Neural Mobilization: A Systematic Review of Randomized Controlled Trials with an Analysis of Therapeutic Efficacy

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Abstract: Neural mobilization is a treatment modality used in relation to pathologies of the nervous system. It has been suggested that neural mobilization is an effective treatment modality, although support of this suggestion is primarily anecdotal. The purpose of this paper was to provide a systematic review of the literature pertaining to the therapeutic efficacy of neural mobilization. A search to identify randomized controlled trials investigating neural mobilization was conducted using the key words *neural mobilisation/mobilization, nerve mobilisation/mobilization, neural manipulative physical therapy, physical therapy, neural/nerve glide, nerve glide exercises, nerve/neural treatment, nerve/neural stretching, neurodynamics*, and *nerve/neural physiotherapy*. The titles and abstracts of the papers identified were reviewed to select papers specifically detailing neural mobilization as a treatment modality. The PEDro scale, a systematic tool used to critique RCTs and grade methodological quality, was used to assess these trials. Methodological assessment allowed an analysis of research investigating therapeutic efficacy of neural mobilization. Ten randomized clinical trials (discussed in 11 retrieved articles) were identified that discussed the therapeutic effect of neural mobilization. This review highlights the lack in quantity and quality of the available research. Qualitative analysis of these studies revealed that there is only limited evidence to support the use of neural mobilization. Future research needs to re-examine the application of neural mobilization with use of more homogeneous study designs and pathologies; in addition, it should standardize the neural mobilization interventions used in the study.

Keywords: Neural Mobilization, Neurodynamics, Randomized Controlled Trial, Systematic Review, Therapeutic Efficacy.

In the past, *neural tension* was used to describe dysfunction of the peripheral nervous system. More recently, there has been a shift away from a purely mechanical rationale to include physiological concepts such as structure and function of the nervous system. *Neurodynamics* is now a more accepted term referring to the integrated biomechanical, physiological, and morphological functions of the nervous system[1-4]. Regardless of the underlying construct, it is vital that the nervous system is able to adapt to mechanical loads, and it must undergo distinct mechanical events such as elongation, sliding, cross-sectional change, angulation, and compression. If these dynamic protective mechanisms fail, the nervous system is vulnerable to neural edema, ischaemia, fibrosis, and hypoxia, which may cause altered neurodynamics[1,2].

When neural mobilization is used for treatment of adverse neurodynamics, the primary theoretical objective is to attempt to restore the dynamic balance between the relative movement of neural tissues and surrounding mechanical interfaces, thereby allowing reduced intrinsic pressures on the neural tissue and thus promoting optimum physiologic function[1,2,4-7]. The hypothesized benefits from such techniques include facilitation of nerve gliding, reduction of nerve adherence, dispersion of noxious fluids, increased neural vascularity, and improvement of axoplasmic flow[1,2,4-10]. However, these etiological mechanisms for the clinically observed effects of neural mobilization still require robust validation. At present, the positive clinically observed effect of neural mo-

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bilization is mainly based on anecdotal evidence. Therefore, the purpose of this paper was to systematically review and assess the therapeutic efficacy of neural mobilization for treatment of altered neurodynamics through evaluation of appropriate randomized controlled trials (RCTs). It was hypothesized that the findings might guide evidence-based practice in the clinical application of neural mobilization.

Methods

Literature Search Strategy

A search to identify RCTs examining neural mobilization was conducted in March 2007. The following electronic databases were searched: MEDLINE via PubMed (from 1966 onwards), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (from 1982 onwards), the Cochrane Controlled Trials Register in the Cochrane Library (latest edition), SPORT-Discus (from 1830 onwards), Allied and Complementary Medicine Database (AMED) (from 1985 onwards), Physiotherapy Evidence Database (PEDro) (from 1953 onwards), ProQuest 5000 International, ProQuest Health and Medical Complete, EBSCO MegaFile Premier, Science Direct (from 1995 onwards) and Web of Science (from 1945 onwards).

The search strategy of these databases included terms and keywords related to the intervention: neural mobilisation/mobilization, nerve mobilisation/mobilization, neural manipulative physical therapy, physical therapy, neural/nerve glide, nerve glide exercises, nerve/neural treatment, nerve/neural stretching, neurodynamics and nerve/neural physiotherapy. Randomized controlled trial or RCT was the key term used in relation to the methodology of the studies.

TABLE 1. PEDro Scale (modified from Maher et al[13]).

	Score	
Criteria	**No**	**Yes**
1. Eligibility criteria were specified*		
2. Subjects randomly allocated to groups	NO (0)	YES (1)
3. Allocation was concealed	NO (0)	YES (1)
4. Groups similar at baseline regarding the most important prognostic factors	NO (0)	YES (1)
5. Blinding of all subjects	NO (0)	YES (1)
6. Blinding of all therapists who administered therapy	NO (0)	YES (1)
7. Blinding of all assessors who measured at least one outcome	NO (0)	YES (1)
8. Measures of at least one key outcome were obtained from more than 85% of initially allocated subjects	NO (0)	YES (1)
9. All subjects for whom outcome measures were available received treatment or control as allocated, or if this was not the case, at least one outcome measure analysed using "intention to treat" analysis	NO (0)	YES (1)
10. The results of between-group statistical comparisons are reported for at least one key outcome	NO (0)	YES (1)
11. The study provides both point measures and measures or variability for at least one key outcome	NO (0)	YES (1)
Total		N/10

* Criteria 1 score is not included in the overall PEDro rating.

