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Neural Priming for Post-Stroke Upper Limb Hemiparesis

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Rush University Medical Center

Learning Objectives

At the conclusion of this activity,

1. Participant will define the concept of motor priming and its relevance to neurorehabilitation
2. Participant will describe three types of motor priming paradigms and their associated neural mechanisms
3. Participants will compare and contrast the clinical benefits, limitations, and underlying mechanisms of the various types of motor priming presented.

Terms and Abbreviations

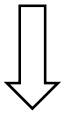
- TMS – Transcranial Magnetic Stimulation
- tDCS- transcranial direct current stim
- M1 motor cortex
- S1 sensory cortex
- BP – Bilateral priming.
- BDNF – Brain Derived Neurotrophic Factor
- Supraspinal – above vertebral column or spine
- RCT – randomized controlled trial
- ALT – Alternating movement
- MIR-Mirror movement
- VO^2 The amount of oxygen individual can utilize during max. exercise
- MEP – motor evoked potential

Presentation on Priming

- Timely
- Need some knowledge in neuroplasticity and the possible neural mechanisms
- You may need to articulate what you are doing
- Need some background in the priming research

NEURAL Priming

Priming: Change in behavior based on previous stimuli or, in some cases, concurrent stimuli (Stoykov & Madhavan, 2015). The behavior change



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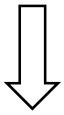


Facilitates
motor learning
and recovery

NEURAL Priming

Priming: Change in behavior based on previous stimuli or, in some cases, concurrent stimuli (Stoykov & Madhavan, 2015). The behavior change

⇩

Facilitates motor learning and recovery ⇨ *Associated with changes in neuroplasticity* that coincide with changes in motor behavior

Mechanisms of Neuroplasticity

Experience-dependent Plasticity

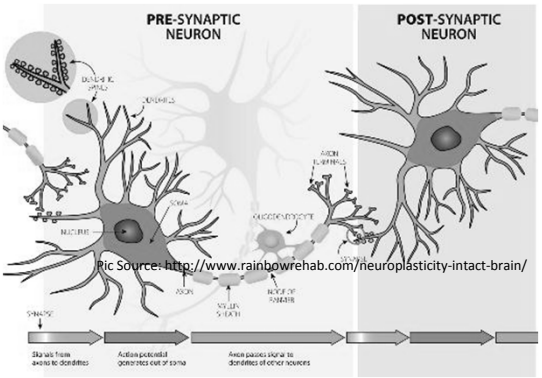
Synaptogenesis
- Change in number of synapses
- Size of synapses

Synaptic Plasticity
- Changes in efficacy of existing synapses
  - Long Term Potentiation (LTP)
  - Long Term Depression (LTD)

Cellular Processes
- Dendritic growth/remodeling

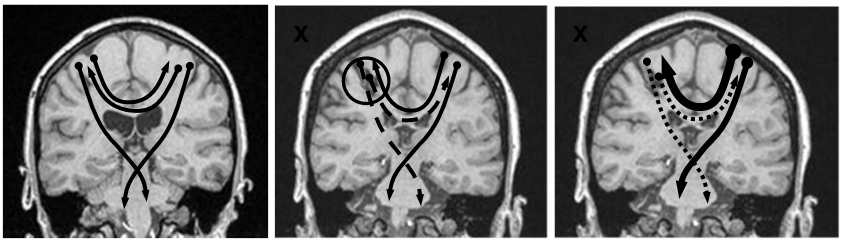
Molecular Processes
- Calcium, potassium, sodium

Adaptive capacity of the central nervous system



Pic Source: http://www.rainbowrehab.com/neuroplasticity-intact-brain/

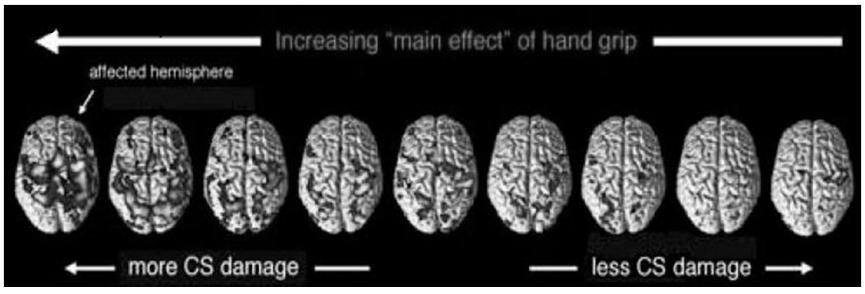
Neural Mechanisms BP- Asymmetry of Post-Stroke Cortical Excitability



