CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Rehabilitation and Recovery following Stroke Evidence Tables

Range of Motion and Spasticity in the Shoulder, Arm and Hand

Teasell R, Salbach NM (Writing Group Chairs)
on Behalf of the Canadian Stroke Best Practice Recommendations
Rehabilitation and Recovery following Stroke Writing Group

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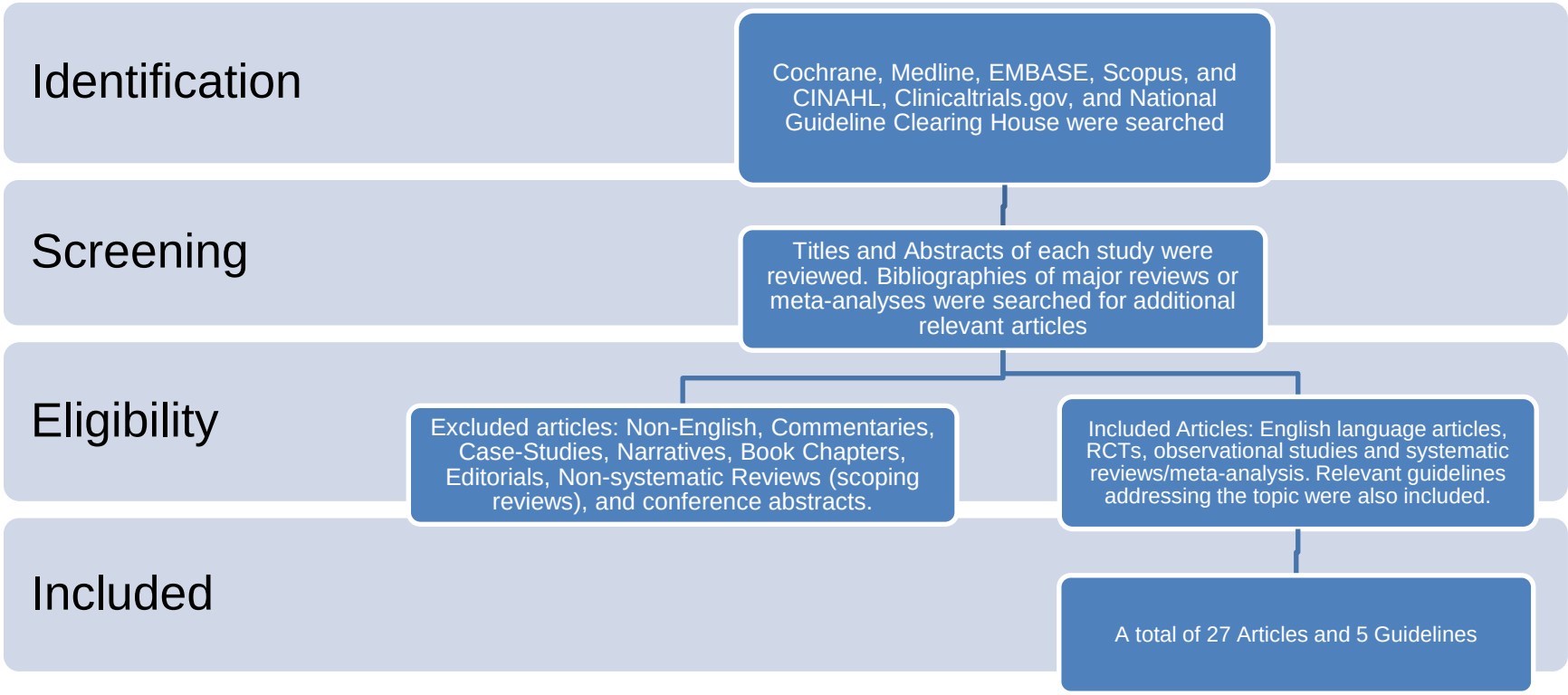
Search Strategy



Cochrane, clinicaltrials.gov, Medline, EMBASE, CINAHL and Scopus were searched using the keywords: Stroke AND (“spasticity” OR “contracture”) AND (“upper extremity” OR “upper limb”) AND (rehabilitation OR therapy OR intervention). Two new sections, stimulation and robotics, were added for the 2014 update. Titles and abstract of each article were reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 27 articles and 5 guidelines were included and were separated into categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
(Australian) Clinical Guidelines for Stroke Management 2017 - Chapter 5 of 8: Rehabilitation - Stroke Foundation	**Spasticity** Hand and wrist orthoses (splints) should not be used as part of routine practice as they have no effect on function, pain or range of movement. (strong recommendation). For stroke survivors with upper limb spasticity, Botulinum Toxin A in addition to rehabilitation therapy may be used to reduce spasticity, but is unlikely to improve activity or motor function. (weak recommendation). For stroke survivors with spasticity, acupuncture should not be used for treatment of spasticity in routine practice other than as part of a research study. (weak recommendation). For stroke survivors with spasticity, adjunct therapies to Botulinum Toxin A, such as electrical stimulation, casting and taping, may be used. (weak recommendation). For stroke survivors, the routine use of stretch to reduce spasticity is not recommended. (weak recommendation). For stroke survivors at risk of developing contracture, routine use of splints or prolonged positioning of upper or lower limb muscles in a lengthened position (stretch) is not recommended. (strong recommendation). **Contracture** For stroke survivors, serial casting may be trialled to reduce severe, persistent contracture when conventional therapy has failed. For stroke survivors at risk of developing contracture or who have developed contracture, active motor training or electrical stimulation to elicit muscle activity should be provided.
Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, Lang CE, MacKay-Lyons M, Ottenbacher KJ, Pugh S, Reeves MJ, Richards LG, Stiers W, Zorowitz RD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. **Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke**	Resting hand/wrist splints, along with regular stretching and spasticity management in patients lacking active hand movement, may be considered. **(C)** Use of serial casting or static adjustable splints may be considered to reduce mild to moderate elbow and wrist contractures. **(C)** Surgical release of brachialis, brachioradialis, and biceps muscles may be considered for substantial elbow contractures and associated pain. **(B)** The use of overhead pulley exercises is not recommended. **(C)** Targeted injection of botulinum toxin into localized upper limb muscles is recommended to reduce spasticity, to improve passive or active range of motion, and to improve dressing, hygiene, and limb positioning. **(A)** Oral antispasticity agents can be useful for generalized spastic dystonia but may result in dose-limiting sedation or other side effects. **(A)** Physical modalities such as NMES or vibration applied to spastic muscles may be reasonable to improve spasticity temporarily as an adjunct to rehabilitation therapy. **(A)** Intrathecal baclofen therapy may be useful for severe spastic hypertonia that does not respond to other interventions. **(A)** The use of splints and taping are not recommended for prevention of wrist and finger spasticity after stroke. **(B)**

