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Sensory re-education after nerve injury of the upper limb: a systematic review

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Objective: To systematically review the available evidence for the effectiveness of sensory re-education to improve the sensibility of the hand in patients with a peripheral nerve injury of the upper limb.
Data sources: Studies were identified by an electronic search in the databases MEDLINE, Cumulative Index to Nursing & Allied Health Literature (CINAHL), EMBASE, the Cochrane Library, the Physiotherapy Evidence Database (PEDro), and the database of the Dutch National Institute of Allied Health Professions (Doconline) and by screening the reference lists of relevant articles.
Review methods: Two reviewers selected studies that met the following inclusion criteria: all designs except case reports, adults with impaired sensibility of the hand due to a peripheral nerve injury of the upper limb, and sensibility and functional sensibility as outcome measures. The methodological quality of the included studies was independently assessed by two reviewers. A best-evidence synthesis was performed, based on design, methodological quality and significant findings on outcome measures.
Results: Seven studies, with sample sizes ranging from 11 to 49, were included in the systematic review and appraised for content. Five of these studies were of poor methodological quality. One uncontrolled study ($N = 13$) was considered to be of sufficient methodological quality, and one randomized controlled trial ($N = 49$) was of high methodological quality. Best-evidence synthesis showed that there is limited evidence for the effectiveness of sensory re-education, provided by a statistically significant improvement in sensibility found in one high-quality randomized controlled trial.
Conclusion: There is a need for further well-defined clinical trials to assess the effectiveness of sensory re-education of patients with impaired sensibility of the hand due to a peripheral nerve injury.

Introduction

'Without sensation the hand is blind'.[1] Indeed, it has been found that, even though motor function is normal, the function of the hand can be severely affected by the sole loss of sensibility of the hand. As a result, the ability to perform activities of daily living can also be impaired to a certain degree.

A peripheral nerve injury of the upper limb often results in impaired sensibility of the hand. Despite microsurgical repair techniques, there is inevitably a distortion of the profile of neural impulses reaching the sensory cortex. Although, the majority of the axons will regenerate and re-innervate the correct type of sensory receptor, some regenerating axons

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will be trapped in the scar interface, and will therefore never reach the receptor. Other axons will be misdirected into a different topographical area. Furthermore, although a certain number of axons will re-grow into the correct topographical area, they will re-innervate the wrong sensory receptor or re-innervate an irreversibly degenerated receptor.[2,3]

From experimental studies with primates it is known that axonal misdirection results in a significant reorganization of the somatosensory cortex, with a new and distorted map of the skin areas originally innervated by the damaged nerve.[4–6] It was found that the former well-defined individual cortical representations of separate fingers disappear, and change into dispersed discontinuous islands. However, it is not yet known whether these significant cortical changes after nerve injury and repair also occur in humans, although clinical experiments strongly indicate that such reorganizational changes do occur.[6,7]

Through the cortical reorganization that results from nerve injury and repair the patient loses functional sensibility, also referred to as tactile gnosis (i.e. the ability to identify shapes and textures).[8] In a normal hand, a stimulus (e.g. a gripped screw) elicits a profile of neural impulses which reach the sensory cortex. These impulses are associated with previous memories or experiences, and turn into a conscious perception. After nerve repair the same stimulus will elicit an altered profile of neural impulses, and when these impulses reach the somatosensory cortex they may find no match in the association cortex. In such cases the sensation is experienced as new, cannot be identified, and may even pass unnoticed.[2,9]

Cortical connections and cortical maps can be remodulated by experience. Experiments have shown that activity, behaviour and the acquisition of skills are factors that can influence the cortical patterns.[10–14] This plasticity of the brain, to respond to changes by peripheral influence, can be used in the rehabilitation of (functional) sensibility of the hand in patients with a peripheral nerve injury of the upper limb. This type of treatment is called sensory re-education. Sensory re-education is aimed at: (1) refining cortical receptive fields with a higher sensory resolution, (2) improving tendency towards reversal and normalization of the distorted hand map, and (3) improving processing in the sensory network at a higher order cortical level, facilitating interpretation of the distorted hand map.[15] This may help to improve functional sensibility, and thus improve the patient's use of the impaired hand.

