Neuroimaging biomarkers and predictors of motor recovery: implications for PTs

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Description:
Stroke is a heterogeneous disease that presents considerable challenges to clinicians with regards to choosing optimal therapies and determining patient outcomes. In medicine, measurements that directly capture a patient's physiological state guide clinical decision-making. For example, a physician assesses coronary function with a cardiac stress test and makes treatment decisions based on test results. In stroke rehabilitation, tests and measures of behavior predominantly guide care delivery. However, behavioral assessments are often imprecise, subjective, and lack the ability to capture the physiological state or recovery potential of the brain– the principal target of stroke therapies. Neuroimaging provides information about the patient beyond what is offered from conventional behavioral assessments. Brain-based information has the potential to enhance clinical decision-making and, ultimately, patient outcomes. The primary objective of this course is to describe the potential role of neuroimaging in stroke rehabilitation with an emphasis on the use of both structural and functional neuroimaging measurements to monitor and predict motor recovery and treatment response in stroke.

Objectives:
Upon completion of this course, the participate will be able to:

1. Describe conventional and advanced structural and functional neuroimaging techniques.

2. Differentiate a neuroimaging biomarker from a predictor in the context of stroke rehabilitation.

3. Identify potential biomarkers and predictors of motor recovery in stroke.

4. Discuss opportunities and barriers to implementing neuroimaging information into clinical stroke rehabilitation across the recovery trajectory.

Session Outline:

1. **Defining stroke biomarkers and predictors: Jessica Cassidy**
   - **a.** Why is stroke a heterogeneous disease?
     - **i.** Spontaneous and therapeutic-induced recovery[1]
     - **ii.** Additional factors influencing recovery
   - **b.** Stroke biomarker[2-4]
   - **c.** Stroke predictor [2]
   - **d.** What is the value of stroke biomarkers and predictors in rehabilitation?

2. **Review of neuroimaging techniques: Jessica Cassidy, Kathryn Hayward**
   - **a.** Considerations
     - **i.** Temporal resolution
     - **ii.** Spatial resolution
     - **iii.** Invasiveness and contraindications
   - **b.** Structural neuroimaging
     - **i.** Magnetic Resonance Imaging (MRI)
       - **1.** Acquisition
         - Scanner with strong magnet (1.5 to 7.0 Tesla)
         - Signal generation
         - Contrasts: T1, T2, T2-FLAIR, and T2*
       - **2.** Analysis
       - **3.** PROs
         - Non-invasive
         - Spatial resolution
       - **4.** CONs
         - Contraindications
         - Expensive
         - Personnel often required
         - Loud
         - Issues of claustrophobia
         - Movement
     - **ii.** Diffusion Tensor Imaging (DTI)
       - **1.** Acquisition
         - Diffusion of water molecules to reveal microstructural properties of white matter tracts
       - **2.** Analysis
         - Considerations: probabilistic vs. deterministic tractography, atlas (standard) vs. native (individual)

space, atlas masks (standard) vs. hand-drawn (individual) regions of interest to reconstruct tracts

3. PROs
    - Spatial resolution
    - Does not require active movement for collection
    - Ability to index motor and non-motor white matter tracts
4. CONs
    - Contraindications
    - Cost to collect and analyze (time-intensive)
    - Access to MRI equipment/technologist/collaborators

c. Functional neuroimaging

i. Functional Magnetic Resonance Imaging (fMRI)

1. Acquisition
    - Signal:
        - Hemodynamic Response Function
        - Blood-Oxygen Level Dependent (BOLD) signal
            - Task-oriented vs. resting-state
2. Analysis
    - Preprocessing pipeline
    - General linear model
3. PROs
    - Non-invasive
    - Spatial resolution
4. CONs
    - Temporal resolution
    - Contraindications
    - Movement
    - Expensive
    - Time-intensive
    - Issues of claustrophobia

ii. Electroencephalography (EEG)

1. Acquisition
    - Recording of electrical activity (cortical oscillations) generated from underlying pyramidal cells
    - Consideration: number of electrodes, electrode arrangement, system (gel-based, solution, dry)
2. Analysis
    - Event-related potential
    - Continuous resting-state
    - Frequency spectrum
    - Quantitative EEG metrics: power and coherence
3. PROs
    - Temporal resolution (millisecond)

- Non-invasive
- Inexpensive (in comparison to MRI/fMRI)
- Accessibility (few contraindications)
- Non-invasive

4. CONs
- Spatial resolution
- Preparation time depending on EEG system

iii. Transcranial Magnetic Stimulation (TMS)

1. Acquisition
- Single vs. paired pulse
- Collection approaches: resting and active motor thresholds, recruitment curves, interhemispheric inhibition
- Brain regions: primary motor vs. non-motor regions
- Considerations: selection of muscle to record electromyography (EMG) signal, subject position, implementation of neuro-navigation

2. Analysis
- Visualizing and quantifying motor-evoked potential (MEP)
- Visualizing and quantifying interhemispheric inhibition

3. PROs
- Able to quantify excitability of primary motor cortex and relationship of non-motor regions to motor cortex
- Non-invasive
- Low cost (in comparison to MRI/fMRI)
- Temporal resolution

4. CONs
- Contraindications
- Primarily quantifies motor system
- Some techniques require MEP presence
- Spatial resolution

3. Structural neuroimaging biomarkers and predictors

a. Corticospinal tract measurements: **Jessica Cassidy**

i. CST injury features and motor recovery prediction[5]

b. Corpus callosum measurements: **Jill Stewart**

i. Interhemispheric pathways between homologous motor regions and their relationship with motor function in health and after stroke[6-9]

ii. Relationship between the motor section of the corpus callosum and motor function after stroke – differences based on level of motor severity[10]

iii. Corpus callosum integrity and skilled reach control[11]

iv. Other relevant white matter pathways – the example of Superior Longitudinal Fasciculus and within session changes in motor performance

c. Corticospinal tract and corpus callosum measurement application in a multi-site study: **Kathryn Hayward**
    i. Background
    ii. Role of data sharing to produce a mega-data set
    iii. Results
    iv. Recommendations for moving forward

4. **Functional neuroimaging biomarkers and predictors**
    a. TMS: **Michael Borich**
        i. Interhemispheric Inhibition
            1. Transcallosal inhibition[12]
        ii. Limitations of standalone TMS for measuring and modulating cortical activity

    b. Combined TMS and EEG: **Michael Borich**
        i. Offline approaches: before vs. after TMS
        ii. Measuring cortical reactivity[13]
        iii. Measuring cortical connectivity
        iv. EEG coherence to evaluate TMS-evoked connectivity
        v. Assessment of interhemispheric inhibition[14]

    c. EEG application in subacute and chronic stroke: **Jessica Cassidy**
        i. Hospital use[15]
        ii. Clinical trial use[16]

5. **Neuroimaging application to clinical practice and current obstacles**
    a. Stroke Recovery and Rehabilitation Roundtable[17]: **Kathryn Hayward**
        i. Goals of the Biomarker working group
            1. What biomarkers are clinical trial-ready?
            2. What biomarkers are developmental priorities?
        ii. Future
            1. Recommendations and moving the field forward

    b. Translation of neuroimaging evidence to clinical practice: **Jill Stewart**

    c. Obstacles and future directions: **Jill Stewart**

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