REHABILITATION AFTER MCA INFARCTION
CONTEMPORARY TRENDS IN REHABILITATION

Health vs. Health Condition

Body Functions & Structures (Functional impairment) (Structural deficit)

ACTIVITY (Activity limitation) *Capacity Qualifier*

PARTICIPATION (Participation restriction) *Performance Qualifier*

Intrinsic Contextual Factors
Environmental Factors
Barriers vs. Facilitators

Extrinsic Contextual Factors
Personal Factors
Barriers vs. Facilitators

Levels of Participation
Restriction/Disability Across the Lifespan

• 0-5 yrs. Play
• 5-18 yrs. School
• 18-65 yrs. Ability to work & Homemaking
• > 65 Ability to be Independent in self-Care & homemaking; participate in recreation & leisure
Persisting Consequences of Stroke
Lai, et al. 2002

- Even in patients following stroke who had a Barthel Index Score over 95 (considered a good recovery) survivors of stroke differed from matched peers in the community, stroke still affected
  - Hand function
  - Activities and instrumental activities of daily living
  - Participation
  - Overall social participation

Self-Reported Long-Term Needs Post CVA
McKevitt, et al. 2011

- About half of stroke survivors reported no unmet needs at 1-5 years post
- Among the remainder, median number of unmet needs was 3
- According to the problem reported
  - 58.4% reported mobility problems and 25% had needs unmet
  - 43.95% reported falls and 21% had needs unmet
  - 38% reported emotional problems and 39% reported needs unmet
- 52% reported a reduction or loss of work

Understanding Stroke Survivorship: Expanding the Concept of Poststroke Disability
Skolarus et al Stroke (2014)

- 892 Stroke Survivors
- 65-121% more likely to receive help with self-care and mobility than controls
- Significantly lower short physical performance battery scores (walking speed, repeated chair stand, and balance tests)
- Lower physical capacity for EVEY measure
- Participation restrictions were higher among stroke survivors (32.8% vs. 23.5%)
- After adjusting for physical capacity, there was NO difference between stroke survivors and controls
- Anxiety and depression predicted participation restrictions
- NEED STROKE SURVIVORSHIP RESEARCH (>70 ON CANCER)
Understanding Stroke In WV 2004, DHHR

► 45% of stroke patients have dysphagia
► 40% need help in everyday living
► 26% dependent in activities of daily living
► 30% are unable to walk without assistance
► Acute care average length of stay less than 5.3 days
► 53% discharged to home
Stroke & Quality of Life
Horstman, et. al 2012

- Individuals reported a significant decrease in ability to participate in social roles and activities following stroke
- There was a correlation between decreased overall life satisfaction and upper and lower extremity motor impairments
- Fatigue was also a factor in predicting life satisfaction and mobility
- Depression is related to post-stroke survivor quality of life

PHYSICAL THERAPY TO MEET THE NEEDS OF INDIVIDUALS POST-STROKE

Contemporary Science & Translation to the Clinic

Benchmark Clinical Trials for Stroke Rehabilitation

- The "EXCITE" clinical trial
- The "LEAPS" clinical trial
Results from EXCITE

- Procedures:
  - This was an NIH-funded RCT in which 106 individuals received the treatment, which was constraint-induced therapy.
  - This consisted of wearing a padded mitt on the unaffected limb 90% of waking hours for 2 weeks (forced use) plus 6 hours per day of upper limb task practice for 10 days (weekdays).
- Outcome Measures included:
  - Wolf Motor Function Test (WMFT)
  - 15 timed and 2 strength tasks
  - Structured Interview about real-world arm use (MAL)
  - Amount of Use Scale
  - Stroke Impact Scale
  - Full spectrum health status interview
- Results measured at baseline, 2 weeks, and at 4 month intervals
  - Improvement on all parameters that was sustained

SAMPLE CHARACTERISTICS IN EXCITE

- Sample Criteria:
  - 3 to 9 months post stroke
  - Lower functioning participants had at least 10 degrees of active wrist extension, at least 10 degrees of thumb abduction and at least 10 degrees of extension in at least 2 additional digits
  - Greater than 24 on the Mini-Mental State Exam

Results from LEAPS

- Procedures:
  - 488 individuals at least two months post stroke stratified into groups according to three categories: moderate vs. severe walking impairment; early vs. late intervention; locomotor treadmill training vs. regular home physical therapy
  - Early intervention was 2 months post stroke and late intervention was 6 months post stroke
  - ALL participants received intervention consisting of 12-16 weeks of PT (36 sessions, or about 3 sessions/week of 90 minutes; the “traditional” group had PT in the home
- Outcome Measures:
  - Gait velocity for 10 m walk; distance walked in 6 minutes; Berg Balance test and other assessments of function, such as the Stroke Impact Scale
- Results:
  - ALL subjects improved in all parameters assessed
  - NO superiority in using the treadmill training intensive practice
  - Subjects in the early treadmill training group reported a higher incidence of dizziness and falls
Summary of Training studies (CI & PWSTT)