- ✓ Interhemispheric asymmetry in M1 excitability Talelli et al., (2006) Clin Neurophysiol
- ✓ Asymmetry in transcallosal inhibition Murase et al., (2004) *Ann Neurol,*
- ✓ "Balanced" hemispheres associated with better recovery Rossini et al., (2003) *Lancet Neurol*

Animation courtesy of J. Stinear & W. Byblow

Association with function



Activation in the non-lesioned hemisphere is associated with poor function

Ward et al. 2007 Eur J Neurosc

Paradigms of Motor Priming

- **Movement-based priming**
  - **Bilateral Motor Priming**
  - **Aerobics Based Priming**
- **Motor imagery and action observation**
- **Sensory-based priming**
  - **Sensory Stimulation**
  - **Transient Functional Deafferentation**
- Pharmacology-based priming
- Stimulation-based priming

Stoykov and Madhavan, JNPT 2014

Movement Based Priming Objectives

I. The benefits of movement based priming
II. The types of **movement-based** *priming*
 a. Bilateral
 b. Aerobics Based priming
III. **Imagery**
 a. Mirror therapy
 b. Action observation
 c. auditory practice
IV. **Sensory Based Priming**
 a. Sensory stimulation
 b. Sensory Deprivation

Benefits of Movement Based Priming

- Cost Effective
- Does Not Require Skilled Operator
- Can include individuals with hx of seizure disorder, pacemakers or metal materials from surgery
- No FDA Approval
- Repetitions

Bilateral **Training** versus Bilateral **Priming**
(B) Arm training with Rythmic Auditory Cueing

- Whitall et al. (2000) reported on a single group study of 14 chronic subjects who improved on the FMUE and strength measures.
- Bilateral symmetrical movement during BAT is the training itself
- Proposed mechanism is the well documented symmetry constraint
- (tendency of both limbs to resort to symmetrical movements at higher speed)

Bilateral Priming

- Bilateral priming **precedes** motor practice to ready the brain for practice of uni/bilateral (synergy) functional tasks
- BP studies have used varying UE training protocols including home programs, Standard care, Wii based training, and TST protocols from previous clinical trials
- Neural mechanism is normalization in cortical inhibitory mechanisms

Bilateral Priming (aka Active Passive Bilateral Therapy)

- Rhythmic wrist flex/ex at frequency of 1 Hz for 15 min prior to training.
- Stinear & Byblow (2004) showed decrease in excitability in the contralesional hemisphere correlating with motor improvement
- FEW Studies

Stinear J & Byblow (2004). J Clin Neuorphysiol

Stinear CM et al (2009) Brain

Stoykov & Stinear (2010) Am J Phys Med Rehabil

Byblow et al (2012) PLoS One

Stoykov & Corcos, (2013) Stroke

Shiner et al (2014) Neurorehabil Neural Rep

Stinear CM et al (2014) Stroke

For Info re: device contact: Richard Little <richard.little@exsurgorehab.com>

Bilateral priming-Lower Level Subjects

Lower level subjects require more support (in terms of strapping, wedging, or assist from therapist) to keep their hand placed in the device. Metronome is also used.

