THE UNIVERSITY OF BRITISH COLUMBIA

PACIFIC PARKINSON'S Research Centre

Effect of cycling on Cortico-Muscular Coupling of PD patients

Update #2 Presentation

University of British Columbia
Pacific Parkinson's Research Centre

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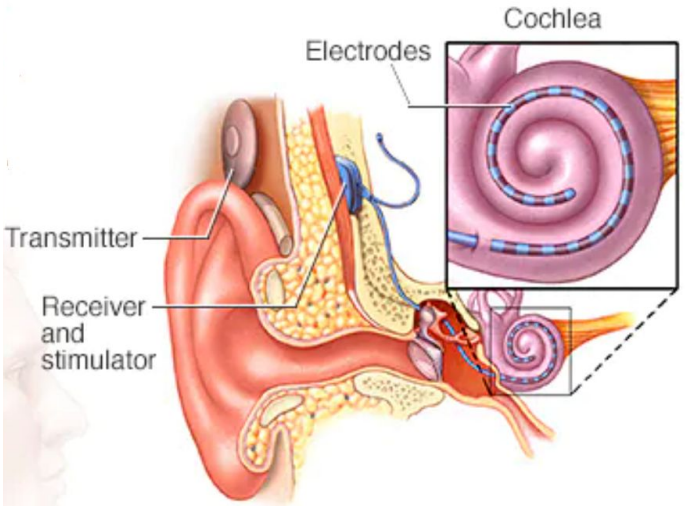
Acquaintance

- 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



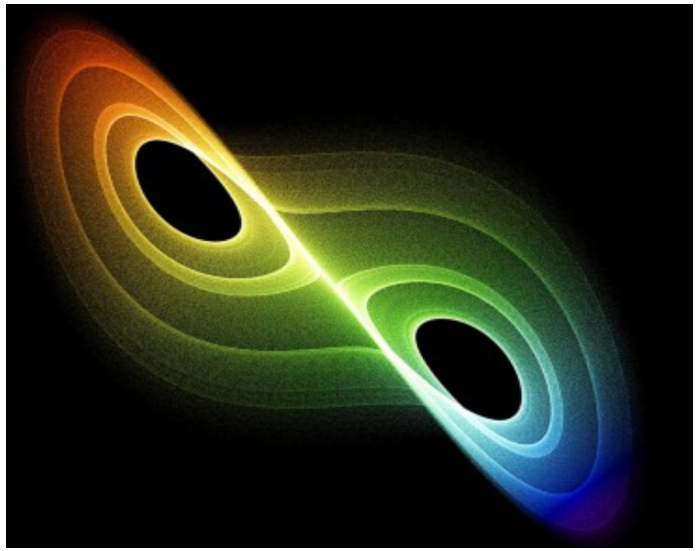


Table of contents

- Introduction
- Literature Review for cleaning
- Cleaning methods
- Literature Review for Coherency
- Coherency methods (Baseline)
- Result of coherence
- Quick glance to the next step + our approac
- Questions

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)

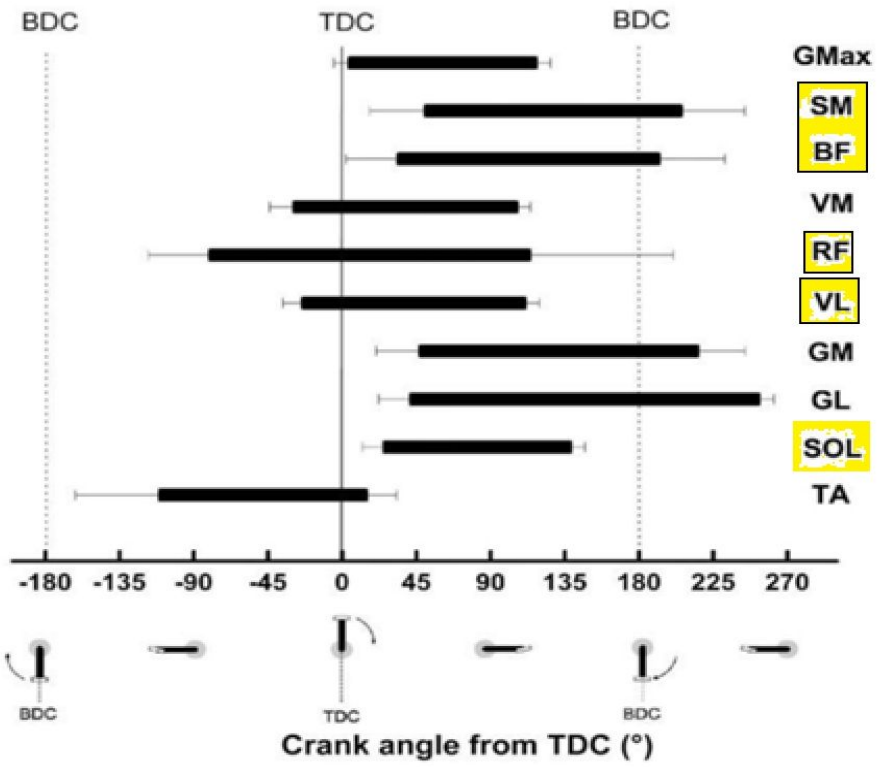


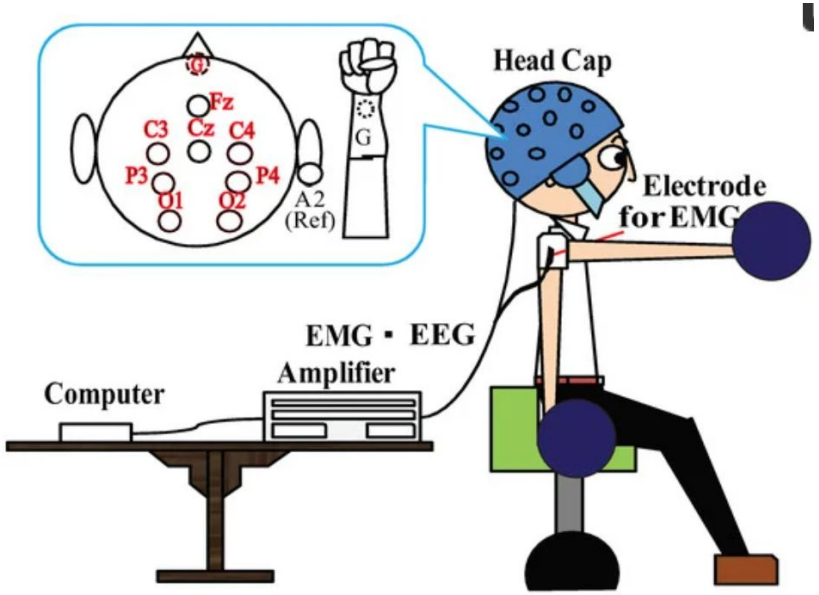
Figure 1: timing of muscles in a bout of pedaling