TABLE 2. Randomized controlled trials of neural mobilization as a treatment modality in order of PEDro score.

	Scores for PEDro Criteria													
	1*	2	3	4	5	6	7	8	9	10	11	QS	Methodological Quality	IVS
Cleland et al[27]	1	1	1	1	0	0	1	1	1	1	1	8	Moderate	5
Coppieters et al[8] (Cervical lateral glide treatment)	1	1	1	1	0	0	1	1	1	1	1	8	Moderate	5
Tal-Akabi & Rushton[31]	1	1	1	1	0	0	1	1	1	1	1	8	Moderate	5
Pinar et al[30]	1	1	1	1	0	0	1	1	1	1	1	8	Moderate	5
Baysal et al[26]	1	1	1	1	0	0	1	1	1	1	1	8	Moderate	5
Allison et al[25]	1	1	1	0	0	0	1	1	1	1	1	7	Moderate	5
Coppieters et al[28] (Neural provocation)	1	1	1	0	0	0	1	1	1	1	0	6	Moderate	5
Akalin et al[24]	1	1	0	1	0	0	0	1	1	1	1	6	Limited	3
Scrimshaw & Maher[10]	1	1	0	0	0	0	1	1	1	1	1	6	Moderate	4
Vicenzino et al[32]	1	1	0	0	0	0	1	1	1	1	1	6	Moderate	4
Drechsler et al[29]	1	1	0	0	0	0	0	1	1	1	1	5	Limited	3

Note: QS = overall quality score; IVS = internal validity score.

*Criteria 1 score is not included in the overall PEDro rating.

The titles and/or abstracts of these citations were reviewed to identify papers specifically detailing neural mobilization used as a treatment modality. The search was limited to studies written in or translated to English and those utilizing human subjects. There was no limitation regarding the date the studies were published, other than the date limitations of each selected database. In addition, the reference lists of each paper were searched to identify other relevant papers.

Study Selection

The method for selection of relevant studies was consistent with suggested guidelines for conducting systematic reviews[11]. The following inclusion criteria were used to select relevant papers for the review:

- Type of participant: participants older than 18, of either gender, and with a clinical diagnosis consistent with neurodynamic dysfunction (musculoskeletal conditions with symptoms of pain and/or paresthesia indicative of compromise of the peripheral nervous system).
- Type of study design: randomized controlled trials.
- Type of intervention: use of a manual or exercise technique designed to have a direct effect on neural tissue with the purpose of dynamically influencing (e.g., sliding, stretching, moving, mobilizing etc.) the neural tissue.
- Outcome measurements: at least one of the following outcome measurements used to assess the status of the nervous system: pain rating (e.g., Visual Analogue Scale [VAS], function-specific pain VAS (i.e., work- or sport-related pain), pain and or range of movement (ROM) during neural tissue provocation tests (NTPT), functional disability scores (e.g., Short-form McGill Pain Questionnaire, Northwick Park Questionnaire, and Oswestry Disability Index).

Methodological Quality Assessment

Three reviewers independently assessed the methodological quality of each RCT. The PEDro Scale (Table 1), developed by *The Centre of Evidence-Based Physiotherapy* (CEBP), was utilized to assess each paper[12]. The PEDro Scale, an 11-item scale, is a validated, reliable, and versatile tool used to rate

RCTs for the PEDro Database[13-15]. The PEDro scale has been used as a measure of methodological quality in many systematic literature reviews[16-20].

An overall score of methodological quality, or quality score (QS), was determined for each paper by each of the three reviewers as a total of positive scores for 10 of the 11 items (i.e., N/10). Unlike the other items, Criterion One of the PEDro scale relates to external validity and was not used in the final total PEDro score[13,15]. A consensus method was used to discuss and resolve discrepancies between the markings of each paper between the reviewers. The agreed QS for each paper is included in Table 2.

The various items of the PEDro Score deal with different aspects of RCT analysis including internal validity, external validity, and statistics. In order to allow quantitative analysis of the methodological quality of a systematic review, van Tulder et al[11] recommended the analysis of the internal validity criteria of any rating tool. For the PEDro Scale, seven items relating to internal validity were identified. These seven items include items 2, 3, and 5 through 9 (Table 1). An internal validity score (IVS) has also been used in other systematic reviews[21] to allow calculation of the number of internal validity criteria met for that particular rating system and to thereby give an assessment of methodological quality. It was decided to calculate an IVS for this review based on the relevant internal validity criteria of the PEDro Scale. The positive scores of each of these seven items were added together to calculate the IVS (Table 2).

