Brain Computer Interface for Stroke Rehabilitation

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**Brain-Computer Interface (BCI)**

From Central Nerve System (CNS) to an external device.

<table>
<thead>
<tr>
<th>BCI Applications:</th>
<th>BCI Challenges:</th>
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</thead>
<tbody>
<tr>
<td>Replace</td>
<td><strong>Responsiveness</strong>&lt;br&gt;Accuracy, adaptability</td>
</tr>
<tr>
<td>Restore</td>
<td><strong>Usability</strong>&lt;br&gt;Convenience, self-administration</td>
</tr>
<tr>
<td>Enhance</td>
<td><strong>Reliability</strong>&lt;br&gt;Sustainability</td>
</tr>
<tr>
<td>Supplement</td>
<td><strong>Affordability</strong>&lt;br&gt;Low-cost, non-recurrent cost</td>
</tr>
<tr>
<td>Improve</td>
<td><strong>Availability</strong>&lt;br&gt;Hospital, rehab center, home</td>
</tr>
<tr>
<td></td>
<td><strong>Efficacy</strong>&lt;br&gt;Effectiveness, ITT</td>
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Stroke

- The leading cause of disabilities
- Third cause of death
- Worldwide
  - 15 million new stroke cases each year worldwide
  - 8000-9000 new cases in Singapore each year
- 33% stroke survivors need various types of rehabilitation
  - movement, speech, concentration, and cognition
About Stroke

• Stroke is a type of cardiovascular disease - affects the arteries leading to and within the brain.

• Type of stroke:
  – Ischemic: when a blood vessel is blocked by a clot
  – Hemorrhagic: when a blood vessel bursts.

• Consequences:
  – Part of the brain cannot get the blood (and oxygen) it needs, so it starts to die.
  – Cause paralysis, affect language and vision, and other problems.
About Stroke (2)

• The average stroke involves 54 milliliters of brain tissue -- about 3 cubic inches -- and takes 10 hours to evolve

• When someone suffers a stroke,
  – 1.9 million nerve cells die, each minute
  – 14 billion synapses and 7.5 miles of nerve fibers were lost, each minute
  – the oxygen-starved brain ages about 3.6 years each hour
  – need for rapid treatment -- time is brain

About Stroke (3)

- Patients need to recognize stroke symptoms and call ambulance right away. ER physicians, neurologists, and nurses need to recognize that stroke is a treatable neuro emergency that has to be handled at the highest triage priority.
- About 70% of patients who suffer a minor stroke or transient ischemic attack (TIA) do not correctly recognize their symptoms.
- About 30% delay seeking medical attention for more than 24 hours.

Post-Stroke Rehabilitation

• Treatment
  • Pharmaceutical, biological and electrophysiological treatment
  • Exercise and Training
  • Potential: stem cell therapy, exogenous tissue engineering and brain-computer interface technologies

• Physio & Occupational Therapy (Gold Standard)
• Bobath approach and the Motor Relearning Program
  • therapists to help patient perform exercises that attempt to overcome motor deficits and improve motor patterns

• Constraint-induced Movement Therapy
  • use of the affected side by restraining the unaffected side

• Challenges
  • Labor intensive and expensive, Lack of repeatability and objective measures

Dimyan & Cohen, 2011
Robot-Assisted Physical Therapy

- Manual assistance is labor intensive and expensive
- Robot performs repetitive exercises on affected limb
  - Ease burden on manpower
  - Consistent and efficient training
  - Pervasive and accurate monitoring
- Clinical data suggests an improvement of functional outcome

Brain Plasticity

Level of Plasticity

Very High
High
Moderate
Low

Young Kids
Children
Adulthood

Stroke: Hebbian Plasticity
Motor Imagery for Stroke

- Motor imagery: a backdoor to the motor system after stroke?  
  

- Mental rotation of the neuronal population vector.


- Evaluation of cortical connectivity during real and imagined rhythmic finger tapping.


- Motor imagery after subcortical stroke: a functional magnetic resonance imaging study.

