.04	0.76	2–4

All receptor nerves were confirmed as nonfunctional by clinical examination, intraoperative nerve stimulation, and images, when appropriate. No patient had any notable donor-related alterations of previously healthy neurological function.

Among the 153 patients, the PGS was grade 1 in 1 patient (0.6%), grade 2 in 21 patients (13.7%), grade 3 in 103 patients (67.3%), and grade 4 in 28 patients (18.3%) (Table 4). For the phrenic nerve, the mean PGS grade was 2.57, with 11 patients having PGS grade 2 (25%) and 33 with PGS grade 3 (75%). The mean PGS grade for the SA nerve was 2.95, with 1 patient having PGS grade 1 (2.5%), 4 patients with PGS grade 2 (10%), 34 with PGS grade 3 (85%), and 1 patient with PGS grade 4 (2.5%). The mean PGS grade for the median and/or ulnar nerve fascicles was 3.27, with 4 patients with PGS grade 2 (9%), 20 with PGS grade 3 (45%), and 20 with PGS grade 4 (45%). The mean PGS grade for the triceps branch was 3.15, with 2 patients with PGS grade 2 (8%), 16 with PGS grade 3 (64%), and 7 with PGS grade 4 (28%). Table 5 summarizes these data.

The Shapiro-Wilk test revealed that all four continuous variables were nonnormally distributed to a p level < 0.001. For this reason, nonparametric tests were used for all intergroup comparisons of continuous variables. These tests revealed significant differences in the final mean PGS grade between either the ulnar/median or triceps nerve and either the phrenic or SA nerve, whether analyzed as four separate groups (by KW-ANOVA) or as a binary variable (intra- vs extraplexual, by Pearson chi-square), with both $p < 0.001$. Patients whose donor was an intra- instead of an extraplexual nerve were statistically younger (25.3 vs 31.3 years, $p = 0.004$), underwent surgery sooner after their injury (at 5.28 vs 7.64 months, $p < 0.001$), had a longer period of postoperative follow-up (63.0 vs 43.4 months, $p < 0.001$), and were less likely to have a good to excellent plasticity outcome at their final assessment (with PGS grade 3–4, 77.1% vs 92.8%, $p = 0.008$) (Table 6).

TABLE 3. Age groups in BPI patients

Age Group, yrs	No. (%) of Pts
<10	5 (3.2%)
10–19	25 (16.5%)
20–29	69 (45.3%)
30–39	32 (21.1%)
40–49	11 (7.2%)
50–59	5 (3.2%)
60–69	6 (3.9%)
≥70	0 (0.0%)
Total	153 (100%)

Pts = patients.

TABLE 4. Global PGS grades of achieved plasticity in the 153 analyzed cases

PGS Grade	No. of Cases (%)
1	1 (0.6%)
2	21 (13.7%)
3	103 (67.3%)
4	28 (18.3%)

When patients with a poor to fair final PGS grade were compared with those whose score was considered good to excellent, the only significant difference was in the percentage whose donor was intra- versus extraplexual (20.8% vs 50.0%, $p = 0.008$).

On multivariable analysis, having an extraplexual donor nerve was the most significant predictor of a good to excellent PGS grade at final follow-up ($p = 0.003$), with younger patient age also predictive ($p = 0.091$). Patient sex ($p = 0.101$), time to surgery ($p = 0.471$), follow-up duration ($p = 0.132$), and compliance scores ($p = 0.885$) were all dropped from the model (Table 7).

Discussion

Nerve transfers are widely used in nerve reconstructive surgery for BPI.[25–29] Success rates for transfers are expressed as the percentage of patients who obtain MRC grade 4 level in strength in the reinnervated muscle.[18] Routinely, the quality of volitional control over the acquired function is not even taken into consideration. The optimal outcome for regaining volitional control is that contraction of the target muscle occurs only in response to the command for the recipient nerve and not the donor (e.g., the elbow flexes in response to a command to flex the elbow, not when commanded to take a deep breath).

The process of central plasticity that underlies the restoration of volitional control can be divided into two steps: disconnection of the donor nerve's primary function and reconnection of the recipient nerve's primary function. These two steps—of disconnection and reconnection—can be analyzed by looking at target muscle contractions when the donor nerve's motor program is activated. To the best of our knowledge, this study is the first to link plastic changes that occur in the brain after a nerve transfer with an objective scale designed to measure these changes.

