HEART & STROKE FOUNDATION
Canadian Partnership for Stroke Recovery

RESTORING LIVES THROUGH RESEARCH

Current and Future Trends in Stroke Rehabilitation

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Objectives

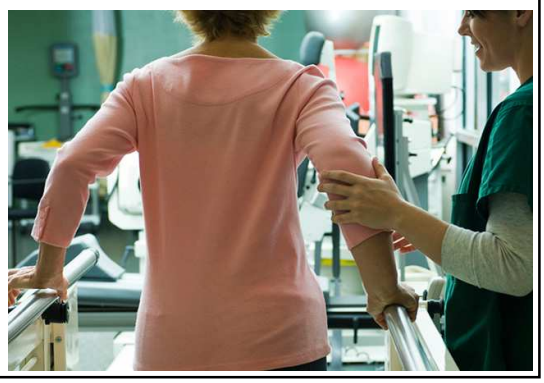
1. **Standardization of Stroke Rehab** – increasing implementation of basic principles of stroke rehab care
2. **Personalized Care** – stroke heterogeneity and limits to standardization of care – biomarkers, algorithms, caregiver availability
3. **Individual Treatment Approaches** – need to move beyond delivering basic principles of care
4. **Integration of Treatment Approaches** – combining different classes of treatments
5. **Shift of Rehab Care to Community**

Neurological Rehab Systems and Standardization of Care

Clinical Best Practice Guidelines aim at standardizing key elements of care

Standardized Care usually focuses on several key principles for which there is wide spread agreement:

1. **Stroke Rehab Units**
2. **Intensive Therapy**
3. **Early Access to Rehab**
4. **Task-Specific Therapy**
5. **Access to Community Based Rehabilitation**



Principles of Rehab, Brain Reorganization and Standardization of Care

Intensity of Therapy: Enough practice to learn new means of achieving lost functions

Task-Specific Training: Practice the function desired

Early Therapy: Taking advantage of brain's greater propensity to learn early on post stroke

Intensity of Therapy

- Research repeatedly shows the benefits of **high dose repetitive task practice**
- Animal studies show need for hundreds of repetitions to learn new movement
- Canadian Stroke Guidelines note stroke rehab patients should receive a **minimum of three hours of direct task-specific therapy, five days a week**
- **In Ontario/Canada average rehab patient gets a little less than 2 hours of direct patient-therapist time** (Foley et al. 2012) 5 days per week.
- Number has been relatively static – culture, cost, pragmatics, poor measurement

Foley et al. *Disability and Rehabilitation* 2012; 34(25):2132-2138.

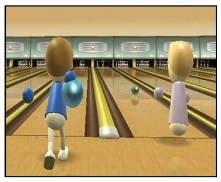
Intensity of Activity in Hospital

- Simpson et al. (2018) observational study of 34 stroke patients.
- Patients had an activity monitor worn continuously for 7 days final week in hospital and first 7 days at home.
- **At home** participants spent more time upright and walking and less time sitting; depression at discharge predicted greater sitting time and less upright time at home (p=0.03).
- **How did rehab get to be less active than being home? Safety overconcerns? Paperwork? Motivation? Culture?**
- Argues very strongly for **early supported discharge.**

Simpson DB et al. *Archives Physical Medicine and Rehabilitation 2018*

Increasing Intensity

- **Group therapy.** Inpatient stroke patients referred to group therapy gait task training or individual gait task training did equally well (Renner et al. 2016).
- **Videogames (non-immersive virtual reality)** improves outcomes but are equal to spending a comparable amount of time playing board games (Saposnik et al. 2016)
- **Weekend therapy** is becoming increasingly common
- **General rehab assistants** are a less expensive alternative to increase intensity and have become very popular; can cross disciplines.



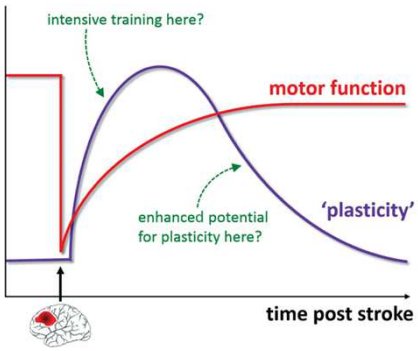
Renner et al. *Clinical Rehabilitation* 2016; 30(7):637-648.
Saposnik et al. *Lancet Neurology* 2016; 15(10):1019-27.