- Key practice variables appear to be critical to evoke neural plasticity and behavioral recovery
  - Task Complexity (Jones et al., 1998)
  - Task Difficulty (Plautz, Milliken and Nudo, 2000)
  - Task Specificity (Nudo, et al., 1999)
  - Task Intensity (Sullivan, et al., 2002)

From Sullivan: Advances in Stroke Rehabilitation, Nov 2007

The Take Home Message for Stroke Rehabilitation

(Sullivan, 2008)

- Perhaps, we should look at rehabilitation interventions more like we look at other (e.g. pharmacologic) interventions as a dose-response relationship and what matters about effectiveness is
  - Timing of intervention
  - Duration of intervention
  - Intensity
  - Complexity
  - Specificity

Summary: What we used to say about post-stroke rehabilitation is mostly wrong

- Most recovery is in the first months after the CVA
- After a certain period (2 years) individuals will not get any further benefit from therapy
- There is limited repair potential for the nervous system after injury
- Therapy once or twice a week for an hour is a lot of therapy and ought to be enough to maximize the person's potential
CASCADE OF EVENTS TRIGGERED BY CORTICAL INJURY

BASELINE LEVEL OF FUNCTION

CHRONIC EVENTS: behavioral compensation, neural repairs, normalization of cerebral metabolism and blood flow, map reorganization, adaptive plasticity

SUBACUTE EVENTS: reversal of diaschisis, release of growth factors, dendritic proliferation and pruning, synaptogenesis, astroglial response, angiogenesis, neurogenesis

ACUTE EVENTS: diaschisis, edema, excitotoxicity, acidosis, release of free radicals, calcium influx, decreased protein metabolism, GABA downregulation, hyperexcitability, apoptosis, early gene responses

1 WK  1 MO  2 MO  3 MO  6 MO  9 MO  1 YEAR  2 YEARS
TIME POST INJURY

From Numa & Dancause (2007)

Kleim
Physical Therapy, 2006

“Therapeutic needs are incompatible with Medicare and other health care policies”

A SEQUEL: WHAT HAPPENS TO INDIVIDUALS AFTER A STROKE IN WV

Are they receiving rehabilitation services in alignment with current projections of dose?
Results
[Questionnaire Return Rate]

<table>
<thead>
<tr>
<th>Participants</th>
<th>n</th>
<th>Percent</th>
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</thead>
<tbody>
<tr>
<td>Eligible</td>
<td>1707</td>
<td></td>
</tr>
<tr>
<td>Returned - Deceased</td>
<td>28</td>
<td>1.64%</td>
</tr>
<tr>
<td>Returned - Bad Address</td>
<td>58</td>
<td>3.40%</td>
</tr>
<tr>
<td>Returned - Unable to Participate</td>
<td>15</td>
<td>0.88%</td>
</tr>
<tr>
<td>Returned - Incomplete</td>
<td>24</td>
<td>1.46%</td>
</tr>
<tr>
<td>Returned - Completed</td>
<td>150</td>
<td>8.79%</td>
</tr>
<tr>
<td>Returned - Agreed to Clinic</td>
<td>100</td>
<td>5.86%</td>
</tr>
<tr>
<td>Total Returned</td>
<td>275</td>
<td>16.11%</td>
</tr>
</tbody>
</table>


Results
Overall sample averages for self reported function

<table>
<thead>
<tr>
<th>Measure</th>
<th>Average</th>
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<tbody>
<tr>
<td>mRMI</td>
<td>12.36/15</td>
</tr>
<tr>
<td>mRNL</td>
<td>9.45/11</td>
</tr>
<tr>
<td>dRNL</td>
<td>6.88/8</td>
</tr>
<tr>
<td>pRNL</td>
<td>2.53/3</td>
</tr>
</tbody>
</table>

MRMI = Modified Rivermead Mobility Index, MRNL = Modified Reintegration to Normal Living, d=daily functioning, p=perception of self

Figure 1: Frequency of RMI and mRNL scores for all subjects
Results: Correlation Relationships

- Good correlation between MRI and mRNL scores (.7581)
- NIHSS with functional outcome
  - mRNL (-.3930) poor
  - RMI (-.4628) fair
- Length of acute care stay
  - mRNL (-.0976) poor
  - RMI (-.1743) poor