To stratify methodological quality, the summated score of the 7-item IVS, calculated from the initial PEDro score (QS), was divided into three categories. A study of *high methodological quality* obtained IVS values of 6–7, a *moderate quality* obtained IVS values between 4–5, and a *limited quality* was scored between 0–3. This decision was made based on even cut-off points between 0 and 7.

Analysis of Therapeutic Efficacy

When RCTs are heterogeneous, there is no available method to quantitatively assess the relative benefit (or lack thereof) of one intervention versus another because the studies compare dissimilar patient populations or interventions. In situations where the heterogeneity of primary studies prevents use of a quantitative meta-analysis to summarize the results, recommendations are typically made based on a qualitative assessment of the strength of the evidence[21]. The RCTs reviewed for this paper were considered heterogeneous because they explored a variety of pathologies and different types of neural mobilization techniques. Consequently, a quantitative meta-analysis was not appropriate and results were analyzed in a qualitative fashion. The qualitative assessment involved the following categories scored specifically for each type of intervention:

- Level 1: Strong evidence: provided by generally consistent findings in multiple RCTs of high quality.
- Level 2: Moderate evidence: provided by generally consistent findings in one RCT of high quality and one or more of lower quality.
- Level 3: Limited evidence: provided by generally consistent findings in one RCT of moderate quality and one or more low-quality RCTs.
- Level 4: Insufficient evidence: provided by generally consistent findings of one or more RCTs of limited quality, or when no RCTs were available, or when studies provided conflicting results.

Clinical Benefit

Lastly, to determine whether a clinical benefit for neural mobilization could be concluded, a ranking system similar to that used by Linton and van Tulder[11] was used. A positive effect was concluded if the intervention (i.e., neural mobilization) was statistically significantly more beneficial compared to the control for at least one key outcome variable, a negative effect if the intervention was less effective than the control, and a neutral effect was concluded where the intervention and control did not statistically differ significantly for any of the outcome variables[23].

Results

Selection of Studies

Ten RCTs, represented by 11 published articles[8,10,24-32], satisfied the inclusion criteria following the electronic and manual reference list searches. The articles published by Coppieters et al[8,28] are from the same subject group and were thus classified as one RCT.

Methodological Quality

The methodological quality for each paper, represented by the IVS, is detailed in Table 2. Nine of 11 studies[8,10,25-28,30-32] reviewed were given an IVS of 4 or 5 and were of moderate methodological quality. Two of the studies[24,29] were given an IVS of 3, suggesting limited methodological quality. Table 3 presents statistics relating to the percentage of each item that was satisfied for an IVS score.

All of the 11 studies satisfied the items relating to random allocation of subjects, measures of one key outcome taken from greater than 85% of the population, use of intention-to-treat analysis (where this was required due to a drop-out group), and results of statistical analysis reported (items 2, 8, 9, and 10). All 11 studies did not satisfy items 5 and 6, which relate to subject and therapist blinding. Two stud-

TABLE 3. Number and percentage of the studies meeting each PEDro criteria.

PEDro Criteria		Number meeting criterion (N)	Percent meeting criterion (%)
1	Eligibility criteria specified (yes/no)	11	100
2.	Subjects randomly allocated to groups (yes/no)	11	100
3.	Allocation was concealed (yes/no)	7	64
4.	Groups similar at baseline (yes/no)	6	55
5.	Subjects were blinded to group allocation (yes/no)	0	0
6.	Therapists who administered therapy were blinded (yes/no)	0	0
7.	Assessors were blinded (yes/no)	9	82
8.	Minimum 85% follow-up (yes/no)	9	100
9.	Intent to treat analysis for at least 1 key variable (yes/no)	9	100
10.	Results of statistical analysis between groups reported (yes/no)	9	100
11.	Point measurements and variability reported (yes/no)	10	91

ies[24,29] did not satisfy item 7, which relates to rater blinding. This suggests that these two studies lacked all three forms of blinding (subject, therapist, and rater). The other 9 studies were single-blinded (rater-blinded) studies. There was no clear trend established for item 4, which relates to concealed allocation of subjects.

Study Characteristics

All ten RCTs used different methods of application of neural mobilization (e.g., cervical lateral glide, slump sliders, peripheral nerve sliders, etc.), and some studies chose to combine these techniques with home-based neural mobilization exercises. There were also differing neurodynamic dysfunctions examined, including lateral epicondylalgia, carpal tunnel syndrome, post-operative spinal surgery, non-radicular low back pain, and neurogenic cervico-brachial pain syndrome. Therefore, all ten RCTs were clinically and therapeutically heterogeneous, necessitating a qualitative analysis for summarizing the results. Table 4 contains details of study characteristics.

Therapeutic Efficacy

Of the 11 studies identified, 6 different categories or types of treatment were identified (Table 5). Using the qualitative rating system, as mentioned earlier, it appears there is limited evidence (Level 3) to support the use of neural mobilization that involves active nerve and flexor tendon gliding exercises of the forearm[24,26,30], cervical contralateral glides[8,28,32], and Upper Limb Tension Test 2b (ULTT2b) mobilization[29,31] in the treatment of altered neurodynamics or neurodynamic dysfunction. There was inconclusive evidence (Level 4) to support the use of neural mobilization involving slump stretches[27] and combinations of neural mobilization techniques[10,25] in the treatment of altered neurodynamics or neurodynamic dysfunction.

