Peripheral somatosensory stimulation and postural recovery after stroke : a systematic review

Peripheral somatosensory stimulation and postural recovery after stroke - a systematic review

Purpose. It is hypothesized that peripheral somatosensory stimulation (PSS) can promote postural recovery after stroke by increasing afferent input and postural contribution of the paretic leg. Therefore, this systematic review aims to investigate which PSS approaches are documented and investigated on effectiveness.

Methods. Five databases (PubMed, Web of Science, PEDro, Cochrane Library Trials, RehabData) have been searched on clinical studies in stroke rehabilitation, investigating PSS, which is defined as a non-motor and focal stimulation to the paretic leg aiming an increase in somatosensory input.

Results. Twenty studies present different PSS approaches (mainly electrical and vibration stimulation) and following results: (I.) There is an immediate effect after a single session of PSS on postural stability. In contrast, (II.) repetitive sessions of isolated PSS led to highly inconsistent results. Finally, (III.) PSS as an adjuvant to exercises did promote long-term postural recovery.

Conclusion. PSS is found to be effective immediately and on a long-term as an adjuvant therapy only in improving postural stability in a chronic stroke population. However, if PSS enhances paretic leg postural contribution remains unclear. Future research is warranted considering promising results and high prevalence of postural instability impacting daily life of stroke survivors.

Keywords: Stroke; Balance; Postural Recovery; Somatosensation; Stimulation; Review

Introduction

More than half of stroke survivors become moderately to severely disabled and are unable to walk, with the majority still experiencing severe disability even after the rehabilitation phase [1-3]. Standing balance control is fundamental for the ability to ambulate [4] and needs to be addressed in postural rehabilitation as soon as possible.

Standing balance control is multifactorial, making it difficult for therapists to determine underlying mechanisms and setting rehabilitation goals. In a cohort by Tyson et al. [5] , weakness and somatosensation are found to be most important. Strengthening after stroke is covered in literature [6] and muscle strength was able to explain only some variability in upright standing performance after stroke [7]. Apparently, other factors predominate. Stroke-related somatosensory impairments are common (50-80% of stroke survivors [8]) and found to be related to balance [5,9], gait [10] and activities of daily living [8]. High prevalence and a functional impact on postural stability suggest addressing somatosensation in postural rehabilitation to be of great importance.

In addition, stroke survivors tend to rely heavily on their non-paretic leg during upright standing [11,12]. They seem to be constrained to the non-paretic side in developing adaptive postural strategies. This asymmetric shift of postural contribution is found to be somehow successful in static [13], but ineffective in dynamic situations, e.g. during gait [14,15]. Therefore, novel therapeutic strategies are warranted which take the functional impact of somatosensation and asymmetric postural contribution into account.

A promising intervention might be peripheral somatosensory stimulation (PSS). Firstly, enhancing afferent input, e.g. by the use of electrical stimulation or vibration, might re-weight sensory processing for balance, leading to the re-integration of the affected leg as a somatosensory organ for postural stability. This might decrease visual over-reliance while keeping an upright posture which is commonly observed after

stroke [16]. Secondly, PSS in the form of low-intensity electrical stimulation aiming to activate cutaneous and proprioceptive sensory fibres is found to drive corticomotor excitability [17] and by that facilitate effects of motor training [18,19]. Similar effects after PSS in postural recovery may firstly promote postural contribution of the paretic leg leading to more symmetric and efficient postural strategies [20] and secondly improve functional gains of balance training [18].

To examine our hypothesis, a systemic review is conducted to investigate which PSS strategies are already documented and investigated on effectiveness in postural recovery after stroke. Therefore, this review aims to investigate whether PSS to the paretic leg in stroke rehabilitation leads to improved balance ability and the development of symmetric postural strategies compared to no additional or sham stimulation.

Methods

The current review was conducted following the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) to guarantee high-quality reporting [21].

Eligibility criteria

Types of studies

Clinical trials (randomized-controlled trials (RCT) and non-randomized observational trials) with full-text publications in English, German or Dutch have been included. There were no publication date limits. Meta-analyses, reviews and case-reports have been excluded.

Types of participants

The population is defined as people after stroke. No limits have been set on the type (infarct/haemorrhage), location (anatomical) or stage (acute/chronic) of the lesion. Studies investigating effects on a stroke population suffering from visuospatial neglect are excluded.

Types of interventions

Stimulation in the current review is defined as a non-motor, peripheral and focal stimulation to the paretic leg aiming an increase in somatosensory input to spinal and supra-spinal levels. Stimulation above motor threshold (e.g. Functional Electrical Stimulation, a stimulation modality aiming to elicit muscle contraction) and stimulation addressing other parts of the body (e.g. non-invasive brain stimulation such as tDCS, a stimulation modality aiming to affect cortical excitability through electrodes attached to the head; or whole-body vibration where patients are standing on a vibrating platform) are excluded. Studies combining exercises with PSS are excluded if the control group did not receive a dose-and-content-matched exercise intervention.

Types of outcome measures

The outcomes are defined as recovery of static and dynamic postural stability.

Information sources

Five databases (PubMed, Web of Science, PEDro, Cochrane Library Trials, RehabData) have been searched.