Task-Specific Training

- In animals, **functional reorganization is greater for tasks which are meaningful** to the animal
- Clinically, repetition of motor skills plays an important role in inducing and maintaining brain changes
- **Repetition**, in the absence of skilled motor learning, **is not enough** for brain reorganization to occur
- This issue has been resolved

The Earlier the Better

- Animal studies suggest there is a time window when brain is "primed" for maximal response to rehab therapies
- **Effects of training after stroke are generally greater when started early after stroke**, to take advantage of a "sensitive period" of enhanced neuroplasticity
- **Brain is "primed" to "recover" early in post-stroke period**



AVERT Trial: Can Rehab Be Too Early?

- Wanted to determine if rehab delivered intensively within first few days, Very Early Mobilization (VEM) was better
- Multi-centre, 56 site randomized controlled trial which took 8 years to complete
- Compared patients in VEM group (n=1054) vs. Usual Care (n=1050)
- Patients in VEM overall did worse – more likely to die or have more severe stroke.
- **Mobilization in first few days after stroke must be carefully done**

The AVERT Trial Collaboration Group. Lancet 2015; 386:46-55

Limits to Standardization of Care

- Standardization of Care – Stroke Rehabilitation Units, Intensity of Task-Specific Therapy, Early Admission to Rehabilitation – has transformed rehab care
- There are limits to Standardization of Care, in particular:

A. Heterogeneity: Stroke patients vary in their impairments and disabilities

B. Limited Consensus on Individual Therapies: Despite thousands of randomized controlled trials

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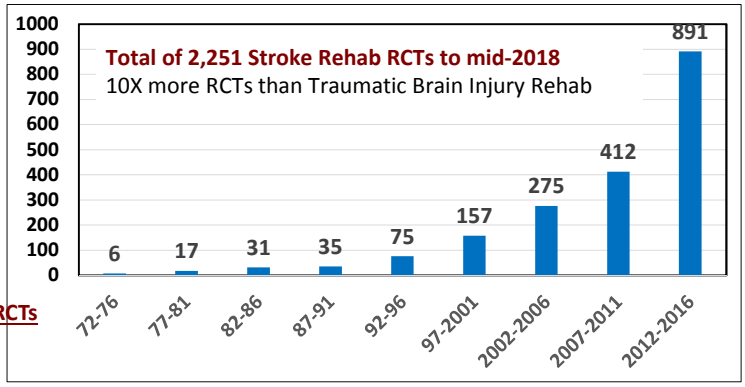

Trends for All Stroke Rehab RCTs Over Time Per Half-Decade

Limits to Standardization of Care: Heterogeneity

1. While stroke is characterized by a focal brain lesion, the size and location of the stroke is highly variable
2. Individual responses to rehabilitation vary; particularly true for more severe strokes

Personalized Medicine Has an Increasing Role

Three examples:

1. **Biomarkers** – i.e. transcranial magnetic stimulation, examining the intactness of corticospinal tract
2. **Evidence-Based Algorithms** i.e upper extremity recovery, will have an increasing role
3. **Psychosocial factors** play an important role, particularly for more severe strokes

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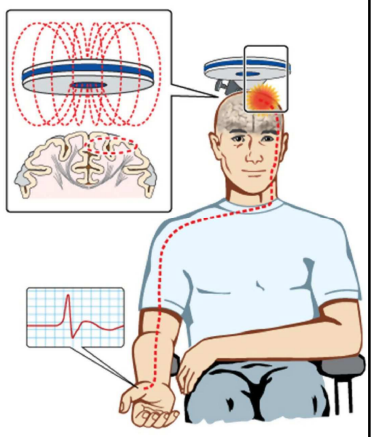
Personalized Medicine: Biomarkers and Proportional Recovery



- Transcranial magnetic stimulation allows measurement of the intactness of the corticospinal tract
- More severe stroke patient with irreversible structural damage to the corticospinal tract severely limits recovery of the upper limb movement (Stinear et al 2007; 2012)
- PREP algorithm combines **clinical measures and biomarkers** (TMS) to predict upper extremity recovery 80% of time(Stinear et al 2017)
- A **comparative study of 192 stroke patients**, in New Zealand, pts with PREP algorithm result revealed had **reduced length of hospital stay of 1 week**

