Why do only some arms recover?

OR

How good are we at predicting upper limb recovery?

NICK WARD, UCL INSTITUTE OF NEUROLOGY, QUEEN SQUARE

Integrating Upper limb research into practice, Queen Square, London, 10-11th April 2013

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Predicting UL recovery after stroke

How do we treat people after stroke?

1. Preservation of tissue
2. Avoid complications
3. Task specific training
4. Enhancement of plasticity
5. Compensation

Rehabilitation → Recovery

Predicting UL recovery after stroke

How do we treat people after stroke?
Upper limb recovery after stroke is unacceptably poor

- 60% of patients with non-functional arms 1 week post-stroke didn’t recover (Wade et al, 1983)
- 18 months post-stroke 55% of patients had limited or no dextrous function (Welmer et al, 2008)
- 4 years post-stroke only 50% had fair to good function (Broeks et al, 1999)
I. Predicting UL recovery after stroke – how good are we?

II. Differences in residual structural & functional architecture

III. Role of non-primary motor areas in supporting recovery

IV. Predicting response to treatment I – cortical stimulation

V. Predicting response to treatment II – motor learning
Predicting UL recovery after stroke

How good are we?

Predictive variables

- Infarct Size
- Infarct Location
- Pre-stroke medical co-morbidities
- Pre-stroke experience, education, age
- Severity of initial stroke deficits
  - Breadth of stroke deficits
  - Acute stroke interventions
  - Medications during stroke recovery period
  - Amount of post stroke therapy
  - Types of post stroke therapy
  - Medical complications after stroke
  - Socioeconomic status
  - Depression
  - Caregiver status
  - Genotype

30-50% of variance in outcomes
Predicting UL recovery after stroke

How good are therapists?

<table>
<thead>
<tr>
<th>Incorrect</th>
<th>PT</th>
<th>Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 m prediction</td>
<td>&lt; 10</td>
<td>14%</td>
</tr>
<tr>
<td></td>
<td>10 – 56</td>
<td>53%</td>
</tr>
<tr>
<td></td>
<td>57</td>
<td>39%</td>
</tr>
<tr>
<td>Overall</td>
<td>41%</td>
<td>30%</td>
</tr>
</tbody>
</table>

Sex
Age
Hemisphere
Stroke type
rTPA
NIHSS
Barthel Index
Motricity Index
Fugl-Meyer
Sitting balance
Days since stroke
Predicting UL recovery after stroke

The PREP algorithm

1. SAFE = shoulder abduction + finger extension (MRC scale) 72 h after stroke (range 0–10)
2. TMS at 2 weeks
3. MRI/DTI at 2 weeks

The PREP algorithm predicts potential for upper limb recovery after stroke

Cathy M. Stinear,¹,², P. Alan Barber,¹,²,³ Matthew Petoe,¹,² Samir Anwar²,⁴ and Winston D. Byblow²,⁵


<table>
<thead>
<tr>
<th>Recovery</th>
<th>Definition</th>
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<tr>
<td>Complete</td>
<td>The patient has the potential to return to normal or near-normal hand and arm function within 12 weeks.</td>
</tr>
<tr>
<td>Notable</td>
<td>The patient has the potential to be using their affected hand and arm in most activities of daily living within 12 weeks, though normal function is unlikely.</td>
</tr>
<tr>
<td>Limited</td>
<td>The patient has the potential to have some movement in their affected hand and arm within 12 weeks, but it is unlikely to be used functionally for activities of daily living.</td>
</tr>
<tr>
<td>None</td>
<td>The patient can expect to have minimal movement in their affected hand and arm, with little improvement at 12 weeks.</td>
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</table>
Predicting UL recovery after stroke