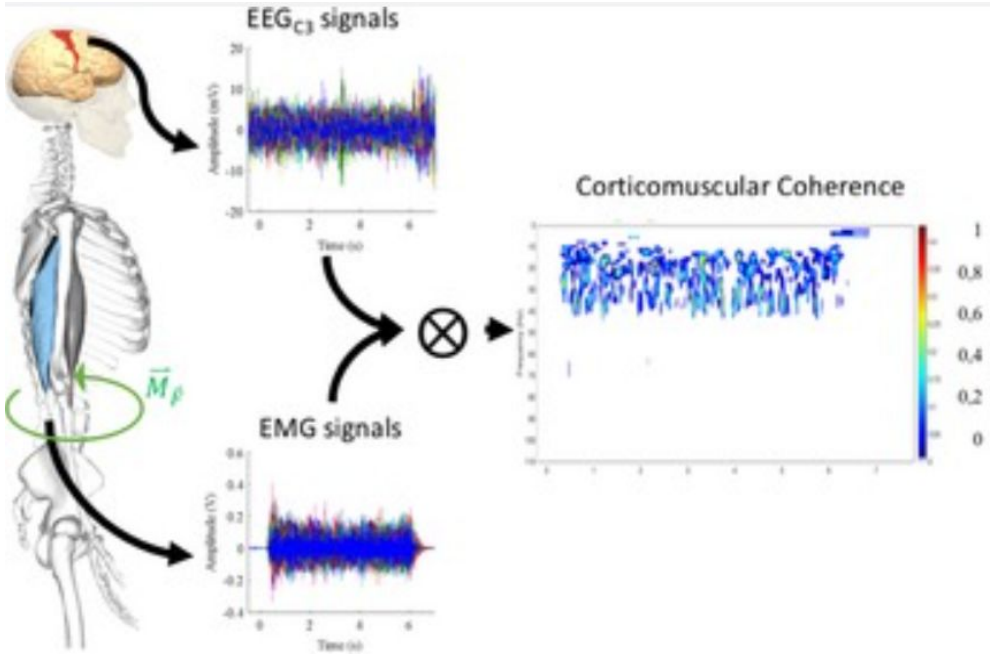
François Hug, Sylvain Dorel. Electromyographic analysis of pedaling: A review. Journal of Electromyography and Kinesiology, 2009, 19 (2), pp.182-198. 10.1016/j.jelekin.2007.10.010. hal- 01839025

