THE FUTURE OF STROKE REHABILITATION

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Disclosure of Financial Relationships

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Has disclosed the following relationships with entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

DISCLOSURES:
RESEARCH: INNOVATIVE NEUROTROCNICS

RESOLUTION OF POTENTIAL CONFLICTS OF INTEREST:
- ALL PRESENTED MATERIAL IS INDEPENDENT OF INDUSTRY PRODUCED CONTENT.
- ONLY MATERIAL SUPPORTED BY PUBLISHED DATA AND EVIDENCE-BASED GUIDELINES WILL BE PRESENTED.

STROKE REHABILITATION

- Where we are –
  - Current stroke rehabilitation
  - The recovery process and effective therapies
  - Recent clinical trials – “the future of stroke rehabilitation”
- Where we are going –
  - Prediction models for stroke outcome
  - Neuromodulation
  - Robotics
  - And beyond.....

U.S. STROKE FACTS

Stroke is 4th leading cause of death and leading cause of disability
- 795,000 new strokes/yr (AHA)
- 700,000 survivors/yr (CDC 2011)

Rehabilitation is needed by 45% - 60%
- At 6 months -
  - 70% - doing well
  - 30% - significantly disabled
STROKE REHABILITATION – WHY DO IT?

Meta-analysis of 10 trials
1586 patients randomized to receive multidisciplinary team rehab vs. general medical care
- 28% reduction in mortality at 4 months
- 21% reduction in mortality at 1 year

For every 100 patients receiving stroke rehab – 5 return home independent

LANGHORNE ET AL, LANCET 1993; LANGHORNE AND DUNCAN, STROKE 2001

STROKE REHABILITATION – WHERE TO DO IT?

What’s the most effective setting? - Comprehensive Stroke Units

Why?
- Dedicated and interested staff - prevent secondary complications
- Early and substantial family involvement - enriches the environment
- The most important “rehab” factor - early mobilization

The Cochrane Library
".... patients who receive (organized stroke unit care) are more likely to survive their stroke, return home and become independent in looking after themselves.....The best results appear to come from those which are based in a dedicated ward.

COCHRANE LIBRARY, 2007

RECOVERY TIME LINE AFTER STROKE
COPENHAGEN STROKE STUDY – 809 PATIENTS

Neurological Recovery:
Scandinavian Stroke Scale

Functional Recovery:
Barthel Index

Time to Reach Maximal Neurologic and Functional Recovery Stratified According to Initial Neurologic Severity

<table>
<thead>
<tr>
<th>Initial Neurologic Severity</th>
<th>Number of Patients</th>
<th>Time (wks) to 80% pts. at Maximum Recovery</th>
<th>Time (wks) to 50% pts. at Maximum Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Severe</td>
<td>83 (9)</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Severe</td>
<td>115 (12)</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Moderate</td>
<td>277 (29)</td>
<td>5.5</td>
<td>7</td>
</tr>
<tr>
<td>Mild</td>
<td>470 (56)</td>
<td>2.5</td>
<td>3</td>
</tr>
</tbody>
</table>

JORGENSEN ET AL, ARCH PHYS MED REHAB, 1995

THE STROKE RECOVERY TIMELINE

Early Mobilization
- Task-oriented practice
- Compensatory learning
- Specific rehab strategies to improve IADLs
- Environmental adaptations and home services

Langhorne, Lancet Neurology 2010
Recommended, Evidence-Based Interventions
Stoke Rehabilitation

**Global Outcomes**
- Multidisciplinary Stroke Unit care
- Early supported discharge services
- Occupational Therapy for ADLs
- Outpatient rehabilitation services to improve ADLs

**Motor Function**
- Constraint-induced Motor Therapy
- Robot-assisted training for arm
- Task-oriented walking and physical fitness training for walking speed and distance

**Cognition/Language**
- Treatment of Depression

**Sensory/Vision**
- None

THE CURRENT “FUTURE” OF STROKE REHAB

Fluoxetine for Motor Recovery after Stroke (FLAME) - Chollet et al., Lancet Neurology, 2012
- Pharmacotherapy for global functional recovery

Extremity Constraint Induced Therapy Evaluation (EXCITE) - Wolf et al., JAMA, 2006
- Rehabilitation training method for arm recovery

FLAME TRIAL - BACKGROUND

Monoamine drugs modulate brain plasticity and outcomes after stroke
- In experimental animals:
  - amphetamines improve outcomes
  - neuroleptics and benzodiazepines impair outcomes
How about selective serotonin reuptake inhibitors (SSRIs)?
- Neuroprotective effects; promote hippocampal neurogenesis
- Several small clinical studies suggested that SSRIs enhance activation of motor cortex and improve stroke outcome.

Fluoxetine modulates motor performance and cerebral activation of patients recovering from stroke
- Pariente et al., Ann Neurol, 2001
**FLAME TRIAL**  
**CHOLLET ET AL., LANCET NEUROLOGY 2011**

- Double-blind, placebo-controlled trial of fluoxetine within 5 - 10 days of ischemic hemiparesis
  - 118 patients received fluoxetine 20 mg daily or placebo x 3 months.
  - All patients received PT

- Primary outcome - Fugl-Meyer Motor Score (FMMS)
- Secondary outcome - Modified Rankin Scale

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**FLAME TRIAL – Fugl-Meyer Score**  
**Chollet et al., Lancet Neurology 2011**

**FLAME TRIAL – Modified Rankin**  
**Chollet et al., Lancet Neurology 2011**

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**EXCITE TRIAL – BACKGROUND**

**Theory of “learned non-use” (Taub)**

- Monkeys with a paretic or sensory deprived limb will “learn” not to use it
- If the intact limb is constrained, movement in the impaired limb improves
- Creatively “forcing” the use of a hemiparetic limb improves functional recovery

**Treatment** - “Constraint-induced therapy”
CONSTRAINT-INDUCED MOTOR THERAPY

Subjects:
- 9 stroke patients; >1 year after a stroke
- Hemiparetic with some use of arm
- 20° wrist extension and 10° finger extension

Method:
- Experimental group (4) – Subjects “forced” to use weak arm, 6 hrs/day x 10 days in rehab; Good arm restrained 90% of waking hours for 2 weeks
- Control group (5) – “lots of attention” + passive movement

Outcome: Functional use of arm

EXCITE TRIAL

WOLF ET AL. JAMA 2006

222 patients - 3 to 9 months post-stroke
- “Good” arm placed in a safety mitt for 90% of waking hours x 2 weeks
- Training (6 hours/day) on pre-selected tasks (e.g. wrapping a present; writing; etc)
- Controls – received “usual care”

Primary outcomes – Function at 1 year
- Real world arm use – Motor Activity Log
- Laboratory arm use – Wolf Motor Function Test

EXCITE TRIAL OUTCOMES
CONSTRAINT-INDUCED MOTOR THERAPY

JAMA EDITORIAL COMMENT
LUFT AND HANLEY, JAMA 2006;296:141-143

• .....constraint-induced therapy, if it were a drug, would probably receive approval based on the EXCITE results. Integration of constraint-induced therapy into routine patient care has begun to occur outside of the United States.

• ....the improvements patients experience are substantial and merit strong consideration of constraint-induced therapy by those responsible for practice guidelines and insurance benefits.