New Directions For Neurorehabilitation

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Outline of Topics

• Predicting recovery in individual patients
• Cortical basis of recovery & neuromodulation
• Wearable robotics
• Promising basic research findings

Disclosure

I have nothing to disclose.
POTENTIAL FOR RECOVERY

General characteristics at population level
- Age
- Infarct size & location
- Acute treatment regimen
- Medical co-morbidities

Exam findings
- Independent digit movements
- Shoulder movements
- Ankle dorsiflexion

What about predicting recovery for individual patients?
- Multimodal assessment shows promise (exam, TMS, MRI)
- Predicting Recovery Potential (PREP) algorithm (Stinear et al., Brain, 2012)

TMS

MULTIMODAL ASSESSMENTS TO PREDICT RECOVERY

PREP Algorithm
- 40 patients with stroke (cortical & subcortical) assessed at day 3 and reevaluated at 3 months
- SAFE (Shoulder Abduction & Finger Extension) Score
- TMS & MEP
- DWI MRI

MULTIMODAL ASSESSMENTS TO PREDICT RECOVERY

ARAT
- Grasp (6)
- Grip (4)
- Pinch (6)
- Gross (3)

Items used...

Adapted from Stinear et al., Brain 2012
CORTICAL BASIS FOR RECOVERY & NEUROMODULATION

NEURAL BASIS FOR RECOVERY

REPAIR MECHANISMS
- Growth factors
- GABA receptor
- Angiogenesis
- Inflammation
- Dendritic branching
- Axonal Sprouting
- Cell-cycle proteins
- Excitability

ARM FUNCTION
- fMRI activity
- glial reaction
- synaptogenesis

Week 0
Week 8

Ipsilesional Hemisphere
Contralesional Hemisphere

Adapted from Cramer, Ann Neurol, 2008

IMBALANCE OF INHIBITION

NON-INVASIVE NEUROMODULATION

Imbalance of inter-hemispheric inhibition

High-frequency (> 3Hz) rTMS

Low-frequency (1 Hz) rTMS

Rheme et al., 2011
Ward and Grefkes, 2013

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NEUROMODULATION WITH R-TMS

- 48 patients, randomized into 3 groups
- Sham, 3Hz and 10 Hz rTMS of affected hemisphere
- 5 days of stimulation at 130% of UH rest MEP
- Rehab regimen?

4=Moderate Severe; Dependent on ADLs; Unable to walk
1=No significant disability; Able to perform usual tasks

Khedr et al., 2010

META-ANALYSIS OF TMS TRIALS

Studies (n=18)
- Small studies with ~10 patients from 2005-2012
- Randomized but not blinded
- 1 Hz rTMS over the unaffected hemisphere (n=8) or HFS rTMS to affected hemisphere
- Outcome measures were variable
- Minimal adverse effects (HA, fatigue)
- Subgroup analysis favored 1Hz rTMS over the unaffected hemisphere

Hsu et al., Stroke 2012

NEUROANATOMICAL BASIS FOR TMS RESPONSE

- 29 patients (16 subcortical, 13 cortical involvement)
- Single dose of 10Hz (5s/25s for 20x over ~6 min)
- 30% increase in speed of finger and hand taps for subcortical only

Ameli et al., Ann Neurol, 2009

WEARABLE ROBOTS
‘WEARABLE’ ROBOTS

Rosen Lab (UCSC)

Univ. Washington

Ekso bionics

INNOVATIVE BASIC SCIENCE

PROMISING BASIC RESEARCH

Pharmacological modulation of perilesional inhibition
- Clarkson et al., Nature 2010
- Blockade of extrasynaptic GABA-R improved motor recovery

Modulation of molecules that inhibit axon sprouting
- NOGO Receptor (Li et al., 2010)
- Ephrin Receptor (Overman et al., 2012)

CONCLUSION

- Decades of basic research has built a foundation for evaluating and developing new treatments
- Individualized predictive models and treatment plans seem quite feasible
- Ongoing research should help develop and refine specific approaches to rehabilitation
- Neuromodulation via stimulation is very promising
- Recent reports of innovative approaches suggest new treatment options