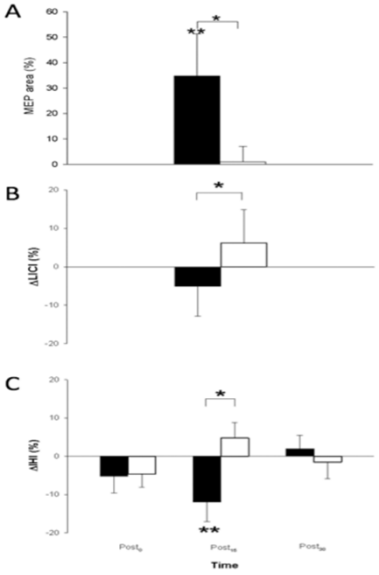
For Info re: device contact: Richard Little <richard.little@exsurgorehab.com>

Evidence for Use of Bilateral Priming in Healthy Population

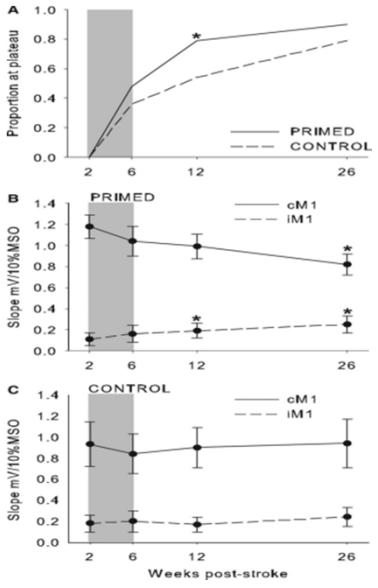
- Experiments 1-3 examined MIR (mirror) (in-phase) wrist flexion and extension
- Compared results to ALT (anti-phase) on various neurophysiologic measures
- (Byblow et al, 2012, PLOS ONE)

Mirror Symmetric versus Asymmetric Bilateral– Healthy Subjects (Byblow et al, 2012)

- Graph A. Increase cortical motor excitability in **MIR** but not **ALT**
- Graph B. Trend of decrease in long interval cortical inhibition in **MIR** & ns increase in **ALT**
- Graph C. Decrease in interhemispheric inhibition from active to passive hemisphere in **MIR**
- No Change in H-reflexes – (B) priming likely supra-spinally mediated



Bilateral Priming Accelerates Motor Recovery (Subacute Phase) Stinear CM et al (2014).



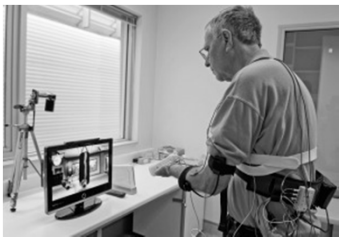
--57 Participants approx 26 days post stroke randomized to BP or control. High level subjects (median FMUE score of 44)

- Graphs B (primed) and C (control)
- Corticomotor excitability of contraM1____ (straight line) decreased in the primed group (B) but not in control group (C)
- CME of ipsilesional hemisphere (iM1) (B) increased in the primed but not control

Stinear CM et al (2014). STROKE

BMP and Wii

- Case-Controlled (N=10) Study using Historical Controls; heterogeneous from 4 months to 10 yrs post; FMUE scores ranged from 5 to 61.
- Individualized Wii 1 hour 10 consecutive weekdays.
- Difference between groups in FMUE 28 weeks post training favoring BP (p= .02); greater UE AROM in BP;



(Shiner, Byblow & McNulty, *Neurorehab Neural Rep*, 2014)

Bilateral priming in treatment

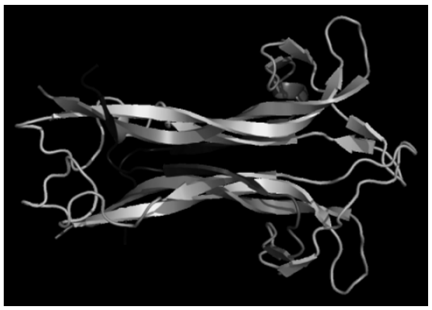
- If spasticity – stretch and heat pack may make it easier.
- Remember, bilateral priming is not the same as bilateral training (purpose & mechanism)
- If wrist contracture – not possible
- Benefits or bilateral priming (in literature) are most evident at follow-up – retaining gains
- Lower level – need to work on keeping them well positioned in rocker
- Metronome helps

Aerobic Exercise – as Priming

- **AEROBIC EXERCISE INCREASES:**
- Aerobic Fitness
- Motor learning
- Cortical Excitability
- Brain-derived neurotrophic factor levels.
- Cognitive Flexibility