Prabhakaran et al. *Neurorehabil Neural Repair* 2008; 22:64-71
Stinear et al. *Brain* 2007; 130:170-80
Stinear et al. *Brain* 2012; 135:2427-35
Stinear et al. Stroke 2017; 48:1011-1019

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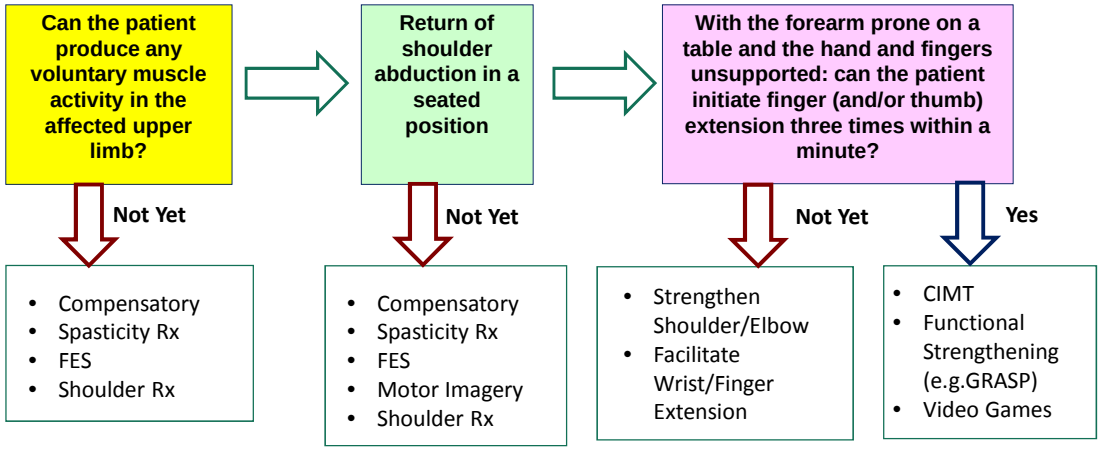
Personalized Medicine: Evidence-Based Algorithms

Viatherapy: A Smartphone App for Post Stroke Arm Recovery

- Wanted to develop an algorithm for post stroke arm recovery
- Used EBRSR, StrokEngine and key literature
- Why an algorithm?
  - Decision making process
  - Based on clear assessment criteria, chosen because of the prognostic indicators
  - Considered the evidence for interventions in the early rehab phase (up to 12 weeks), then after this when rehab may be provided in a less intense manner
- www.viatherapy.org
- Brought together best world experts on upper extremity recovery post stroke.

Wolf et al. Physiotherapy 2016; 102(1):1-4.

Prognostic treatment algorithm for the upper paretic limb

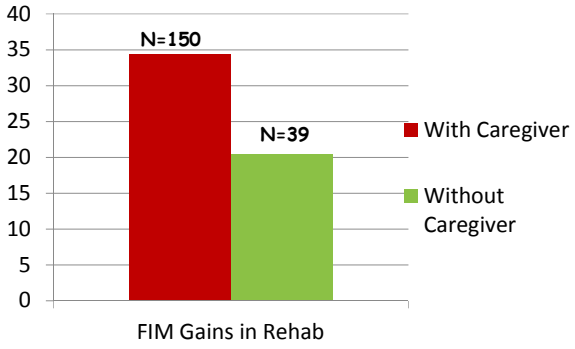


Need to ReEvaluate at 12 Weeks

Wolf et al. Physiotherapy 2016; 102(1):1-4.