The intervention consists of touching different shapes (e.g. circular, square), textures (e.g. smooth, rough) and (familiar) objects. To maximize functional sensibility, higher cortical functions, that is attention, learning and memory, are used. The sequence of object grasp is first with eyes open, then eyes shut with concentration on perception, and finally again with eyes open for reinforcement. Attention will be maximized by training in a quiet room for short intervals. Daily practice sessions over several weeks reinforces the learning.[2,16]

The evidence for the effectiveness of sensory re-education to improve (functional) sensibility of the hand in patients with a peripheral nerve injury has not yet been reviewed systematically. Therefore a systematic review of published studies was conducted to evaluate the effect of sensory re-education in these patients.

Materials and methods

Search strategy

A broad computerized search was conducted in the following databases: MEDLINE, Cumulative Index to Nursing & Allied Health Literature (CINAHL), EMBASE, the Cochrane Library (2006 Issue 2), the Physiotherapy Evidence Database (PEDro), and the database of the Dutch National Institute of Allied Health Professions (Doconline) from the earliest available date until April 2006. The specific search strategy for the MEDLINE database is described in Appendix 1. Furthermore, the reference lists of all identified articles were scanned for additional relevant studies.

Selection for inclusion

Because studies focusing on this problem were expected to be sparse, study designs other than controlled clinical trials were also included in this systematic review. Studies with the following designs were included: (1) randomized controlled trials (RCTs); (2) controlled clinical trials (CCTs); (3) other designs (experiments without a control group) with $N \geq 10$.

Studies of adult patients ($\geq$18 years) with impaired sensibility of the hand due to a peripheral nerve injury of the upper limb (partial/complete cut and sutured) were included. If a study included adults as well as children, the results of the adults had to be presented separately. Studies evaluating rehabilitation treatment for the loss of sensibility, with outcome measures of 'sensibility' (moving and constant touch and vibratory stimuli) or 'functional sensibility', also called tactile gnosis (ability to identify shapes and textures)[7] were included. Language was restricted to English, German, French or Dutch, and only full-length articles were included.

Studies involving patients with neuropathy, complex regional pain syndrome type I, and skin diseases were excluded.

Procedure for inclusion

The procedure for inclusion of the studies was based on the recommendations described by Van Tulder *et al.*[17] The first selection was performed by one reviewer (TO) based on the following two inclusion criteria: 'peripheral nerve injury of the upper limb' and 'impaired sensibility'. Subsequently, two reviewers (TO and EE) independently applied all the selection criteria to the abstracts of the remaining studies. If there was any doubt, the full article was retrieved. Disagreements regarding inclusion status were resolved by discussion, but if no consensus was achieved, a third reviewer (AB) made the final decision.

Methodological quality

The methodological quality of the RCTs and CCTs was rated according to a list of criteria recommended by Van Tulder *et al.*[17] The list consists of 11 criteria for internal validity, six descriptive criteria and two statistical criteria (see Appendix 2). All criteria were scored as 'Yes', 'No' or 'Don't know'. Studies were considered to be of high quality if the scores were positive for at least six criteria for internal validity, three descriptive criteria and one statistical criterion.

The methodological quality of the other designs was rated according to an adapted version of the van Tulder's list.[18] This list of criteria consists of seven criteria for internal validity, four descriptive criteria and two statistical criteria. Studies were considered to be of sufficient quality if the scores were positive for at least four of the seven criteria for internal validity, two descriptive criteria and one statistical criterion.

The methodological quality of the included studies was independently assessed by two reviewers (TO and EE). Disagreements were resolved by discussion, but if no consensus was achieved, a third reviewer (AB) made the final decision.

Data extraction and analysis

Using a predefined form, the two reviewers independently extracted details on design, number of participants and their age and diagnosis, the intervention, the start, frequency and duration of training, the baseline and follow-up data concerning the outcome measures, and the authors' conclusions.

Since clinical heterogeneity with respect to patients, interventions and outcome measures was expected, a best-evidence synthesis was applied. For this review the adapted version of the Van Tulder *et al.* best-evidence synthesis, as described by Steultjens *et al.*[18] was used. The rating system consists of five levels of scientific evidence, based on the study design, the methodological quality, the type of outcome measures, and the statistical significance of the findings.