A search strategy in PubMed [see appendix] (on 26/06/2017) led to 900 hits. A similar strategy in Web of Science (on 26/06/2017) resulted in 464 hits. The search-term combination of "stroke", "stimulation" and "balance" was used in the PEDro database (54), RehabData (24) and Cochrane Library Trials (135) (on 01/07/2017) leading to additional 213 hits. A two-phase selection procedure is performed to detect studies fulfilling inclusion criteria.

Methodological quality

The risk of bias was evaluated for RCTs with the PEDro scale. Items are rated by two independent and trained reviewers. A score of 8/10 or higher is defined as good (1++) and 6-7/10 as fair quality (1+). A score below 6 is considered poor quality (1-). Non-randomized studies were rated by two independent reviewers with a rating system based on the Newcastle-Ottawa Scale (NOS). A score of 4/6 or higher is considered fair quality (2+). A score below is considered poor quality (2-). Finally, methodological quality and level of evidence was rated based on a grading system proposed by Harbour et al. [22] [see Table 1 & 2].

Analysis

Data of included studies are extracted into a spreadsheet listing study characteristics and observed effects [see Table 3]. Extraction happened independently and was double checked.

INSERT TABLE 1 AND 2 HERE

Results

Study selection

After screening on title and deduplication, 96 unique studies were obtained for a detailed screening. Eleven additional studies were added by hand screening, derived from previously published literature reviews in this field of research. After screening, 19 studies have been selected for analysis [see Figure 1].

Studies were excluded based on following reasons: Population did not consist of stroke survivors; stroke survivors suffer from visuospatial neglect; stimulation was above motor threshold or not applied to the lower limb; study design was either a review or a case report/series.

INSERT FIGURE 1 HERE

Population

A total number of 691 stroke survivors were observed. The majority received sensory-amplitude electrical stimulation (SES) (N=479). Local vibration (N=91), thermal stimulation (N=89) and hands-on stimulation (N=32) are less investigated.

In the current review (sub-)acute is defined as less than, and chronic more than six months since stroke onset. The majority of included studies investigated effects in a chronic population [23-36] compared to the acute phase [37-41].

Included studies selected participants on the ability to keep an upright posture or to ambulate, as they had to stand, walk or transfer during the intervention and assessment. Few studies included stroke survivors with ankle spasticity [30-32,34,35] or foot drop only [23].

Outcome measures

Outcome measures are divided into static and dynamic postural stability.

Static postural stability is measured technically via posturography assessing postural sway (defined as center-of-pressure displacement) [30,33,35,36] or distribution of weight [25] during upright standing. Clinical assessments include the Berg Balance Scale (BBS) [29,38-40], the Postural Assessment Scale for Stroke [41] and the Functional Reach Test [27].

Dynamic postural stability includes outcomes measuring the ability to ambulate and to transfer. Few studies utilized a gait analysis assessing kinematics [23,37], spatiotemporal characteristics [23,24,33,36,37] and gait speed [23,26-28,31-33,36,37]. Clinical measures include the Timed Up and Go test (TUG) [32,34,36,40] the modified Motor Assessment Scale [28,38,39], the basic mobility section of the Stroke Rehabilitation Assessment of Movement [41], the Functional Ambulation Classification [38,39,41] and the 6-Minute Walking Test [32,40].

Methodological quality

Two out of the 15 included RCTs present good or 1++ quality [23,32]. Scores of other RCTs vary between 7/10 [33,37-40] and 6/10 [25,27,31,36,41] indicating 1+ quality. Two RCTs present a high risk of bias or 1- quality [30,34]. A single RCT has not yet been rated. Therefore the authors of the current review conducted the rating based on the PEDro scale, leading to a score of 7/10 and 1+ quality [35]. The NOS scores for non-randomized trials vary from fair (2+) [24,28] to poor (2-) [26,29].

PSS approaches, observed effects and level of evidence

Different PSS approaches are identified (SES, vibration, thermal and hands-on stimulation) and grouped according to the following classification: (I.) Immediate

effects after or during a single session of PSS; (II.) effects after repetitive sessions of isolated PSS compared to no stimulation; (III.) effects of PSS combined with exercises compared to a dose-and-content-matched exercise group which got no or sham stimulation.

(I.) Beneficial effects during SES were observed for static postural stability [27,30] compared to sham stimulation. In addition, speed [27] and locomotor control [24] of gait improved during SES which is similar to those effects seen during local vibration [26]. A single session of hands-on stimulation, aiming improvements in soft tissue elasticity and somatosensation of the paretic foot, led to an improved static postural stability [29]. All immediate effects are reported in a chronic population based on level B evidence.

(II.) Exposing the paretic foot repetitively to a thermal agent led to beneficial effects on dynamic but inconsistent effects on static postural stability in an acute population [38,39]. In addition, effects disappeared at a 6-month follow-up [39]. Hsu et al. [41] found noxious stimulation (heat 46-47C; cold 2-3C) to be superior for regaining dynamic postural stability. Paoloni et al. [23] investigated isolated local vibration added to usual care and found improved gait. In contrast, repetitive application of isolated SES (e.g. TENS) led to neutral effects on gait ability [28,31,32,37] and only a small improvement in the TUG compared to no stimulation [32] according to level A evidence.