Psychosocial Factors and Severe Stroke Rehab

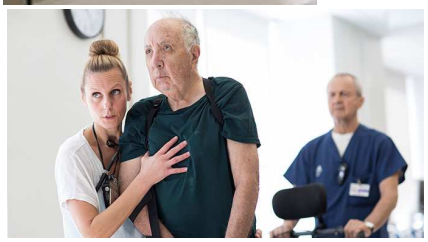
- Take longer to achieve same functional gains with traditional rehab approach
- **<u>Supportive family and resources becomes critical</u>**
- 190 severe stroke inpt rehab; **Only 1 of 121 discharged home in absence of caregiver** (120/151 with caregiver vs. 1/39 without caregiver)
- Individuals with caregivers found to make significantly greater FIM® gains
- **Limits success of rehabilitation of very elderly severe stroke patients with no family supports!**
- Alternatively rehab of severe stroke patients with strong family supports is more likely to be successful



Rehabilitation = Therapy

Ideally delivered Intensively, started Early and focused on Tasks important to the stroke patient

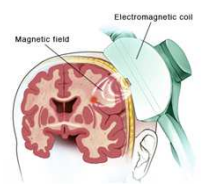
Involve one-on-one practicing with a skilled therapist

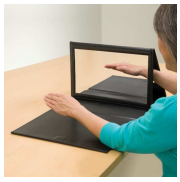


Deciding on Individual Treatment Approaches

EBRSR www.ebrsr.com

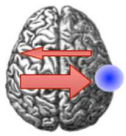
- There is limited clinical consensus as to what individual therapies should be consistently applied (i.e., CIMT, technologies).
- There are 1410 motor RCTs alone to mid-2018 but most are small single site usual care control studies (more proof-of-principle studies)
- With larger, more sophisticated motor RCTs with active controls, **both groups often improve similarly with dose matched therapy** (LEAPS, EVREST, SIRRACT)
- How one delivers the basic therapy seems to be not important
- **Primers and facilitators** of rehabilitation recovery becomes more important





Duncan PW et al. *NEJM* 2011;364:2026-36

Primers and Facilitators of Motor Recovery



Interhemispheric inhibitory imbalance

Excite Ipsilesional Brain Activity
Task Specific Activities
Intensity of Therapy
Constraint-Induced Movement Therapy
Action Observation
Mirror Therapy
Motor Imagery
rTMS (10 Hz)
tDCS anode
Pharmacological Stimulants

Reduce Contralesional Brain Activity
rTMS (1 Hz)
tDCS cathode
Constraint-Induced Movement Therapy

Facilitate Affected Side Activity
Intensity of Therapy
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Functional Electrical Stimulation
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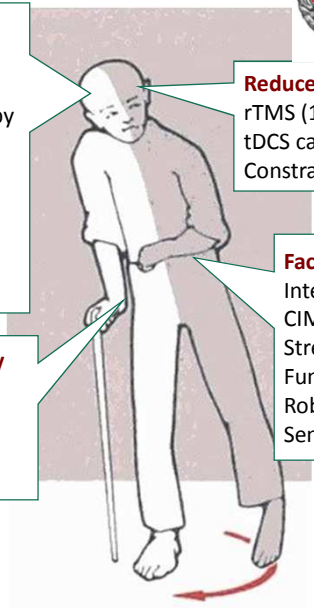
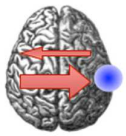


Primers and Facilitators of Motor Recovery: Influencing Brain Motor Pathways



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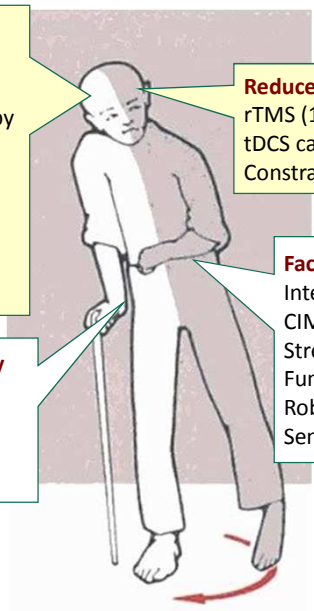


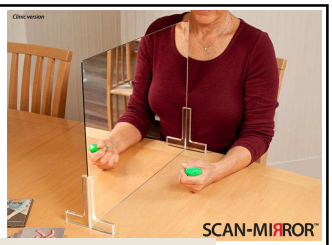
Prime the Ipsilesional Brain Motor Pathway: Action Observation Therapy (AOT)