Clinical Benefit

Table 4 lists the study details of the 11 studies. More studies found a positive effect[8,24-28,30,32] than a neutral effect[10,29,31] .

Discussion

A search to identify RCTs investigating neural mobilization yielded 11 studies that met the inclusion criteria for this review. Analyses of these studies, using the criteria of Linton and van Tulder[11], indicated that 8 of the 11 studies[8,24-28,30,32] concluded a positive benefit from using neural mobilization in the treatment of altered neurodynamics or neurodynamic dysfunction. Three of the 11 studies[10,29,31] concluded a neutral benefit, which suggests that neural mobilization was no more beneficial than standard treatment or no treatment. Nine of the 11 studies[8,10,25-28,30-32] reviewed demonstrated moderate methodological quality; the two remaining studies[24,29] yielded limited methodological quality. Studies exhibited weaknesses in random allocation, intention to treat, concealed allocation, and blinding; consequently, our ability

TABLE 4. Randomized controlled trials of neural mobilization as a treatment modality .

Author	Patient demographics	Intervention Group (IG)	Comparison Group (CG)	Outcome	Result	IVS	QS
Cleland et al[27]	N=30 (9 male, 21 female) —Age range 18–60 years —Mean age (years) IG 40.0 (±12.2), CG 39.4 (±11.3) Duration symptoms (weeks) IG 14.5 (±8.0), CG 18.5 (±12.5)	16 subjects with low back pain Same as control plus: Slumped stretching exercise (position held 30 seconds, 5 repetitions) Home exercise slump stretches (2 repetitions for 30 seconds) 2 x week for 3 weeks	14 subjects with low back pain 5-minute cycle warm-up Lumbar spine mobilization (Posterior-anterior mobilizations to hypomobile lumbar segments, grade 3–4) Standardized exercise program (pelvic tilts, bridging, squats, quadruped alternate arm/leg activities; 2 sets 10 repetitions each exercise) 2 x week for 3 weeks	Outcomes were measured pre- and post-treatment 1)Body diagram (for distribution of symptoms) 2)Numeric pain rating scale (NPRS) 3)Modified Oswestry disability index (ODI) 4)Fear avoidance beliefs questionnaire	No baseline differences between groups ($p > 0.05$). At discharge, patients who received slumped stretching demonstrated significantly greater improvements in disability (9.7 points on the ODI, $p < 0.001$), pain (0.93 points on the NPRS, $p=0.001$), and centralization of symptoms ($p<0.01$) than patients who did not. The between-group comparisons suggest that slump stretching is beneficial for improving short-term disability, pain, and centralization of symptoms.	*5*	*8*
Baysal et al[26]	N=36 (36 female patients—all with clinical and electrophysiological evidence of CTS All with bilateral involvement Mean age— Grp 1 47.8 ± 5.5; Grp 2 50.1 ± 7.3; Grp 3 51.4 ± 5.2 Mean duration of symptoms (years)— Grp 1 1.5 ± 1.6; Grp 2 1.4 ± 0.8; Grp 3 1.4 ± 0.8 8 eventual dropouts	*Group 1* (N=12) *custom made neutral volar splint* (worn for 3 weeks); *exercise therapy* (nerve and tendon gliding exercises as described by Totten & Hunter, 1991) 5 sessions daily, each exercise repeated 10x/session—for 3 weeks *Group 2*—(N=12) *custom made neutral volar splint* (worn for 3 weeks); *Ultrasound* (15min/session to palmar carpal tunnel, 1mhz,	Experimental groups 1 and 3 that incorporated nerve gliding exercises and a comparison group that did not incorporate these exercises. Comparison between groups 2 and 3 as the only difference in intervention programs was that group 3 used nerve gliding exercises and group 2 did not.	All measures pre-Rx, end of Rx, and 8 weeks F/U 1. pain (VAS) 2. Tinel's sign 3. Phalen's sign 4. mean static two-point discrimination—pulp of radial three digits 5. hand-grip strength—hand-held dynamometer 6. pinch strength—between thumb and little finger—dynamometer 7. symptom-severity scale questionnaire (11 items)	No significant differences between groups at the end of Rx and 8 weeks follow-up of all measures of Treatment Effect (measures 1, 5, 6, 7, 8, 9, 10) Within group comparisons showed significant improvement seen in all 3 grps in Tinels and Phalen's signs at end of Rx and 8 weeks follow-up Significant improvement seen in all 3 grps in grip and pinch strength at 8 weeks follow-up. No changes seen in two-pt discrimination	*4*	*8*

TABLE 4. Randomized controlled trials of neural mobilization as a treatment modality *(continued)*.