  N Sharma, et al, Stroke 2009

- Imagining the impossible: intact motor representations in hemiplegics


- Intact motor imagery in chronic upper limb hemiplegics: evidence for activity-independent action representations.

<table>
<thead>
<tr>
<th>Research on BCI for Stroke Rehab</th>
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<tbody>
<tr>
<td>• Think to move: a neuromagnetic brain-computer interface (BCI) system for chronic stroke</td>
</tr>
<tr>
<td>• Applying a brain-computer interface to support motor imagery practice in people with stroke for upper limb recovery: a feasibility study</td>
</tr>
<tr>
<td>• Brain-computer interface controlled functional electrical stimulation system for ankle movement</td>
</tr>
</tbody>
</table>
Research on BCI for Stroke Rehab (2)

- First Steps Toward a Motor Imagery Based Stroke BCI: New Strategy to Set up a Classifier  

- A Large Clinical Study on the Ability of Stroke Patients to Use EEG-Based Motor Imagery Brain-Computer Interface  
  K. Ang, et al, Clinical EEG and Neuroscience, 2011

- Relationship Between Electrical Brain Responses to Motor Imagery and Motor Impairment in Stroke  

- Resting State Changes in Functional Connectivity Correlate With Movement Recovery for BCI and Robot-Assisted Upper-Extremity Training After Stroke  


- Brain-Machine Interface in Chronic Stroke Rehabilitation: a Controlled Study  

- Brain-Computer Interface in Stroke Rehabilitation  
Clinical Studies on Stroke Rehab

- BCI-based Upper Limb Stroke Rehab
  - 25 chronic sub-cortical stroke patients
  - Compared to robotic rehab
  - 4 week rehab, fMRI

- tDCS Combined with BCI-based Upper Limb Stroke Rehab
  - 18 chronic sub-cortical stroke patients
  - Real-tDCS (20m) vs sham-tDCS (1m)
  - 2 week rehab, fMRI/DTI/TMS

- BCI-based Grip/Wrist Stroke Rehab
  - 21 chronic sub-cortical stroke patients
  - Compared to haptic rehab and human therapist
  - 6 week rehab
Motor Imagery Brain-Computer Interface (MI-BCI)-based upper limb robotic rehabilitation for stroke patients is introduced. The architecture of the proposed MI-BCI-based robotic rehabilitation is illustrated in Fig. 1, which synergizes MI-BCI with the clinical implementation details. The purpose of this calibration phase is to address subject variability with respect to the characteristics of the CSP features. These 4 stages collectively construct a specific motor imagery detection model.

In the calibration phase, the subject is presented with a pre-defined period of 2 seconds. If motor intent is detected, the MIT-Manus robot directly assists the subject in moving the impaired limb towards the goal. The main difference in the calibration phase is that the former initiates robot-assisted movement if voluntary drive is detected whereas the latter initiates robot-assisted movement if voluntary drive and directly involves the primary motor system at all stages of stroke recovery is known to influence motor training. For the "stop" cue, the subject is instructed not to imagine moving the stroke-affected limb.

In the proposed MI-BCI-based robotic rehabilitation, the upper limb rehabilitation using the MIT-Manus robot is employed with a non-invasive EEG system. In the calibration phase, the subject is presented with a pre-defined period of 2 seconds. If motor intent is detected, the MIT-Manus robot directly assists the subject in moving the impaired limb towards the goal. The main difference in the calibration phase is that the former initiates robot-assisted movement if voluntary drive is detected whereas the latter initiates robot-assisted movement if voluntary drive and directly involves the primary motor system at all stages of stroke recovery is known to influence motor training.

On the other hand, motor imagery incorporates the use of imagination to recruit the motor system at all stages of stroke recovery is known to influence motor training. For the "stop" cue, the subject is instructed not to imagine moving the stroke-affected limb.