The PREP algorithm

1. SAFE = shoulder abduction + finger extension (MRC scale) 72 h after stroke (range 0–10)
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<th>Definition</th>
<th>Goal</th>
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<td>Complete</td>
<td>The patient has the potential to return to normal or near-normal hand and arm function within 12 weeks.</td>
<td>Rehabilitation could focus on task-specific therapy in order to facilitate a return to full or near-full use of the hand and arm in activities of daily living.</td>
</tr>
<tr>
<td>Notable</td>
<td>The patient has the potential to be using their affected hand and arm in most activities of daily living within 12 weeks, though normal function is unlikely.</td>
<td>Rehabilitation could focus on strength, coordination and fine motor control, in order to maximize recovery of function and minimize compensation with the other hand.</td>
</tr>
<tr>
<td>Limited</td>
<td>The patient has the potential to have some movement in their affected hand and arm within 12 weeks, but it is unlikely to be used functionally for activities of daily living.</td>
<td>Rehabilitation could focus on reducing impairment by strengthening the paretic upper limb and improving active range of motion, in order to promote adaptation and incorporation of the affected upper limb in daily activities wherever possible.</td>
</tr>
<tr>
<td>None</td>
<td>The patient can expect to have minimal movement in their affected hand and arm, with little improvement at 12 weeks.</td>
<td>Rehabilitation could focus on prevention of secondary complications, such as spasticity and shoulder instability, and reducing disability by learning to complete activities of daily living with the unaffected hand and arm.</td>
</tr>
</tbody>
</table>
Predicting UL recovery after stroke

What are the useful predictive variables?

Predictors of upper limb recovery after stroke: a systematic review and meta-analysis

Fiona Coupar¹, Alex Pollock², Phil Rowe³, Christopher Weir³ and Peter Langhorne³

Abstract

Objective: To systematically review and summarize the current available literature on prognostic variables relating to upper limb recovery following stroke. To identify which, if any variables predict upper limb recovery following stroke.

Data sources: We completed searches in MEDLINE, EMBASE, AMED, CINAHL and Cochrane CENTRAL databases. Searches were completed in November 2010.

Review methods: Studies were included if predictor variables were measured at baseline and linked to an outcome of upper limb recovery at a future time point. Exclusion criteria included predictor variables relating to response to treatment and outcome measures of very specific upper limb impairments such as spasticity or pain. Two independent reviewers completed data extraction and assessed study quality.

Results: Fifty-eight studies met the inclusion criteria. Predictor variables which have been considered within these studies include; age, sex, lesion site, initial motor impairment, motor-evoked potentials and somatosensory-evoked potentials. Initial measures of upper limb impairment and function were found to be the most significant predictors of upper limb recovery; odds ratio 14.84 (95% confidence intervals (CI) 9.08–24.25) and 38.62 (95% CI 8.40–177.53), respectively.

Conclusions: Interpretation of these results is complicated by methodological factors including variations in study populations, upper limb motor outcome scales, timing of baseline and outcome assessments and predictors selected. The most important predictive factors for upper limb recovery following stroke appear to be the initial severity of motor impairment or function.
Predicting UL recovery after stroke

Understanding stroke anatomy

stroke damage
damaged pathways
damaged cortex
Predicting UL recovery after stroke
Assessing corticospinal tract damage

Track from fMRI-defined hand areas in 4 different cortical motor areas

Correlation with post-stroke hand grip strength

Shultz et al, Stroke 2012
Predicting UL recovery after stroke

Predicting response through corticospinal tract damage

Can treatment response be predicted from CST damage?

Robot-based hand motor therapy after stroke

Craig D. Takahashi,* Lucy Der-Yeghiaian, Yu Le, Rehan R. Motiwala and Steven C. Cramer

Damage to M1 pathway limits response to robot assisted therapy

Riley et al., Stroke 2011; 42: 421-6
Predicting UL recovery after stroke

Differences in residual functional architecture

Increasing ‘main effect’ of left hand grip

affected hemisphere

more CS damage

less CS damage

Ward et al., Brain 2006
Predicting UL recovery after stroke

Differences in residual functional architecture

Increasing ‘main effect’ of left hand grip

more CS damage

less CS damage

affected hemisphere
Predicting UL recovery after stroke

Predicting response with functional imaging

Robot-based hand motor therapy after stroke

Craig D. Takahashi, Lucy Der-Yeghaian, Vu Le, Rehan R. Motiwalla and Steven C. Cramer

Less activity in M1 limits response to robot assisted therapy

Cramer et al., Stroke 2007; 38: 2108-14
Predicting UL recovery after stroke

**Left versus right hemisphere damage**

left hemisphere for *predicting and accounting for limb dynamics*
right hemisphere for *stabilizing limb position through impedance control mechanisms*

left hemisphere damage - greater errors in movement direction
right hemisphere damage - greater errors in movement extent
Predicting UL recovery after stroke

Central compensation?

