Neurorehabilitation and Brain Plasticity

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Overview

1. What is plasticity?
2. How do we treat upper limb impairment?
3. Variability in lesion induced structure and organisation
4. Predicting outcomes?
1. Preservation of tissue
2. Avoid complications
3. Task specific training
4. Enhancement of plasticity
5. Compensation

Rehabilitation & Plasticity

*Treating Stroke*

Rehabilitation

Recovery
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)
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What is brain plasticity?

PLASTICITY is

- the formation of new functional connections between nerve cells
- the withdrawal of inappropriate connections
- the modulation of strength between the cell-cell connections called synapses

changes that occur in the organization of the brain as a result of experience
Activity takes advantage of plastic changes, but also enhances them.

These are therefore therapeutic targets for the promotion of recovery after stroke.

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*What is brain plasticity?*

**lesion induced changes**

**activity**

**inactivity**
Brain plasticity! Hold on ..... the cortex is not capable of plasticity but is hardwired and immutable. Once damage occurs, cortical neurons either die or at best do not change their projection patterns....."
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What is brain plasticity?

Dendritic growth *in vivo*

Axon arborisation *in vivo*

Niell et al., Nat Neurosci 2004; 7: 254-260

Hua et al., Nature 2005; 434: 1022-1026

dendrites

axon
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What is brain plasticity?

“... the cortex is not capable of plasticity but is hardwired and immutable. Once damage occurred, cortical neurons either died or at best did not change their projection patterns.....”

The structure of the brain is constantly changing – this is the basis of learning both in health and disease.

However, it requires ‘activity’ to take advantage of these processes and create new connections and networks.
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.

Treatments aimed at reducing impairments

Task-specific training

- cortical stimulation
- other
- drugs
Task specific training is better than general exercise – motor learning?

Works better in patients with reasonable residual motor control

Optimal dose is important but not clear

Motor practice/ Motor learning
Constraint induced therapy
Robotic assisted devices
Virtual environments
Performance improvement proportional to amount of practice

1. *Distributed practice* - frequent and longer rest periods
2. *Variable practice* - varying parameters of task
3. *Contextual interference* - random ordering of related tasks

Better retention and generalisation of learning to new tasks

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How do we treat upper limb impairment?

- 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
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How do we treat upper limb impairment?

Effect of Constraint-Induced Movement Therapy on Upper Extremity Function 3 to 9 Months After Stroke
The EXCITE Randomized Clinical Trial

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

The New England Journal of Medicine

Original Article

N Engl J Med 362;19 NEJM.ORG May 13, 2010
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How do we treat upper limb impairment?

Robotic treadmill training

Home video arm/hand training

Robotic arm training
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How do we treat upper limb impairment?
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How do we treat upper limb impairment?
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.

Treatments aimed at reducing impairments:

- Task-specific training
  - cortical stimulation
  - other
  - drugs
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How do we treat upper limb impairment?


### TABLE 2. Fixed-effects Meta-analysis of Eight Studies that Examined the Pre–Post Effects of Anodal tDCS on Motor Function in Stroke Survivors

<table>
<thead>
<tr>
<th>Included Studies</th>
<th>Outcome Measure</th>
<th>Baseline Measure</th>
<th></th>
<th>Post-measure</th>
<th>Standard Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total (n)</td>
<td>Mean</td>
</tr>
<tr>
<td>Boggio et al.1</td>
<td>JTT</td>
<td>54</td>
<td>16.2</td>
<td>4</td>
<td>49.33</td>
</tr>
<tr>
<td>Fregni et al.2</td>
<td>JTT</td>
<td>63.8</td>
<td>18.22</td>
<td>6</td>
<td>59.33</td>
</tr>
<tr>
<td>Hummel, 2005</td>
<td>JTT</td>
<td>43.57</td>
<td>2.36</td>
<td>6</td>
<td>39.72</td>
</tr>
<tr>
<td>Hummel et al.13</td>
<td>RT</td>
<td>273.5</td>
<td>15.4</td>
<td>11</td>
<td>256.6</td>
</tr>
<tr>
<td>Hummel et al.13</td>
<td>PS</td>
<td>118.8</td>
<td>23</td>
<td>11</td>
<td>124.8</td>
</tr>
<tr>
<td>Kim et al.11</td>
<td>BBT</td>
<td>35.8</td>
<td>18.59</td>
<td>10</td>
<td>43.3</td>
</tr>
<tr>
<td>Kim et al.12</td>
<td>FM Test</td>
<td>31</td>
<td>11.17</td>
<td>6</td>
<td>45.5</td>
</tr>
<tr>
<td>Mahmoudi et al.22</td>
<td>JTT</td>
<td>10.6</td>
<td>7.43</td>
<td>10</td>
<td>9.46</td>
</tr>
<tr>
<td>Stagg et al.14</td>
<td>RT</td>
<td>59.9</td>
<td>25.92</td>
<td>13</td>
<td>551.89</td>
</tr>
<tr>
<td>Stagg et al.14</td>
<td>GS</td>
<td>1.59</td>
<td>1.55</td>
<td>13</td>
<td>1.47</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>90</td>
<td></td>
<td>90</td>
<td>100</td>
</tr>
</tbody>
</table>
Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial

François Chollet, Jean Tardy, Jean-François Albucher, Claire Thalamas, Emilie Berard, Catherine Lamy, Yannick Bejot, Sandrine Deltour, Assia Jaillard, Philippe Niclot, Benoît Guillon, Thierry Moulin, Philippe Marque, Jérémie Pariente, Catherine Arnaud, Isabelle Loubinoux

118 patients with ischemic stroke and hemiparesis (Fugl-Meyer scores ≤55)
fluoxetine (n=59; 20 mg once per day, orally) or placebo (n=59)
3 months starting 5 to 10 days after the onset of stroke
All patients had physiotherapy as delivered in local unit
The primary outcome measure was change in the FM score between day 0 and 90
Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial

François Chollet, Jean Tardy, Jean-François Albucher, Claire Thalamas, Emilie Berard, Catherine Lamy, Yannick Bejot, Sandrine Deltour, Assia Jaillard, Philippe Niclot, Benoît Guillot, Thierry Moulin, Philippe Marque, Jérémie Pariente, Catherine Arnaud, Isabelle Loubinoux

Lancet Neurol 2011;10:123-30

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How do we treat upper limb impairment?

Improved FM score at 90 days

Improved mRS score at 90 days
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.

Treatments aimed at reducing impairments

Task-specific training

- cortical stimulation
- other
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Variability in lesion induced structure and organisation

stroke damage

damaged pathways

cortical reorganisation?
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Variability in lesion induced structure and organisation

T1 structural
DTI
fMRI
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Variability in lesion induced structure and organisation

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

Correlation with post-stroke hand grip strength

Schulz et al, Stroke 2012; 43:2248-51
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Variability in lesion induced structure and organisation

<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>
Will the same treatment strategy work in these patients?
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Predicting outcomes

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

<table>
<thead>
<tr>
<th>Recovery</th>
<th>Definition</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<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>
<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>

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
Advances in neurorehabilitation are coming about through advances in neuroscience.

The dose of treatment is critical - more is generally better.

Enhancement of plasticity is possible.

Neuroimaging should help in stratification.

Understanding the mechanisms of recovery and treatment might allow targeted or individualised therapy after stroke in future.
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