In our patients, complete disconnection of the prior CNS pathway and full restoration of independent volitional motor control (PGS grade 4) occurred in less than one-fifth of 153 patients. In more than two-thirds of the patients, however, only a subtle contraction (MRC grade 1) of the target muscle was noticeable in response to a command related to the donor nerve (PGS grade 3). In other words, in the vast majority of our patients, good voluntary control returned because of either good or excellent

TABLE 5. Nerve transfers employed in BPI (n = 153) and plasticity score (PGS grade) achieved

Nerve Transfer	Total No. of Cases	No. of Cases w/ PGS Grade				
		1	2	3	4	Mean
Phrenic to ADUT, LC, MCN, or BB	44	0	11	33	0	2.57
SA to MCN	40	1	4	34	1	2.95
Median &/or ulnar fascicle to MCN	44	0	4	20	20	3.27
Triceps to axillary	25	0	2	16	7	3.15

ADUT = anterior division of the upper trunk; BB = biceps brachialis; LC = lateral cord.

plasticity (PGS grade 3 or 4). Plasticity was poor in the remaining approximately 15% of patients in whom the effect of donor program activation remained MRC grade 2–4 muscle contraction.

Interestingly, the degree of plasticity did not differ significantly between the four different donor nerves we used, nor were there any correlations between our PGS grade and a patient's age, time to surgery, length of follow-up, or extent of compliance with rehabilitation.

Central plasticity predominantly takes place at a synaptic level, and less so by sprouting of dendrites.[9,30–32] The development of central plasticity takes time and different phases can be discerned. At the beginning of reinnervation, the target muscle can be contracted only via a command linked to the donor nerve (for example, if the surgeon connects the phrenic nerve, originally designed for inspiration by contracting the diaphragm, to elbow flexion muscles triggered by the MCN, then initially the patient flexes the elbow during inspiration). As time passes, usually over a couple of months, patients become increasingly able to activate their target muscle by focusing on the recipient nerve's primary function. Toward the end stages of reinnervation, the process of disconnection from the donor nerve may continue to the point that target muscle contractions may become possible solely based on acceptor muscle commands[4] through changes that have been correlated with a shift in motor cortex activity.[33–36] The main and original finding of this study is that this independence is rarely complete, and that a trace of the donor motor program (as in the above example of inspiration) remains when the patient flexes the elbow.

Two prerequisites have already been identified for plastic changes to occur and good volitional control to be restored. Both concern neuroanatomical CNS factors: 1) the donor and recipient nerve areas must have intrinsic connections prior to the transfer; and 2) the closer the donor and acceptor cortical areas are located to each other, the easier it becomes for the patient to regain voluntary control.[7,10,11]

As might be expected, in our 153 patients, the level of plasticity ultimately achieved was superior in patients whose donor nerve was derived from within the plexus (ulnar and/or median nerve fascicles or the triceps nerve) compared with patients whose donor nerve was drawn from outside the plexus (either the phrenic or SA nerve), which is consistent with the superior outcomes generally achieved when nerve transfers travel a shorter distance. This finding is especially notable given that the average postoperative follow-up for patients whose donor was extraplexual was almost 20 months longer than that for their intraplexual counterparts, and that this longer duration of follow-up was perhaps secondary to the inferior plasticity outcomes for extraplexual donors. Similarly unsurprising to us was the finding that younger patients (aged 20 years and younger) generally achieved higher plasticity levels than patients who were older, as also published elsewhere.[12,13,42] This finding was true on both univariable and multivariable analysis for the former variable—nerve donor—but only on multivariable analysis for patient age. This discrepancy might be explained, however, by the

TABLE 6. Comparing patients with intra- versus extraplexual donor nerves

Variable	Donor Nerve		p Value
	Extraplexual (n = 84)	Intraplexual (n = 69)	
Age, yrs	25.31	31.28	**0.004**
Age ≤20 yrs	31.0%	20.3%	0.135
Female sex	8.3%	7.2%	0.803
Time to op, mos	5.28	7.64	**<0.001**
Duration of follow-up, mos	63.00	43.41	**<0.001**
Therapy compliance (RQS) score	3.08	2.99	0.430
Final PGS grade	2.81	3.35	**<0.001**
Final PGS grade 3–4	77.1%	92.8%	**0.008**

Values are presented as means or percentages unless otherwise indicated. Boldface type indicates statistical significance.