Results

Study selection

The search identified 760 publications, but after applying the selection criteria, only six studies could be included. Screening the references of the retrieved articles produced one additional study, so a total of seven studies could be subjected to quality assessment and data extraction.

Methodological quality

The inter-rater agreement on the scores for methodological quality was good (overall agreement 82% [93/113], kappa 0.72). For 10 of the 113 items scored the final decision was made by the third reviewer (AB). The methodological quality of one RCT,[19] two CCTs,[20,21] and four studies with other designs[22–25] was assessed (Table 1). The RCT was of high methodological quality. It appeared that the two CCTs carried out by Imai *et al.*[20,21] focused on the same participants and the same intervention, but reported different outcome measures. These two CCTs had a low score for methodological quality, and one of the four studies with other designs[24] had sufficient methodological quality.

Study characteristics

The study characteristics are presented in detail in Table 2. The RCT and CCTs compared treatment with no treatment. Sample sizes ranged from 11 (study

Table 1 Quality assessment of the studies[a]

First author	Internal validity	Descriptive criteria	Statistical criteria	Methodological quality
Randomized controlled trial				
Cheng[19]	b1, f, g, j, l, n	a, c, d, m1	o, q	High
Controlled clinical trial				
Imai[20]	g, j, l, p	a	o	Low
Imai[21]	g, j, l, p	a	o, q	Low
Other designs				
Daniele[22]	g, j, l	a, d	o	Low
Wei[24]	g, j, l, n, p	a, d, m1	o, q	Sufficient
Parry[23]	j, n, p	a, m1	–	Low
Wynn-Parry[25]	j, n	a, d, m1, m2	–	Low

[a]See supplement to Appendix 2 for definitions. Only the fulfilled criteria are reported.

with no control group) to 49 (RCT; intervention group $N = 24$; control group $N = 25$). In six studies the patients had a nerve injury which had been repaired. Wei and Ma[24] included patients with a toe-to-hand transfer.

The treatment of sensibility varied with regard to treatment modality and time of onset. Cheng *et al.*[19] used two specific treatment techniques, the rotating tactile stimulation disc and the pocket size tactile stimulator. Parry[23] and Wynn-Parry and Salter[25] used familiar objects with different shapes and textures. Wei and Ma[24] combined the method described by Dellon[2] (early and late phase sensory re-education) with a Disk-Criminator (Baltimore, MD, USA). Daniele and Aguado[22] also used the method described by Dellon,[2] with additional recognition of hidden objects in beans, and the use and recognition of plastic letters. A combination of the methods described by Dellon,[2] Dellon and Jabaley[3] and Wynn-Parry[16] was used by Imai *et al.*[20,21]

In three of the six studies[21,23,25] the treatment started as soon as a patient could feel moving touch at the fingertips. In three studies[19,20,22] the treatment started earlier. In the Wei and Ma[24] study the treatment started much later, at a mean of 33 months after surgery (range 13–98 months).

Outcome of interventions

In their high methodological quality RCT, Cheng *et al.*[19] reported a significant positive effect of sensory re-education on sensibility at six months. A moving two-point discrimination of 2–6 mm was achieved in 10 patients (41%) in the intervention group, versus four patients (16%) in the control group ($P = 0.0144$). A constant two-point discrimination of 2–6 mm was achieved in nine patients (38%) in the intervention group, versus three patients (12%) in the control group ($P = 0.0023$). The Medical Research Council grading of S3+ to S4 was achieved in 22 patients (92%) in the intervention group, but only in nine patients (36%) in the control group ($P = 0.0009$). There was no significance difference between the groups with regard to cutaneous pressure threshold. Twelve patients (50%) in the intervention group and 10 patients (40%) in the control group had a cutaneous pressure threshold of 3.61 or less ($P = 0.097$).

The Wei and Ma[24] study was of sufficient methodological quality, and also reported a significant increase in sensibility after sensory re-education. The constant and moving two-point discrimination improved significantly ($P < 0.0001$).

These findings are supported by the other five studies which were of low methodological quality, and which also reported a positive effect of sensory re-education.