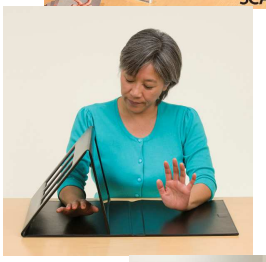
Action Observation

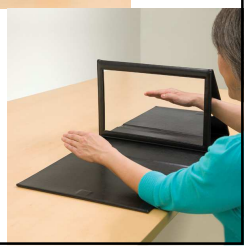
- AOT is a top down approach and is grounded in basic neuroscience and the recent discovery of the mirror neuron system (MNS)
- Individual observes another individual performing a motor task, either on a video or a real demonstration, and then attempts to mimic what they see
- Shown to improve motor recovery

Prime the Ipsilesional Brain: Mirror Therapy

- Mirror is used to create a reflection of the *non*-affected arm or hand in place of the affected side during therapy
- **Perform various stroke recovery exercises with the *non*-affected side**
- The mirror image 'tricks' brain into thinking that affected arm is moving like unaffected arm
- Primes motor pathway for the actual movement







Prime the Ipsilesional Brain: Mental Imagery or Practice

- Adapted from the field of sports psychology as a supplement to exercise
- Mental practice involves rehearsing a specific task or series of tasks, mentally
- Stored motor plans for executing movements can be accessed and reinforced during mental practice
- Improves upper extremity motor function when compared to standard care

Motor Imagery

Constraint Induced Movement Therapy (CIMT)

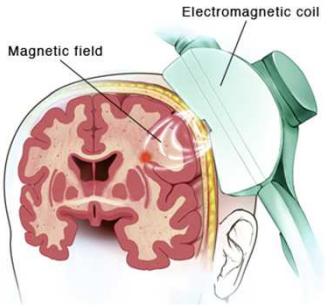
Interhemispheric inhibitory imbalance

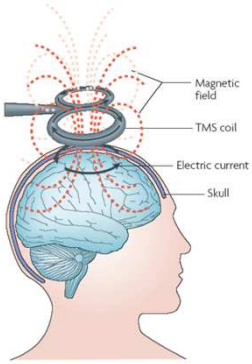
- CIMT involves restraint of unaffected hand/arm and increased practice/use of the affected hand/arm
- **Traditional CIMT:** 2 week training program with 6 hours of intensive upper extremity training with restraint of the unaffected arm for at least 90% of waking hours
- Opportunity to increase intensity of therapy at minimal cost
- Strong research evidence it works, especially for chronic stroke; helps overcome inhibition of stronger side

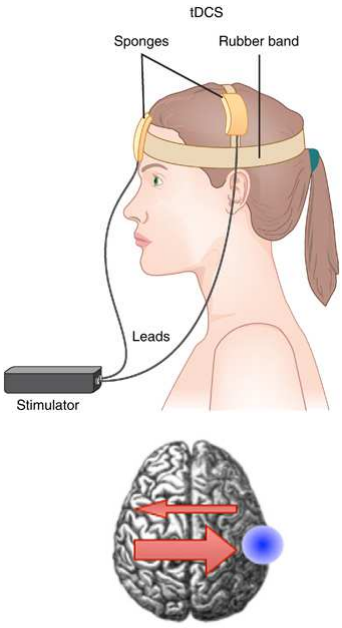
Brain Stimulation

Brain stimulation involves primarily non-invasive motor cortex stimulation:

1. Repetitive transcranial magnetic stimulation (rTMS)
2. Transcranial direct current stimulation (tDCS)

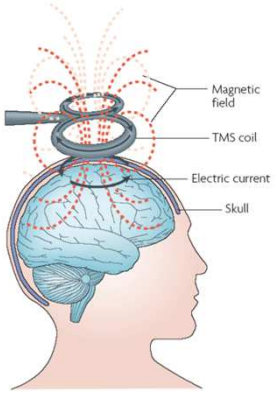


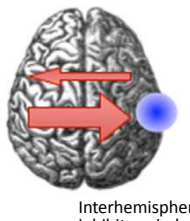




Repetitive Transcranial Magnetic Stimulation (rTMS)

- Involves use of a coil that produces a magnetic field that passes through the skull to cerebral cortex
- **Low frequency stimulation** tends to **inhibit** cortical excitability while **high frequency stimulation increases** cortical excitability
- Motor improvement can occur with inhibition of unaffected hemisphere (which is inhibiting the affected side) and exciting the affected hemisphere