(III.) Combining SES with exercises (task-oriented training) did improve static, as assed by posturography [35,36] and the BBS [40], and dynamic [31,32,36,40] postural stability compared to a dose-and-content-matched sham-stimulation group. The latter notion includes for example improvements on the TUG [32,36,40] and in gait speed [31,32]. Effects persisted even at a follow-up measurement as reported by level A evidence [31,32,40]. However, a single RCT with a high risk of bias found no superior effects on the TUG [34]. Performing exercises during local vibration, as well as applying hands-on stimulation as

184 a part of a sensorimotor therapy protocol, did improve static postural stability according
185 to posturographic measures [25,33].
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187 INSERT TABLE 3 HERE

Discussion

As somatosensory loss impacts rehabilitation after stroke negatively [8,42], the question arose whether enhancing somatosensory input during rehabilitation by means of PSS promotes postural recovery gains. Different stimulation approaches were grouped leading to the following results: (I.) There is an immediate effect after a single session of PSS on postural stability, in contrast with (II.) repetitive sessions of isolated PSS which led to highly inconsistent results. Finally, (III.) combining PSS with exercises did promote long-term postural recovery in a chronic population compared to a dose-and-content-matched exercise group and these results persisted at follow-up.

One might concern that supplementary stimulation might increase risk of falling, as the integration of additional input will increase cognitive demands. However, this hypothesis cannot be confirmed by the current review. Firstly, immediately after PSS performance on the Forward Reach Test [27] and the BBS [29] improved along with postural sway normalization [30]. Secondly, adding PSS to exercises did not lead to more adverse events or higher drop-out rates. Contrary, postural stability improved suggesting, if anything, that additional stimulation can decrease fall risk after stroke.

PSS as a novel therapeutic strategy for postural recovery

In the introduction, PSS is suggested as a novel therapeutic strategy in postural rehabilitation as it might restore somatosensation and increase postural contribution of the paretic leg. Only a single trial measured weight-bearing symmetry and found improvements after six weeks of stimulation and exercises [25]. One might suggest that participants relied more on the paretic leg while keeping an upright posture. However, it remains unclear whether symmetry remediated because of “true” recovery or a learned compensation strategy, where true recovery is defined as restoring of a symmetric

bearing of weight resulting from equal contribution of both legs to upright postural stability [20]. In fact, only 10-20% of regulatory activity happened through the paretic leg during upright standing [43] and stroke survivors recovered without any improvements in paretic leg regulatory activity [44]. Apparently, postural recovery after stroke is mainly driven by compensatory strategies, e.g. shifting postural contribution to the non-paretic side leading to weight-bearing asymmetry [12,13]. In the study of Goliwas et al. [25], weight-bearing symmetry gains did not reach significance during visual deprivation, a condition where participants highly depend on somatosensory input from and regulatory activity of the paretic leg in order to achieve symmetry. Therefore, improvements during the eyes-open, but not during the eyes-closed condition, most likely suggest a learned strategy based on visual information rather than an increase in paretic leg postural contribution.

Still, some evidence supports the hypothesis. Somatosensory functions improved [27-29] and normalization of postural sway was more evident in the eyes closed condition after PSS [30,33,35]. It is suggested that stimulation did promote central integration of afferent input rising from the paretic leg, leading to a decrease in visual dependence while maintaining an upright posture. However, these observations result from single force plate set-ups which do not give definite insights to which extend the paretic leg is involved in postural stability. A lack of evidence concerning PSS as a therapeutic strategy to enhance paretic leg postural contribution is identified and future research is warranted.

Spinal and supra-spinal effects of PSS

Immediate effects after PSS on postural stability [24,26,27,29,30] are similar to those seen after PSS to the upper limb, as performance on the Jebsen-Taylor Hand Function Test improved immediately after combining PSS with training [45,46]. This indicates a close

functional relation between somatosensory input and motor output. Underlying mechanisms are an issue of discussion.

Some authors found reduced spasticity immediately post-stimulation [30] and after repetitive sessions of PSS [31,34-36] in the current review. In animal studies, application of TENS increased release of GABA in the dorsal horn [47], which acts as an inhibitory neurotransmitter to spinal reflex activity leading to a decrease in spasticity. This mechanism is similar to baclofen and short-term effectiveness of both interventions is found to be equivalent in a recent review [48]. The authors conclude that TENS is a safe and effective adjuvant therapy in limb spasticity management.

Beside a possible spinal anti-spastic effect, evidence on supra-spinal effects is growing. Stimulation to the hand led to increased blood flow in the primary sensorimotor cortex [49] and increased cortico-motor excitability [17,49]. How these cortical sensorimotor interactions work is still unclear. Findings of Tyson et al. [27] who observed improved somatosensation along with improved postural stability during TENS might suggest that enhanced afferent input is centrally transmitted to the primary sensory cortex (S1) and that S1-activity drives motor cortex excitation leading to improved motor output. Brodie et al. [50] observed after non-invasive central stimulation to S1 improvements in somatosensory functions and motor learning. This reinforces the increasingly clear importance of somatosensation in motor learning [51] considering that skill learning is an adaptive process triggered by afferent input as described by the internal model [52]. Central sensory disorders, which are common after stroke [8], may disrupt this mechanism and hamper learning [51] leading to poorer recovery [42]. PSS might remediate somatosensory integration and restore learning capacity. Indeed, PSS combined with exercises increased long-term postural recovery after stroke [31,32,35,36,40].

