Effect of cycling on Cortico-Muscular Coupling of PD patients

Update #2 Presentation

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Acquaintance

• I am Zahra
• Graduated from Amirkabir University of Technology, with dual degrees, Electrical engineering and Biomedical engineering
• Doing Capstone project in the Integrated Circuit design field, designing stimulator of cochlear implant -> where I found signal processing more attractive 😊
• Starting to learn signal processing after graduation, and doing some projects to gain more insights
• doing EEG-EMG coupling research to build a better foundation in this field
• My other favorite field is nonlinear dynamic and chaos theory, in neuronal models, which led me doing some relevant courses and projects
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Cycling

• Important muscles of lower limb in pedaling:
  • Gluteus maximus
  • Semimembranosus + Semitendinosus + biceps femoris (Hamstring muscles) (hip extension + knee flexion)
    • Controversial, from TDC to BDC, some said from TDC to 270
  • Vastus lateralis and Vastus medialis (knee extension)
    • Activated from just before TDC to just after 90
  • Rectus femoris (knee extension + hip flexion)
    • Activated from 270 to 90
  • Gastrocnemius lateralis and Gastrocnemius medialis
  • Soleus (ankle extension)
    • From 45 to 135

• Coordinated and orderly activation of important muscles in a one bout of cycling (Figure 1)

Coupling

EEG-EMG coupling

• Cortico Muscular coupling: An index that reflect the synchrony and interaction, linear or nonlinear, between the Brain and muscles.
• Factors affecting CMC: band frequencies, force levels, age correlation, and diseases [1]
• Different from multimodal research

Our sensor data

- Dataset contains 23 subjects, 15 PD and 8 control
- 30 signals were recorded from each subject
  - 2 EOG
  - 3 ECG
  - 9 EEG (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4)
  - 16 EMG (bipolar recording) (Hamstring, Soleus, Rectus Femoris, and vastus lateralis muscle for each side)
- Pedaling in 5 intensities, each for 3 minutes approximately
- Between two rounds, they have a 3-min rest to recover
- Data is recorded about 30-35 minutes
Our clinical data

• Mood assessment excel file
  • Including their scores in multiple feelings such as alertness, hostility, proudness, guiltiness, etc. before, after, and while they take their meds (Levodopa)

• Motor assessment
  • Investigation of Pegboard, Finger tapping for both hands, and time up and go (TUG) for both group

• Cognitive assessment
  • Investigation of Montreal cognitive assessment, trail making test (TMT), response time (RT), and verbal fluency in pre, post and while they take their made.
Experimental protocol

Inclusion Criteria:
• Adult between 40-80 years
• Hoehn and Yahr stage I-III
• Exercise on a regular basis (at least 100 minutes of aerobic exercise per week)
• Montreal Cognitive Assessment score >/= 24
• Beck’s depression inventory </= 13
• Beck’s anxiety inventory </= 9
• Able to communicate with study personnel
• Able to be informed of the nature of the study and willing to give written consent form
Research questions

• **Aim1:** To investigate if activity that arises in the motor cortex and contributes to the muscle activity during moderate pedaling is altered in patients with PD compared to healthy gender- and age-matched controls.

• **Aim2:** To examine whether different levels of intensity during the pedaling intervention cause different neuronal activity patterns in distinct areas of the brain.

• **Aim3:** To determine whether a single bout of exercise has an impact on cognitive functioning in patients with PD and whether this is different to healthy age and gender-matched controls.

• **Aim4:** To investigate whether a single bout of a cycling exercise leads to changes in motor function in PD subjects.

• **Aim5:** To determine whether a single bout of exercise has an influence on the mood and fatigue in patients with PD and healthy controls.
Research questions

• Aim1: To investigate if activity that arises in the motor cortex and contributes to the muscle activity during moderate pedaling is altered in patients with PD compared to healthy gender- and age-matched controls.

• Aim2: To examine whether different levels of intensity during the pedaling intervention cause different neuronal activity patterns in distinct areas of the brain.