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

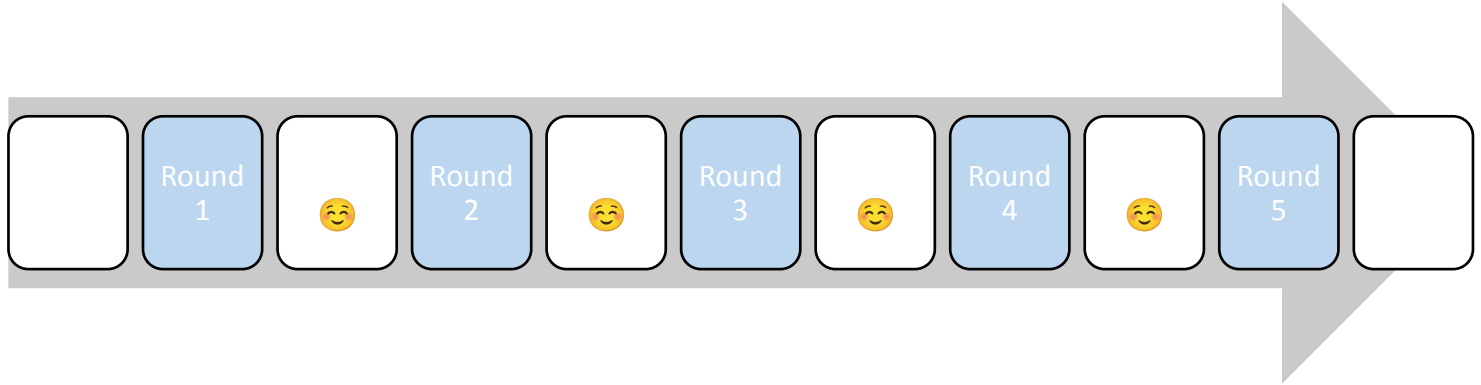


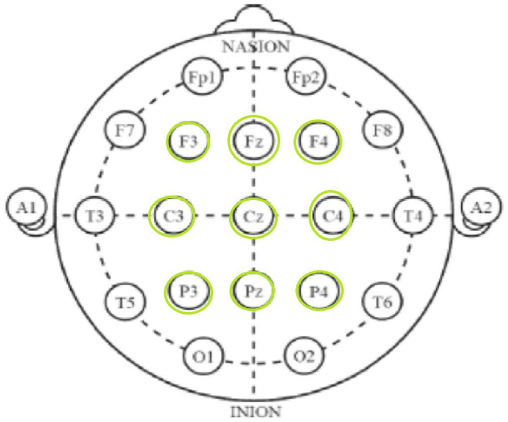


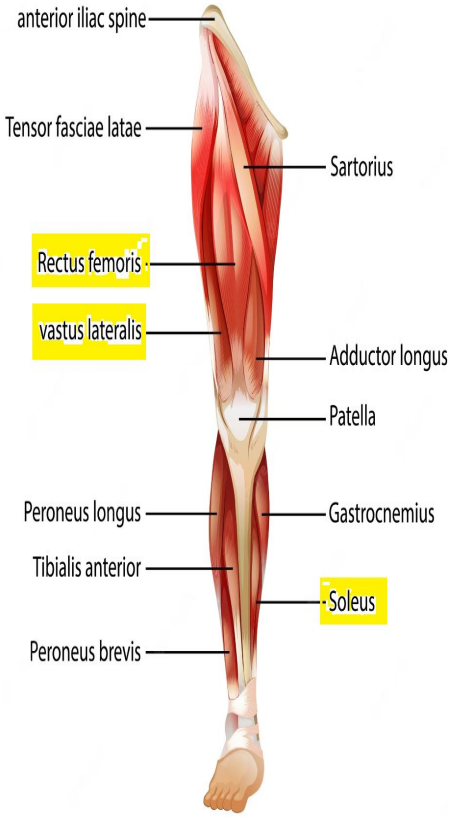
[1] Liu J, Sheng Y and Liu H (2019) Corticomuscular Coherence and Its Applications: A Review. Front. Hum. Neurosci. 13:100. doi: 10.3389/fnhum.2019.00100

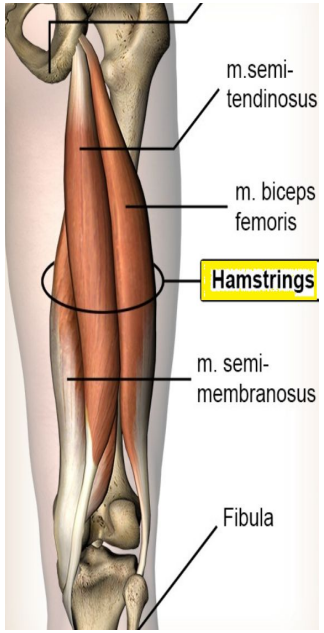
Our sensor data

- 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



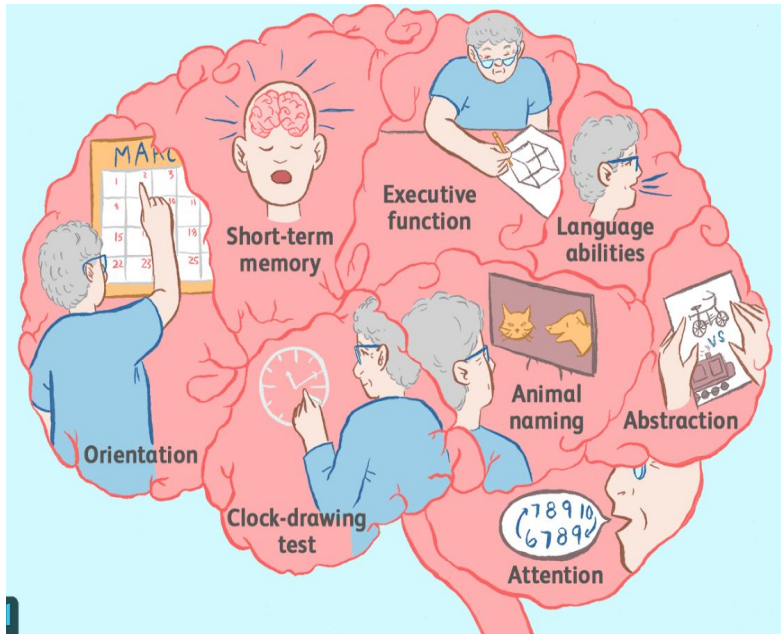






Our clinical data

- 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

Statistical Tests

- 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

Classification of 5-level intensities

- 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 clinical information

- 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

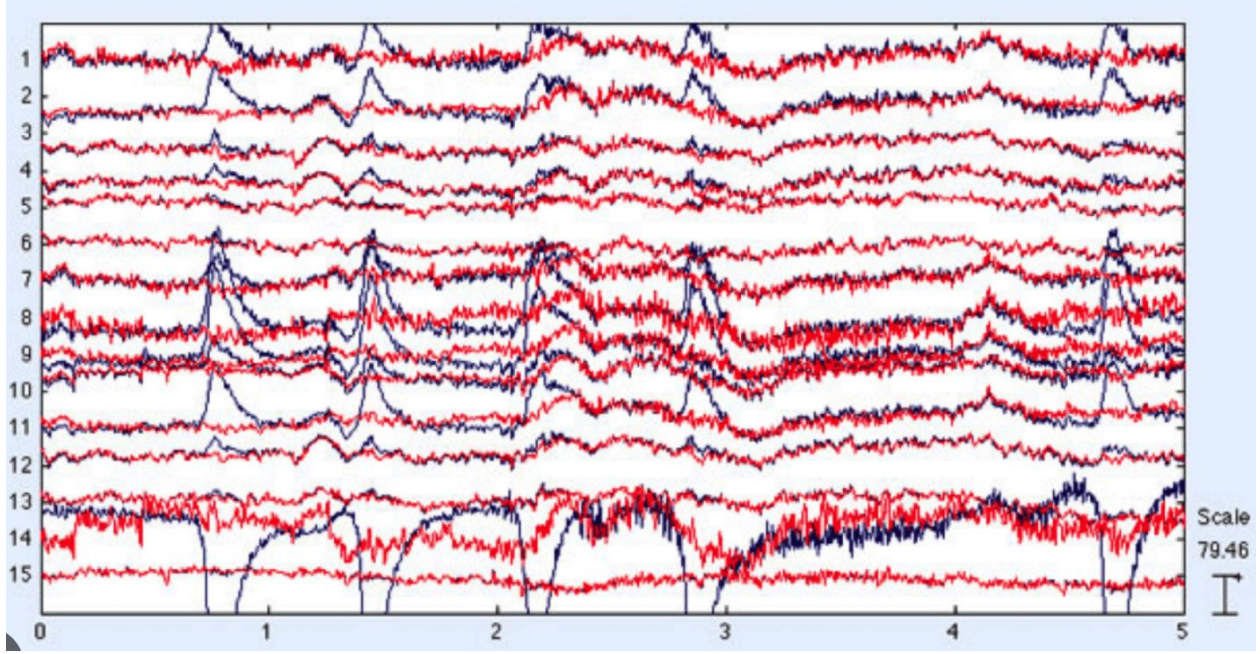
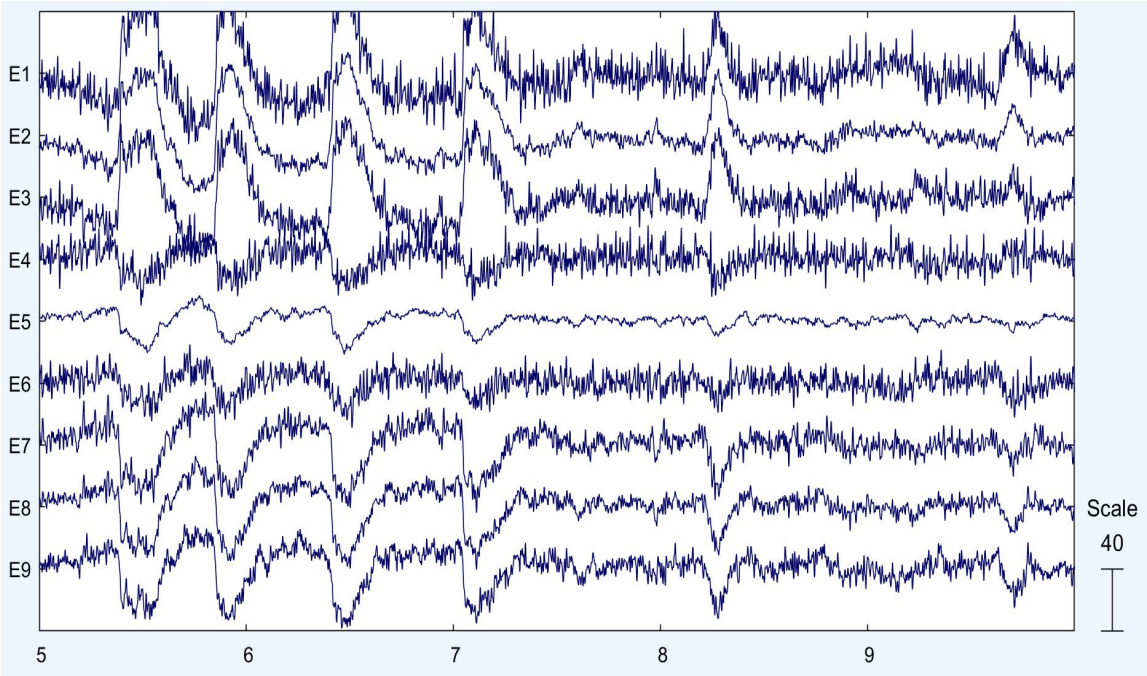