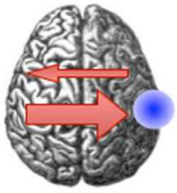


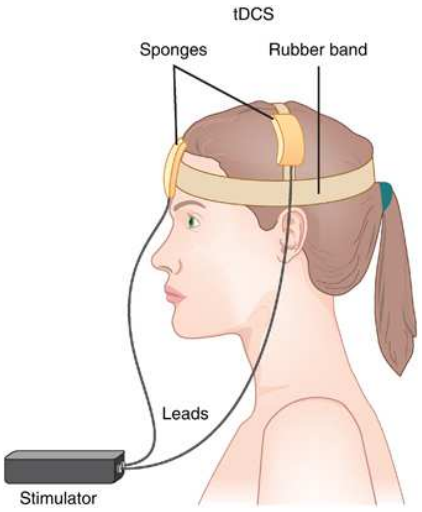


Interhemispheric inhibitory imbalance

Transcranial Direct Current Stimulation

- Mild electrical currents (1-2 mA) conducted through 2 surface electrodes applied to scalp
- **Anodal stimulation increases** cortical excitability
- **Cathodal stimulation decreases** cortical excitability





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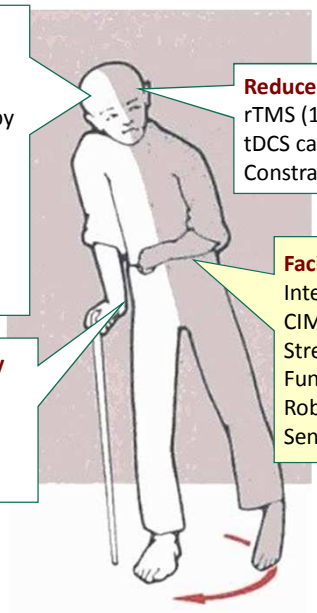
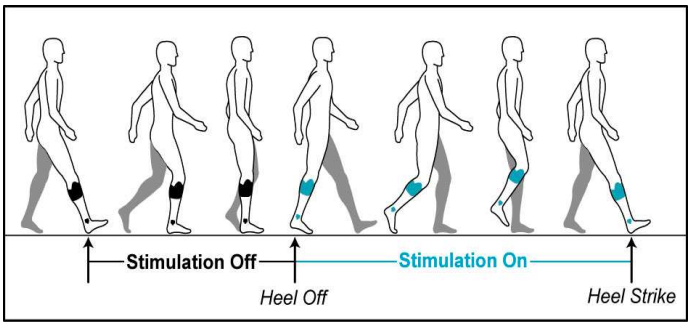


Functional Electrical Stimulation (FES)

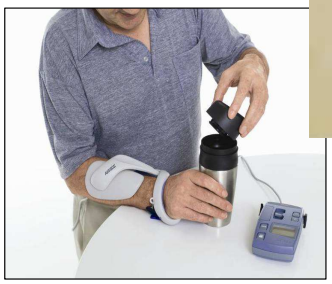
- Weak ankle dorsiflexion (DF) with plantarflexion hypertonicity results in drop foot, typically corrected with an ankle foot brace
- FES of common peroneal nerve enhances ankle DF during swing phase of gait

Ness L300®



Hand Functional Electrical Stimulation

Ness H200®



- Electrostimulation of peripheral nerves and muscles with external electrodes are applied to stimulate movement during training of activities
- Uses electrical stimulation to open and close grasp

Electromechanical and Robotic Assisted Walking

- Patient is suspended over a treadmill and a electromechanical walker moves the legs in walking motion
- Canadian Practice Guidelines recommend consider for more severe or early stroke patient who would not otherwise practice walking
- Exoskeleton allows the patient to stand and walk in upright position
- Thought to be most effective for early more severe strokes