Author	Patient demographics	Intervention Group (IG)	Comparison Group (CG)	Outcome	Result	IVS	QS
		1.0w/cm2, 1:4, 5cm2 transducer) 1 Rx/day, every 5 days for 3 weeks (total 15 Rx's) *Group 3*—(N=12) *custom made neutral volar splint* (worn for 3 weeks); *exercise therapy* (nerve and tendon gliding exercises as described by Totten & Hunter, 1991) 5 sessions daily, each exercise repeated 10x/session—continued for 3 weeks; *Ultrasound* (15minutes/session to palmar carpal tunnel, 1mhz, 1.0w/cm2, 1:4, 5cm2 transducer) 1 Rx/day, every 5 days for 3 weeks (total 15 Rx's)		8. functional status scale questionnaire (8 items) 9. median motor nerve conduction—motor distal latency EMG of abductor pollicis 10. sensory distal latency—EMG of abductor pollicis 11. needle EMG of abductor pollicis brevis—looking for denervation 12. patient satisfaction survey (at 8weeks follow-up only)	Within-group analysis showed significant improvement in pain, symptom and functional scales of all three groups at end-Rx and 8 weeks follow-up Grp 3 had significantly the best results at 8 weeks follow-up patient satisfaction questionnaire Median sensory distal latency significantly decreased in grps 1 and 3 at end-Rx and 8 weeks follow-up No significant change seen in median motor distal latency of all 3 grps $P<0.05$ In summary, between-group analysis revealed no difference between groups, but within-group analysis showed that all groups improved a statistically significant amount for a majority of outcome measures.		
Pinar et al[30]	N =26 (female) Age range 35–55 years Duration of symptoms (mo) CG 47.6 (± 6.8), IG 49.6 (± 5.2)	14 patients (19 hands) patients diagnosed with early-middle stages CTS In addition to splint wearing and patient training program treated with nerve gliding exercises 10 repetitions 5 sets a	12 patients (16 hands) patients diagnosed with early-middle stages CTS Treated in volar splint in neutral worn day & night for 6-weeks, then night only from week 6-10, and a	Undertaken before and after a 10-week treatment program. 1. Tinel Test 2. Phalen Test 3 Pain (VAS) over a day 4. Motor Function—manual muscle testing, and grip strength (Jamar hand	Between-group comparisons for these same variables showed no statistically significant differences pre-treatment or post-treatment, so the groups were similar. Both groups made statistically significant improvements in pain, pinch & grip strength, and sensitivity testing according	*5*	*8*

		day for 10 weeks, combined with a conservative treatment program	patient training program for the modification of functional activities (avoid repetitive activities, etc.) with a conservative treatment program.	dynamometer) 5. Sensory evaluation (Semmes-Weistein monofilament [SWM] &2-point discrimination test [2PD]) 6. Electrophysiological test—median & ulnar nerve. distal latencies	to intra-group or "within-group" analysis ($p< 0.05$). A statistically significant result favoring the incorporation of neural gliding exercises—with more rapid pain reduction, and greater functional improvement especially in grip strength ($p< 0.05$). Tables 2–4 provide post-treatment data on electrophysiologic, Tinel, and Phalen test findings. Since all subjects had "positive/pathologic" findings pre-treatment, the authors could use these 2x2 contingency tables to generate a number needed to treat to see whether there was a clinically important effect favoring neural gliding exercises on these particular outcomes.		
Coppieters et al[8] (cervical lateral glide) References described together due to papers' different outcomes on the same subject sample with the same intervention technique.	N=20 (16 females, 4 males) Age range 35–65 years —Mean age (years) IG 49.1 (±14.1), CG 46.6 (±12.1) —Mean duration of symptoms (mo) IG 2.7, CG 3.2 As above	10 subjects with brachial or cervicobrachial neurogenic pain Received neural mobilization treatment (contralateral l glide of cervical segment) Cervical contralateral glide C5-T1. Several components of the neural tension provocation test of the median nerve (NTPT1) were applied. Patients in supine	10 subjects with brachial or cervicobrachial neurogenic pain Received ultrasound dose of 0.5 W/cm^2, 5 minutes sonation time, 20% size of head 5cm^2, frequency 1MHz. Pulsed ultrasound for 5 minutes over the most painful area (0.5 W/cm^2, 1MHz, treatment head 5cm^2). Arm was in unloaded position. Ultrasound	Outcomes were measured pre- and post-treatment 1)Elbow extension ROM during NTPT1 2) Pain (VAS) 3) Symptom distribution Measurements taken pre- and post-treatment 1. Elbow extension ROM during NTPT1 2. Pain intensity during the NTPT1 VAS	Significant differences in treatment effects between two groups could be observed for all outcome measures ($p\leq0.306$). For the mobilization group, the increase in elbow extension from 137.3° to 156.7°, the 43% decrease in area of symptom distribution and decrease in pain from 7.3 to 5.8 were significant ($p\leq.0003$). For ultrasound group, there were no significant differences On the involved side, the shoulder girdle elevation	*5* *5*	*8* *6*

TABLE 4. Randomized controlled trials of neural mobilization as a treatment modality *(continued)*.