Neural Mechanisms of Aerobic Exercise: Brain Derived Neurotrophic Factor (BDNF)

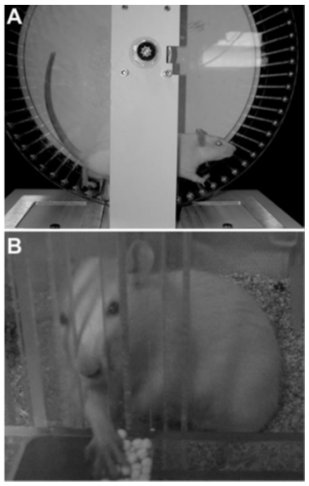
- Most abundant neurotrophin (secreted protein) effecting neuronal proliferation, differentiation and survival
- Lower levels are associated with mental disorders
- Increases after exercise



Endurance Exercise facilitates relearning of forelimb motor skill

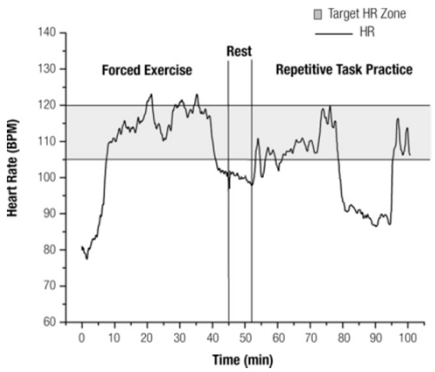
(Ploughman et al, 2015, *Eur J Neurosci*)

- Ploughman et al randomized 36 **stroke- induced rats** to one of four groups:
  - No rehabilitation
  - Reaching only
  - Motorized run only
  - RUN/REACH
  - Reaching /running tasks were systematically upgraded each week
  - **Improvement** on Wheel/Reach task and increased expression of Messenger RNA in Run/Reach group



Forced Aerobic Exercise prior to Task Specific Training)

- 45 yo male 10.5 months post-stroke
- Heart rate (HR) response during a representative 45-min session of forced aerobic exercise followed by a 45-min session of OT-based repetitive task practice (RTP).
- Within or above his target HR zone (105–120) during
  - 94% of this forced exercise session
  - 51% of this OT session.
- Variable response during OT dependent on the task position (standing or sitting) & difficulty



BPM = beats per minute

(Linder et al,2015, *Am J Occup Ther)*

Forced Aerobic Exercise Enhances Motor Recovery after Stroke (Linder et al, 2015)

POST-TX RESULTS:

*30% improvement in VO_2 Peak

*From 35 to 55 on FMUE (20 point improvement)

*43 meter improvement post-tx on 6 minute Walk Test,

*Improved on WMFT functional ability scale

Forced Aerobics

- Collaborate with physical therapy
- Try to have patients stand while doing upper limb training
- Don't worry about tiring patients out – they should be working
- Check with doctor

- Research has shown that it reduces cognitive deficits
- Good for younger patients

Another Type of Priming – Motor Imagery

- Definition
- 3 types of motor imagery,
- Possible neural mechanisms
- Studies of Mirror Therapy
- Clinical Tips for Mirror Therapy

III. Motor Imagery

- Voluntary Cognitive Process of imagining movement without movement actually occurring.
- Important when physical practice is limited by impairment

III. Imagery Based Priming - Types

- Mirror therapy
- Action Observation
- Mental rehearsal via auditory feedback

Tools

- Mirror with a stand set up in sagittal plane

Mirror Box

- Plastic mirror which is covered

http://ireflex.co.uk/mirrorboxtherapy.com/make-a-mirror-box/

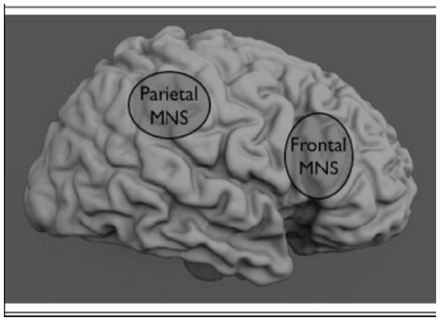
A. Action Observation B. Mental Rehearsal

Evidence

- Mirror Therapy – numerous case studies as well as RCTs
- Action Observation – (Ertelt, 2007) in stroke. It has also been used in Parkinson's, pediatric, orthopedic population (hip replacements)
- Mental Practice via auditory tape – numerous articles by Stephen Page with patients listening to tapes and instructed in mental practice (after physical practice)

NEURAL MECHANISM: Mirror Neuron System?