• Correlation with Excel sheets:
  • Aim3: To determine whether a single bout of exercise has an impact on cognitive functioning in patients with PD and whether this is different to healthy age and gender-matched controls.
  • Aim4: To investigate whether a single bout of a cycling exercise leads to changes in motor function in PD subjects.
  • Aim5: To determine whether a single bout of exercise has an influence on the mood and fatigue in patients with PD and healthy controls.
EEG Cleaning

• Using butterworth for line noise (60 hz), removing DC (0.1 hz), and cutting high frequency (more than 100 hz)
• Using RLS for removing EOG artifact
• Using PCA for removing EMG artifact
• Using ICA and ICLabel for remaining artifacts

Figure 1: EEGLAB window, after preprocessing
EEG: RLS for removing EOG

- Using this algorithm by the EEGLAB plugin: AAR (Automatic Artifact Removal)
  - Could not remove all type of EOG artifacts

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EEG: PCA Removing EMG artifacts

- Using this algorithm by the EEGLAB plugin: AAR (Automatic Artifact Removal)
- Providing CCA, PCA and other algorithms in this plugin
- Choosing PCA by visualization

EEG: removing remaining artifact

- Using ICA and ICLabel for remaining artifacts (two components were removed for each subject)

![Figure 1: Output of ICA algorithm after removing IC 2 and 7 black: signal with artifact, red: clean signal](image1)

![Figure 2: Output of ICLabel plugin as labels for ICs](image2)
EMG cleaning

• Using butterworth for line noise and removing DC (bandpass 0.1-400 hz)
• Using RMS for envelope detection
EMG cleaning

- Bipolar Recording: Disappearing large ECG artifact and extra movement after using in a bipolar way (Figure 1)
- Bipolar Sol: Sol L1 – Sol L2
- ECG artifact (Figure 2)
Literature Review: 

Coherence

General categories for computing Cortico-Muscular Coherence

• Magnitude Squared coherence and enhanced version of it
• Wavelet coherence and enhanced version of it
• Transfer entropy
• Auto regressive based methods such as: Granger causality, Partial directed coherence (PDC) and generalized partial directed coherence (GPDC)

Literature review for Coherence


- Greater CMC in 6-15 hz in patients with tremor
- Lower CMC in Older adults in beta and higher in alpha than younger
- Assessing methods of rehabilitations and electrical stimulation in stroke or PD patients
- Parkinson’s:
  - CMC increased after STN-DBS in 10-30 hz
  - Slight increase after DBS implantation
- ALS: CMC dramatically reduced in ALS patients

Literature review for Coherence

[4] Cortico-muscular coherence increases with tremor improvement after deep brain stimulation in Parkinson's disease

- 7 PD patients
- EMG: abductor pollicis brevis (APB), first dorsalis interosseus muscles (FDI), with references localized over the distal interphalangeal joint of the thumb (APB) and the distal interphalangeal joint of the index finger
- EEG: FC1, C1, CP1, FC3, C3, CP3, FC2, C2, CP2, FC4, C4, CP4
- Movement: isometric precision grip task in four perioperative sessions
  - 1 day before (D0)
  - 1 day after (D1)
  - 8 day after, Stim off
  - 8 day after, Stim on

Method:
- Cross spectral analysis

Result:
- Significant decrease of CMC in the theta band, and increase in the low-beta frequency band on D8StimOn (upper fig)
- In D1, an increase of coherence in the high beta band during ‘precision grip’ compared with ‘rest’ in all subjects (coherence of MI and contralateral hand muscles) (lower fig)
- Significant increase in the high-beta band during ‘precision grip’ compared with ‘rest’ (coherence of STN and contralateral hand muscles)

Literature review for Coherence

[6] Brain-muscle connectivity during gait: corticomuscular coherence as quantification of the cognitive reserve

• Young (<30) and elderly (>65) group
• 3 different walking
  • Spontaneous walking (SW)
  • Walking with cognitive tasks (counting down and saying loud) (DW)
  • Walking with targets on the floor (TW)
• RF and SM are excluded. C3 and C4 are meaningful.
• Contralateral relationship: c3 with right distal leg muscle, c4 with left

Method:
• Continuous Wavelet transform and wavelet coherence
• 4 possible portion: Beta and Gamma band for frequency, 20%-40% and 70%-90% for time are chosen.