Author	Patient demographics	Intervention Group (IG)	Comparison Group (CG)	Outcome	Result	IVS	QS
Coppieters et al[28] (neural provocation)		received a lateral translation movement away from their involved side, while mimicking cervical side flexion lor rotation. After 2 trials, 3 repetitions were performed.	chosen because it does not involve any movement of peripheral nerves.		force occurred earlier and the amount of force at the end of the test was substantially though not significantly greater on the uninvolved side at the corresponding ROM. Together with a significant reduction in pain perception after the cervical mobilizations, a clear tendency toward normalization of the force curve could be observed, namely, a significant decrease in force generation and a delayed onset. The control group demonstrated no differences.		
Allison et al[25]	N=30 (20 females, 10 males) Age range 18–75 years Median duration of symptoms (mo) NT 12 IQR 48 AT 72 IQR 72 CG 12 IQR 91	Neural tissue manual therapy (NT)—Cervical lateral glide, shoulder girdle oscillation, muscle re-education, home mobilization. For 8 weeks. Articular treatment group (AT) Glenohumeral joint mobilization, thoracic mobilization and home exercise. For 8 weeks.	Received no intervention for the initial 8 weeks (Then at the end of the study they were given neural treatment as a cross-over protocol.)	Measurements taken pre-treatment 4 weeks into treatment and post-treatment. 1. McGill pain questionnaire 2. Northwick Park questionnaire 3. Pain (VAS)	Both intervention groups were effective in improving pain intensity, pain quality scores, and functional disability levels. However, a group difference was observed for the VAS scores at 8 weeks with the "neural manual therapy" group having a significantly lower score.	*5*	*7*
Akalin et al[24]	N=36 (2 male, 34 female) Age range 38–64 years	18 subjects with CTS Same as control plus: Tendon glides in 5. positions	18 subjects with CTS Custom-made neutral volar	Undertaken pre-treatment and 8 weeks post-treatment	At the end of treatment, within-group analysis showed a significant improvement was	*3*	*6*

	Mean age 51.93 ±5.1 years Mean group age (years) CG 52.16 (±5.6), IG 51.7 (±5.5) Duration of symptoms (mo) CG 47.6 (± 6.8), IG 49.6 (± 5.2)	Median nerve exercises in 6 positions. (Each position was maintained for 5 seconds; 10 repetitions of each exercise were done 5 times a day) For 4 weeks	wrist splint was instructed to be worn all night and during the day as much as possible for 4 weeks	1) Phalen's sign 2) Tinel's sign 3) 2-point discrimination 4) Grip strength 5) Pinch strength 6) Symptom severity score 7) Functional status score A patient satisfaction investigation undertaken by telephone 8.3 (± 2.5) months post-treatment	obtained in all parameters in both groups. The nerve and tendon glide group had slightly greater scores but the difference between groups was not significant except for lateral pinch strength. A total of 72% of the control group and 93% nerve and tendon slide group reported good or excellent results in the patient satisfaction investigation, but the difference between the groups was not significant. In summary, both groups improved by a statistically significant amount according to within-group analysis comparing before and after treatment, but except for lateral pinch strength, both groups improved a similar amount because between-group analysis revealed no statistically significant differences after treatment While patient satisfaction percentages were higher in the neural mobilization group, this difference between groups was not statistically significant.		
Scrimshaw & Maher[10]	N=81 (30 female, 51 male) Mean age (years) IG 55 (±17) CG 59 (±16)	35 subjects undergoing lumbar discectomy (N=9), fusion (N=6) or laminectomy (N=20)	46 subjects undergoing lumbar discectomy (N=7), fusion (N=9) or laminectomy (N=30)	Measured at baseline, 6 weeks, 6 months, and 12 months. 1. Global perceived effect (GPE) 2. Pain (VAS)	All patients received the treatment as allocated with 12-month follow-up data available for 94% of those randomized. There were no statistically significant or clinically significant benefits provided by the neural	4	6

TABLE 4. Randomized controlled trials of neural mobilization as a treatment modality *(continued)*.

Author	Patient demographics	Intervention Group (IG)	Comparison Group (CG)	Outcome	Result	IVS	QS
		Same as control plus neural mobilization added. Exercises were 6 weeks post-discharge	Standard post-operative care (exercises for lower limb and trunk) Exercises were encouraged for up to 6 weeks post-discharge	3. McGill pain questionnaire 4. Quebec disability scale 5. Straight leg raise 6. Time taken to return to work	mobilizations treatment for any outcome.		
Tal-Akabi & Rushton[31]	N=21 Age range 29–85 years Mean age 47.1 (±14.8) Duration of symptoms (years) 2.3 (±2.5, range 1–3) All subjects are on the waiting list for surgery	*Group 1:* 7 subjects with CTS received ULTT 2a mobilization *Group 2*–7 subjects with CTS received carpal bone mobilization (anterior-posterior and or posterior-anterior) and a flexor retinaculum stretch	*Group 3* 7 subjects with CTS received no intervention	All except PRS were taken pre- and post-treatment 1. Symptoms diary (24hr VAS) 2. Functional box scale (FBS) 3. Range of motion (ROM)—wrist flexion/ extension 4. ULTT2a 5. Pain relief scale (PRS) 6. Continuing on to have surgery	An effect of neural mobilization on pain demonstrated a statistically significant difference between the 3 groups ($p<0.01$). However, although this improvement was better than no treatment, it was not superior to the effect that could be achieved with carpal bone mobilization, with no statistical difference in effectiveness of treatment demonstrated between the two intervention groups.	5	8
Vicenzino et al[32]	N=15 with lateral epicondylalgia (7 male, 8 female) Age range 22.5–66 years Mean age 44 ± 2 years Duration of symptoms 8 ± 2 months	*Treatment group* Contralateral glide C5/6 grade 3 with affected arm in a predetermined position	*Control group* Subject's arm rested on abdomen Subjects received 1 of the 3 treatment	Recorded immediately before and after treatment 1. ULTT2b (measuring degrees of abduction)	The treatment group produced significant improvements in pressure pain threshold, pain-free grip strength, neurodynamics, and pain scores relative	*4*	*6*