This motivates the development of a Motor Imagery Brain-Computer Interface (MI-BCI)-based robotic rehabilitation for stroke patients.
BCI System

EEG Acquisition → Temporal Filtering → Feature Selection → Classifier → Decision

Spatial Filtering → Feature Extraction → Adaptation/Learning

Co-adaptation

Feedback and Control
BCI-based Upper Limb Stroke Rehab
Funding: TEC. Hospitals: TTSH, NNI

• **Protocol**
  - 3 rehab sessions per week
  - 4 week rehabilitation
  - 2 fMRI scans at pre- & post-
  - Manus robot: 960 repetitions (1 Hour)
  - BCI-Manus: 160 repetitions (1 Hour)

• **Clinical Outcome Measurement:**
  - **Fugl-Meyer Assessment (FMA)** - quantitatively estimated the extent of neurological deficit of the upper extremity
  - Grip Strength
  - Motor FIM, MAS, MOTAS, PAIN
  - Measured at week 0, 2, 4 and 12

<table>
<thead>
<tr>
<th></th>
<th>Screening</th>
<th>Robotic Group</th>
<th>BCI Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>N=14</td>
<td>N=11</td>
<td></td>
</tr>
<tr>
<td>In training</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Graph:**
- **Robotic Group**
- **BCI Group**

**Timeline:**
- 0 weeks
- 2 weeks
- 4 weeks
- 12 weeks

**Legend:**
- ●
- ●●
- ●●●
- ●●●●
- ●●●●●
### Demographic of Patients (N=25)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Manus group (n=15)</th>
<th>BCI+Manus (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54 ± 10</td>
<td>49 ± 145</td>
</tr>
<tr>
<td>Gender N(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Male</td>
<td>7 (46.7%)</td>
<td>9 (81.8%)</td>
</tr>
<tr>
<td>- Female</td>
<td>8 (53.3%)</td>
<td>2 (18.2%)</td>
</tr>
<tr>
<td>Stroke type N(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Infarction</td>
<td>5 (33.3%)</td>
<td>5 (45.5%)</td>
</tr>
<tr>
<td>- Hemorrhagic</td>
<td>10 (66.7%)</td>
<td>6 (54.4%)</td>
</tr>
<tr>
<td>Stroke nature N(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cortical</td>
<td>5 (33.3%)</td>
<td>3 (27.3%)</td>
</tr>
<tr>
<td>- Subcortical</td>
<td>10 (66.7%)</td>
<td>8 (72.7%)</td>
</tr>
<tr>
<td>Paresis side N(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Right</td>
<td>9 (60.0%)</td>
<td>6 (54.5%)</td>
</tr>
<tr>
<td>- Left</td>
<td>6 (40.0%)</td>
<td>5 (45.5%)</td>
</tr>
<tr>
<td>Duration post stroke (days)</td>
<td>235±184</td>
<td>384±291</td>
</tr>
</tbody>
</table>

Clinical Outcome (FMA)

**Robotic Group**

- Week 2: 6.2
- Week 4: 4.5
- Week 12: 5.3

**BCI Group**

- Week 2: 5.0
- Week 4: 3.2
- Week 12: 2.3

**Relative FMA improvement (wrt week 0)**

- Week 2: Manus 3.2 (P=0.020) BCI+Manus 1.1 (P=0.402)
- Week 4: Manus 6.2 (P=0.003) BCI+Manus 4.5 (P=0.032)
- Week 12: Manus 7.3 (P=0.013) BCI+Manus 5.3 (P=0.020)
IC map post

= FCC map

Grefkes et al, 2011,
Westlake, et al, 2011
## Functional Connectivity Changes

<table>
<thead>
<tr>
<th>Area</th>
<th>Description</th>
<th>BCI group shows consistently higher increase in FCC than Robotics group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsilesional Motor Cortex and contralesional Cerebellum and Superior Temporal Gyrus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contralesional Motor Cortex and ipsilesional Precuneus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supplementary Motor Area with Ipsilesional Inferior Parietal Lobe (IPL), Anterior Cingulate Cortex (ACC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visuospatial System with Superior Temporal Gyrus (STG) and Superior Medial Gyrus (SMG)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Varkuti, et al, 2012*
tDCS Combined with BCI for Upper Limb Stroke Rehab
Funding: NMRC. Hospital: NUH