Result:
• Higher CMC during targeted walking in both group (greater increase in young group)
• Significant difference in ‘left TA - C4’ pair for EG between the SW and TW in beta band both in both 20%-40% (p-value = 0.020) and 70%-90% (p-value = 0.003)
• A significant difference for YG between SW and TW (p-value = 0.023)
Literature review for Coherence

[7] Corticomuscular Coherence and Motor Control Adaptations after Isometric Maximal Strength Training

Corticomuscular Coherence and Motor Control Adaptations after Isometric Maximal Strength Training

• 13 healthy men
• tibialis anterior (TA), gastrocnemius lateralis (GL), soleus (SOL), and gastrocnemius medialis (GM)
• Fp1, F3, Fz, F4, C3, Cz, C4, P3, Pz, and P4
• 3-week maximal strength training

Method:
• Wavelet coherence

Result:
• CMC was not changed despite muscle adaptation.
• Discussed (based on other paper) that CMC changed with fine motor tasks, or change after at least 3 years of exercise

Literature review for Coherence

[9] Coupling Analysis of EEG and EMG Signals Based on Transfer Entropy after Consistent Empirical Fourier Decomposition

- Two movement
  - Knee-jerk reflex (cerebellar to muscle is weaker)
  - Inhibited knee-jerk reflex (cerebellar to muscle would be greater)
- C3 EEG, quadriceps muscle EMG

Method:
- Consistent empirical Fourier Decomposition (CEFD) firstly (more in appendix) +
- transfer entropy for coherence
- Variational Mode Decomposition (VMD) is used as a benchmark in this paper

Result:
- Significant coupling of **beta band** in both knee-jerk reflex and inhibited knee-jerk reflex
- EMG->EEG is significantly higher than EEG->EMG in knee jerk reflex (fig 1)
- EEG->EMG is significantly higher than EMG->EEG in inhibited knee jerk reflex (fig 2)

Literature review for Coherence

[10] Electroencephalogram–Electromyography Coupling Analysis in Stroke Based on Symbolic Transfer Entropy

- 5 post stroke patients, and 7 control subjects
- 32 EEG channels: FP1, FP2, F7, F8, F4, F3, FZ, FC5, FC1, FC2, FC6, T7, C3, CZ, C4, T8, CP5, CP1, CP2, CP6, TP9, P7, P3, PZ, P4, P8, TP10, PO9, O1, OZ, O2, PO10
- 12 EMG channel: flexor digitorum superficialis (FDS), brachioradialis muscle, radial wrist flexor, ulnar wrist flexor, musculus biceps brachii (MBB), and triceps
- 2 movement with 2 hands
  - Left and right hand gripping (5 kg and 10 kg)
  - Left and right elbow bending

Method:
- Variable scale symbolic transfer entropy (VS-STE)
- Baseline method: symbolic transfer entropy
- Result:
  - Greater CMC in post-stroke patients in both directions (EEG -> EMG and EMG -> EEG)
  - Strongest CMC in beta band
Literature review for Coherence

[12] Alpha Band Cortico-Muscular Coherence Occurs in Healthy Individuals during Mechanically-Induced Tremor

- Considering CMC in alpha band by inducing artificial tremor, given the absence of it in healthy people
- 13 volunteers, biceps brachii (BB) muscle EMG, C3, C5, FC5, FC3, CP5 and CP3 EEG
- Elbow flexor against a spring load and isometric condition of 20% of Maximal Voluntary Isometric Contraction (MVIC)

Method:
- Partial directed coherence using vector autoregressive

Result:
- Significant beta CMC against isometric contraction
- Significant alpha CMC against a spring load (figure:)

Coherence methods

Implemented methods:

• Magnitude squared coherence
• Wavelet coherence
• Transfer entropy
• Partial directed coherence
• Generalized partial directed methods
• Direct transfer function

RQ1: Does pedaling have different impact on PD patients than control group?
Result of coherence: spectral coherence

Magnitude Squared Coherence:

- FFT and welch can be used to produce power spectral density (PSD)
- Considering welch as a more robust method to extract PSD
- Computing MSC via welch, hamming window 1000 time points (1 second)
Result of coherence: spectral coherence

Magnitude Squared Coherence:

- Trying to figure out whether there is a significant difference between PD and healthy group in each intensities
- Trying to figure out whether cycling has different effect on two groups at the end
- F and P channels are not investigated to avoid fake results (omitting based on literature)
- Delta and theta bands are not investigated to avoid fake results (omitting based on literature)
- Extracting Alpha band coherence for injury and pathology (this band is omitted in several literature that are about the difference of movements)
Result of coherence: spectral coherence