TABLE 7. Predictors of the new PGS grade

Variable	PGS Grade		p Value
	1–2 (n = 22)	3–4 (n = 131)	
Age, yrs	30.42	27.62	0.311
Age ≤20 yrs	12.5%	28.1%	0.108
Female sex	16.7%	6.3%	0.082
Time to op, mos	6.22	6.40	0.795
Duration of follow-up, mos	49.83	54.71	0.535
Therapy compliance (RQS) score	2.96	3.05	0.572
Donor nerve, % intraplexual*	20.8%	50.0%	**0.008**

Values are presented as means unless otherwise indicated. Boldface type indicates statistical significance.
* Ulnar/median or triceps nerve.

higher percentage of younger patients who had either a phrenic or SA nerve donor (31% vs 20%). Indeed, even among the relatively small number of patients younger than 21 years, the 25 patients whose donor was extraplexual achieved a statistically worse PGS grade than the 14 patients whose donor was intraplexual (2.96 vs 3.43, p = 0.020). This study adds to our knowledge regarding the level of plastic changes that occur within these central networks. The study results also demonstrate the sensitivity of this scale, which was able to detect significant differences between intra- and extraplexual nerve donors and between younger and older patients, for which both of these findings were expected and were supported by the literature.

Rehabilitation is widely recognized as beneficial, assisting with the restoration of motor function.[18,21,37–41] In our study, however, we were unable to detect any indication that rehabilitation frequency or intensity had any significant impact on the plasticity process. It seems, therefore, that the role of rehabilitation was limited. New rehabilitation techniques might need to be developed to reduce the effect of donor motor nerve activation by enhancing the process of disconnection and, thereby, improve volitional control.

The potential for plastic changes decreases with increasing age.[12,13,42] However, we were unable to identify any relationship between patient age and the level of plasticity they achieved in this large series. One possible reason for the lack of this finding might be that the age distribution of our patients was too narrow for us to detect this relationship.

Study Strengths and Limitations

Our study has strengths and weaknesses. One major strength is that the level of disconnection and volitional control was studied empirically for the first time, to our knowledge, in a relatively large series of patients and spanning four different donor nerves.

One weakness of this study is that we only asked patients to activate their target muscle in two ways: 1) purely via donor nerve activation and 2) following this step, without using the donor nerve, at least volitionally. With the latter step, patients might not have unintentionally activated the donor nerve's primary function. For the phrenic nerve, it was easy for us to observe whether this was the case, as just asking the patient to avoid inspiration eliminates any influence of this donor nerve. For the SA or ulnar/median nerve, fascicles were used as donors. This procedure requires simultaneous observations while grading MRC strength in the target muscle, for instance, measuring whether and to what extent the shoulder is shrugged during an attempt of maximal elbow flexion. Consequently, we may have missed some level of combined activation. In the clinical setting, this type of activation can be quite hard to discern. Simultaneous recording of muscle action potentials related to both donor and acceptor muscle function may prove helpful in future analyses.[33]

Both a strength and weakness of our study is that we developed our own 4-point scale to score the level of neuroplastic disconnection achieved after nerve transfers. Although MRC grade 1 contractions might have been missed, our scale was nonetheless able to detect expected differences between donor nerves and patient groups (younger vs older) among whom outcome differences were expected.

We did not look at the relationship between the number of avulsed roots, global arm function following nerve repair, and our plasticity scale, which might have provided additional insights because the level of initial denervation might have been affected by long-range connections and strongly reduced functional connectivity within the motor cortex.[5]

Conclusions

Nerve transfers are widely used to restore motor function in BPI patients. However, complete disconnection between the donor nerve's initial function and the reinnervated muscle restored function is achieved in less than 20% of patients, at least when the phrenic nerve, SA nerve, median nerve and/or ulnar fascicles, or a triceps branch is used. Incomplete disconnection as shown by at least a trace of donor nerve program activity was present in the majority of the patients. The level of disconnection and control was poor in approximately 15% of the patients, and both the choice of donor nerve and patient age were predictive of this outcome.