	Range of duration 2–36 months	*Placebo group* Manual contact was applied as in the treatment group with patient's arm rested on abdomen but no glide was applied All treatments were applied in 3 lots of 30 seconds with 60-second rest periods	conditions for 3 days in a random order.	2. Pain-free grip strength (hand held dynamometer) 3. Pressure pain threshold 4. Pain via VAS (over 24 hours) 5. function VAS (over 24hours)	to the placebo and control groups ($p< 0.05$)		
Drechsler et al[29]	N=18 (8 male, 10 female) Age range 30–57 years Mean age 46 years Mean age of groups (years) IG 46.4, CG 45.5	8 subjects with lateral epicondylitis Neural tension group ULTT 2b with . . . 1. Graded flexion and or shoulder abduction 2. Anterior-posterior mobilizations of radial head if radial head mobility was judged hypomobile Home exercise plan to mimic ULTT2b 10 repetitions a day increasing but not exceeding 2 sets a day. 2x week for 6–8 weeks	10 subjects with lateral epicondylitis Standard treatment group 2 times a week for 6–8 weeks 1. Ultrasound over common extensor tendon 2. Transverse friction to tendon (1 minute per session) 3. Stretch and strengthen wrist extensors 5–10 repetitions 30 seconds. Dumbbells gradually increasing to 3 sets 15 repetitions 4. Home exercise program stretch and strengthen	Undertaken pre treatment, post treatment and 3 month Follow up 1. Self-report questionnaire 2. Grip strength (hand-held dynamometer) 3.Iisometric testing extension of 3rd finger 4. ULTT2b (measuring abduction) 5. Radial head mobility (ant/post glides, graded as hypo/normal/ hyper 6. Elbow extension ROM during ULTT	Subjects who received radial head mobilizations improved over time ($p<0.05$) Results from neural tension group were linked to radial head treatment and isolated effects could not be determined. There were no long-term positive results in the standard treatment group.	3	5

Legend: N = number of subjects, IG = intervention group, CG = control group, VAS = visual analogue scale, CTS = carpal tunnel syndrome, Grp = group, Rx = treatment, mHz = mega-hertz, EMG = electromyography, F/U = follow-up, NT = neural treatment, AT = articular treatment, ROM = range of movement, mo = months, yrs = years, ULTT = upper limb tension tests, ant = anterior, post = after, IQR = interquartile range, ULTT2a = median nerve bias neurodynamic test, ULTT2b = radial nerve bias neurodynamic test.

to review and assess the therapeutic efficacy of neural mobilization for treatment of altered neurodynamics through evaluation of appropriate randomized controlled trials was substantially limited.

Methodological weaknesses can lead to over- or underestimations of actual outcomes. For example, blinding can significantly eliminate bias and confounding, and is essential in maintaining the robustness of an RCT. Blinding is difficult for use in studies involving manual therapy[33,34], although in this review only 9 of the 11 studies blinded the raters. Some have argued that blinding for use in manual therapy studies is useful[34], although it is arguable that non-masked raters could bias outcome findings.

The outcome measures used by the RCTs in this review also lacked homogeneity. A battery of different scales was used, and findings are not transferable across populations. One method used to standardize measures of success is the use of a minimal clinically important different score (MCID). MCID relates to the smallest change in a clinical outcome measure, which correlates to a person feeling "slightly better" than the initially recorded state[33]. Findings can be dichotomized into success or failure. In research that analyzes the therapeutic benefit of an intervention, the MCID is an important statistic, as it represents a level of therapeutic benefit significant enough to change clinical practice[34]. MCIDs are population- and pathology-specific, and they require analysis to determine a properly computed value. To our knowledge, all or a majority of the outcome scales used have not been evaluated for an MCID for the population examined in our study.