Plots of some Significant difference in:

- **Contralateral:**
  - Figure 1: (C3-right vas), intensity 50, beta band (p-value = 0.0062)

- **Ipsilateral:**
  - Figure 2: (C3-left vas), intensity 60, alpha bands (p-value = 0.0052)
Result of coherence: spectral coherence

Significant difference in:

**In pedaling:**

- **Contralateral:**
  - C3-right vas, intensity 30, beta band (0.029)
  - C4-left sol, intensity 30, gamma band (0.027)
  - C4-left Vas, intensity 30, gamma band (0.017)
  - C4-left Vas, intensity 40, beta band (0.008)
  - C3-right ham, intensity 40, beta band (0.027)
  - C3-right vas, intensity 50, beta band (0.0062)
  - C4-left sol, intensity 60, beta band (0.035)
  - C4-left Ham, intensity 60, alpha band (0.02)
- **Ipsilateral:**
  - C3-left sol, intensity 30, alpha band (0.037)
  - C3-left ham, intensity 40, beta band (0.027)
  - C3-left Fem, intensity 40, beta band (0.038)
  - C4-Right sol, intensity 50, alpha band (0.014)
  - C3-left vas, intensity 60, alpha bans (0.0052)
  - Cz-Right Vas, intensity 30, beta band (0.022)
  - Cz-left Vas, intensity 30, gamma band (0.043)
  - Cz-left Fem, intensity 40, alpha band (0.033)
  - Cz-right Ham, intensity 50, gamma band (0.027)
  - Cz-right Vas), intensity 50, beta band (0.044)
Result of coherence: spectral coherence

Significant difference in:

**In warm up and cool down:**

- **Warm up**
  - Cz-left ham, beta band (0.01)
  - Cz-right ham, alpha band (0.01)
  - Cz-right ham, gamma band (0.03)
  - Contralateral:
    - C3-right vas, beta band (0.02)
    - C3-right fem, beta band (0.034)

- **Cool down**
  - Cz-left vas, alpha band (0.03)
  - Contralateral:
    - C3-right Ham, beta band (0.04)
wavelet Coherence:

- Computing Continuous wavelet transform (CWT) of both signals, producing coherence signal by complex conjugate
- Using the Morlet (and Morse) wavelet method for CWT
Result of coherence: wavelet coherence

Plots of some Significant difference in:

- Cz-Right Fem, intensity 40, alpha band (0.009)
- Figure 1: all coefficients without separating sub bands of EEG
- Figure 2: coherence coefficients of alpha band
Result of coherence: wavelet coherence

Plots of some Significant difference in:

- Ipsilateral:
  - C3-left Sol, intensity 60, alpha band (0.009)
- Figure 1: all coefficients without separating sub bands of EEG
- Figure 2: coherence of alpha band

Figure 1

Figure 2
Result of coherence: wavelet coherence

Significant difference in:

**In pedaling:**
- Cz-left fem, intensity 40, beta band (0.007)
- Cz-right fem, intensity 40, alpha band (0.004)
- Cz-left sol, intensity 60, alpha band (0.009)

**Contralateral:**
- C3-right ham, intensity 30, alpha band (0.04)
- C4-left sol, intensity 40, alpha band (0.031)
- C4-left fem, intensity 40, alpha band (0.05)
- C4-left fem, intensity 50, alpha band (0.039)
- C4-left sol, intensity 60, alpha band (0.036)
- C4-left fem, intensity 60, alpha band (0.016)

**Ipsilateral:**
- C4-right fem, intensity 40, alpha band (0.006)
- C4-right fem, intensity 50, alpha band (0.04)
- C3-left sol, intensity 60, alpha band (0.009)
- C3-left Vas, intensity 70, alpha band (0.047)
Result of coherence: wavelet coherence

Significant difference in:

**In Cool down and warm up:**
- Cool down
  - No significant difference
- Warm up
- Cz-right sol, warm up, alpha band (0.039)
- Contralateral
  - C4-left ham, warm up, alpha band (0.032)
  - C4-left vas, warm up, alpha band (0.012)
- Ipsilateral
  - (C3-left ham), warm up, alpha band (0.037)
  - (C3-left Vas), warm up, alpha band (0.02)
Result of coherence: mutual information

Mutual Information: (in time domain)