Cognitive Rehab Post Stroke

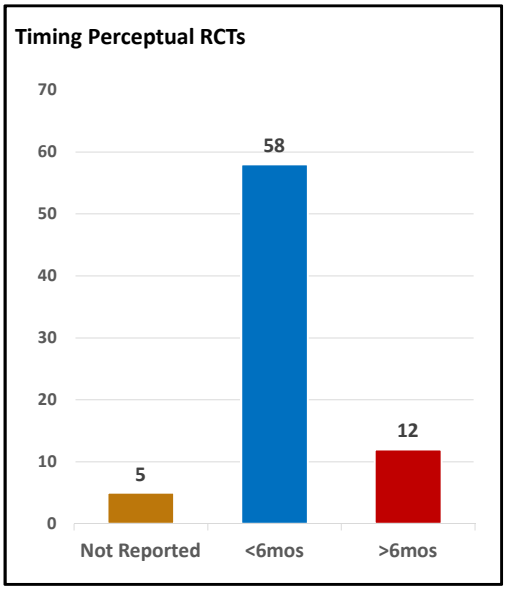
EBRSR www.ebrsr.com

- **Evidence for cognitive rehab is less clea**r than motor rehab as there are fewer RCTs (1/5 of motor RCTs) and effectiveness for interventions less certain (Cumming et al. 2013; Bruno-Petrina 2014)
- Effective treatments for **memory and executive function**, often associated with **more diffuse lesions**, are lacking (Ballard et al. 2003)
- Good evidence that **rehab is effective in treating more focal deficits** such as **visual spatial** rehab or interventions for **aphasia** (Cicerone et al. 2011; Brady et al. 2012)
- There are fundamental differences between how visual spatial and aphasia recover which influences rehab care

Cumming et al. International J Stroke 2013; 8(1):38-45

Stroke Rehab Perceptual Evidence

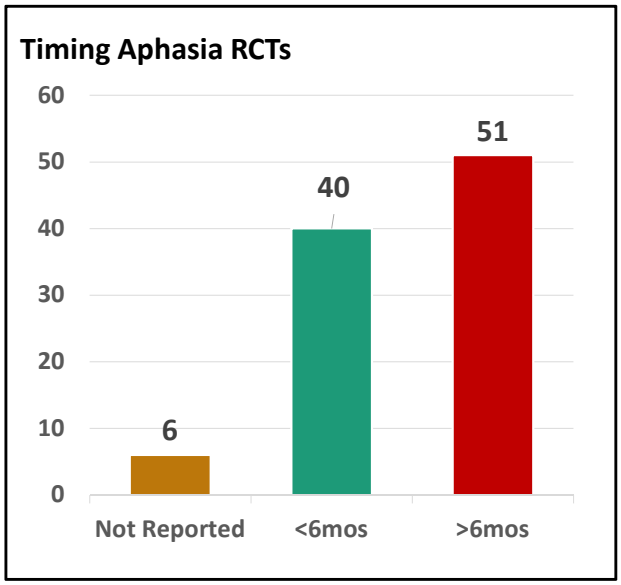
Eye Patching – 12 RCTs - Conflicting evidence of benefit
Prism Glasses -13 RCTs - Strong evidence of benefit but does not persist long-term
Visual Scanning – 12 RCTs - Strong evidence of benefit with associated improvements in function



Stroke Rehab Aphasia

Cochrane review 2016

- **Comparison of SLT vs. no SLT** – significant benefit for functional communication, reading compression, general and written expression; not significant for auditory comprehension and naming
- **Comparison of high level SLT (vs. low level SLT)** has shown greater intensity, dosage and duration benefits some language outcomes



Integration of Therapeutic Approaches

Involves integrating treatments or combining motor treatment with something else

Integration of different therapeutic approaches such as:

1. Cognitive-motor interference
2. Motor-sensory integration
3. Music Therapy for Aphasia
4. Pharmacological Treatment and Rehab

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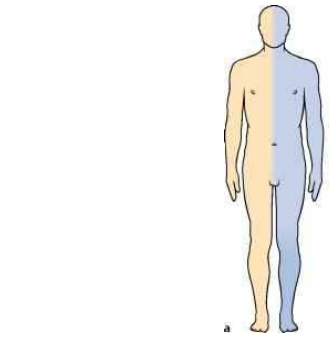
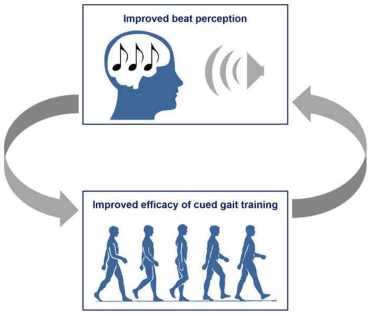
Cognitive-Motor Interference (Mobility)