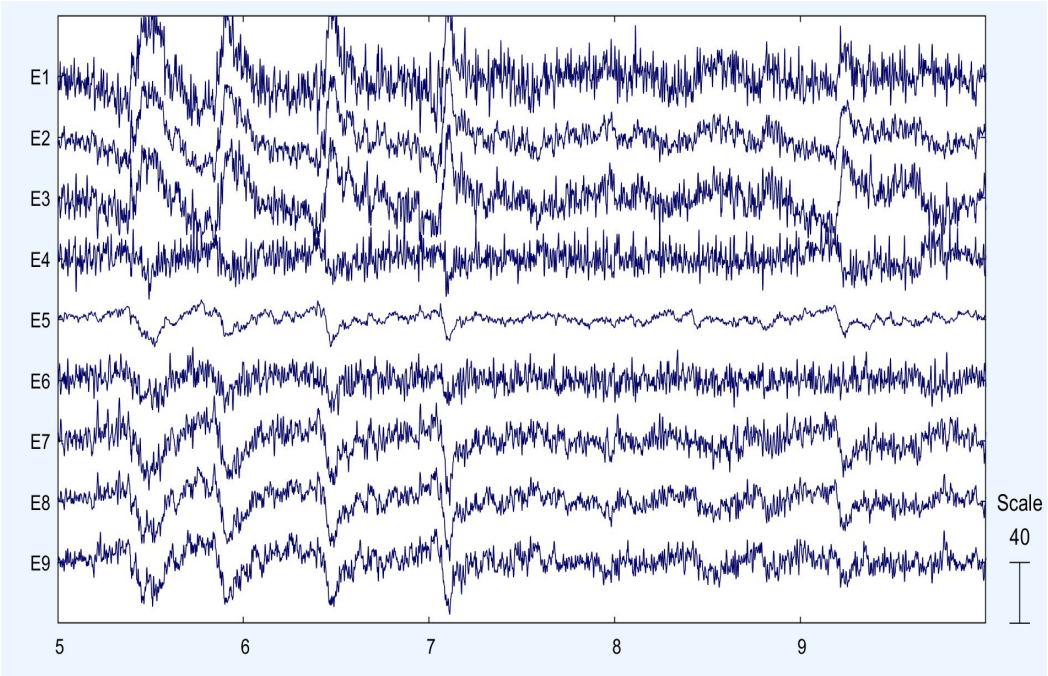
Figure 1: EEGLAB window, after preprocessing