- Inferior Frontal gyrus, ventral pre-motor and inferior parietal lobe
- Mirror Neurons Fire while observing object oriented actions
- Speculation that Mirror Neurons active during motor imagery
- Limited Evidence for Mirror therapy

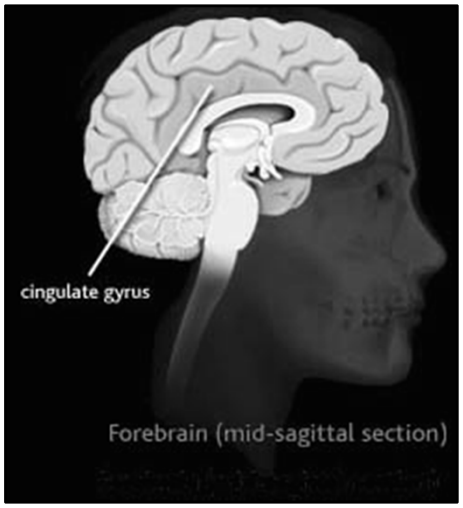


Cingulate Gyrus

Michielsen, Smits et al (2011)

fMRI study examining bilateral movement with mirror reflection

Sense of self and spatial awareness



Neural Mechanisms

- Studies (with TMS) indicated increased corticomotor excitability in the M1 which modulates the hidden hand
- Ventriloquism
- Possibly using same neural pathways during normal movement.

Randomized Controlled Trial

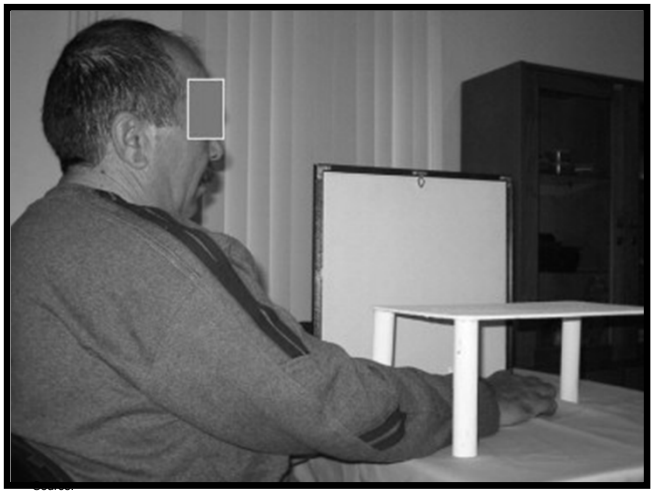
- Randomized Controlled Trial (Yavuzer et al, 2008)
- Mirror Group and Group that looked at the back of the mirror
- 20 acute stroke patients randomized to each group (N=40)

Yavuzer G, Selles R, Sezer N, Sütbeyaz S, Bussmann JB, Köseoğlu F, Atay MB, Stam HJ. Arch Phys Med Rehabil. 2008 Mar;89(3):393-8.

Fig 2

Source: Archives of Physical Medicine and Rehabilitation 2008; 89:393-398
(DOI:10.1016/j.apmr.2007.08.162)

Fig 3



Archives of Physical Medicine and Rehabilitation 2008; 89:393-398
(DOI:10.1016/j.apmr.2007.08.162)

Mirror Therapy Protocol

- Start out with simple movement in cardinal planes - Progress to multi-joint
- At all times, the subject is observing the limb in the mirror
- Move to tasks requiring prehension such as putting cut out letters into a word (Backwards letters), writing, rolling a small ball with the therapist

Points

- Take off rings or jewelry
- A variety of diagnoses – brain injury, pain syndromes & orthopedic conditions
- Strong effect with lower level
- Bedside and when precautions limit limb movement
- Bilateral or Unilateral
- Several times per day if possible
- Do not let patient look at the moving hand. They must look in the mirror.