- During gait activities with an added cognitive task, people with stroke are likely to demonstrate significant decrements in motor tasks only or in both motor and cognitive tasks
- Longitudinal studies show conventional therapy has minimal effects on Cognitive-Motor Interference (CMI)
- Initial work suggests that dual-task interventions may reduce CMI during gait in stroke survivors living in community
- Dual-task training has been shown to improve gait and balance training while performing direct cognitive tasks such as counting or repeating sentences (He Ying et al. 2018)

Sensory Aspect of Post-Stroke Motor Rehab

- Successful movement relies on efficient sensori-motor integration; however, sensory therapy and sensori-motor reintegration is seldom targeted
- Neurological patients who have lost one or more of their senses may show profoundly affected motor functions
- Perceptual attentional deficits, such as hemispatial neglect, represent a well known negative prognostic factor in motor functional recovery
- There are a large number of treatments focused on sensory stimulation, FES, biofeedback, music therapy, mirror therapy in upper and lower extremities and combining these with motor therapies may be helpful





Music Therapy for Aphasia

Melodic Intonation Therapy (MIT)

Two main components of music based therapy:

1) Melodic Intonation (singing) - reduces rate at which words are articulated and allows better stringing of words to enhance fluency

2) Rhythmic tapping while words and eventually phrases are repeated - may engage the right hemisphere sensorimotor network and improve verbal production

Fluoxetine for Motor Recovery After Ischemic Stroke

- FLAME trial examined use of fluoxetine within 5-10 days of stroke onset for 3 months; patients receiving fluoxetine made a better neurological recovery
- Mechanism uncertain: Rx depression and/or facilitate/prolong reorganization of brain
- Recent trials not able to duplicate this work in terms of neurological recovery (Kim et al. 2017, FOCUS Study 2018)

Chollet et al. *Lancet Neurol* 2011; 10(2):123-30

Shift to Community Rehabilitation

- Community rehab reduces rehospitalization and allows earlier discharge home
- NNT in order to spare one person from experiencing a poor outcome was 14
- Two often competing principles – value of home-based therapy and the importance of continuity of care (hospital to home)

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Hospital and Community-Based Outpatient Therapy

- London experience is patients in **home-based** outpatient therapy (who tend to be older and more disabled) made **greater gains** than those in hospital based outpatient therapy
- Outpatient therapy in the home allows for **practicing skills in a real-life setting** which may account for greater gains
- Early supported discharge shows that it is just not enough to provide the resources; **continuity of care matters**

COMMUNITY Stroke Rehabilitation TEAM

Early Supported Discharge

EBRSR www.ebrsr.com

In-Patient and ESD Same Team	Significant Benefit
In Patient Team / ESD Team	Trend to Benefit
In Patient Team / ESD Team	Trend to Less Benefit

- It is just not enough to provide the resources; **continuity of care matters**

Fearon P, Langhorne P. *Cochrane Database of Systematic Reviews* 2012 Issue 9

Summary of Talk

- Stroke Rehabilitation has the **strongest evidence-base** of any of the neurorehabilitation disease groups
- **First Principles** in stroke rehab are generally agreed upon and established as **Standardized Practice** – stroke rehab units, intensity, early admission, task-specific training – **Operationalizing** evidence to practice still incomplete
- Research Evidence for **Specific Therapies/Treatments** is strong but evidence for one better than another is often not evident
- Next wave is **Primers and Facilitators** of Recovery
- **Individualized Care** (biomarkers, algorithms and social supports) and **Integration of Therapeutic Approaches** (cognitive-interference, motor-sensory, pharm-therapy) are potentially new approaches
- The **Shift of Rehab from Hospitals to Home** is inevitable and we need well evidenced models of care

HEART & STROKE FOUNDATION
Canadian Partnership for Stroke Recovery

RESTORING LIVES THROUGH RESEARCH

The End

Western

ST JOSEPH'S HEALTH CARE LONDON

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