Guideline	Recommendations
Association. ***Stroke* 2016;47:e98–e169**	
Intercollegiate Stroke Working Party. *National clinical guideline for stroke,* 5th edition. London: Royal College of Physicians, 2016.	*4.15.1 Recommendations* A. People with motor weakness after stroke should be assessed for spasticity as a cause of pain, as a factor limiting activities or care, and as a risk factor for the development of contractures. B. People with stroke should be supported to set and monitor specific goals for interventions for spasticity using appropriate clinical measures for ease of care, pain and/or range of movement. C. People with spasticity after stroke should be monitored to determine the extent of the problem and the effect of simple measures to reduce spasticity e.g. positioning, passive movement, active movement (with monitoring of the range of movement and alteration in function) and/or pain control. D. People with persistent or progressive focal spasticity after stroke affecting one or two areas for whom a therapeutic goal can be identified (e.g. ease of care, pain) should be offered intramuscular botulinum toxin. This should be within a specialist multidisciplinary team and be accompanied by rehabilitation therapy and/or splinting or casting for up to 12 weeks after the injections. Goal attainment should be assessed 3-4 months after the injections and further treatment planned according to response. E. People with generalised or diffuse spasticity after stroke should be offered treatment with skeletal muscle relaxants (e.g. baclofen, tizanidine) and monitored for adverse effects, in particular sedation and increased weakness. Combinations of antispasticity drugs should only be initiated by healthcare professionals with specific expertise in managing spasticity. F. People with stroke should only receive intrathecal baclofen, intraneural phenol or similar interventions in the context of a specialist multidisciplinary spasticity service. G. People with stroke with increased tone that is reducing passive or active movement around a joint should have the range of passive joint movement assessed. They should only be offered splinting or casting following individualised assessment and with monitoring by appropriately skilled staff. H. People with stroke should not be routinely offered splinting for the arm and hand.
Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: rehabilitation, prevention and management of complications, and discharge planning. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Jun. 101 p.31	**4.9.1 Summary of recommendations** **Not recommended** routine resting splinting of the upper limb *Clostridium botulinum* toxin type A **Insufficient evidence** routine functional electrical stimulation robot-mediated passive therapy oral antispasticity agents intrathecal antispasticity agents alcohol neurolysis tibial nerve neurotomy
Management of Stroke Rehabilitation Working Group. VA/DoD clinical practice guideline	Use of antispastic positioning, range of motion exercises, stretching, splinting, serial casting or surgical correction for spasticity. **C** Use of tizanidine (in chronic stroke patients), dantrolene, and oral baclofen for spasticity **B** Avoid drugs with central nervous system effects that may impair recovery **D** Use of botulinum toxin improves spasticity **B**

Guideline	Recommendations
for the management of stroke rehabilitation. Washington (DC): Veterans Health Administration, Department of Defense; 2010. p. 87	Use of intrathecal baclofen for chronic stroke patients **B** Use of certain neurosurgical procedures **I**