However, improved somatosensation after S1-stimulation showed only a small effect on motor functions [50] and Kaelin-Lang et al. [17] found increased motor cortex excitability after PSS without any change in S1 excitability. The authors consider short-term plastic changes in the motor cortex to be directly induced by afferent input, as the motor cortex receives somatotopically projections from the sensory cortex [17]. Apparently, somatosensory input can drive not only somatosensory but also motor cortex excitability. Plastic changes in the motor cortex directly after PSS are probably responsible for immediate functional improvements [24,26,27,29,30]. The immediate character of these effects seems to mimic those seen after rapid motor learning [53] suggesting that afferent-induced changes in motor excitability is fundamental for learning.

The latter notion emphasizes PSS to be a potential adjuvant therapy in rehabilitation after stroke. Considering that immediate [24,26,27,29,30] and long-term improvements [6,25,31-33,35,36] are found in a chronic population, one might suggest that enhanced afferent input triggers remaining plastic capacity for sensorimotor re-organization. Therefore, the current review suggests PSS to be considered a motor learning *booster* and a valuable adjuvant to task-oriented exercises in rehabilitation after stroke.

Limitations of the current review

All included studies except for two RCTs [23,32] present methodological weakness. Observational trials lack a randomized-controlled design [24,26,28,29] and the majority of RCTs present low PEDro scores due to inadequate blinding of patients, therapists and/or assessors and a lack of an intention-to-treat analysis [27,30,31,33,34,36-40]. In addition, PSS approaches and dosage varied widely between studies. This prevents drawing firm conclusions and therefore the readers should interpret the current review not as definite

therapeutic guidelines, but rather a state-of-the-evidence document rising questions and giving recommendations for clinical practice and research.

Recommendations for future research

Future trials of robust methodological quality and adequate blinding should take characteristics of PSS into account: Postural stability improved immediately [24,26,27,29,30] and stimulation prior to exercises is effective in improving recovery [31,32,35]. An observational trial found a peak of cortical excitability at 45-60 minutes of PSS [54], similar to the amount of adjuvant PSS given in a high-quality clinical trial [32]. Aftereffects are described by Walker et al. [24]. Similar, Golaszweksi et al. [55] reported effects 1h after stimulation to be even stronger compared to immediate effects post-stimulation. Kaelin-Lang et al. [17] applied sensory stimulation to the nervus ulnaris and found that motor evoked potentials of ulnar nerve-innervated muscles improved only. To sum up, cortical effects of PSS are immediate, relatively short-lasting and focal. This emphasizes, similar to the conclusion of the current review, that PSS is effective only as an adjuvant therapy in improving functional recovery after stroke. If PSS should be delivered above or below sensory threshold remains unclear. The current review found beneficial effects after supra-sensory PSS [24,27,30-32,35,40]. However, Conforto et al.[18] found sub-sensory PSS to facilitate motor training, similar to Park et al. [36]. This issue needs further investigation.

Beside PSS characteristics, outcome measures should include dual force plate posturography[13] to gain insights to which extent the paretic leg contributes to postural stability after PSS. Comparing different sensory conditions will further distinguish between true or compensatory recovery. Finally, combining neuro-imaging with clinical assessments can close the gap between fundamental and clinical research, which can provide a groundwork to develop evidence-based rehabilitation strategies.

Conclusion

Somatosensory integration is fundamental for postural stability and motor learning, suggesting that enhancing somatosensory input during rehabilitation can promote postural recovery gains after stroke. Indeed, PSS, in most included studies provided as low-intensive electrical stimulation, is found to be effective immediately and on a long-term as an adjuvant therapy only in improving postural stability in a chronic population. However, a lack of evidence concerning PSS as therapeutic strategy to enhance paretic leg postural contribution is identified. Future research is warranted considering those promising results after exercise therapy combined with PSS and high prevalence of postural instability impacting daily life of stroke survivors.

Declarations of interest

Finally, the author(s) declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

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Tables

Table 1: assessing methodological quality adapted from the SIGN guidelines

1++	RCT's with a very low risk of bias (high quality)
1+	RCT's with a low risk of bias (fair quality)
1-	RCT's with a high risk of bias (poor quality)
2+	well conducted observational studies with a low risk of bias (fair quality)
2-	observational studies with a high risk of bias (poor quality)

Table 2: rating level of evidence adapted from the SIGN guidelines

	Conclusion based on …
A	≥ 1 study of 1++ quality or ≥ 2 studies of 1+ quality
B	≥ 2 studies with a quality of at least 2++
C	≥ 2 studies with a quality of 2+
D	lower

