Post-stroke upper limb rehabilitation – next steps

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STROKE IS A CHRONIC AND PROGRESSIVE DISEASE

- 17 million people a year experience first stroke
- Survival is improving but still 1.5M survivors in UK
- Economic burden is high - £9B a year in UK
- Turn attention towards treatments to promote recovery
- Funding for stroke research lags behind dementia, CHD and cancer
Promoting Recovery After Stroke

Elements of upper limb treatment after stroke

1. Avoid complications
2. Motor training
3. Enhance plasticity

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*Upper limb treatment – which intervention?*

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Ulf Function</th>
<th>Ulf Improvement</th>
<th>ADL</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral arm training + other</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Low quality evidence for comparison of bilateral arm training with usual care or other interventions.</td>
</tr>
<tr>
<td>Bilateral arm training + unilateral arm training</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Moderate quality evidence that unilateral arm training is more effective than bilateral arm training at improving upper limb function.</td>
</tr>
<tr>
<td>Biofeedback</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Up-to-date high quality review required.</td>
</tr>
<tr>
<td>Bobath therapy</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Up-to-date high quality review required.</td>
</tr>
<tr>
<td>Brain stimulation: TDCS</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Moderate quality evidence of benefit on impairment, as compared to placebo or control. Higher quality evidence of no benefit or harm on ADL outcomes.</td>
</tr>
<tr>
<td>Brain stimulation: TMS</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Low quality evidence when range of upper limb function outcomes pooled, but moderate quality evidence from five trials (15 participants) showed no benefit or harm of TMS on arm function.</td>
</tr>
<tr>
<td>CIMT</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>High quality systematic review of impairment and ADL outcomes required.</td>
</tr>
<tr>
<td>Electrical stimulation</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Differences between trials, and risk of bias within trials, limit ability to pool data from trials.</td>
</tr>
<tr>
<td>“Hands-on” therapy</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Moderate quality evidence of a beneficial effect of mental practice.</td>
</tr>
<tr>
<td>Mental practice</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Moderate quality evidence of a beneficial effect of mental practice.</td>
</tr>
<tr>
<td>Mirror therapy</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Data for upper limb function and impairment measures pooled together; moderate quality evidence of benefit on pooled result.</td>
</tr>
<tr>
<td>Music therapy</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>High quality trial evidence required.</td>
</tr>
<tr>
<td>Pharmacological interventions</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Need for high quality, adequately powered trials. Reviews require updating.</td>
</tr>
<tr>
<td>Repetitive task training + &gt; 20 hours dose</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Pooling all trials of repetitive task training demonstrates moderate quality evidence of no benefit or harm. When combined with CIMT trials, moderate quality evidence of a beneficial effect.</td>
</tr>
<tr>
<td>Repetitive task training + &gt; 20 hours dose</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Subgroup with a dose of &gt; 20 hours, provides moderate quality evidence of beneficial effect.</td>
</tr>
<tr>
<td>Robotics</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Beneficial effect on Fugl-Meyer and ADL measures. Moderate quality evidence of no benefit or harm on strength. Subgroup analyses showed no benefit or harm on Fugl-Meyer, when compared to the same duration of conventional rehabilitation.</td>
</tr>
<tr>
<td>Sensory interventions</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Moderate quality evidence from one trial (n=28) of thermal stimulation as compared to no treatment. Low quality evidence for comparisons with placebo or control. High quality trial evidence required.</td>
</tr>
<tr>
<td>Strength training</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Low quality evidence due to poor reporting on information within review. High quality up-to-date review and RCTs required.</td>
</tr>
<tr>
<td>Stretching &amp; positioning</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Moderate quality evidence from review pooling data from trials with a wide range of populations, interventions and comparison groups. High quality subgroup analyses are required.</td>
</tr>
<tr>
<td>Task-specific training</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Up-to-date high quality review required.</td>
</tr>
<tr>
<td>Virtual reality</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Moderate quality evidence of a beneficial effect on upper limb function and impairment, measured by Fugl-Meyer. Moderate quality evidence of no benefit or harm on grip strength.</td>
</tr>
<tr>
<td>Factors in service delivery:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose of intervention</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Moderate quality evidence of no benefit or harm from increased dose of intervention. High quality trial evidence, and subgroup analysis relating to dose quantity, required.</td>
</tr>
<tr>
<td>Location of intervention - home-based therapy</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>This evidence relates to home-based therapy programs compared to usual care. Evidence comparing delivery at home or at hospital is low quality.</td>
</tr>
<tr>
<td>Location of intervention - telehealth</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Evidence from comparison of computer-based training program with usual care.</td>
</tr>
</tbody>
</table>

Interventions for improving upper limb function after stroke (Review)

Pollock A, Farmer SE, Brady MG, Langhorne P, Mead GE, Mehrholz J, van Wijck F.
We need a step change in the provision of rehabilitation and long-term support for stroke survivors and their families. All stroke survivors should get an early assessment for rehabilitation in hospital, and receive appropriate levels of therapy both in hospital and following discharge. Post-hospital reviews should be available to all stroke survivors, wherever they live in Europe, and they should be able to get therapy (including for their psychological and non-physical needs) as long as they need it.
People with stroke should accumulate **at least 45 minutes** of each appropriate therapy every day, at a frequency that enables them to meet their rehabilitation goals, and for as long as they are willing and capable of participating and showing measurable benefit from treatment.