<table>
<thead>
<tr>
<th>OUTCOMES</th>
<th>Barthel</th>
<th>ARAT</th>
<th>GRIP</th>
<th>NHPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient A</td>
<td>20/20</td>
<td>57/57</td>
<td>98.7%</td>
<td>78.9%</td>
</tr>
<tr>
<td>Patient B</td>
<td>20/20</td>
<td>57/57</td>
<td>64.2%</td>
<td>14.9%</td>
</tr>
</tbody>
</table>
Power and Coherence are measures of changes in MEG data at particular frequencies...

- **Power** is an increase or decrease in synchrony of the underlying neuronal population = 1 source
- **Coherence** represents the amplitude and phase correlation between two sources = 2 sources
Predicting UL recovery after stroke

Central compensation?
Predicting UL recovery after stroke

Central compensation?

Beta coherence

Gamma coherence

Rossiter et al 2012
Predicting UL recovery after stroke

Other factors?

Co-factors
- Side of stroke
- Sensory loss
- Cognitive dysfunction
- Visual disorders

Fatigue
- Spasticity / loss of ROM
- Genotype
Rehabilitation is a process of active change by which a person who has become disabled acquires the knowledge and skills needed for optimum physical, psychological and social function.

Predicting UL recovery after stroke

Which treatment?

Treatments aimed at reducing impairments

Task-specific training

- cortical stimulation
- other
- drugs
Predicting UL recovery after stroke

Cortical stimulation to promote upper limb recovery


<table>
<thead>
<tr>
<th>Table 2. Fixed-effects Meta-analysis of Eight Studies that Examined the Pre-Post Effects of Anodal tDCS on Motor Function in Stroke Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Included Studies</strong></td>
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<tr>
<td>----------------------</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
</tr>
<tr>
<td>Boggio et al.</td>
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<tr>
<td>Fregni et al.</td>
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<tr>
<td>Hummel, 2005</td>
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<tr>
<td>Mahmoudi et al.</td>
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<tr>
<td>Stagg et al.</td>
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<tr>
<td>Stagg et al.</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>
Predicting UL recovery after stroke

What is cortical stimulation doing after stroke?

Enhancing plasticity in the motor cortex

Modulation of GABAergic and glutamatergic synapses
Predicting UL recovery after stroke

Predicting response to cortical stimulation with structural imaging
Predicting UL recovery after stroke

Predicting response to cortical stimulation with functional imaging

Will the same treatment strategy work in these patients?
Predicting UL recovery after stroke

Predicting response to treatment

Ward and Cohen, Arch Neurol 2004
ADAPTATION

• Motor system responds to altered environment in order to regain former levels of performance
• Driven by prediction error
• Can occur in single session
• Short lived after effect

SKILL LEARNING

• Acquiring new patterns of muscle activation to achieve higher levels of performance
• Not just faster or more accurate – both
• Driven by reward and reinforcement
• Occurs within session and over extended practice
• Number of repetitions determines acquisition
• Other factors promote retention and generalisability
  - distributed practice
  - variable practice
  - contextual interference
Predicting UL recovery after stroke

Increasing the dose

Effect of Constraint-Induced Movement Therapy on Upper Extremity Function 3 to 9 Months After Stroke

The EXCITE Randomized Clinical Trial

A Self-Administered Graded Repetitive Arm Supplementary Program (GRASP) Improves Arm Function During Inpatient Stroke Rehabilitation

A Multi-Site Randomized Controlled Trial

Jocelyn E. Harris, MSc; Janice J. Eng, PhD; William C. Miller, PhD; Andrew S. Dawson, MD

**Background and Purpose.** More than 70% of individuals who have a stroke experience upper limb deficits that impact daily activities. Increased amount of upper limb therapy has positive effect; however, practical and inexpensive methods of therapy are needed to deliver this increase in therapy.