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Table 3: characteristics of included studies, observed effects (*, p<0.05; †, p<0.01) and methodological quality

	population	**intervention**	**control**	**time effect** (difference pre/post within group)	**interaction effect** (difference pre/post between groups)	**MQ**
(I.) immediate effects of a single session PSS						
Kawahira 2004[26]	chronic (>5m); walk 10m with aid; N=13	during loc vib (83Hz) to m. tib ant and m. glut med	/	gait speed (+0.05 m/s)†		2-
Walker 2014[24]	chronic (>6m); walk independently; N=12	during SES (95% motor threshold, 30Hz) to malleolis med	/	foot placement ML† AP, gait kinematics (less hip circumduction†)		2+
Tyson 2013[27]	chronic; standing independently 20s; N=29	during TENS via sock-electrode (> sens threshold, 70-130 Hz)	sham		forward reach (+4.16 cm)†, gait speed (+0.03 m/s)†	1+
Kim 2015[29]	chronic; N=12 (6 walker, 6 non-walker)	immediately after 30 min hands-on foot activation	/	BBS (+5,25)*		2-
Cho 2013[30]	chronic (14,5m); spasticity; stand unassisted 10min;N=42	immediately after 60 min of TENS (2-3x sens threshold, 100Hz) to m. gastro	sham	COPdis EO (-10.14cm)*, EC (-20.74cm)*, US EO (-34.76cm)*	COPdis EO (-10.14cm)*, EC (-20.74cm)*, US EO (-34.76cm)*	1-
(II.) repetitive sessions of isolated PSS						
Chen 2011[38]	acute (<4w); BS<4; FAC<2; N=36	6w thermal stim for 48min, 5x/w	talking session	BBS (+28.0)†, mMAS (+16.0)†, FAC (+2)†	BBS (+7.5)†, mMAS (+6)†, FAC (+1)†	1+

Liang 2012[39]	acute (<4w); BS <4; N=30	6w thermal stim for 40min, 5x/w	talking session	BBS (+30,3)†, mMAS (+18,3)†, FAC (+2,3)†	BBS (+9.3), mMAS (+6,5)†, FAC (+0.8)†	1+
Hsu 2013[41]	subacute (>3m); sit independently >30min; N=23	8w noxious thermal stim for 30min, 3x/w	innocuous stim	PASS (+1.1), mob-STREAM (+2.8)†, FAC (+0.8)†	PASS (+0.9), mob-STREAM (+2.5), FAC (+0.4)	1+
Peurala 2002[28]	chronic (+-3,3y); N=19	3w SES via sock-electrode (sub-sens, 50 Hz) for 2x20min, 2x/day	/	gait speed(+0.03 m/s), mMAS (+2.4)*		2+
Yavuzer 2007[37]	subacute (+-3,5 mos); BS <4; stand unassisted; N=30	4w SES to n. peron (> sens threshold, 35Hz) for 30min, 5x/w	no stim	gait kinematics, ST gait analysis, gait speed (+0.03 m/s)	gait kinematics, ST gait analysis, gait speed (+0.02 m/s)	1+
Ng 2007[31]	chronic (>1y); walk 10m unassisted; spasticity; N=88	4w TENS (2-3x sens threshold, 100 Hz) to n. peronealis for 60 min, 5x/w	no stim	gait speed (+0.08 m/s)	gait speed (+0.07 m/s)	1+
Ng 2009[32]	chronic (>1y); spasticity; N=109	4w TENS (2x sens threshold, 100 Hz) to n. peronealis for 60 min, 5x/w	no stim	gait speed (+0.03 m/s), 6MWT (+18.4cm), TUG (-2.1)	gait speed (+0.01 m/s), 6MWT (+17.8cm), TUG (-2.1)†	1++
(III.) repetitive sessions of PSS combined with exercises						
Lee 2013[33]	chronic (>6 months); walk 10m independently; N=34	6w EX during loc vib (90Hz) to achilles tendon and m. tib ant for 30 min, 3x/w	EX + sham	COPdis EO (–11.91)*, EC (–20.67)*, COPv EO (–0.40)*, EC (–0.69)*, ST gait analysis*, gait speed (+0.15 m/s)*	COPdis EO (–12.71)*, EC (–20.33)*, COPv EO (–0.43)*, EC (–0.68)*, ST gait analysis*, gait speed (+0.12 m/s)*	1+

Laddha 2016[34]	chronic (+-15,7 m); spasticity; walk 10m unassisted; N=30	6w EX + prior 30 or 60min TENS (2-3x sens threshold, 100Hz) to n. peron, 5x/w	EX	TUG (n/r) *	TUG (n/r)	1-
Jung 2017[35]	chronic (6,5 m); sit-to-stand unassisted; spasticity; BS=3; N=40	6w EX + prior 30min TENS (2x sens threshold, 100Hz) to n. peron, 5x/w	EX + sham	COPdis EO (-21.0 cm)*, COPdis EC (-26.4 cm)*	COPdis EO (-12.2 cm)*, COPdis EC (-13.3 cm)*	1+
Ng 2007[31]	chronic (>1y); walk 10m unassisted; spasticity; N=88	4w EX + 60 min prior TENS (2-3x sens threshold, 100Hz) to n. peron, 5x/w	EX + sham	gait speed (+0.13 m/s)†	gait speed (+0.09 m/s)†	1+
Ng 2009[32]	chronic (>1y); spasticity; N=109	4w EX + 60 min prior TENS (2x sens threshold, 100Hz) to n. peron, 5x/w	EX + sham	gait speed (+0.19 m/s)†, 6MWT (+50.1 cm), TUG (-6.8)	gait speed (+0.09 m/s)†, 6MWT (+19.3 cm)†, TUG (-3.6)†	1++
Ng 2016[40]	acute (6,2w); stand 1min unassisted; FAC >2; N=76	8w EX + prior 60 min TENS (2x sens threshold, 100Hz) to n. peron, 2x/w	EX + sham	BBS (+9.9)†, 6MWT (+69.9m)†, TUG (+20.1s)†	BBS (+1.1)†, 6MWT (+5.9m), TUG (+6.2s)†	1+