TYPES - SENSORY BASED PRIMING

IV. Sensory based priming

A. Sensory Stimulation

PNS

Muscle Vibration

B. Sensory Deprivation

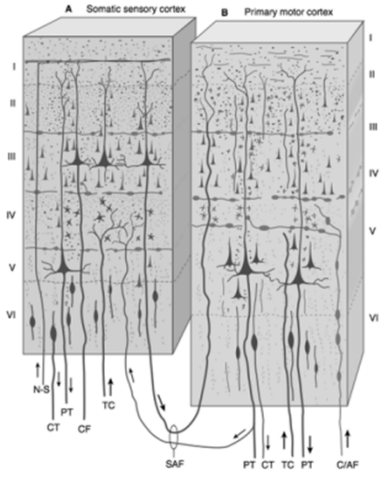
Temporary functional deafferentation

BENEFITS OF SENSORY PRIMING

- Sensory priming enhances motor and sensory feedback
- BECOMING MORE
  - CLINICALLY RELEVANT
  - & COST-EFFECTIVE

Sources:
Fitzgerald, M.J., Gruener, G., & Mtui, E. (2012)
Clincal neuroanatomy and neuroscience,
6th edition pp. 300-303.

- Short Association fibers fr pyramidal neurons
- U



SENSORY STIM - Peripheral Nerve Stimulation

- Bursts of electrical stimuli delivered to the skin overlying peripheral nerves at regular intervals
- Ulnar, median, radial
- An extended period of peripheral nerve stim prior to training can:

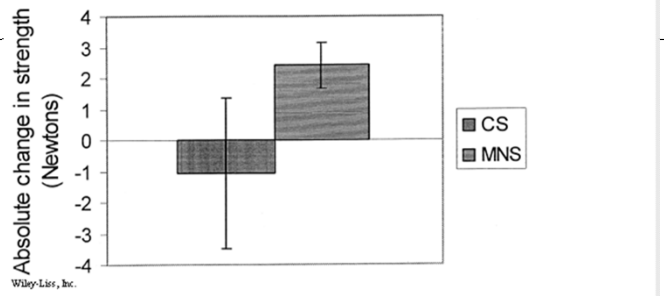
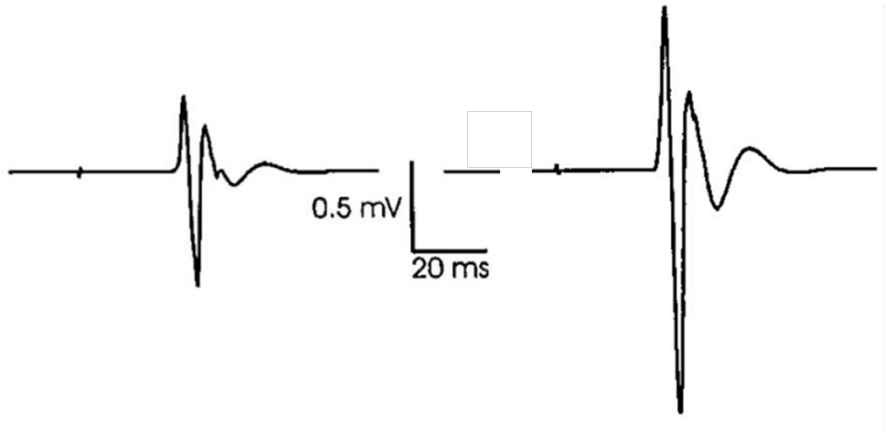


Figure 2. Absolute changes in muscle strength (Newtons) in the control stimulation session and the median nerve stimulation session (n = 7). Error bars represent standard errors of the mean.