Evidence Tables

Stretching Programs +/- Splinting to Prevent Contracture

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Harvey et al. 2017 **Australia** **Cochrane Review**	N/A	49 RCTs (2,135 participants) including participants with neurological condition, advance age, those with a history of trauma and those with underlying joint or muscle pathology. 11 trials included stroke cohorts treated for upper limb impairments.	Trials evaluated the effect of stretching programs (casting, splinting, self-administered, positioning, and sustained passive stretch) on preventing contractures. Intervention comparisons include: stretch vs. no stretch, stretch vs. place or sham, and stretch plus co-intervention vs. co-intervention, including splints.	**Primary Outcomes:** Joint mobility (active range of motion, passive range of motion, passive joint stiffness) **Secondary Outcomes:** Pain (VAS), spasticity (Modified Ashworth Scale, Tardieu Scale), activity limitation (Functional Independence Measure, Motor Assessment Scale).	**Stroke specific results** *Joint mobility:* Immediate effects (n=11): MD=0.56 degrees, 95% CI -1.56 to 2.68, p=0.6. Long- term effects (n=4): MD=-0.32 degrees, 95% CI -4.09 to 3.44, p=0.87. *Pain* Immediate effect (n=4): SMD=0.31, 95% CI -0.03 to 0.66, p=0.072. Long term effects (n=4): SMD=0.03, 95% CI -0.41 to 0.47, p=0.09. *Spasticity* Immediate effects (n=4): SMD=0.05, 95% CI -0.29 to 0.39, p=0.76. Long term effects (n=1): SMD=-0.5, 95% CI -1.12 to 0.11, p=0.11. *Activity limitation* Immediate effects (n=5): SMD=0.27, 95% CI -0.09 to 0.63, p=0.14. Long term effects (n=4): SMD=0.14, 95% CI -0.29 to 0.58, p=0.52.
Choi et al. 2016 **Korea** **RCT**	CA: ☒ Blinding: assessor ☒ patient ☒ ITT: ☒	30 patients with pain, edema and paralysis of the hand in the acute stage of stroke recovery between 2 to 6mo.	Participants in the experimental group wore resting hand splints for a max 10hr/d for 12wk. The control group did not receive splinting therapy. All participants received general rehabilitation for 30min/d, 5d/wk for 12 wk.	**Primary Outcomes:** Visual analog scale for pain (VAS), hand voltmeter for edema, Modified Ashworth Scale (MAS) for wrist. Outcomes were assessed before and after the intervention.	Significant differences were found in the experimental group compared to the control group on the VAS, and in volume of hand ($p<0.05$) but not on the MAS.
Basaran et al. 2012	CA: ☑ Blinding: assessor ☑	39 subjects, 5-120 months post stroke with a wrist MAS score of ≥1	Examination of a 5-week, home-based exercise program.	**Primary Outcome:** MAS	No significant differences within or among the groups on any of the outcomes assessed.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Turkey **RCT**	ITT:☒		Patients were advised to stretch wrist and finger flexors for 10 repetitions and to try reaching and grasping an object for 10 repetitions 3x/day in addition to conventional therapy. Patients in 2 groups wore either a volar or dorsal splint for up to 10 hours overnight throughout the study period. Patients in the control group did not wear a splint	Outcomes were assessed before and after treatment, at least 2 hours after the splint had been removed.	
Lannin et al. 2007 **Australia** **RCT**	CA: ☑ Blinding: assessor ☑ ITT: ☑	63 subjects who had experienced a stroke in the previous 8 weeks with no active wrist extension.	Comparison of 2 different splints. Subjects in all groups received routine therapy. Subjects in the intervention groups wore one of 2 custom-made, static, palmar mitt splints- one placed the subject's wrist in a neutral position, the other, in an extended position (>45^{o}). Subjects wore the splints for up to 12 hours overnight for 8. Subjects in the control group received therapy only.	**Primary Outcome:** Extensibility of the wrist and finger flexor muscles. **Secondary Outcomes:** Motor Assessment Scale, Tardieu Scale, Disabilities of the Arm, Shoulder and Outcome Measure (DASH) Assessments were conducted at baseline, at the end of treatment (4 weeks) and 6 weeks.	There were no statistically significant differences between groups on any of the outcomes over the study period. Mean changes in wrist extensibility (degrees) from baseline to 6 weeks: Neutral splint group: 62.1 ± 16.4 to 48.8 ± 14.5 Extended splint group: 65.2 ± 15.0 to 42.5 ± 14.9 Control group: 64.5 ± 10.1 to 39.4 ±17.8 Mean changes in UE-MAS from baseline to 6 weeks: Neutral splint group: 0.3 ± 0.9 to 0.9 ± 2.0 Extended splint group: 0.3 ± 0.4 to 0.8 ± 2.0 Control group: 0.1 ± 0.3 to 0.5 ± 0.8 Mean changes in DASH scores from baseline to 6 weeks: Neutral splint group: 57.6 ± 24.0 to 56.5 ± 22.9 Extended splint group: 62.8 ± 24.4 to 58.0 ± 18.9 Control group: 60.8 ± 21.7 to 67.0 ± 19.8
Horsley et al. 2007 **Australia** **RCT**	CA: ☑ Blinding: assessor ☑ ITT: ☑	40 patients admitted for inpatient rehabilitation > 40 days on average, who were unable to actively extend their wrist past the neutral position.	Patients in the experimental group received 30 minutes of stretch of wrist and finger flexors 5 days a week for 4 weeks. Patients in both groups received	**Primary Outcome:** Passive wrist extension **Secondary Outcomes:** Pain (10 cm VAS), Motor Assessment Scale	There were no statistically significant differences between groups on any of the outcomes over the study period. Mean changes in passive wrist extensibility (degrees) from baseline to 9 weeks: Stretch group: 69.5± 13.6 to 63.4 ± 14.7

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			conventional task-specific therapy from physiotherapists and occupational therapists.	Assessments were conducted at baseline, weeks 4, 5 and 9.	Control group: 65.7 ± 13.1 to 57.0 ± 15.9 Mean Δ change = 3.5 degrees, 95% CI -4.6 to 11.7 Mean changes in pain at rest from baseline to 9 weeks: Stretch group: 1.1 ± 1.8 to 1.5 ± 2.6 Control group: 0.4 ± 1.1 to 1.5 ± 2.6 Mean Δ change = 0.2, 95% CI -1.5 to 2.0 Mean changes in UE-MAS from baseline to 9 weeks: Stretch group: 0.9 ± 1.8 to 5.9 ± 6.6 Control group: 0.3 ± 0.6 to 1.9 ± 3.3 Mean Δ change = 2.3, 95% CI -0.7 to 5.3

Centrally Acting Oral Agents

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Simpson et al. 2009 **USA** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	60 patients with stroke or traumatic brain injury of at least 3 months duration with a MAS score of ≥3 of the wrist flexors and difficulty with dressing or hygiene	Comparison of BT-A vs. tizanidine vs. placebo Subjects were randomized to 1 of 3 groups: BT-A + oral placebo (n=20), oral tizanidine + placebo injection (n=21) or placebo injection + oral placebo (n=19). Patients in the BT-A group received a single injection of BT-A (Botox), (average of 400U). The wrist flexors were the primary target site, although muscles in the shoulder or fingers could also be injected at the discretion of the investigator.	**Primary Outcome:** Modified Ashworth Scale (MAS) wrist **Secondary Outcomes:** Disability Assessment Scale, Modified Frenchay Scale, grip strength Assessments were conducted at baseline, 3, 6,12 and 18 weeks	Mean change from baseline to week 3 in MAS scores: BT-A: -1.55 ± 1.2; tizanidine: -0.25 ± 0.64; placebo: -0.67 ± 0.91, p<0.001 (BT-A was more effective compared with other 2 groups). The differences persisted at week 6, but by weeks18 and 22 there appeared to be no differences between the groups. Results from inferential statistics not reported, but by looking at figure, the mean reductions were <1 in all study groups. Mean change from baseline to week 6 in Principal Therapeutic Target of DAS scores: BT-A: -1.13 ± 1.1; tizanidine: -0.47 ± 1.18; placebo: -0.67 ± 1.08, p=0.20 Frenchay Scale scores to be reported in future publication Early terminations: BT-A group: 6; tizanidine group: 8; placebo: 5