MQ, methodological quality; PSS, peripheral somatosensory stimulation; m, months; w, weeks; min, minutes; loc vib, local vibration; SES, sensory-amplitude electrical stimulation; ML, medio-lateral; AP, antero-posterior; BBS, Berg Balance Scale; COPdis, displacement of center-of-pressure; COPv velocity of displacement of center-of-pressure; EO, eyes open; EC, eyes closed; US, unsupported surface; UC, usual care; FAC, Functional Ambulation Classification; BS, Brunnstrom Stages of Stroke Recovery; mMAS, modified Motor Assessment Scale; PASS, Postural Assessment Scale for Stroke Survivors; mob-STREAM, mobility section of the Stroke Rehabiliation Assessment of Movement; ST, spatiotemporal; 6MWT, 6-Minute Walking Test; TUG, Timed-up and Go Test; EX, exercises

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Appendix

Search Strategy in PubMed:

("Cerebrovascular Disorders/rehabilitation"[Mesh] OR "Stroke/rehabilitation"[Mesh] OR "Stroke Rehabilitation"[Mesh] OR "Stroke/therapy"[Mesh]) AND ("Sensation/rehabilitation"[Mesh] OR "Somatosensory disorders/rehabilitation"[Mesh] OR "Somatosensory Disorders/therapy"[Mesh] OR "Hypesthesia/rehabilitation"[Mesh] OR "proprioception"[Mesh] OR "physical stimulation"[Mesh] OR "Transcutaneous Electric Nerve Stimulation"[Mesh] OR "pressure"[Mesh] OR "touch"[Mesh] OR "Vibration/therapeutic use"[Mesh] OR "Electric Stimulation Therapy"[Mesh] OR stimulation[All Fields] OR "somatosensory stimulation"[All Fields]) AND ("gait"[Mesh] OR "postural balance"[Mesh] OR "walking"[Mesh] OR "activities of daily living”[Mesh])

table 1: assessing methodological quality adapted from the SIGN guidelines

1++	RCT’s with a very low risk of bias
1+	RCT's with a low risk of bias
1-	RCT's with a high risk of bias
2++	high-quality observational studies with a very low risk of bias
2+	well conducted observational studies with a low risk of bias
2-	observational studies with a high risk of bias

table 2: rating level of evidence adapted from the SIGN guidelines

	Conclusion based on
A	≥ 1 study of 1++ quality or ≥ 2 studies of 1+ quality
B	≥ 2 studies with a quality of at least 2++
C	≥ 2 studies with a quality of 2+
D	Lower