Functional Outcome by Type of Stroke

<table>
<thead>
<tr>
<th></th>
<th>Ischemic</th>
<th>Hemorrhages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean AGE</td>
<td>62.19</td>
<td>73.18</td>
</tr>
<tr>
<td>Mean RMI</td>
<td>12.36</td>
<td>12.78</td>
</tr>
<tr>
<td>Mean RNL</td>
<td>9.45</td>
<td>8.69</td>
</tr>
<tr>
<td>Total Number</td>
<td>147</td>
<td>27</td>
</tr>
<tr>
<td>Number received PT</td>
<td>66</td>
<td>11</td>
</tr>
</tbody>
</table>

Functional Outcome by Characteristics of Intervention

<table>
<thead>
<tr>
<th></th>
<th>Received tpa</th>
<th>No tpa</th>
<th>Received PT post discharge</th>
<th>No PT post Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RMI</td>
<td>13.96</td>
<td>11.95</td>
<td>11.25</td>
<td>13.51</td>
</tr>
<tr>
<td>Mean RNL</td>
<td>10.39</td>
<td>9.2</td>
<td>8.75</td>
<td>10.11</td>
</tr>
</tbody>
</table>

* Differences are significant
Results

No significant difference between discharge physical therapy compared to:
- Distance from the hospital (p=.1298)

Significant difference between discharge physical therapy and self-reported function:
- Functional level on the MRMI total score (p<0.001)
- RNL score (p<0.001)
- Difference was in OPPOSITE DIRECTION of prediction

Results

| Patient response to acute care rehab and satisfaction with rehab services |
|-----------------------------|----------------|----------------|
| Patient Response            | Yes | No | Not Answered |
| Rehabilitation              | 62  | 101| 11           |
| Discharge PT                | 78  | 95 | 1            |
| Satisfaction                | 89  | 37 | 48           |

Rehabilitation = rehab while hospitalized, Satisfaction = satisfaction with amount of physical therapy
Results

Figure 2: Frequency of RMI and RNL scores for subjects unsatisfied with amount of PT

So, what does it mean?

- First, a mail survey is biased to receive the high performing responders
- People are receiving physical therapy after they have a CVA, regardless of how far away they are from the primary stroke center
- HOWEVER, the people who are receiving physical therapy may be the ones who will benefit the least
- People in the higher levels of function were DISSATISFIED with the amount of therapy they received

PREDICTING THE FUTURE OF STROKE REHABILITATION
What are emerging treatments?

- Focus of emerging treatments is how to potentiate positive neuroplastic changes and block negative changes from occurring
- Also, how to predict recovery using genetics
  - APOE4 poly morphism & val.66 polymorphism for brain derived neurotrophic factor associated with poor recovery

Pharmacotherapeutics

- Changing the excitability of the CNS neurons
- Amphetamine studies in animals vs. humans
  - Papadopoulos, et Al Stroke 2009

NIH focused clinical trial: Amphetamine-Enhanced Stroke Recovery (AESR)

SSRIs (anti-depressants) seem to facilitate neuroplasticity

PREDICTING THE FUTURE OF STROKE REHABILITATION

TASK ORIENTED TRAINING
Constraint-Induced (CIT) and Bimanual Hand-Arm Intensive Therapy (HABIT)
**HABIT**

- Consists of structured practice increasing in complexity
- Provision of functional activities that necessitate bimanual hand use
- Child-friendly

**Outcomes**

**PREDICTING THE FUTURE OF STROKE REHABILITATION**

Non-Invasive Brain Stimulation

- Noninvasive method to alter excitability of neurons in the brain
- **Transcranial Magnetic Stimulation**
  - Single or paired pulse
  - Evaluate CNS area contribution to task by examining Motor Evoked Potential MEP
  - “Virtual Lesions”
- **Repetitive (rTMS)**
  - More likely to change excitability of corticospinal or other pathways
  - LTP vs. LTD
  - Low frequency tends to LTD; High frequency to LTP
- **Transcranial Direct Current Stimulation (tDCS or TES)**
  - Anode vs. cathode stimulation
  - Anode stimulation increases cortical excitability; cathodal decreases
Non Invasive Brain Stimulation

Ipsilesional vs. contralesional hemisphere effects

Motor Demand dependent activation of ipsilateral motor cortex 

- Examines relationship of cortical hemispheres in motor tasks, particularly ipsilesional cortex
- Conclusion:
  - Control of hand movements via ipsilateral corticospinal connections is weak
  - Task differentiated between patterns of activation with pointing being primarily bilateral but tapping shows more contralateral connections
PREDICTING THE FUTURE OF STROKE REHABILITATION