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			Patients in the tizanidine group received a maximum daily dose of 36 mg/day, which was achieved by day 28 if increments (4 mg q 3-4 days were tolerated). No mention of additional therapy Study duration was 22-24 weeks.		Number of adverse events: BT-A group: 8; tizanidine group n=15; placebo group: n=10
Gelber et al. 2001 **USA** **Single group intervention study**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	47 subjects at least 6 months post stroke with moderate spasticity (MAS scores of 2 or 3 in major muscle groups) with functional limitations or pain as a result	Open label study where subjects received a maximum daily dose of tizanidine 36 mg/day, titrated in 2 mg increments Subjects were tapered off the drug after 16 weeks	**Primary Outcomes:** Modified Ashworth Scale (MAS), elbow, wrist, finger **Secondary Outcomes:** NIHSS, muscle strength assessed using the British Medical Research Council scale, ARAT, Pain (0-4 scale) BI, physician assessed functional disability (0-4 scale) Outcomes were assessed at baseline and weeks 16 and 18.	Total Mean UE MAS score: Baseline: 9.03 ± 0.41 Week 16: 6.47 ± 0.54 Week 18 (off-meds): 7.46 ± 0.49 Changes from baseline were statistically significant. There were no significant decreases in muscle strength using any of the BMRC sub scales. No significant improvement in any of the 4 domains of the ARAT. Mean improvement for grasp, grip, pinch and gross movement scores ranged from 0 to 0.4. No significant decrease in the frequency of pain, but there was a decrease in the intensity of pain at week 16 (1.6 ± 0.20 to 1.4 ± 0.23, p=0.038). Significant improvement in disability assessed by the physician ay week 16 (2.5 ± 0.12 to 1.9 ± 0.19, p<0.0001). No significant improvement in BI scores at week 16 (80.2 ± 2.7 to 81.1 ± 2.9, p=ns) Adverse events: 89% of subjects reported at least 1 adverse event. 28% of subjects discontinued the study due to an adverse event.

Botulinum Toxin-Type A (BT-A)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Elovic et al. 2016 **USA** **RCT**	CA: ☒ Blinding: assessor ☑ patient ☑ ITT: ☑	317 stroke patients >3mo after stroke with upper limb spasticity with muscle tone ≥2 on the Ashworth Scale	A total dose of 400U botulinum toxin A (BT-A) or placebo was administered guided by electromyography or electrical nerve stimulation. A primary target clinical pattern (PTCP) was determined that included the elbow (200U), wrist (150U) or fist for injection (100U). Muscles other than the PTCP the investigators discretion was used.	**Primary Outcomes:** Ashworth Scale (AS), Investigator's Global Impression of Change (IGIC). **Secondary Outcomes:** Disability Assessment Scale (DAS). Assessments were conducted at baseline, 4wk, 8wk, and 12wks.	AS significantly improved in the experimental group compared to the placebo group at all time points ($p<0.001$; $p<0.001$, $p=0.041$). IGIC was significantly higher in the experimental group than the placebo group at 4wk ($p<0.05$). DAS improved in a higher proportion of experimental group than in placebo group at 4wk ($p=0.007$).
Wissel et al. 2016 (pain) **Ward et al. 2014 (function)** **International** **RCT** ***BOTOX® Economic Spasticity Trial (BEST)***	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	273 persons with post-stroke spasticity. Mean age was 62 years. 86% of participants had their stroke >12 months previous. 74.3% of patients reported pain at baseline. Persons with upper and lower-limb spasticity were included.	Participants were randomized to receive a single dose of BT-A or placebo in addition to usual care. Dosing and site of injection was based on clinician judgement. An optional second dose was administered ≥ 12 weeks after the first injection. The double-blind phase lasted for 22 to 34 weeks, depending on the timing of the second injection, followed by an open label extension through week 52.	**Primary outcome:** Physician Assessment of Success, as Determined by Percentage of Patients Who Achieve Their Principal Active Functional Goal at Week 24 **Secondary outcomes:** Pain, HRQoL	The median first and optional second injection doses of BT-A were 340 U and 365 U. *Function* There were no significant differences between the groups at weeks 12, 24 or 52 with respect to the percentage of patients who achieved their principal active functional goal (33.1 vs. 28.9, 40.9 vs. 33.3 and 45.0 vs. 52.4, respectively). There were no differences between groups in the number of persons who achieved their secondary active functional goals. A higher number of persons in the BT-A groups achieved their secondary passive functional goals at 24 weeks, (60.6% vs. 38.6%, $p=0.016$), but not at weeks 12 or 52. The mean change from baseline in resistance to passive movement Scale Summated total score in persons with upper-limb spasticity was –4.3 (95% CI –5.7 to –2.8) in the BT-A group and –1.7 (95% CI –2.9 to –0.4) in the placebo group. *Pain*