figure 1: detailed flowchart of search process with reasons of exclusion

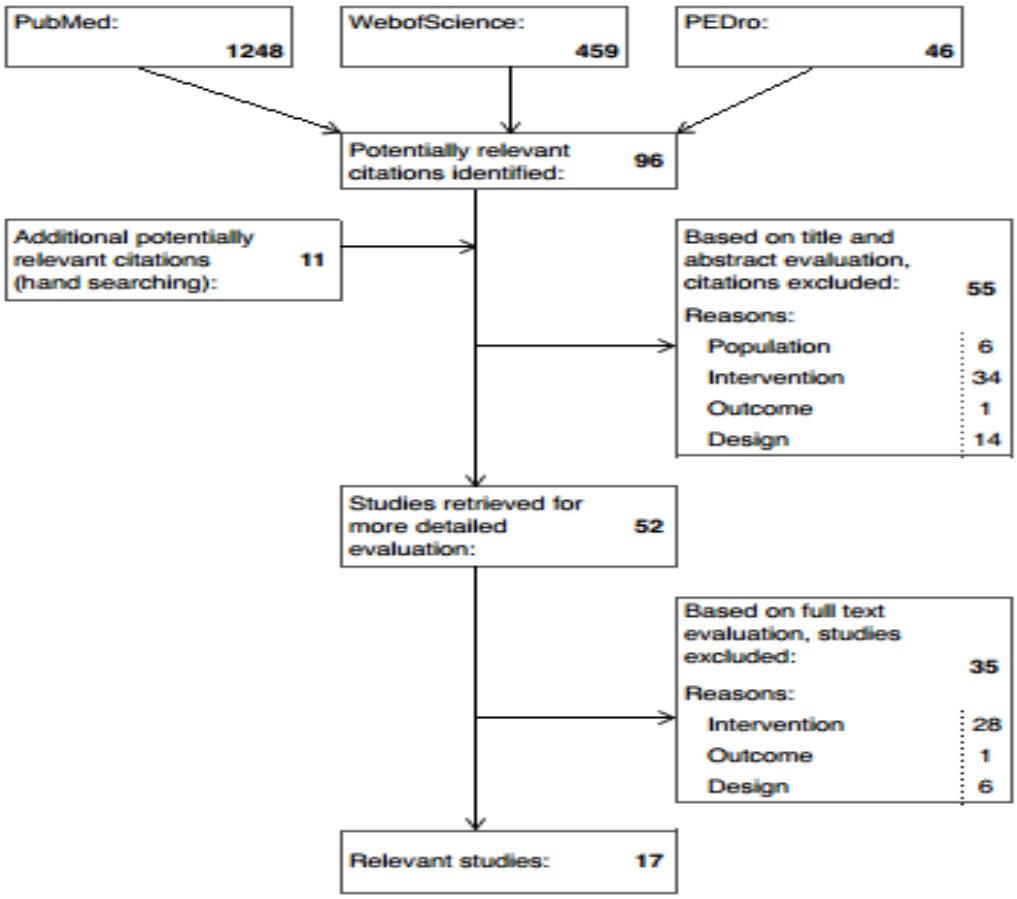

table 3: characteristics and methodological quality of included studies

artikel	population	intervention	control/compare	PEDro/ NOS*	quality
Chan, 2012	chronic (>6m), walking 100m; N=32	single session WBV (12Hz) 2x10 min	sham	8/10	1+
van Nes, 2004	chronic (>6m); stand 30s; N=23	single session WBV (30Hz, 3mm amplitude) 4x45 sec		4/6*	2+
van Nes, 2006	acute (<6w); BBS <40; N=53	SC + 6 weeks WBV (30Hz, 3mm amplitude) 4x45 sec 5x/w	SC + exercises	3/6*	2-
Paoloni, 2010	chronic (>6m); walk 10m unassisted, foot drop; N=44	SC + 4 weeks local vibration (120Hz) 30min 3x/w	SC	8/10	1+
Kawahira, 2004	chronic (>5m); walk with aid; N=13	single session local vibration (83Hz)		8/10	1+
Chen, 2011	acute (<4w); BS<4, FAC<2; N=36	SC + 6w thermal intervention 48min 5x/w	SC + talking sessions	7/10	1-
Liang, 2012	acute (<4w); BS <4; N=30	SC + 6w thermal intervention 40min 5x/w	SC + talking sessions	7/10	1-
Hsu, 2013	subacute (>3m); sit independently >30min; N=23	SC + 8w noxious stimulation 30min 3x/w	SC + innocuous stimulation	6/10	1-
Walker, 2014	chronic (>6m); walk independently; N=12	single session CES to n. plantaris med. (supra-sens, bi-phasic, 30Hz), while active		5/6*	2+
Tyson, 2013	chronic; standing independently 20s; N=29	single session CES via sock-electrode (supra-sens, biphasic, 70-130 Hz), while active	sham	6/10	1-
Peurala, 2002	chronic (+-3,3y); N=19	SC + 3w CES via sock-electrode (sub-sens, monophasic, 50 Hz) 2x20min		4/6*	2+
Yavuzer, 2007	subacute (+-3,5m); BS <4, stand independently; N=30	SC + 4w CES to n. peronealis (supra-sens, biphasic, 35Hz) 30min, 5x/w	SC	7/10	1-
Kim, 2015a	chronic; N=12 (6 walker, 6 non-walker)	single session foot activation 30min		3/6*	2-
Kim, 2015b	chronic (>1y); N=30	8w foot activation 30min, 3x/w		3/6*	2-
Goliwas, 2015	chronic (>12m); standing independently >30sec; N=20	SC + 6w sensorimotor foot stimulation 15min 5x/w	SC	6/10	1-
Lynch, 2007	acute (+- 50d), SS loss; walk 10m assisted; N=21	SC + 2w retraining program 30min 5x/week	SC + relaxation	6/10	1-
Morioka, 2003	subacute (+- 64d), standing independently; N=26	SC + 2w hardness discrimination task 5x/w	SC	6/10	1-

WBV, whole body vibration; SC, standard care; BBS, Berg balance scale; BS, Brunnstrom stage; FAC, functional ambulation classification; CES, cutaneous electrical stimulation; SS, somatosensory; y, years; m, months; w, weeks; d, days

table 4: observed effects of included studies

intervention	outcome measure	gain-EXP (95% CI)	time effect (p value)	gain-CTL	Diff (95% CI)	interactioneffect (p value)
I. somatosensory recovery						
- during or directly after stimulation						
ES (Tyson)	joint position sense - DF (degree)	+1,8 (0.19, 3.16)	**0.029***			
	~ PF	+1.67 (-0.22, 3.82)	0.078			
SMS (Kim.a)	monofilament - 5th toe (thickness)	-0.95	**<0.05***			
	~ 1st toe	-0.23	>0.05			
	~ dorsal	+0.03	>0.05			
- after repetitive stimulation sessions						
WBV (Van Nes 06)	monofilament (thickness)	-0.25	**<0.05***	-2,32		>0.05
ES (Peurala)	VAS	+1.3	>0.05			
	SEPs	n/r	**<0.05***			
SRe (Lynch)	monofilament test - heel (thickness)	n/r	**0.026***	n/r		>0.05
	~ lateral border	n/r	**0.024***	n/r		>0.05
	~ 1st toe	n/r	**0.011***	n/r		>0.05
	distal proprioception test	n/r	0.55	n/r		0.057
SMS (Kim.b)	monofilament- 5th toe (thickness)	-1,14	**<0.01***			
	~ 1st toe	-1,12	**<0.01***			
	~ dorsal	-1.11	**<0.01***			
IIa. immediate carry-over effect on …						
- balance						
WBV (Chan)	weight distribution symmetry	+3.47		+ 0.2	-3.27 (-6.02, -0.51)	**0.022***
WBV (Van Nes 04)	postural sway EC	n/r	**0.009***			
	weight distribution symmetry	n/r	**0.027***			
ES (Tyson)	forward reach (cm)	+4.16	**0.009***			
SMS (Kim.a)	BBS	+5,25	**<0.05***			
SMS (Kim.b)	TIS - static	-0.19	>0.05			