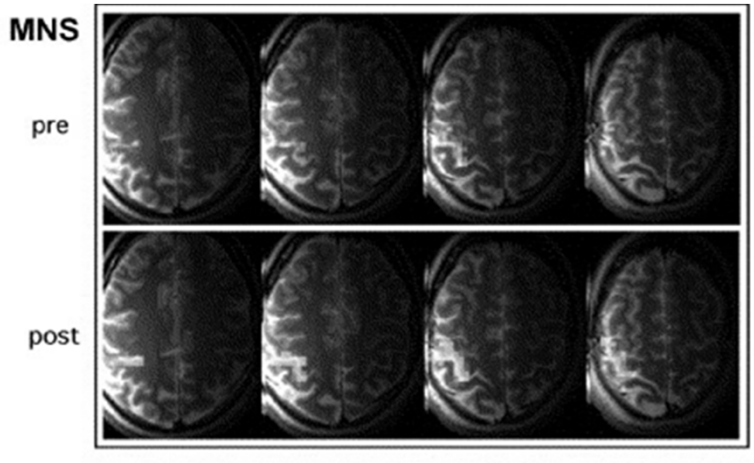
Cortical excitability is increased with sensory stimulation



Pre MEP Post MEP

Ridding et al, *Exp Brain Res*, 2000

Enlarge cortical areas activated by movement



Wu et al. *Neuroimage,* 2005

SENSORY STIM: Vibration to Agonist

- **Agonist (Extensor Carpi Radialis)**
- After 5 minutes of vibration:
  - 20% improvement in Box & Block
  - Increase in Cortical silent period of antagonist

Liepert and Binder, 2010, Restorative Neurol Neuroscience

Sensory Stimulation: Different possibilities for vibration.

TheraBracelet LLC

SENSORY DEPRIVATION- TFD

- TEMPORARY FUNCTIONAL DEAFFERENTATION- Deafferentation of a body part induced by mechanical or pharmacological agents as a priming mechanism prior to motor training
  - Type of Anesthetic Modality
  - Anesthetized Limb Area
  - Neural Mechanism – location of anesthesia

Temporary Functional Deafferentation

- Anesthetic block to the shoulder and/or upper arm
- Followed by motor training (pinch task)
- Improvements in pinch of the affected hand
- Larger Motor evoked potentials
- **Muellbacher et al, 2002**

Temporary Functional Deafferentation

- EMLA® 2.5% lidocaine and 2.5% prilocaine (EMLA, AstraZeneca,) applied to volar forearm then **CIMT**
- Tested for tactile resolution (grating oriented task) at fingertips and found to be better (t=3.76; $p<0.01$).
- Petoe et al (2013) found that increased, after EMLA, there was increase intracortical inhibition which was related to movement precision (Healthy subjects)

Weiss et al, 2011

Sensory Based Priming

- Almost always beneficial – most stroke patients have some reduction in sensation
- Vibration and PNS have research behind them and definite neural mechanisms. That is not to say that other types of sensory stim (rice bowl, mesh glove) would not work. It just hasn't been studied.
- Use your imagination
- EMLA – if your physician is on board

Summary

- Priming is associated with motor learning and neuroplasticity
- The neural mechanism for bilateral priming is change in interhemispheric inhibition.
- For chronic stroke, Asymmetry of cortical excitability is an underlying neural mechanism which explains many of the priming mechanisms.

- Aerobics based priming – associated with increase in BDNF
- Priming, by itself, is not therapy. It needs to be followed by training of the upper extremity (Task specific training, CIMT,)

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Stroke Treatment Across The Care Continuum

http://www.occupationaltherapy.com/general/stroke-awareness-month-virtual-conference

Mon 5/16	**Stroke Recovery and OT Implications within the Continuum** Salvador Bondoc, OTD, OTR/L, FAOTA
Tues 5/17	**Taking the Mystery Out of Mastery in Stroke Rehabilitation Practice** Robert Ferguson, MHS, OTR/L
Wed 5/18	**Neural Priming for Post-Stroke Upper Limb Hemiparesis** Mary Stoykov, PhD, OTR/L
Thur 5/19	**Occupational Therapy's Role in Managing Functional Implications of Visual and Cognitive Impairments** Lisa Rivera, MS, OTR/L
Fri 5/20	**Facilitating Return to Work after Stroke across the Continuum of Care** Shannon Scott, OTD, OTR/L

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