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Mean pain reduction from baseline at week 12 was significantly greater with BT-A group (-0.77, 95% CI -1.14 to -0.40) than placebo (-0.13, 95% CI -0.51 to -0.24; P < 0.05). Higher proportions of patients with pain in the BT-A group achieved ≥30% and ≥50% reductions in pain at week 12 (53.7% and 37.0%, respectively) compared with placebo (28.8% and 18.6%, respectively; P < 0.05).
Shaw et al. 2011 **UK** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☒ ITT: ☑	333 subjects < 1 month following stroke with spasticity of the elbow (MAS>2) and/or spasticity of the shoulder, wrist or hand with reduced arm function	Comparison of BT-A vs. therapy Subjects were randomized to receive 100 or 200 U BT-A (Dysport) (n=170) + a standardized therapy program (1 hour/day, 2x/week for 4 weeks) vs. therapy program only (n=163). Subjects in the BT-A group received injections injected into the shoulder, arm, wrist, elbow and/or fingers Repeat injections were available to subjects in the intervention group at 3, 6 and 9 mos. 2 therapy menus were available depending on baseline arm function. Subjects with no active arm function participated in stretching (20 minutes), positioning (10 minutes) and passive/active assisted upper arm activity (20 minutes), while subjects with some arm function participated in stretching (10 minutes)	**Primary Outcome:** A successful outcome-defined as an increase in score of ≥3 ARAT points for subjects with initial ARAT scores of 0 to 3; ≥6 points for subjects with initial scores of 4 to 51 and a final ARAT score of 57 for baseline scores between 52 and 56. **Secondary Outcomes:** MAS, Motricity Index (arm), grip strength, 9-Hole Peg Test, BI, Pain (0-10 verbal rating Scale) Outcomes were assessed at baseline, 1,3- and 12-months following randomization	At 1 month, there was no significant difference in the proportion of subjects who achieved a successful outcome between groups. 25.1% in BT-A group vs. 19.5% in control group, p=0.232. There were no significant differences at months 3 or 12. There was a significant reduction in MAS scores at 1 month favouring the BT-A group (median change score of 0 vs. -1, p=0.001), but not at 3 or 12 months (median change score 0 vs. 0). There were no significant differences between groups for the following outcomes at any of the assessment points for either group: Motricity Index (median change 0 vs. 3 at 1 month, 0 vs. 4 at 3 months and 5 vs. 5 at 12 months), 9-hole Peg Test (median change 0 vs. 0 at all assessment points), grip strength (median change score of 0 vs. 0 at 1 and 3 months, 0.5 vs. 0 at 12 months), BI (median change score of 0 vs. 0 at months 1 and 3, -1 vs. -1 at 12 months). There was a significant decrease in pain score at 12 months favouring the BT-A group (0 vs. -2, p=0.004).12-month assessments were completed for 92 subjects in the control group and 170 subjects in the BT-A group. Adverse events: There were 52 serious adverse events in the BT-A group and 50 in the control group. Only 1 serious adverse event was believed to have been related to BT-A treatment.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			and task-oriented practice (40 minutes).		
McCrory et al. 2009 **USA** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	102 subjects with moderate to severe spasticity of the arm, (minimum MAS score of 2 in at least 2 out of the 3 of the wrist, elbow and finger flexor muscles and a minimum of 1+ in the third area) an average of 6 years following stroke	Comparison of BT-A (n=54) vs. placebo (n=42) First treatment: Placebo vs. 750 to 1,000 U Dysport injected into elbow, wrist and fingers muscles under EMG guidance. Second treatment at 12 weeks: additional 500 to 1,000 U Dysport into same sites Concurrent therapy: none stated	**Primary Outcome:** Assessment of Quality of Life (AQoL) (0 to 1.0) **Secondary Outcomes:** Pain (100-mm VAS), Depression (Hospital Anxiety and Depression Scale), goal Attainment Scaling (GAS), spasticity (MAS), (Modified) Motor Assessment Scale, Patient Disability Scale (PDS), Carer Burden Scale (CBS) Outcomes were assessed at baseline, weeks 8, 12, 20 and 24	Between group differences from baseline to week 20 (mean Δ, 95% CI). AQoL: -0.03, -0.09 to 0.02, p=0.27 Pain: 10.14, -8.1 to 27.4, p=0.25 HADS: -0.07, -0.87 to 1.47, p=0.61 GAS: -5.20, -9.08 to 1.28, p<0.001 (favours BT-A group) There must be a typo in this reporting. Significant p value not possible given 95% CI MAS across all joint: 1.59, 0.98 to 2.00, p<0.001 (favours BT-A group) MMAS: -0.22, -0.75 to 0.31, p=0.41 PDS: -0.01, -0.27 to 0.25, p=0.94 CBS: -0.02, -0.65 to 0.61, p=0.95 20-week assessments were completed for 37 subjects in the control group and 53 subjects in the BT-A group. Adverse events: Treatment related adverse events were reported in 5.55 of subjects in the BT-A group and 9.5% in the placebo group. Most adverse events were mild.

Intrathecal Baclofen (ITB)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Meythaler et al. 2001 **USA** **RCT crossover**	Screening period: assessor ☑ patient ☑ Open-label portion: assessor ☒ patient ☒ ITT: ☒	21 subjects with disabling and painful intractable hypertonia (defined by an Ashworth Scale score of at least 3 in one affected extremity or an average spasm score of at least 2 in the affected extremities on the day of screening) following stroke of at least 6	Subjects were randomized to receive a screening bolus trial of either 50 µg baclofen or saline placebo. 17 subjects responded to the active drug and were then implanted with a continuous-infusion pump and continued to receive treatment for up to a year.	**Primary Outcome:** Ashworth Scale **Secondary Outcomes:** 5-point Penn Spasm Frequency Scale, 6-point reflex scale (elbow) 13 subjects were followed for 1 year, 4 for 6 months.	Mean (± sd) scores at baseline and 12 months Ashworth scores: 3.2 ± 1.1 to 1.8 ±0.09, p<0.0001. Spasm score: 0.7±1.0 to 0.5, p=ns (12 month result extrapolated from figures) Reflex Score: 2.4 ±0.8 to 1.5, p=ns (12 month result extrapolated from figures) Adverse events: Several mild and transient adverse events were reported.