EEG:RLS for removing EOG

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



Raw EEG, before using RLS

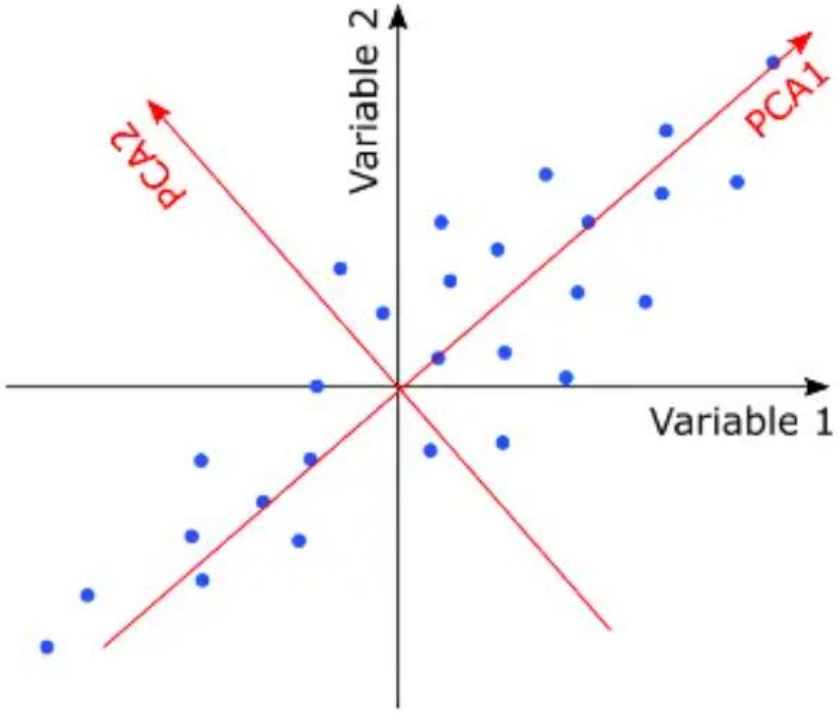


clean EEG, after using RLS

Gomez-Herrero, G. et al., *Automatic Removal of Ocular Artifacts in the EEG without an EOG Reference Channel*, In Proceedings of the 7th Nordic Signal Processing Symposium, 2006. 10.1109/NORSIG.2006.275210.

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



Introduction
Literature Review cleaning
Cleaning Methods
Literature Review coherence
Coherence Methods
Result of Coherence
Quick Glance to The future
questions

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EEG: removing remaining artifact

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

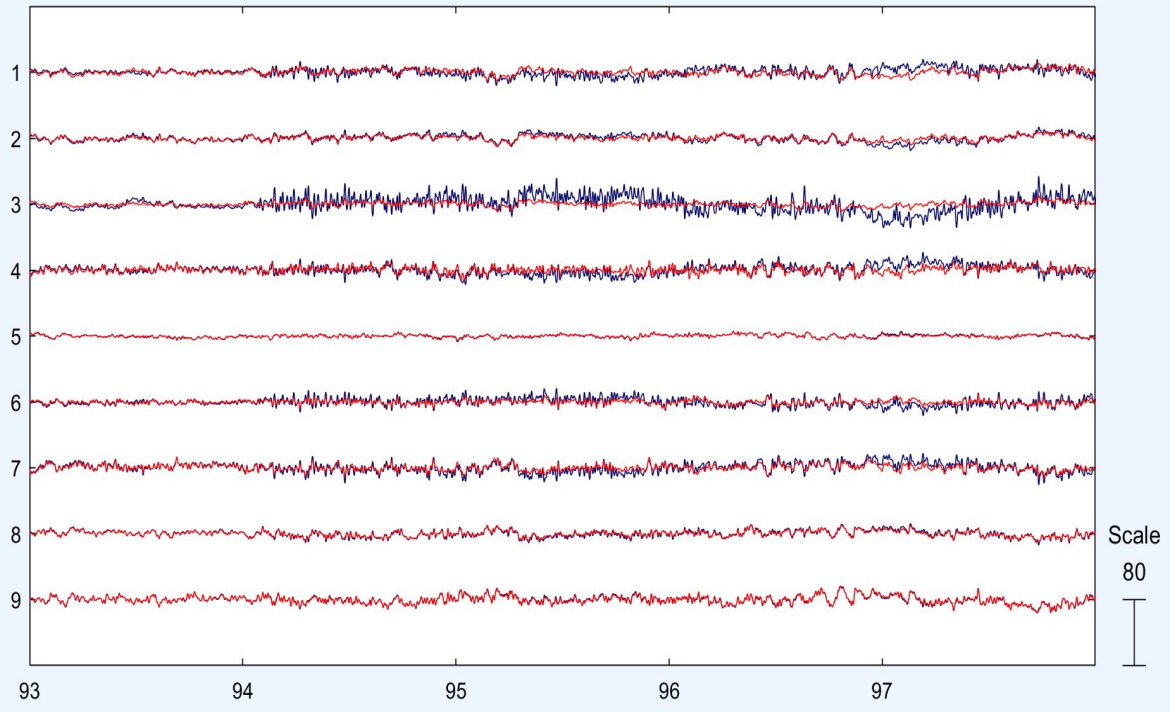


Figure 1: Output of ICA algorithm after removing IC 2 and 7 black: signal with artifact, red: clean signal