References

1. Cushing H. The surgical treatment of facial paralysis by nerve anastomosis: with the report of a successful case. *Ann Surg*. 1903;37(5):641-659.
2. Körte W, Bernhardt M. Ein fall von nervenpfropfung des nervus facialis auf den nervus hypoglossus. *Dtsch Med Wochenschr*. 1903;29:293-295.
3. Lurje A. Concerning surgical treatment of traumatic injury of the upper division of the brachial plexus (Erb's-type). *Ann Surg*. 1948;127(2):317-326.
4. Malessy MJ, van Dijk JG, Thomeer RT. Respiration-related activity in the biceps brachii muscle after intercostal-musculocutaneous nerve transfer. *Clin Neurol Neurosurg*. 1993; 95(suppl):S95-S102.
5. Fraiman D, Miranda MF, Erthal F, et al. Reduced functional connectivity within the primary motor cortex of patients with brachial plexus injury. *Neuroimage Clin*. 2016;12:277-284.
6. Socolovsky M, di Masi G, Bonilla G, Domínguez Paez M, Robla J, Calvache Cabrera C. The phrenic nerve as a donor for brachial plexus injuries: is it safe and effective? Case series and literature analysis. *Acta Neurochir (Wien)*. 2015; 157(6):1077-1086.
7. Socolovsky M, Malessy M, Lopez D, Guedes F, Flores L. Current concepts in plasticity and nerve transfers: relationship between surgical techniques and outcomes. *Neurosurg Focus*. 2017;42(3):E13.
8. Simon NG, Franz CK, Gupta N, Alden T, Kliot M. Central adaptation following brachial plexus injury. *World Neurosurg*. 2016;85:325-332.
9. Jensen JL, Marstrand PCD, Nielsen JB. Motor skill training and strength training are associated with different plastic changes in the central nervous system. *J Appl Physiol (1985)*. 2005;99(4):1558-1568.
10. Osborne NR, Anastakis DJ, Davis KD. Peripheral nerve injuries, pain, and neuroplasticity. *J Hand Ther*. 2018;31(2): 184-194.
11. Socolovsky M, Malessy M. Brain changes after peripheral nerve repair: limitations of neuroplasticity. *J Neurosurg Sci*. 2021;65(4):421-430.