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		months duration, and failure to respond to oral antispasticity medications.	Subjects were initiated to continued treatment at 100 µg/day with dose increases up to an average of 268 ± 175 µg/day.		

Alcohol or Phenol Neurolysis

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Kong & Chua 1999 **Singapore** **Single group intervention study**	Blinding: assessor ☒ patient ☒	20 subjects an average of 12 months following stroke with severe elbow flexor spasticity causing fixed contracture and flexion deformity	The musculocutaneous nerve was localized and blocked with a solution of 50% ethyl alcohol in water at a rate of 1-2 mL/mm until muscle contraction ceased (mean total volume was 4 mL). No mention of concurrent therapy	**Primary Outcome:** MAS (elbow) **Secondary Outcomes:** Passive ROM (elbow), Medical Research council (MRC) scale Outcomes were assessed at baseline (t0), 4, weeks (t1), 3 (t2) and 6 months (t3) post treatment.	Mean (± sd) scores at t0, t1, t2 & t3 MAS: 3.7 ± 0.6, 1.7±1.0, 2.0±0.8, 2.1±0.8, p<0.001) PROM (degrees): 87.3±20.2, 104.3±20.1, 103.8±18.9, 101.6± 19.7, p=0.018 MRC: 0.6 ±0.8, 0.6±0.8, 0.6±0.8, 0.6±0.8, p=ns Adverse events: 3 subjects reported pain over the lateral aspect of the forearm

Robotics

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Veerbeek et al. 2017 **Netherlands** **Systematic review and meta-analysis**	N/A	34 RCTs (1362 subjects) evaluated the effect of robotic treatment on upper limb motor function	Intervention comparison includes robot treatment versus nonrobotic treatment for motor control of the paretic arm.	**Outcomes:** Motor control: Fugl Mayer Assessment (FMA-UE) Muscle tone: Modified Ashworth Scale (MAS) Upper limb capacity: Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Box and Blocks Test (BBT), Arm Motor Ability test (AMAT) Muscle strength: Motricity	Muscle tone of the paretic arm was assessed with the MAS in 13 RCTs (N = 429) with a total of 18 comparisons, yielding a significant homogeneous summary effect size (SMD 0.24, 95% CI 0.04 to 0.44; Z = 2.36, P = .02, I 2 = 25%), in favor of the control group. Pooling muscle tone scores of individual muscle groups resulted in a nonsignificant homogeneous summary effect size (SMD −0.16, 95% CI −0.55 to 0.23; Z = 0.82, P = .41, I 2 = 46%; 4 RCTs, N = 107) for the elbow flexors and a nonsignificant

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Index (MI), Motor Power Scale (MPS) Basic activities of daily living: Functional Independence Measure (FIM), modified Ranking Scale (mRS), Barthel Index (BI).	heterogeneous summary effect size (SMD 0.28, 95% CI −0.91 to 1.46; Z = 0.46, P = .65, I 2 = 75%; 3 RCTs, N = 54) for the wrist flexors. The meta-analyses in the early and late-start trials were nonsignificant for muscle strength, muscle tone, upper limb capacity, and basic ADL.
Lee et al. 2016 **Korea** **RCT**	CA: ☒ Blinding: assessor ☒ patient ☒ ITT: ☒	58 patients with upper limb spasticity >1 on the MAS. Time post stroke onset: experimental group=40.91, control group=41.86d	The experimental group received robot-assisted therapy with the Neuro-X upper limb training robot, and the control group received conventional rehabilitation therapy. Training was given for 30min, 2x/d, 5x/wk, for 2wk.	**Primary Outcomes:** Modified Ashworth Scale (MAS); Manual Muscle Test (MMT); Manual Function Test (MFT); Brunnstrom Stage (BBS); Modified Barthel Index (MBI). All measures were evaluated at baseline and post-intervention.	There were significant increases in MAS, MMT, MFT, BBS, and MBI in both groups ($p<0.05$); however, no significant differences between groups were found.
Taveggia et al. 2016 **Italy** **RCT**	CA: ☒ Blinding: assessor ☑ patient ☒ ITT: ☒	54 patients admitted from 3 hospitals within the acute phase of stroke (0.5 to 12mo post stroke onset).	The experimental group received a passive mobilization of the upper limb through the robotic device ARMEO Spring and conventional therapy for 5d/wk, for 6wk. The control group received traditional passive mobilization of the limb for 6 consecutive weeks (5 days/week).	**Primary Outcomes:** Functional Independence Measure (FIM), Motricity Index (MI). **Secondary Outcomes:** Modified Ashworth Scale (MAS), pain (VAS). Outcomes were evaluated at baseline, after the intervention and at 6wk post intervention.	There were significant between group differences on the FIM ($p=0.037$), MI ($p<0.001$), and on the VAS ($p<0.01$), but not on the MAS.
Masiero et al. 2014 **Italy** **RCT**	CA: ☒ Blinding: assessor ☑ patient ☒ ITT: ☑	34 patients with hemiparesis enrolled within 15d of stroke onset.	The experimental group received standard therapy (65% of exercise time) associated with robotic (NeReBot) training (35% of exercise time) while the control group received standard therapy for the upper limb. All participants received total daily rehabilitation experimental	**Primary Outcomes:** Modified Ashworth Scale (MAS), Medical Research Council (MRC), Fugl-Meyer Assessment (FMA-UE), Functional Independence Measure (FIM), Box and Blocks Test (BBT), dexterity, Frenchay Arm Test (FAT). All assessments were	There were no significant between-group differences with respect MRC, FMA-UE, FIM, BBT, FAT and MAS from baseline to follow-up.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			group for 120 minutes, 5 days per week, for 5 weeks.	performed at baseline, at the end of therapy time, at 3 months and at 7 months after entry.	