The best-evidence synthesis showed that there is limited evidence that sensory re-education leads to an improvement in (functional) sensibility, provided by the findings in the high-quality RCT.

Discussion

The objective of this review was to systematically review the available evidence for the effectiveness of

Table 2 Characteristics of included studies

First author	Design[a]	Participants[b]	Intervention[c]	Frequency and duration of intervention	Baseline and follow-up	Results[d]	Conclusion of authors	Notes
Cheng[19]	RCT	$N=60$: 49 analyzed (I: $n=24$, C: $n=25$). In: adults, nerve injury distal to MCP joint, nerve repair. Ex: diabetes mellitus, skin diseases, (local) skin graft, painful neuroma I: mean age 42 years C: mean age 39 years	I: routine rehabilitation: ROM exercises, strengthening and scar and oedema treatment, and tactile stimulation: office programme; rotating tactile stimulation disc and home programme: pocket size tactile stimulator C: routine rehabilitation	Start: 3 weeks after surgery. Office programme 20 min twice a week until patient returned to work Home programme: several times a day. Stop: average 5 weeks after returned to work Duration: ranged from 6 weeks to 4.5 months	Baseline: 3 weeks after surgery Follow-up: after 23 weeks	At 6 months: CPT $\leq$0.217 g in 12/24 I vs. 10/25 C: $P=0.097$ M2PD 2–6 mm in 10/24 I vs. 4/25 C; $P=0.0144$ S2PD 2–6 mm in 9/24 I vs. 3/25 C; $P=0.00023$ MRC (S3+/S4) in 22/24 I vs. 9/25 C; $P=0.0009$	At 6 months, the results of the intervention group were significantly better than those of the control group	Purpose is to improve functional sensation. Outcome is only at the level of function sensibility
Imai[20]	CCT	$N=46$ (I: $n=22$, C: $n=24$). In: adults, median nerve repair at the wrist. Ex: not described I: mean age 42.8 years (range 20–55 years) C: mean age 37.5 years (range 20–55 years)	I: formal programme of sensory re-education: combination of that described by Wynn-Parry and Dellon C: no formal sensory re-education	Start: when sensibility was recovered in the palm of the hand Frequency and duration are described in reference	One-time measurement I: 1–2 years after nerve repair C: range 1–16 years	CPT of I-patients was better than of C-patients: $P<0.001$ Subgroup age <30 years: $P<0.003$ Subgroup age >30 years: $P<0.05$	Sensory re-education following median nerve repair at the wrist can significantly improve the level of cutaneous threshold achieved and help that level to be reached more quickly than when patients are permitted to recover on their own without a programme	The subscript of figure 1 of the article states that no significant difference was found between the two groups

(continued)

Table 2 (Continued)

First author	Design[a]	Participants[b,c]	Intervention[c]	Frequency and duration of intervention	Baseline and follow-up	Results[d]	Conclusion of authors	Notes
Imai[21]	CCT	$N = 46$ (I: $n = 22$, C: $n = 24$). In: adults, clean-cut median nerve injury at the wrist, primary microsurgical grouped fascicular repair. Ex: not described I: mean age 42.8 years C: mean age 37.5 years	I: sensory re-education (combination of that proposed by Wynn-Parry and Dellon) C: no intervention	Start: when moving touch is first perceived either over the pulp of the thumb, index or long finger. Once or twice a day for 15–20 min each time. Every two weeks follow-up by therapist. Duration not reported	One time measurement I: 1–2 years after nerve repair C: mean 6.6 years (range 1–16 years)	Paraesthesia (mild/none) in 17/22 I vs. 9/24 C: $P<0.01$ ORT: 9/12 objects in 19/22 I vs. C 2/24: $P<0.05$ S2PD and M2PD I vs. C: no significant difference	Sensory re-education is a cost-efficient technique for improving recovery of sensibility after median nerve repair at the wrist	In abstract ORT $P<0.005$
Daniele[22]	OD	$N = 11$, 13 digital nerves involved. In: adults (20–45 years), clean cut digital nerve injury, repaired. Ex: not described	Method described by Dellon,[2] with additional recognition of hidden objects in beans, use and recognition of plastic letters	Start: first postoperative day Daily short sessions every 4–5 hours. Monday to Friday visiting the therapist	One assessment after 4–7 weeks rehabilitation	All patients acquired useful protective sensibility (pain and temperature) S2PD: 4–9 mm M2PD: 2–9 mm Moberg-Dellon tests: 50% to normal S3+ = 23% and S4 = 77 %	Our method of early compensatory sensory re-education is comparable in its results to other programmes, but these results will be achieved in less time	In the table the patients were 20–45 years old. In text they were 15–45 years old
Wei[24]	OD	$N = 13$; 22 toe-to-hand transfers. In: adults (19–35 years, mean age 27.5 years), microneurovascular toe-to-hand transfer, ability and willingness to return for monthly follow-up	Sensory re-education followed the 1981 recommendations of Dellon[2] (early and late phase sensory re-education), modification that a Disk-Criminator	Start: mean 33 months (range 13–98 months) 4 times a day for 5 min each time. Mean duration 3.3 months (range 1–6 months). Monthly visit to therapist	Baseline at start of therapy Follow-up: mean 3.3 months (range 1–6 months)	S2PD ↓; $P<0.0001$ M2PD ↓; $P<0.0001$ In all of 22 transferred toes there was a decrease in millimetres	A programme of sensory re-education can significantly improve the measured sensibility of a toe transferred by microneurovascular technique to the hand	Purpose is to improve functional sensation. Outcome is only at the level of function sensibility