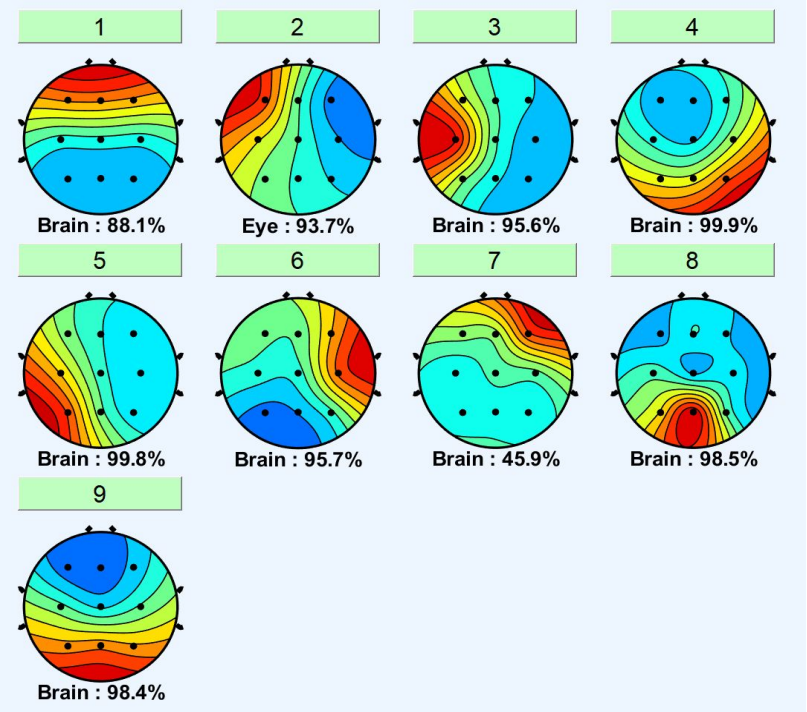
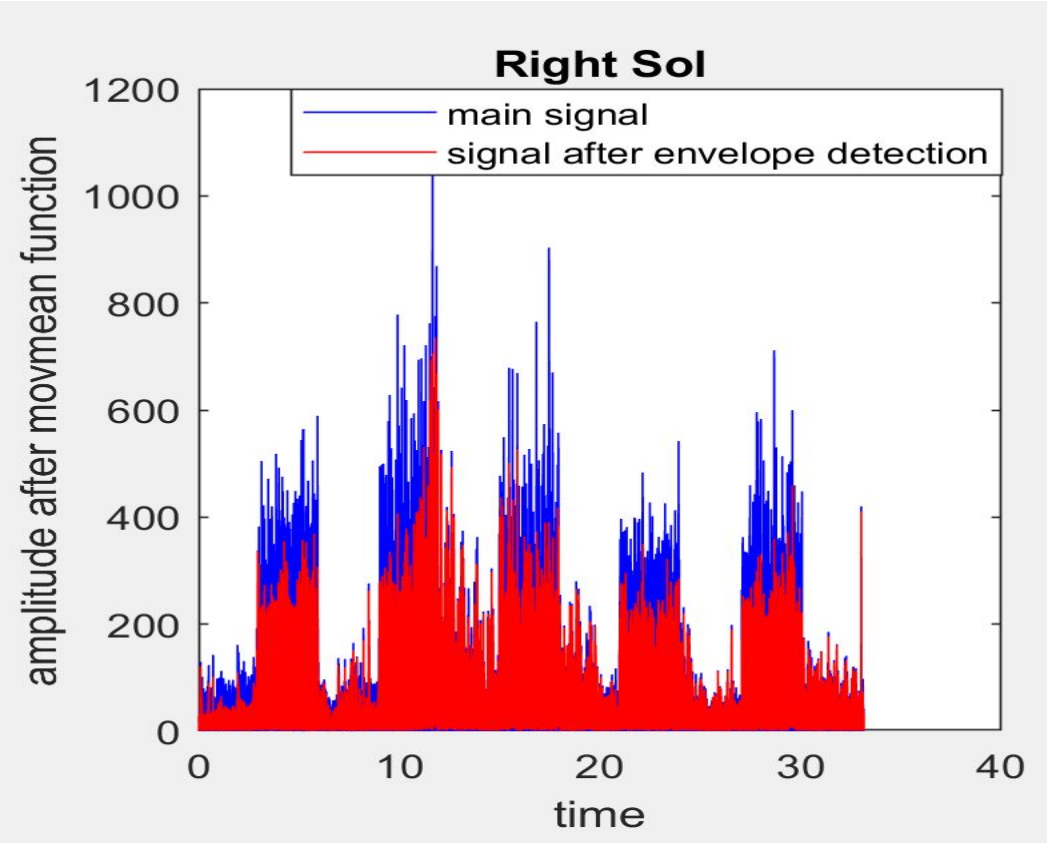


Figure 2: Output of ICLabel plugin as labels for ICs

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)