• Computing entropy of both signals and joint entropy, and producing coherence signal

• No significant difference in each pair (p-value of each pair between two groups > 0.05)

• Figure 1: MI of PD and control group in a c3-left sol pair, alpha band, intensity 30

Figure 1: MI of PD and control subject
Partial Directed coherence:
• Autoregressive-based model
• Model should be stable, white, and consistent by tuning order, window length, and step size
• Useful toolbox: SIFT
Result of coherence: PDC

**Brain to muscle**
- No significant difference

**Muscle to brain**
Significant difference in:
- Cz-Right Ham, int 40, beta band (0.013)
- Contralateral
  - C4-left sol, int 60, beta band (0.04)
- Ipsilateral
  - No significant difference
Result of coherence: GPDC

Generalized Partial Directed coherence:

• Autoregressive-based model
• Model should be stable, white, and consistent by tuning order, window length, and step size
• Useful toolbox: SIFT
• Figure 1: output figure of subject 1, in SIFT toolbox
Result of coherence: GPDC

**Muscle to brain**

Significant difference in:
- Cz-Left Sol, int 40, beta band (0.023)
- Cz-left sol, int 70, gamma band (0.006)
- Cz-left vas, int 70, gamma band (0.006)
- Cz-right ham, int 70, gamma band (0.017)

**Contralateral**
- C4-Left fem, int 40, alpha band (0.04)
- C4-left sol, int 70, alpha band (0.046)
- C4-left Vas, int 70, beta band (0.015)

**Ipsilateral**
- C4-Right vas, int 50, alpha band (0.023)
- C4-Right vas, int 50, beta band (0.021)
- C4-Right vas, int 50, gamma band (0.015)
- C4-right fem, int 50, alpha band (0.023)
- C4-Right ham, int 50, alpha band (0.006)
- C3-left sol, int 70, gamma band (0.009)
- C4-right vas, int 70, gamma band (0.008)
- C4-right fem, int 70, gamma band (0.04)

**Brain to muscle**

Significant difference in:
- **Contralateral**
  - C3-Right Vas, int 30, alpha band (0.028)
  - C3-Right Ham, int 50, alpha band (0.01)
- **Ipsilateral**
  - C3-Left Vas, int 40, alpha band (0.045)
  - C3-Left Fem, int 50, alpha band (0.024)
  - C3-Left Ham, int 50, Gamma band (0.046)
  - C3-Left Fem, int 50, Gamma band (0.024)
  - C3-Left Fem, int 70, Gamma band (0.019)
Result of coherence: DTF

Direct Transfer Function:
• Autoregressive-based model
• Model should be stable, white, and consistent by tuning order, window length, and step size
• Useful toolbox: SIFT
Result of coherence : DTF

**Muscle to brain**

Significant difference in:
- Cz-Right Ham, int 30, alpha (0.03)
- Cz- left sol, int 40, alpha (0.007)
- Cz- left sol, int 40, beta (0.009)
- Cz-right ham, int 40, alpha (0.027)
- Cz-right ham, int 40, beta (0.027)
- Cz-right ham, int 40, gamma (0.035)
- Cz-left sol, int 60, alpha (0.03)
- Cz-left sol, int 60, gamma (0.04)
- Cz-left sol, int 40, gamma (0.015)

- Contralateral
  - C3 - left sol, int 40, Gamma (0.038)

- Ipsilateral
  - C4-Right Ham, int 30, beta (0.039)
  - C4-right ham, int 40, alpha (0.04)
  - C4-right ham, int 40, beta (0.013)

**Brain to muscle**

- No significant difference
Conclusion

• Advantage of Frequency domain over time domain methods in this research
• Advantage of GPDC over PDC in this research
• DTF shows significant difference in EMG->EEG while there was no EEG->EMG difference
Quick glance to the future

- Focusing on a fraction of time for each muscle (e.g.: 0-0.5 sec for Ham, and 0.5-1 sec for SoL)
- Using ML methods to classify coherence signals or finding well-suited features (biomarkers) to find the role of intensity (RQ2)
- Using ML to find the impact of intensity or suitable figures which show effect of intensity
- Using ML for investigating impact of cycling on mood, fatigue, and motor function (data of excel file, RQ 3, 4, 5)
Questions

Any question? 😊
Thanks for your attention 😊