**Methods.** This was a multi-site single blind randomized controlled trial to determine the effectiveness of a 4-week self-administered graded repetitive upper limb supplementary program (GRASP) on arm recovery in stroke. 103 participants with stroke were randomized to the experimental group (GRASP group, n=53) or the control group (education protocol, n=50). The primary outcome measure was the Chedoke Arm and Hand Activity Inventory (CAHA), a measure of upper limb function in activities of daily living. Secondary measures were used to evaluate grip strength and passive upper limb use outside of therapy time. Intention-to-treat analysis was performed. Group differences were tested using analysis of covariance.

**Results.** At the end of the 4-week intervention (approximately 7 weeks poststroke), the GRASP group showed greater improvement in upper limb function (CAHA) compared to the control group (mean difference 6.5, 95% CI 3.4 to 9.6, P<0.001). The GRASP group maintained this significant gain at 5 months poststroke. Significant differences were also found in favor of the GRASP protocol for grip strength and passive upper limb use. No serious adverse effects were experienced.

**Conclusion.** A self-administered homework exercise program provides a cost-, time-, and treatment-effective delivery model for improving upper limb recovery in subacute stroke. (Stroke. 2009;40:2123-2128.)

Key Words: stroke ■ rehabilitation ■ upper limb

Robot-Assisted Therapy for Long-Term Upper-Limb Impairment after Stroke

ORIGINAL ARTICLE

**N Engl J Med 362:219; NEJM.org May 13, 2010**

**Motor – 1000’s of repetitions**

**Language – 100 hours**
Predicting UL recovery after stroke

*Increasing the dose*

**A Self-Administered Graded Repetitive Arm Supplementary Program (GRASP) Improves Arm Function During Inpatient Stroke Rehabilitation**

A Multi-Site Randomized Controlled Trial

Jocelyn E. Harris, MSc; Janice J. Eng, PhD; William C. Miller, PhD; Andrew S. Dawson, MD

*(Stroke. 2009;40:2123-2128.)*

- multi-site single blind randomized controlled trial
- 4-week self-administered graded repetitive upper limb program in 103 stroke patients approx 3 weeks post stroke
- 3 grades (mild, moderate, severe)
- Provided with exercise book with instructions
- Repetitions, inexpensive equipment
- strength, range of motion, gross and fine motor skills
- GRASP group showed greater improvement in upper limb function
- GRASP group maintained this significant gain at 5 months post-stroke
Predicting UL recovery after stroke

*Increasing the dose*

- Robotic treadmill training
- Home video arm/hand training
- Robotic arm training
Predicting UL recovery after stroke

*When to treat?*
Predicting UL recovery after stroke

Increasing the dose – specialist clinics

Upper Limb Rehabilitation Clinic

Does your patient still have difficulty using their arm after a stroke?

The National Hospital for Neurology and Neurosurgery (NHHN) offers a multidisciplinary service with expertise in assessing and treating upper limb problems.

The clinic offers advice on the management of patients with neurological upper limb deficits secondary to central nervous system disease. It is particularly interested in seeing stroke survivors who might benefit from more intense treatment of upper limb deficits, especially early after stroke.

For more information, see the Upper Limb Rehabilitation Clinic page on the UCL website.

Contacts

Dr Nick Ward, e: n.ward@ucl.ac.uk
Reader in Clinical Neurology & Honorary Consultant Neurologist
The National Hospital for Neurology and Neurosurgery (Box 146)
Queen Square, WC1N 3BG

www.camden.nhs.uk/gps/upper-limb-rehabilitation-clinic
Predicting UL recovery after stroke

Summary

• We are not that good at predicting – would this help?
• Understanding residual brain structures might help
  • Predict outcome
  • Predict response to treatment
• A number of factors might contribute to poor outcome
• Increasing the dose would undoubtedly help
• Is capacity for motor learning preserved after stroke?
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Holly Rossiter
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Karine Gazarian
Ella Clark
John Rothwell
Penny Talelli

Some more slides at www.ucl.ac.uk/ion/departments/sobell/Research/NWard

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Brain Research Trust Plasticise

European Research Consortium ★★★ Help the brain recover from damage