*Royal College of Physicians – National Clinical Guideline for Stroke*
UK SSNAP (stroke audit) data

<table>
<thead>
<tr>
<th></th>
<th>Three monthly</th>
<th>Four monthly</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.1 Percentage of patients reported as requiring physiotherapy</td>
<td>85.6%</td>
<td>85.2%</td>
</tr>
<tr>
<td>6.2 Median number of minutes per day on which physiotherapy is received</td>
<td>35.0</td>
<td>33.8</td>
</tr>
<tr>
<td>6.3 Median % of days as an inpatient on which physiotherapy is received</td>
<td>71.9%</td>
<td>69.9%</td>
</tr>
</tbody>
</table>

- Av stay in ASU = 17 Days
- 35 mins*74%*17 days = 7.3 hrs PT
- 4.5 hrs SLT
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*Upper limb treatment – how much are we giving?*

People are still INACTIVE and ALONE after stroke.
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Upper limb behavioural treatment – early

Effect of a Task-Oriented Rehabilitation Program on Upper Extremity Recovery Following Motor Stroke
The ICARE Randomized Clinical Trial

Carolee J. Weinstein, PhD; Steven L. Wolf, PhD; Alexander W. Dromerick, MD; Christianne J. Lane, PhD; Monica A. Nelsen, DPT; Rebecca Lewthwaite, PhD; Steven Yong Cen, PhD; Stanley P. Azen, PhD; for the Interdisciplinary Comprehensive Arm Rehabilitation Evaluation (ICARE) Investigative Team

JAMA. 2016;315(6):571-581

30 hours over 10 weeks
Effects of intensity of arm training on hemiplegic upper extremity motor recovery in stroke patients: a randomized controlled trial

Chao Han, Qiang Wang, Ping-ping Meng and Ming-zhu Qi

Table 2. Comparisons of outcomes of patients in three groups (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FMA (UE)</td>
<td>6.70 ± 2.26</td>
<td>8.20 ± 3.43</td>
<td>6.50 ± 3.06</td>
<td>0.386</td>
</tr>
<tr>
<td>ARAT</td>
<td>0.80 ± 1.14</td>
<td>1.50 ± 1.58</td>
<td>1.00 ± 1.52</td>
<td>0.553</td>
</tr>
<tr>
<td>BI</td>
<td>51.50 ± 22.49</td>
<td>62.50 ± 20.98</td>
<td>50.50 ± 23.33</td>
<td>0.422</td>
</tr>
<tr>
<td><strong>6 weeks after treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FMA (UE)</td>
<td>13.00 ± 6.38</td>
<td>19.70 ± 7.09</td>
<td>24.50 ± 7.96</td>
<td>0.005</td>
</tr>
<tr>
<td>ARAT</td>
<td>5.30 ± 3.40</td>
<td>8.70 ± 4.62</td>
<td>10.90 ± 3.60</td>
<td>0.008</td>
</tr>
<tr>
<td>BI</td>
<td>85.00 ± 11.79</td>
<td>88.00 ± 10.33</td>
<td>89.50 ± 6.85</td>
<td>0.590</td>
</tr>
</tbody>
</table>

FMA (UE), Fugl-Meyer Assessment (upper extremity); ARAT, Action Research Arm Test; BI, Barthel Index; Group A, Group B and Group C, each group received arm rehabilitation training for 1 hour, 2 hours and 3 hours a day respectively.

- Patients 40 (+/-20) days post-stroke
- Mean baseline FM 6-8
- Arm training 1, 2, 3 hrs/day, 5 days/wk, 6 wks
- Training depending on patient’s impairments
- Included correct positioning and caring of the arm; passive, assisted and active movements; strength training; practice of functional activities.