Neuromuscular Electrical Stimulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Qian et al. 2017 **Hong Kong** **RCT**	CA: ☒ Blinding: Assessor ☑ Patient ☒ ITT: ☑	24 participants with upper limb motor deficits in the acute stage of stroke recovery (NMES-robot group: 25d, control group: 14d).	Participants were randomized to receive either upper limb motor training using an EMG-driven NMES robotic arm, or traditional therapy. Each participant received a total of 20 sessions with the robot, at an intensity of 5 sessions/wk, 1session/d, within 1mo.	**Primary Outcomes:** Fugl Meyer Assessment (FMA-UE), Action Research Arm Test (ARAT), Modified Ashworth Scale (MAS), Functional Independence Measure (FIM). Outcomes were assessed at pre-, post-intervention and at 3mo follow-up.	There were significant differences between the groups in the pre-post and pre-3mo changes in FMA-UE scores (total score, shoulder/elbow, and wrist/hand scores) (all $p<0.05$). There were significant differences between groups in the pre-post and pre-3mo changes in the MAS for elbow and wrist (all $p<0.05$); only the change in MAS for finger at pre-3mo was significantly different between the groups ($p<0.001$). There was no significant difference between the groups regarding ARAT and FIM score changes.
Miyasaka et al. 2016 **Japan** **RCT**	CA: ☒ Blinding: Assessor ☒ Patient ☒ ITT: ☒	30 subacute stroke patients.	The experimental group received robot training with neuromuscular electrical simulation, and the control group received only robot training. Training was performed 1h/d 5x/d for 2wk.	**Primary Outcomes:** Active Range of Motion (ROM), Fugl Meyer Assessment (FMA-UE) total score, FMA-shoulder/ elbow. Outcomes were assessed before and after the intervention.	Only the experimental group demonstrated a significant improvement on ROM for shoulder flexion and shoulder abduction ($p<0.01$). There were significant differences between the groups on the ROM ($p<0.05$). Within-group differences revealed that both groups improved on the FMA-shoulder/elbow measure at post intervention ($p<0.01$), and on the FMA-UE total score (experimental group: $p<0.01$; control group: $p<0.05$). No significant between-group differences were groups on the FMA-UE.
Stein et al. 2015 **Brazil** **Systematic**	N/A	29 RCTs (940 subjects).	Evaluate the evidence for the use of NMES on both upper and lower limb spasticity and range of	**Primary Outcomes:** Modified Ashworth Scale (MAS) for upper extremity (wrist and elbow).	MAS (wrist; n=6): MD=0.12, 95% CI -0.41 to 0.64, I^2=81%, p=0.66. Only 1 RCT included participants in the acute/subacute stage of stroke recovery, with the remainder evaluating stroke patients in the chronic stage.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
review and meta-analysis			motion over control interventions.	**Secondary Outcomes:** Range of motion (ROM) for upper extremity (wrist and elbow).	MAS (elbow; n=4): MD=-0.39, 95% CI -0.89 to 0.11, I^2=54%, p=0.13. All RCTs were in chronic stroke participants. ROM (wrist; n=7): MD=0.46, 95% CI -2.28 to 3.21, I^2=60%, p=0.74. Only 1 RCT included participants in the acute/subacute stage of stroke recovery, with the remainder evaluating stroke patients in the chronic stage. ROM (elbow; n=3): MD=4.57, 95% CI 0.57 to 8.57, I^2=0%, p=0.03. All RCTs were in chronic stroke participants. Adverse events: Not reported.
Cui et al. 2015 **China** **RCT**	CA: ☒ Blinding: Assessor ☑ Patient ☒ ITT: ☑	45 patients with subacute stroke (12hr-NMES group: 12.6wk; 30min-NMES group: 12.8wk; control group: 14.4wk).	Participants were randomized to one of three groups: (1) 12hr-NMES group which received 12 hours of NMES and conventional rehabilitation, (2) 30min-NMES group which received 30min of NMES and conventional rehabilitation, or (3) control group which received conventional rehabilitation. Electrical stimulation treatment was provided for 12hr or 30min session/d respectively, 6d/wk for 4wk.	**Primary Outcomes:** Modified Ashworth Scale (MAS), Fugl Meyer Assessment-proximal (shoulder/elbow) (FMA-p), Fugl Meyer Assessment-distal (wrist/hand) (FMA-d), Action Research Arm Test (ARAT). Outcomes were assessed at pre-, post-intervention and at 8wk follow-up.	There were no significant within-group and between-group differences regarding the MAS scores at 4 or 8wk. All groups demonstrated within-group improvements at 4 and 8wk on the FMA-p, FMA-d and the ARAT (all p<0.05). Significant improvements in the FMA-d were found in the 12h-NMES group compared with the NMES group at 4 and 8wk (p=0.007; p=0.003). Significant improvements in the FMA-p were obtained in the 12h-NMES group compared with the control group at 4 and 8wk (p=0.01; p=0.000).
Shimodozono et al. 2014 **Japan** **RCT**	CA: ☑ Blinding: Assessor ☒ Patient ☑ ITT: ☑	27 adults with severe arm impairment within 13 weeks of stroke onset (RFE-NMES group: 6.2wk, RFE group: 6.8wk, control group: 6.7wk).	The repetitive facilitative exercise (RFE)-under-surface neuromuscular electrical stimulation (NMES) group was given 100-150 repetitions of standardized movements of shoulder, elbow, wrist	**Primary Outcomes:** Fugl Meyer Assessment (FMA-UE), Active Range of Motion (ROM). Outcomes were assessed at baseline and at post intervention.	All groups demonstrated a significant improvement in ROM elbow extension over the study period (p=0.034). The RFE-NMES group demonstrated a significantly greater improvement on the ROM of the elbow compared to the control group (p=0.003) but not to do RFE group. T

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			joints of their affected arm with concurrent low amplitude NMES for each corresponding musculature. The RFE-only group received the same exercise regimen, without NMES. The control group received a conventional rehabilitation programme without NMES. All experimental groups were provided for 4 weeks, 40 minutes per day, for 5 days per week.		here was no statistically significant difference between groups over the study period regarding of ROM on shoulder flexion and wrist dorsiflexion. There were statistically significant differences between groups across the study period for the FMA-UE (p=0.014). The RFE-NMES group demonstrated a significantly greater improvement on the FMA-UE compared to the control group (p=0.003) but not to do RFE group.