- **Protocol**
  - 5 rehab sessions per week
  - 2 week rehabilitation
  - 3 fMRI scans at screening, pre- & post-
  - 160 repetitions (1 Hour)

- **Clinical Outcome Measurement:**
  - **Fugl-Meyer Assessment (FMA)**
  - Grip Strength, Box-Block
  - Modified Ashworth
  - Measured at week 0, 3, 6

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Control</td>
<td></td>
</tr>
<tr>
<td>BCI + Real tDCS</td>
<td></td>
</tr>
<tr>
<td>BCI + Sham tDCS</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Screening</th>
<th>33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>tDCS</td>
</tr>
<tr>
<td>In training</td>
<td>N=9</td>
</tr>
</tbody>
</table>

Weeks

-2 0 2 4 6
Clinical Outcome (FMA)

<table>
<thead>
<tr>
<th></th>
<th>Week 2</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>tDCS</td>
<td>0.9</td>
<td>5.6</td>
</tr>
<tr>
<td>Sham</td>
<td>2.8</td>
<td>5.4</td>
</tr>
</tbody>
</table>

P-values:
- Week 2: tDCS vs. Sham, P=0.420
- Week 4: tDCS vs. Sham, P=0.005
- Week 4: Sham vs. real-tDCS, P=0.069
- Week 4: Sham vs. real-tDCS, P=0.021
Resting State Functional Connectivity: Central Sulcus to ACC

- All patients showed enhancement in connectivity from bilateral central sulcus to ACC region with and without transcranial direct stimulation (tDCS).
- This suggested enhanced motor control and motivation from ACC to motor cortex.
- Threshold at $p<0.001$ (height) and $p<0.05$ FWE corrected (extent=150 voxels).

BCI-based Grip/Wrist Stroke Rehab

Funding: A*STAR. Hospital: TTSH

- **Protocol**
  - 3 rehab sessions per week
  - 6 week rehabilitation
  - 160 repetitions (1 Hour) + 0.5 standard therapy

- **Clinical Outcome Measurement:**
  - Fugl-Meyer Assessment (FMA)
  - Grip Strength, Box-Block
  - Modified Ashworth
  - Measured at week 0, 3, 6, 12, and 24

<table>
<thead>
<tr>
<th>Screening</th>
<th>45</th>
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<tbody>
<tr>
<td><strong>Group</strong></td>
<td><strong>SC</strong></td>
</tr>
<tr>
<td>In training</td>
<td>N=7</td>
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</tbody>
</table>

### Standard Control Group
- SC Group

### Haptic Group
- HK Group

### BCI-HK Group
- BCI-HK Group

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Weeks: 0, 3, 6, 12, 24
Clinical Outcome (FMA)

<table>
<thead>
<tr>
<th></th>
<th>Week 3</th>
<th>Week 6</th>
<th>Week 12</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCI+HK</td>
<td>5.8</td>
<td>7.2</td>
<td>8.2</td>
<td>9.7</td>
</tr>
<tr>
<td>HK</td>
<td>3.9</td>
<td>7.3</td>
<td>6.5</td>
<td>8.3</td>
</tr>
<tr>
<td>SC</td>
<td>1.6</td>
<td>4.9</td>
<td>3.6</td>
<td>3.6</td>
</tr>
</tbody>
</table>

Relative FMA improvement (wrt week 0)

- BCI: P=0.029, P=0.039, P=0.111
- Haptic: P=0.001, P=0.021, P=0.139
- Therapist: P=0.001, P=0.004, P=0.002, P=0.0005, P=0.002

Note: P-values indicate statistical significance.
Conclusion

• Statistically & clinically significant clinical outcomes were observed comparing the pre- and post-rehabilitation FMA measurements.
• Functional imaging shows statistically significant enhancement in functional connectivity after rehabilitation.
• Initial indication of structural change might imply possible neuroplasticity effects.
• tDCS is helpful in enhancing patients’ recovery.
• EEG coherence could provide prediction for clinical outcome.
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For additional information, please visit our website, http://nsp.i2r.a-star.edu.sg/