	~ dynamic	+1.87	**<0.01***			
	~ coordination	+0.56	>0.05			
- mobility						
WBV (Chan)	TUG	-6.48		- 0.45	6.03 (3.17, 8.89)	**0.0003***
	10MWT	-2.09		- 0.10	1.99 (0.11, 3.87)	**0.039***
LV (Kawahira)	gait speed (m/s)	+0.05	**<0.01***			
ES (Walker)	foot placement - ML		**0.006***			
	~ AP		>0.05			
ES (Tyson)	gait speed (m/s)	+0.03	**0.002***			
IIb. long term carry-over effect						
- on balance						
WBV (Van Nes 06)	BBS	+16.7	**<0.01***	+17.4	-0.7	>0.05
	TCT	+5.5	**<0.01***	+10.5	-5.0	>0.05
TS (Chen)	PASS-TC	+5.0	**<0.001***	+5.0	+- 0	0.597
	BBS	+28.0	**<0.001***	+15.5	+7.5	**0.007***
TS (Liang)	BBS	+30.3	**<0.05***	+ 21	+9.3	0.050
TS (Hsu)	PASS	+1.1	>0.05	+ 0.2	+0.9	0.206
SMS (Kim.b)	TIS - static	+0.22	>0.05			
	~ dynamic	+3.07	**<0.01**			
	~ coordination	+1.14	**<0.01**			
SMS (Goliwas)	weight distribution symmetry EO	+12.2%	**<0.05**	+2.4%	+9.8%	**<0.05***
	~ EC	+8.1%	**<0.05**	+2.4%	+6.7%	>0.05
SRe (Lynch)	BBS	+5,1	**<0.005**	+3,81	+1.29 (–3.16, 5.74)	>0.05
SRe (Morioka)	postural sway EO	-11.6	**<0.01**	-1.7	+9.9	**<0.05***
	~ EC	-9.9	**<0.05**	-4.6	+4.3	>0.05
- on mobility						
WBV (Van Nes 06)	RMI	+3.4	**<0.01***	+3.6	-0.2	>0.05
	FAC	+2	**<0.01***	+2	+- 0	>0.05
LVib (Paoloni)	DF angle at heel-contact (detailed gait analysis in article)	+6.71	**0.001**	+1.54	+5.17	>0.05
	gait speed (m/s)	+0.09	**0.047**	+0.02	+0.07	>0.05
TS (Chen)	mMAS	+16.0	**<0.001***	+10.5	+6	**0.010***

	FAC	+2	**<0.001***	+1	+1	**<0.001***
TS (Liang)	mMAS	+18.3	**<0.05***	+11.8	+6.5	**<0.05***
	FAC	+2.3	**<0.05***	+1.5	+0.8	**<0.05***
TS (Hsu)	mob-STREAM	+2.8	**<0.01***	+0.3	+2.5	0.087
	FAC	+0.8	**<0.01***	+0.4	+0.4	0.177
ES (Peurala)	10MWT (s)	-6.3	>0.05			
	mMAS	+2.4	**<0.05***			
ES (Yavuzer)	gait kinematics (detailed gait analysis in article)		>0.05			>0.05
	gait speed (m/s)	+0.03	>0.05	+0.01	+0.02	>0.05
SRe (Lynch)	gait speed (m/s)	n/r	**.012***	n/r		0.337
	ILA	n/r	.376	n/r		0.114

EXP, experimental; CTL, control; ES, electrical stimulation; DF, dorsalflexion; PF, plantarflexion; SMS, sensorimotor stimulation; WBV, whole body vibration; VAS, visual analogue scale; SEPs, sensory-evoked potentials; n/r, not reported; SRe, sensory retraining; EC, eyes closed condition; BBS, berg balance scale; ES electrical stimulation; LV, local vibration; TIS, trunk impairment scale; TUG, timed up and go test; 10MWT, 10 meter walking test; ML, medio-lateral; antero-posterior; TCT, trunk control test; TS, thermal stimulation; PASS(-TC), postural assessment scale for stroke patients (- trunk control); EO, eyes open condition; RMI, Rivermead mobility index; FAC, functional ambulation classification; mMAS, modified Motor Assessment Scale; ILA, Iowa level of assistance; mob-STREAM, mobility section - Stroke Rehabilitation Assessment of Movement;