Somatosensory Stimulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Cai et al. 2017 **Australia** **Systematic review and meta-analysis**	N/A	22 RCTs (1425 subjects). Only 7 studies evaluated upper extremity outcomes. Of these, 4 RCTs evaluated spasticity, and 4 RCTs evaluated motor function (1 RCT evaluated both). Of these, 3 did not report on the time post stroke, 1 evaluated participants in the acute phase of stroke recovery, and 3 corresponded to the sub-acute phase of stroke.	Interventions for the 7 RCTs evaluating upper limb recovery included: electroacupuncture combined with rehabilitation versus rehabilitation only (n=6), and electroacupuncture combined with rehabilitation and baclofen versus rehabilitation with baclofen (n=1).	**Primary Outcomes:** Modified Ashworth Scale (MAS). **Secondary Outcomes:** Fugl Meyer Assessment (FMA), adverse events.	MAS (n=4) SMD=-0.57, 95% CI -0.84 to -0.29, I^2=0%, p<0.0001. FMA (n=4) SMD=13.32, 95% CI -6.53 to 33.17, I^2=100%, p=0.19. The review reported high heterogeneity in treatment protocols among the studies evaluating upper extremity motor function. Adverse events: No reporting.
Calabro et al. 2017 **Italy** **RCT**	CA: ☒ Blinding: Assessor ☑ Patient ☑	20 patients with first ever left hemisphere stroke experienced more than 3 months before enrollment (experimental	Participants in the experimental group received Armeo-Power robotic training coupled with focal muscle vibration therapy, while the control group received Armeo-	**Primary Outcomes:** Modified Ashworth Scale (MAS). **Secondary Outcomes:**	There was a significant decrease in the MAS scores for the experimental group after the intervention (p<0.001), and at follow-up (p=0.007). There was no

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: ☒	group=5±2mo; control group=6±2mo).	Power training only. The therapy was provided for 1hr/session, 5 sessions/wk, for 8wk. A total of 40 sessions were conducted.	Fugl Meyer Assessment (FMA), Functional Independence Measure (FIM), Hamilton Rating for Anxiety (HRS-A) and Depression (HRS-D). Outcomes were assessed at baseline before the intervention, after the intervention, and at one-month follow-up.	significant change in MAS scores at post intervention and at follow-up for the control group (p=0.3; p=0.4). A time x group interaction for the MAS showed a significant difference between the groups, and at post intervention and follow-up (p<0.001). The experimental group demonstrated a significant decrease in the FIM score, FMA, HRS-A and HRS-D at post intervention (p<0.001; p=0.001; p=0.001; p=0.001) and at follow-up, respectively (p=0.01; p=0.007; p=0.001; p=0.001). The control group demonstrated a significant decrease in the FMA scores at post intervention (p=0.04); no other outcomes were found to be significant.

Non-invasive Brain Stimulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
rTMS					
McIntyre et al. 2017 **Canada** **Systematic review and meta-analysis**	N/A	10 studies (2 RCTs and 8 pre-post) with a mean stroke duration from 6mo to 10yr evaluating rTMS for upper limb spasticity	Intervention comparisons included rTMS plus rehabilitation or rTMS plus medication versus sham stimulation with medication or no comparison for pre-post studies. The stimulation location included both contralesional and bihemispheric.	**Primary Outcomes:** Modified Ashworth Scale (MAS) for elbow, wrist, and finger. Outcomes were assessed at post intervention and at follow-up.	The uncontrolled pre-post studies found significant improvements in MAS for elbow (P < .001), wrist (P < .001), and finger flexors (P < .001). However, a meta-analysis of the 2 available RCTs failed to find a significant rTMS treatment effect on MAS for the wrist (standardized difference=0.34, p=0.30).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
tDCS					
Mazzoleni et al. 2017 **Italy** **RCT**	CA: ☒ Blinding: assessor ☒ patient ☑ ITT: ☒	24 stroke patients within 9 to 60 days from stroke onset with upper limb hemiparesis	Patients were randomly assigned to the experimental (EG) or control group (CG). All participants performed wrist robot-assisted training a) in conjunction with tDCS (real stimulation for patients in EG) or b) without tDCS (sham stimulation for patients in CG). Each patient was asked to perform 5 sessions/wk, each session lasted 30 minutes, for 6 weeks of goal-directed planar reaching tasks.	**Primary Outcomes**: Fugl Meyer Assessment (FMA-UE), Modified Ashworth Scale (MAS), Motricity Index (MI), Box and Blocks Test (BBT). Outcomes were assessed before and after therapy.	There were significant improvements in both groups on the FMA-UE, FMA-wrist, MI, and BBT after the intervention ($p<0.05$ all). There were however no significant improvements on the MAS-wrist in either group. No significant differences between groups were observed on any of the outcome measures after the intervention.

Abbreviations

CA = Concealed Allocation	MD = Mean Difference
CG = control group	N/A = Not Applicable
CI = Confidence Interval	NMES = Neuromuscular electrical stimulation
EG = experimental group	OR = Odds Ratio
FES = Functional electrical stimulation	RCT= Randomized Controlled Trial
IQR = Interquartile Range	RFE = Repetitive facilitative exercise
ITT = Intention to treat	rTMS = repetitive transcranial magnetic stimulation
MAS = Modified Ashworth Scale	tDCS = transcranial direct current stimulation

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