90 hours over 6 weeks
Patients recruited 2 weeks post-stroke
Self-administered repetitive practice
FM 39.5 (14.2) vs 40.0 (12.6)
1 hour 6 days a week for 4 weeks
Continued for further 3 months at
Difference maintained at retention

Table 3. ANCOVA Results for the Primary Outcome Measure, Chedoke Arm and Hand Activity Inventory at Postintervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline Score</th>
<th>Posttest Score (95% CI)</th>
<th>Change Score (95% CI)</th>
<th>ANCOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRASP</td>
<td>32.6</td>
<td>46.7 (44.9–48.8)</td>
<td>14.1 (11.8–16.2)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Control</td>
<td>32.7</td>
<td>40.1 (38.9–42.8)</td>
<td>7.9 (5.0–10.3)</td>
<td></td>
</tr>
</tbody>
</table>

24 hours over 4 weeks
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*Upper limb behavioural treatment – early*

**MIT-Manus**

36 hours over 12 weeks
127 patients (36 x 60 mins)
robot vs matched = -0.1 on UL-FM*
robot vs usual = +2.17 on UL-FM*

**ARMin**

18 hours over 8 weeks
73 patients (24 x 45 mins)
robot vs matched = +0.8 on UL-FM

*not significant*
300 hours of UL therapy over 12 weeks = 8-11 points on UL-FM

Table 5: Within-group gains in impaired coordination (FM) for each of the 3 treatment groups

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Coordination Measure</th>
<th>Pretreatment (points)</th>
<th>Posttreatment (points)</th>
<th>Median Gain Score (95% CI)</th>
<th>P</th>
<th>Mean Gain Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>ML</td>
<td>FM</td>
<td>23.6±5.8</td>
<td>33.5±8.3</td>
<td>9 (7.5–12.5)</td>
<td>.003*</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>FM scale for shoulders/elbows</td>
<td>12.7±2.9</td>
<td>16.4±3.9</td>
<td>3.5 (2.5–4.5)</td>
<td>.003*</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>FM scale for wrists/hands</td>
<td>9.1±2.6</td>
<td>14.7±4.7</td>
<td>5 (4.0–7.5)</td>
<td>.003*</td>
<td>6</td>
</tr>
<tr>
<td>FES+ML</td>
<td>FM</td>
<td>23.5±6.5</td>
<td>32.3±7.9</td>
<td>8 (5.5–12)</td>
<td>.002*</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>FM scale for shoulders/elbows</td>
<td>12.7±3.5</td>
<td>16.5±3.9</td>
<td>4 (2.0–6.0)</td>
<td>.005*</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>FM scale for wrists/hands</td>
<td>8.8±3.5</td>
<td>13.4±4.2</td>
<td>5 (2.0–7.0)</td>
<td>.003*</td>
<td>5</td>
</tr>
<tr>
<td>ROB+ML</td>
<td>FM</td>
<td>23.6±5.9</td>
<td>31.3±6.2</td>
<td>7.8 (4.5–11)</td>
<td>.003*</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>FM scale for shoulders/elbows</td>
<td>12.9±1.9</td>
<td>16.6±2.5</td>
<td>3.5 (2.5–5.0)</td>
<td>.002*</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>FM scale for wrists/hands</td>
<td>8.3±4.3</td>
<td>12.0±4.1</td>
<td>4.0 (1.5–5.0)</td>
<td>.007*</td>
<td>4</td>
</tr>
</tbody>
</table>

300 hours over 12 weeks
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Upper limb treatment – Queen Square Programme

FUGL MEYER Scores at Admission, Discharge, 6 Weeks and 6 Months

Δ = 8.2

Upper Limb Rehabilitation Clinic

Do you still have difficulty using your arm after a stroke?

If you or a relative have suffered a stroke and still have problems using your arm, then you might be interested in this NHS service at The National Hospital for Neurology and Neurosurgery (NHN), Queen Square.

The multidisciplinary service is run by Dr Nick Ward (Consultant Neurologist), Fran Brander (Physiotherapist), and Kate Kelly (Occupational Therapist) with expertise in assessing and treating upper limb problems.

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

www.ucl.ac.uk/cnr/clinical/qs/nswmd

90 hours over 3 weeks

= 8.2 points on modified UL-FM
Upper limb therapy - summary

- We don’t give enough to know what is possible through motor/behavioural training
- Simple task specific training seems less effective
- Treat at level of impairment, activity and participation = better ‘buy in’ and ultimately higher ‘dose’
- Dose response ‘emerging’ from clinical trials
- Pick appropriate outcome measure – e.g. impairment vs activity vs participation
- Need aspirational studies not pragmatic in rehab/restoration
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Recovery after stroke is proportional

1. How to turn non-recoverers into (proportional) recoverers?
2. How to improve on regaining 70% of what is lost?
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Does recovery depend on plasticity?

Dendritic growth in vivo

LIII pyramidal cell

Axon arborisation in vivo

Upregulation of growth-promoting factors

Stroke

Critical period of rehabilitation

Sustained

Upregulation of growth-inhibiting factors

Late

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Stratification in clinical trials

Ward NS, Nat Rev Neurol 2017
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Does outcome depend on anatomy?

Classification accuracy

CST = 73%

MOTOR = 87%

Rondina et al JNNP (2017)
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**Next steps**

**Prediction**

- New models to predict upper limb outcome

**Mechanism**

- Mechanistic understanding of early recovery in humans

**Therapy**

- Fluoxetine?

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