		appointments, intelligence, willingness to co-operate with the rehabilitation protocol. Ex: not described	was employed as a home rehabilitation device					
Parry[23]	OD	$N=40$. In: adults, median nerve injury, surgical repair. Ex: not described Age: not described	Sensory re-education: recognize objects and textures blindfolded, comparing with the normal hand and also with eyes open. Instruct relatives, encourage patients to train at home and to indulge in activities that demand sensory function. Co-intervention: full-time rehabilitation programme, preferably as inpatients	Start: as soon as patient can feel moving touch at fingertips. Frequency: not described. Duration: usually for 3 weeks	Follow-up 3–12 months. Assessment at start of training and after training, but not described exactly when	Texture recognition: Start: 5/9 in mean 15 s; after training: 7/9 in mean 9 s. Object recognition: Start: 11/17 in mean 17 s; after training: 16/18 in mean 9 s 2PD: after training: 2 patients (5%) <10 mm. Localization almost perfect in all patients	Formal sensory retraining procedures are well worthwhile in adult patients after median nerve lesions, provided that they are well motivated and are likely to use their sensory function in the hand in their work or hobbies	In the conclusion, they described duration of 1–2 weeks 2PD: not clear whether they mean S2PD or M2PD
Wynn Parry[25]	OD	$N=23$. In: adult inpatients, lesion of median nerve or median and ulnar nerve, sutured. Ex: not described Age: not described	Recognition of shapes using wooden blocks of circular, oblong, square and hexagonal shape. Recognition of 10 different textures. Finally, recognition of	Start: once the patient had some recovery of sensation in the fingers. Frequency: 4 times a day for 10 min. Duration: not reported	Measurements at 1 and 3 months, on discharge from treatment, and at follow-up (normally at 6 months and then at yearly intervals for	Recognition of textures: start: 4 textures in mean 34 s; after training: 7 textures in mean 19 s. Recognition of objects: Start: mean 23 s; after training: mean 11 s (including 7 additional	Our results have been most encouraging and we believe that sensory retraining should be a part of rehabilitation after suture of the median nerve or median	–

Table 2 (*Continued*)

First author	Design[a]	Participants[b,c]	Intervention[c]	Frequency and duration of intervention	Baseline and follow-up	Results[d]	Conclusion of authors	Notes
			large and then small everyday objects. All exercises: blindfolded; when patient failed the blindfold was removed, and the exercise was repeated with eyes open		5 years	objects) Localization: 1 of 23 patients had not regained normal localization at 3 months follow-up. Long-term results not explicitly described	and ulnar nerve lesion	