Due to the heterogeneity in respect to the neural mobilization interventions used in these RCTs, it is difficult to make general conclusions regarding neural mobilization as a general therapeutic tool. Over all, six different categories or types of neural mobilization treatments were identified (Table 5). Of these, there was limited evidence to support the use of active nerve and flexor tendon gliding exercises of the forearm[24,26,30], cervical contralateral glides[8,28,32], and Upper Limb Tension Test 2b (ULTT2b) mobilization[29,31] in the treatment of altered neurodynamics or neurodynamic dysfunction. There was inconclusive evidence to support the use of slump stretches[27] and combinations of neural mobilization techniques[10,25] in the treatment of altered neurodynamics or neurodynamic dysfunction.

Future studies are needed and a larger, more comprehensive body of work is required before conclusive evidence is available. We found only 10 RCTs met the inclusion criteria for this systematic review. Unfortunately, all studies were clinically heterogeneous in that each looked at a number of different pathologies and different types of neural mobilization. This made quantitative analysis of therapeutic efficacy impossible. As Reid and Rivett[21] have stated, direct quantitative comparison, within the realms of systematic review, is very difficult when pathologies, interventions, and outcome measures are heterogeneous. For example, even for this review there were a number of studies that looked at neural mobilization in treatment for lateral epicondylalgia[29,32], carpal tunnel syndrome[24,26,30,31], and cervicobrachial pain[8,25,28]. The specific neural mobilization intervention differed be-

TABLE 5. Level of evidence for therapeutic efficacy per intervention type.

Number	Type of Intervention	Studies per Intervention	Evidence for Intervention
1	Slump stretches	Cleland et al[27]	Insufficient (Level 4)
2	Active nerve and flexor tendon gliding exercises (forearm)	Baysal et al[26] Pinar et al[30] Akalin et al[24]	Limited (Level 3)
3	Cervical contralateral glide (nerve mobilization)	Coppieters et al[8] Coppieters et al[28] Vicenzino et al[32]	Limited (Level 3)
4	Combination (neural tissue manual therapy, cervical lateral glide, and shoulder girdle oscillations)	Allison et al[25]	Insufficient (Level 4)
5	Combination (Straight leg raise, knee flexion/extension, and passive cervical flexion)	Scrimshaw & Maher[10]	Insufficient (Level 4)
6	Upper limb tension test 2b (ULTT 2b) neural mobilization	Tal-Akabi & Rushton[31] Drechsler et al[29]	Limited (Level 3)

tween studies, making, in these cases, the treatments too heterogeneous for statistical pooling.

With respect to the clinical implications of these findings, it is interesting to note that generally all the RCTs that looked at neural mobilization for upper quadrant (i.e., cervical spine, shoulder girdle, and upper limb) problems, with the exception of one study [25], concluded that there was limited evidence for therapeutic efficacy. This is in direct contrast to studies that examined neural mobilization for lower quadrant (i.e., lumbar spine, pelvic girdle, and lower limb) problems[10,25,27] in that all provided inconclusive evidence for therapeutic efficacy. From a more specific pathological perspective, for neural mobilization of cervical nerve roots, three papers supported the use of cervical contralateral glide mobilization. For neural mobilization of the median nerve in people with carpal tunnel syndrome, three papers supported the use of active nerve and flexor tendon gliding exercises of the forearm[24,26,30].

Future Research

Considering the results of the extensive literature search carried out for this review, there is an obvious paucity of research concerning the therapeutic use of neural mobilization. Not only is there a lack in quantity of such research, upon dissection of the scarce research that is available, there is also a lack of quality. Future research should look not only at similar pathologies but also at similar neural mobilization techniques.

Another key feature of these studies is that only clinical outcome measures were used. In the introduction, we discussed the biomechanical, physiological, and morphological theories underlying neural mobilization. One of the key theories for using neural mobilization is to exploit the mechanical effect that this form of mobilization has on the neural tissue and its mechanical interface. It is possible to use objective *in-vivo* measurements of neural movement (i.e., glide, slide, stretch, etc.) via real-time diagnostic ultrasound. It will be important to eventually substantiate clinical improvements with objective measurement of neural movement. For example, recent unpublished data have demonstrated that it is possible to visualize and quantify, with reasonable reliability, sciatic nerve movement during neural mobilization[35]. As it has been postulated that an improvement in nerve mobility may explain any perceived benefits of neural mobilization, it would be relevant to make a comparison of clinical measures with objective measures (e.g., ROM and neural mobility) in an *in-vivo* situation in studies that examine neural mobilization. Such a comparison may give clues as to whether neural mobilization is more likely to impose a mechanical effect or a neurophysiological effect on the nervous system.

Conclusion

Neural mobilization is advocated for treatment of neurodynamic dysfunction. To date, the primary justification for using neural mobilization has been based on a few clinical trials and primarily anecdotal evidence. Following a systematic review of the literature examining the therapeutic efficacy of neural mobilisation, 10 RCTs discussed in 11 studies were retrieved. A majority of these studies concluded a positive therapeutic benefit from using neural mobilization. However, in consideration of their methodological quality, qualitative analysis of these studies revealed that there is only limited evidence to support the use of neural mobilization. Future research needs to examine more homogeneous studies (with regard to design, pathology, and intervention), and we suggest that they combine clinical outcome measures with *in-vivo* objective assessment of neural movement. ■

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