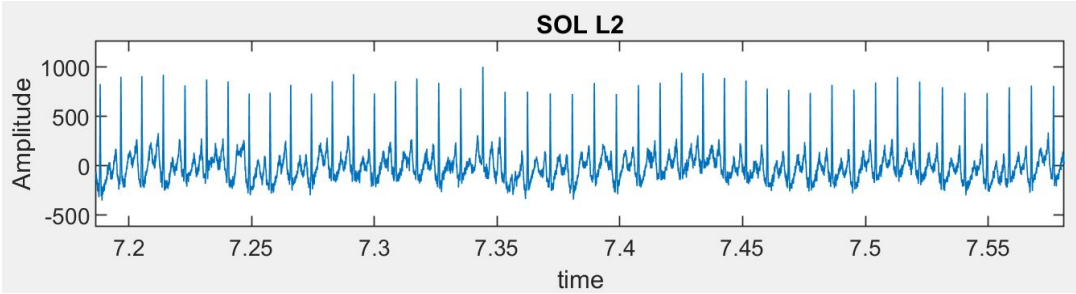


Figure 2

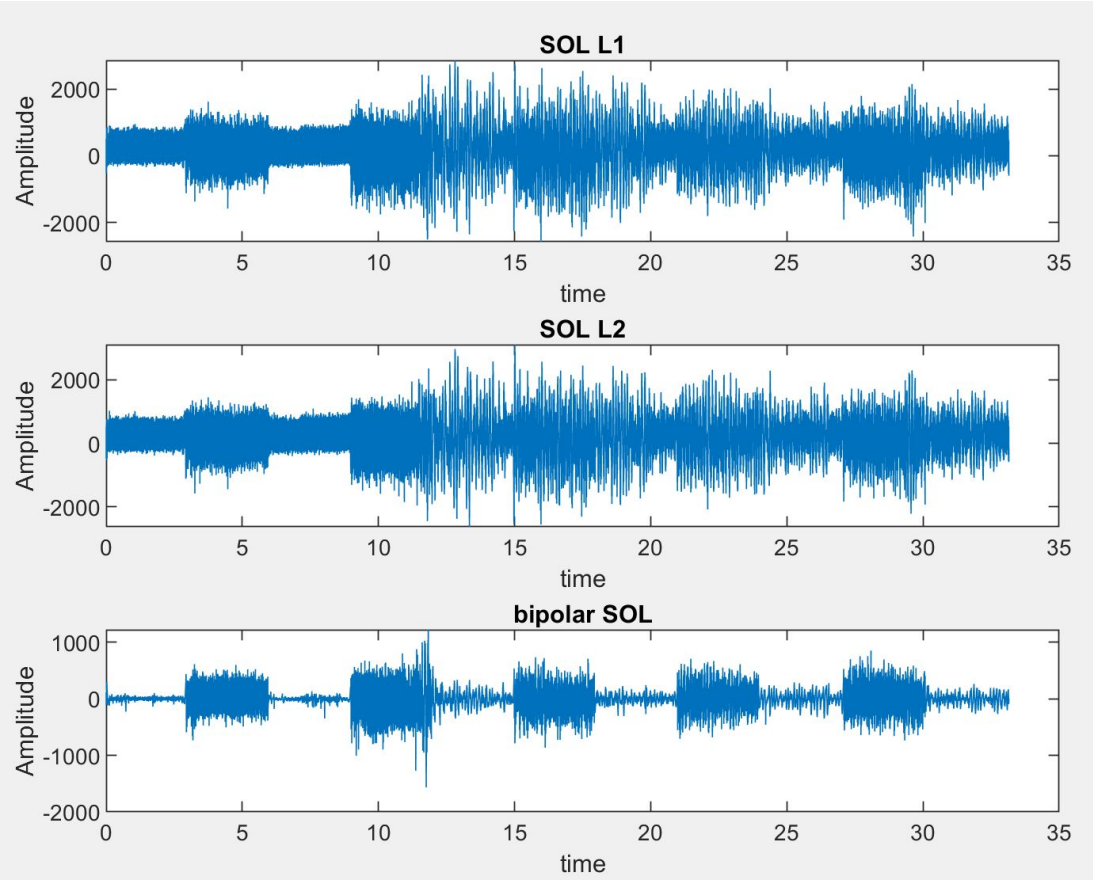


Figure 1

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)

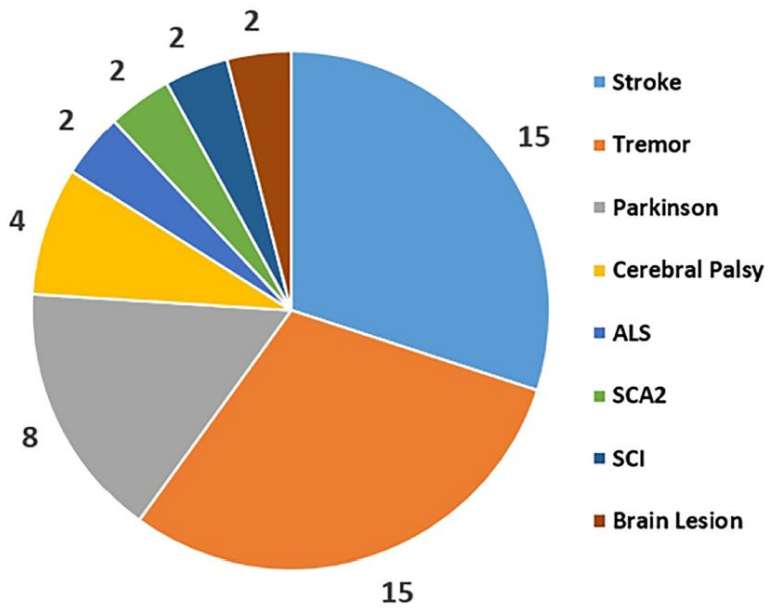
Cremoux, S., Tallet, J., Dal Maso, F., Berton, E. and Amarantini, D. (2017), Impaired corticomuscular coherence during isometric elbow flexion contractions in humans with cervical spinal cord injury. Eur J Neurosci, 46: 1991-2000. https://doi.org/10.1111/ejn.13641

Introduction
Literature Review cleaning
Cleaning Methods
Literature Review coherence
Coherence Methods
Result of Coherence
Quick Glance to The future
questions

Literature review for Coherence

[2] Corticomuscular Coherence and Its Applications: A Review

- 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



Liu J, Sheng Y and Liu H (2019) Corticomuscular Coherence and Its Applications: A Review. Front. Hum. Neurosci. 13:100.
doi: 10.3389/fnhum.2019.00100

Literature review for Coherence

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

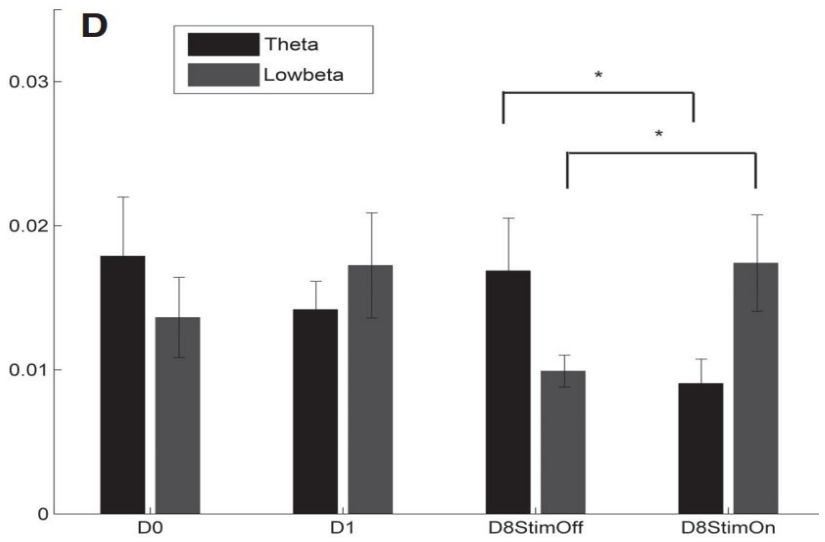
- 7 PD patients
- EMG: abductor pollicis brevis (APB), first dorsalis interosseus muscles (FDI), with references localized over the distal interphalangeal joint of the thumb (APB) and the distal interphalangeal joint of the index finger
- EEG: FC1, C1, CP1, FC3, C3, CP3, FC2, C2, CP2, FC4, C4, CP4
- 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

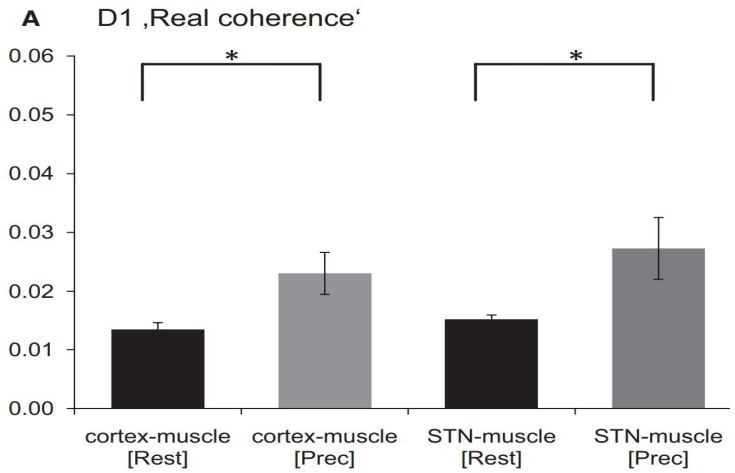
Method:

- 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)





Park H, Kim JS, Paek SH, Jeon BS, Lee JY, Chung CK. Cortico-muscular coherence increases with tremor improvement after deep brain stimulation in Parkinson's disease. Neuroreport. 2009 Oct 28;20(16):1444-9. doi: 10.1097/WNR.0b013e328331a51a. PMID: 19738496.