[a]RCT, randomized controlled trial; CCT, controlled clinical trial; OD, other design.
[b]In, inclusion criteria; Ex, exclusion criteria.
[c]I, intervention group; C, control group.
[d]CPT, cutaneous pressure threshold; M2PD, moving two-point discrimination (↓, improvement); S2PD, constant two-point discrimination (↓, improvement); 2PD, two-point discrimination; MRC grading, Medical Research Council (UK) sensibility grading scheme (range: S0, absence of sensibility, up to S4, normal sensibility); paraesthesia (4-point scale: none, mild, moderate, severe); ORT, object recognition test.

sensory re-education to improve (functional) sensibility of the hand in patients with a peripheral nerve injury of the upper limb. Based on the seven studies that were included, there is limited evidence for the effectiveness of sensory re-education to improve (functional) sensibility of the hand.

The following remarks must be made with respect to this review. Although efforts were made to identify all relevant studies, trials published in non-indexed journals could have been missed. However, by searching through several different databases and by checking the references it seems unlikely that this occurred.

Apart from one RCT and two CCTs, four studies with other designs were also included in this review. A distinction was made between studies with sufficient methodological quality and those with insufficient methodological quality. Due to the weak internal validity of the studies with 'other designs', the studies that were of sufficient methodological quality made only a limited contribution to the best-evidence synthesis (indicative findings).

The conclusions of a review depend on the criteria that are applied to assess the methodological quality of the studies, to define the cut-off point, and to assess the strength of the evidence. These criteria are arbitrary, and may influence the outcome of a systematic review. For example, Juni *et al.*[26] have shown that the use of different methods of quality appraisal may lead to different conclusions with regard to the effectiveness of the treatment, based on the same set of trials. There is still no consensus on how to assess methodological quality, how to define the cut-off point, or how to assess the strength of evidence. However, using the data presented in this review, any reader can retrace the steps and conduct a best-evidence synthesis based on the rating system of his/her own preference.

With respect to the design of the studies, two comments should be made. Three of the seven studies, including the studies that were of high or sufficient quality, only included outcome measures on sensibility (i.e. moving and constant touch and vibratory stimuli) so it is not clear whether the applied methods are also effective for functional sensibility (i.e. the recognition of objects and textures). Moreover, since none of the studies described the long-term effectiveness of the sensory re-education programme, it is not possible to determine whether the treatment had a lasting effect.

Sensory re-education is based on the principle of remoduling cortical maps by experience.[15] Therefore, the patient has to practise several times a day, for weeks or months. This demands considerable motivation from the patient, and the practice sessions should therefore be challenging. Using different types of sensory stimuli, as described by Dellon,[2] Parry[23] and Wynn-Parry,[16,25] will be more challenging than using just two specific treatment techniques. Cheng *et al.*[19] only used a rotating tactile stimulation disc and a pocket-size tactile stimulator, and made no use of familiar objects with different shapes and textures. Furthermore, memory is used for the recognition of a stimulus, so it is likely that familiar shapes, textures and objects will be easier to recognize than specific treatment objects, and therefore functional sensibility will improve more rapidly and, possibly, to a greater extent.

Because of the limited evidence available and the variation between the interventions studied, no specific sensory re-education intervention can be recommended yet. On theoretical grounds, the methods of treatment described by Dellon and Wynn-Parry may be most promising to restore functional sensibility. Their effectiveness should be assessed in randomized trials with blinded assessment of functional sensibility as primary outcome at the International Classification of Functioning, Disability and Health (ICF) level[27] of activities.

Clinical messages

- There is limited evidence for the effectiveness of sensory re-education to improve the (functional) sensibility of the hand in patients with a peripheral nerve injury.
- Well-defined clinical trials are needed to assess the effectiveness of sensory re-education.

Competing interest

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

Contributors

The study was initiated and designed by TO, AB and FN. TO, EE and AB included, selected and assessed the methodological quality of the studies.

The best-evidence synthesis was performed by TO. The draft of the article was prepared by TO and AB, and critically revised by EE and FN. The guarantor of the study is FN.