Robotics

Non-invasive Brain Stimulation in Neurorehabilitation: Local and Distant Effects for Recovery Frontiers in Neuroscience, Liew et al 2014

Enhanced Gait-Related Improvements After Therapist-Versus Robotic-Assisted Locomotor Training in Subjects with Chronic Stroke: A Randomized Controlled Study

Purpose and Methods

• Purpose
  • To determine the extent of walking related improvements obtained after therapist versus robotic assisted locomotor training

• Methods
  • Subjects: N=48 with hemiparesis of greater than 6 months duration
  • Intervention: 12 sessions (30 minutes/session) of locomotor training

Results

• Significant main effect for treatment group
  • Nearly 2 fold difference in SSV
  • Difference in FV noted at post LT
  • Main effect for single limb stance at FV but not SSV
  • No significant main effect for step length asymmetry
  • SF36 scores improved in subjects with severe locomotor deficit who received therapist assisted LT

Conclusion

• Therapist assistance was superior to robotic driven treadmill training in most parameters

• Discussion
Telerehabilitation

Effects of Telerehabilitation on Physical Function and Disability for Stroke Patients: A Randomized, Controlled Trial
Chumbler, Neale R. PhD et al  Stroke 2012. 43(8)

• Done on group of patients from VA
• “Telerehabilitation” was monitoring phone calls from therapist to adjust exercise program
• Showed small and in some cases statistically significant difference between those who received the program and those who did not

Rehabilitation

The NIH has created the NIH StrokeNET to conduct a small and large clinical trials and research studies to advance acute stroke treatment, stroke prevention, and recovery and rehabilitation following a stroke. The network of 25 regional centers across the U.S., which involves more than 200 hospitals, is designed to serve as the infrastructure and pipeline for exciting new potential treatments for patients with stroke and those at risk at stroke. In addition, NIH StrokeNet will provide an educational platform for stroke physicians and clinical trial coordinators.

https://www.nihstrokenet.org/clinical-trials/trials
TELEREHABILITATION IN THE HOME VERSUS THERAPY IN-CLINIC FOR PATIENTS WITH STROKE: An Assessor-blind, Randomized, Non-inferiority Trial

**Trial Purpose:**
Study to improve arm function after stroke

Many people who have had a stroke continue to have weakness in an arm. Extra therapy is known to help the arm improve after stroke, but the best approach remains uncertain. This study will examine this issue by comparing therapy provided in a clinic with therapy provided in your home via a computer.

If you had a stroke 4-20 weeks ago and still have weakness in your arm, you might be eligible for this study. Participation involves between 4 and 22 visits to a study site, as well as some therapy in your home. There is no charge to you or your insurance company, and you will be provided $50 payment for transportation expenses.

If interested, contact the Telerehablitation Study:
- Phone Line: (855) 472-0072 (toll free),
- Email: stroke@uci.edu and ask about the “Telerehab Stroke Study”

Harborview Medical Center
Seattle, WA 98104-2420
PI David Tirschwell, MD

Emory Rehabilitation Hospital
Atlanta, GA 30322-1059
PI Steven L. Wolf PhD

MUSC Center for Rehabilitation Research in Neurological Conditions
Charleston, SC 29425
PI Michelle L. Woodbury, PhD

Burke Rehabilitation Hospital
White Plains, NY 10605-2523
PI David Putrino, PhD

Rehabilitation Institute of Chicago
345 E Superior St.
Chicago, IL 60611-4805
PI Elliot J. Roth, MD

UC Irvine Medical Center
Orange, CA 92868-3201
PI Steve Cramer, MD

Spaulding Rehabilitation Hospital
Charlestown, MA 02129-3109
PI: Ross ZaFonte, DO
Co-PI: Randie Black-Shaffer, MD

MetroHealth Rehabilitation Institute of Ohio
Cleveland, OH 44109-4218
PI John Chae, MD

This trial is funded by the NIH National Institute of Neurological Disorders and Stroke under 1U01NS091951.

For more info on this study, visit: www.clinicaltrials.gov Identifier NCT02360488

Conclusions

- Preventive strategies that are pharmacologic continue to emerge
- Neuroprotective strategies will continue to improve
- Therapy will be characterized by:
  - “priming” the cortex for neuroplastic changes (medications, NIBS)
  - Dosage will be a focus
  - Paradigms which shape learning will be emphasized
- Technology and telerehabilitation to deliver dose

“Despite the advances made in acute stroke care, stroke remains the leading cause of adult disability in Americans. World-wide there is an estimated 50 million stroke survivors coping with significant physical, cognitive and emotional deficits. The field of stroke recovery and restorative neuroscience is still young and provides a rich environment for innovative trials.” Stroke Net