12. Feng JT, Liu HQ, Xu JG, Gu YD, Shen YD. Differences in brain adaptive functional reorganization in right and left total brachial plexus injury patients. *World Neurosurg*. 2015;84(3):702-708.
13. Auer T, Pinter S, Kovacs N, et al. Does obstetric brachial plexus injury influence speech dominance? *Ann Neurol*. 2009;65(1):57-66.
14. Qiu TM, Chen L, Mao Y, et al. Sensorimotor cortical changes assessed with resting-state fMRI following total brachial plexus root avulsion. *J Neurol Neurosurg Psychiatry*. 2014;85(1):99–105.
15. Florence SL, Kaas JH. Large-scale reorganization at multiple levels of the somatosensory pathway follows therapeutic amputation of the hand in monkeys. *J Neurosci*. 1995;15(12):8083-8095.
16. Malessy MJ, Hoffmann CF, Thomeer RT. Initial report on the limited value of hypoglossal nerve transfer to treat brachial plexus root avulsions. *J Neurosurg*. 1999;91(4):601-604.
17. Ferraresi S, Garozzo D, Ravenni R, Dainese R, De Grandis D, Buffatti P. Hemihypoglossal nerve transfer in brachial plexus repair: technique and results. *Neurosurgery*. 2002;50(2):332-335.
18. Socolovsky M, Di Masi G, Battaglia D. Use of long autologous nerve grafts in brachial plexus reconstruction: factors that affect the outcome. *Acta Neurochir (Wien)*. 2011;153(11):2231-2240.
19. Socolovsky M, Malessy M, Bonilla G, Di Masi G, Conti ME, Lovaglio A. Phrenic to musculocutaneous nerve transfer for traumatic brachial plexus injuries: analyzing respiratory effects on elbow flexion control. *J Neurosurg*. 2018;131(1):165-174.
20. Flores LP, Socolovsky M. Phrenic nerve transfer for reconstruction of elbow extension in severe brachial plexus injuries. *J Reconstr Microsurg*. 2016;32(7):546-550.
21. Havton LA, Carlstedt T. Repair and rehabilitation of plexus and root avulsions in animal models and patients. *Curr Opin Neurol*. 2009;22(6):570-574.
22. Solanki C, Socolovsky M, Devi BI, Bhat DI. Nerve repair: bridging the gap from "limp" to "limb". *Neurol India*. 2019;67(suppl):S16-S19.
23. Socolovsky M, Martins RS, Di Masi G, Siqueira M. Upper brachial plexus injuries: grafts vs ulnar fascicle transfer to restore biceps muscle function. *Neurosurgery*. 2012;71(2 Suppl Operative):ons227-ons232.
24. Kim DH, Murovic JA, Tiel RL, Kline DG. Mechanisms of injury in operative brachial plexus lesions. *Neurosurg Focus*. 2004;16(5):E2.
25. Oberlin C, Béal D, Leechavengvongs S, Salon A, Dauge MC, Sarcy JJ. Nerve transfer to biceps muscle using a part of ulnar nerve for C5-C6 avulsion of the brachial plexus: anatomical study and report of four cases. *J Hand Surg Am*. 1994;19(2):232-237.
26. Liverneaux PA, Diaz LC, Beaulieu JY, Durand S, Oberlin C. Preliminary results of double nerve transfer to restore elbow flexion in upper type brachial plexus palsies. *Plast Reconstr Surg*. 2006;117(3):915-919.
27. Leechavengvongs S, Malungpaishorpe K, Uerpairojkit C, Ng CY, Witoonchart K. Nerve transfers to restore shoulder function. *Hand Clin*. 2016;32(2):153-164.
28. Leechavengvongs S, Witoonchart K, Uerpairojkit C, Thuvasethakul P. Nerve transfer to deltoid muscle using the nerve to the long head of the triceps, part II: a report of 7 cases. *J Hand Surg Am*. 2003;28(4):633-638.
29. Leechavengvongs S, Witoonchart K, Uerpairojkit C, Thuvasethakul P, Malungpaishrope K. Combined nerve transfers for C5 and C6 brachial plexus avulsion injury. *J Hand Surg Am*. 2006;31(2):183-189.
30. Malessy MJ, Thomeer RT. Evaluation of intercostal to musculocutaneous nerve transfer in reconstructive brachial plexus surgery. *J Neurosurg*. 1998;88(2):266-271.
31. Malessy MJ, Thomeer RT, van Dijk JG. Changing central nervous system control following intercostal nerve transfer. *J Neurosurg*. 1998;89(4):568-574.
32. Malessy MJ, van der Kamp W, Thomeer RT, van Dijk JG. Cortical excitability of the biceps muscle after intercostal-to-musculocutaneous nerve transfer. *Neurosurgery*. 1998;42(4):787-795.
33. Kwee RM, Chhabra A, Wang KC, Marker DR, Carrino JA. Accuracy of MRI in diagnosing peripheral nerve disease: a systematic review of the literature. *AJR Am J Roentgenol*. 2014;203(6):1303-1309.
34. Iwase Y, Mashiko T, Ochiai N, Kurosawa H. Postoperative changes on functional mapping of the motor cortex in patients with brachial plexus injury: comparative study of magnetoencephalography and functional magnetic resonance imaging. *J Orthop Sci*. 2001;6(5):397-402.
35. Malessy MJ, Bakker D, Dekker AJ, Van Duk JG, Thomeer RT. Functional magnetic resonance imaging and control over the biceps muscle after intercostal-musculocutaneous nerve transfer. *J Neurosurg*. 2003;98(2):261-268.
36. Dai TH, Liu JZ, Sahgal V, Brown RW, Yue GH. Relationship between muscle output and functional MRI-measured brain activation. *Exp Brain Res*. 2001;140(3):290-300.
37. Scott KR, Ahmed A, Scott L, Kothari MJ. Rehabilitation of brachial plexus and peripheral nerve disorders. *Handb Clin Neurol*. 2013;110:499-514.
38. Couzan S, Martin JM, Chave É, Le Hello C. Update on the thoracic outlet syndrome and plexus brachial syndrome: specific clinical examination (for all) and rehabilitation protocol. *J Med Vasc*. 2021;46(5-6):232-240.
39. Milicin C, Sîrbu E. A comparative study of rehabilitation therapy in traumatic upper limb peripheral nerve injuries. *NeuroRehabilitation*. 2018;42(1):113-119.
40. Smania N, Berto G, La Marchina E, et al. Rehabilitation of brachial plexus injuries in adults and children. *Eur J Phys Rehabil Med*. 2012;48(3):483-506.
41. Janssen RMJ, Satink T, Ijspeert J, et al. Reflections of patients and therapists on a multidisciplinary rehabilitation programme for persons with brachial plexus injuries. *Disabil Rehabil*. 2019;41(12):1427-1434.
42. Anastakis DJ, Malessy MJ, Chen R, Davis KD, Mikulis D. Cortical plasticity following nerve transfer in the upper extremity. *Hand Clin*. 2008;24(4):425-444, vi-vii.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Socolovsky, Bonilla, Di Masi, Malessy. Acquisition of data: Socolovsky, Barillaro, Bonilla, Di Masi. Analysis and interpretation of data: Socolovsky, Barillaro, Bonilla, Di Masi, Malessy. Drafting the article: Socolovsky, Malessy. Critically revising the article: Socolovsky, Bonilla, Di Masi, Malessy. Reviewed submitted version of manuscript: Socolovsky. Approved the final version of the manuscript on behalf of all authors: Socolovsky.

Correspondence

Mariano Socolovsky: University of Buenos Aires School of Medicine, Buenos Aires, Argentina. marianosocolovsky@gmail.com.