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Appendix 1 – Search strategy MEDLINE (PubMed)

arm injuries[mesh]
hand injuries[mesh]
peripheral nerves[mesh]
nerve regeneration[mesh]
1 or 2 or 3 or 4
hand
wrist
digits
6 or 7 or 8
sensation[mesh]

somatosensory disorders[mesh]
10 or 11
reeducation or re-education
relearning or re-learning
retraining or re-training
rehabilitation
stimulation
recovery
13 or 14 or 15 or 16 or 17 or 18
5 and 9 and 12 and 19
20 limited to: adults and humans

Appendix 2 – Criteria for methodological quality

Note: Internal validity = b1, b2, e, f, g, h, i, j, l, n, p; descriptive criteria = a, c, d, k, m1, m2; statistical criteria = o, q.

Randomized clinical trials, controlled clinical trials

Patient selection

a) Were the eligibility criteria specified? In order to score a YES, the nerve involved and the mechanism of injury must be described appropriately.
b) Treatment allocation
   1) Was a method of randomization performed? A random (unpredictable) assignment sequence (e.g. numbered opaque sealed envelopes). Methods of allocation using date of birth, date of admission, hospital numbers, or alternation are not regarded as appropriate (No).
   2) Was the treatment allocation concealed? Assignment generated by an independent person not responsible for determining eligibility of the patient. This person has no information about the persons included in the trial and has no influence on the assignment sequence or the decision about eligibility of the patient.
c) Were the groups similar at baseline with regard to the most important prognostic indicators? In order to score a 'Yes', groups have to be similar with regard to age, level of injury, mechanism of injury, and baseline main outcome measures. If a baseline difference exists in one of these factors, a 'No' is scored.

Intervention

d) Were the index and control interventions explicitly described? Adequate description of type, modality, application technique, intensity, duration and frequency of sessions for both the index intervention and control intervention(s) in order to be able to replicate the study.
e) Was the care provider blinded for the intervention? The reviewer determines when enough information about the blinding is given in order to score a 'Yes'. For exercise therapy a 'No' is always scored for this item.
f) Were co-interventions avoided or comparable? Co-interventions should either be avoided or comparable between the index and control groups.
g) Was the compliance acceptable in all groups? The reviewer determines (per outcome parameter) when enough information about the blinding is given to score a 'Yes'. For exercise therapy a 'No' is always scored for this item.
h) Was the patient blinded for the intervention? The reviewer determines (per outcome parameter) when enough information about the blinding is given to score a 'Yes'. For exercise therapy a 'No' is always scored for this item.

Outcome measurement

i) Was the outcome assessor blinded for the intervention? The reviewer determines (per outcome parameter) when enough information about blinding is given to score a 'Yes'.
j) Were the outcome measures relevant? The reviewer determines whether the outcome measures were relevant. For this review: sensibility or functional sensibility.
k) Was there a description of adverse effects? Each event should be described and correctly attributed to allocated treatment: if it is explicitly reported that 'no adverse effects' have occurred, a 'Yes' is scored.
l) Was the withdrawal/drop-out rate described and acceptable? Participants who were included in the study but did not complete the observation period, or were not included in the analysis, must be

described. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up, and does not lead to substantial bias, a 'Yes' is scored. No report of drop-outs is scored as 'Don't know'.

m) Timing of follow-up measurements
   1) Was a short-term follow-up measurement performed? Outcome assessment at the end of the intervention period.
   2) Was a long-term follow-up measurement performed? Outcome assessment $\geqslant 3$ months after the end of the intervention period.

n) Was the timing of the outcome assessment in all patients comparable? Timing of outcome assessment identical for all intervention groups; for all important outcome assessments.

Statistics

o) Was the sample of the patient group described? To be presented for each group at randomization and for the most important outcome assessments.

p) Did the analysis include an intention-to-treat analysis? All randomized patients are reported/analyzed for the most important moments of effect measurement (minus missing values), irrespective of non-compliance and co-interventions.

q) Were the point estimates and measures of variability presented for the primary outcome measures? For all of the important outcome measures both point estimates and measures of variability should be presented separately. Point estimates are: means, medians, modes, etc.; measures of variability are: standard deviations, 95% confidence intervals, etc. For dichotomous or categorical data, proportions have to be presented.

Other designs

The adapted version of the Amsterdam-Maastricht consensus list includes criteria a, d, f, g, i, j, k, l, m1, m2, n, o, p, q.