Literature review for Coherence

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

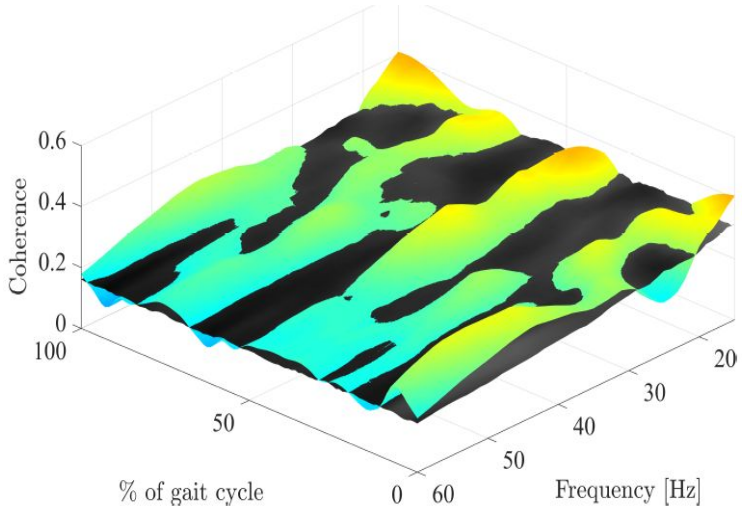
- Young (<30) and elderly (>65) group
- 3 different walking
  - Spontaneous walking (SW)
  - Walking with cognitive tasks (counting down and saying loud) (DW)
  - Walking with targets on the floor (TW)
- RF and SM are excluded. C3 and C4 are meaningful.
- Contralateral relationship: c3 with right distal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



Introduction
Literature Review cleaning
Cleaning Methods
Literature Review coherence
Coherence Methods
Result of Coherence
Quick Glance to The future
questions

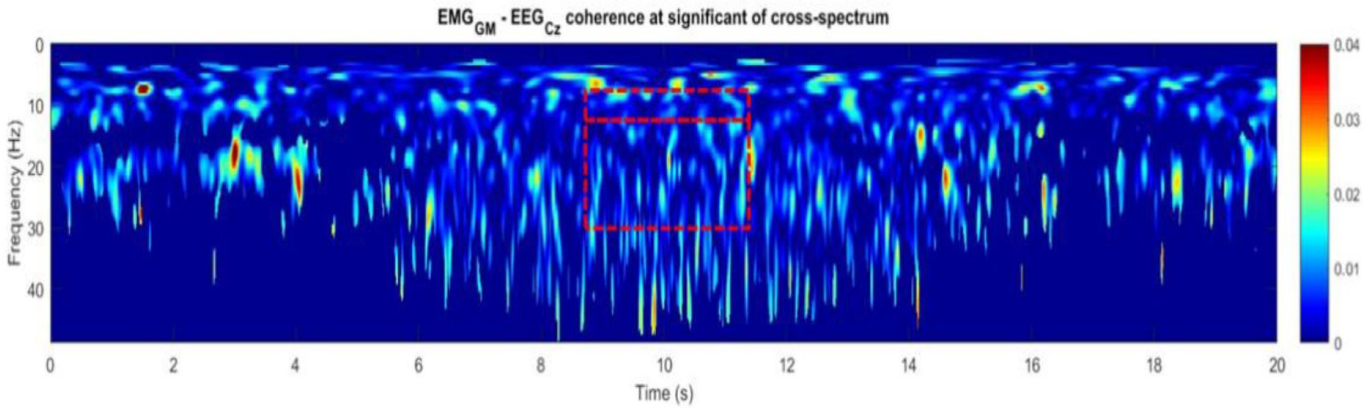
L. Caffi, S. Boccia, V. Longatelli, E. Guanziroli, F. Molteni, A. Pedrocchi
bioRxiv 2022.05.19.492238; doi: https://doi.org/10.1101/2022.05.19.492238

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

Elie, D.; Barbier, F.; Ido, G.; Cremoux, S. Corticomuscular Coherence and Motor Control Adaptations after Isometric Maximal Strength Training. *Brain Sci.* **2021**, *11*, 254. https://doi.org/10.3390/brainsci11020254

Literature review for Coherence

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

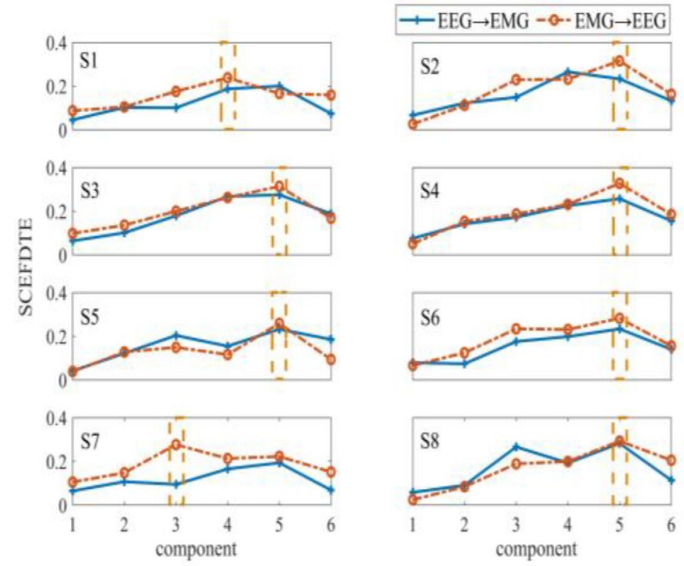
- Two movement
  - Knee-jerk reflex (cerebellar to muscle is weaker)
  - Inhibited knee-jerk reflex (cerrebellar to muscle would be greater)
- C3 EEG, quadriceps muscle EMG

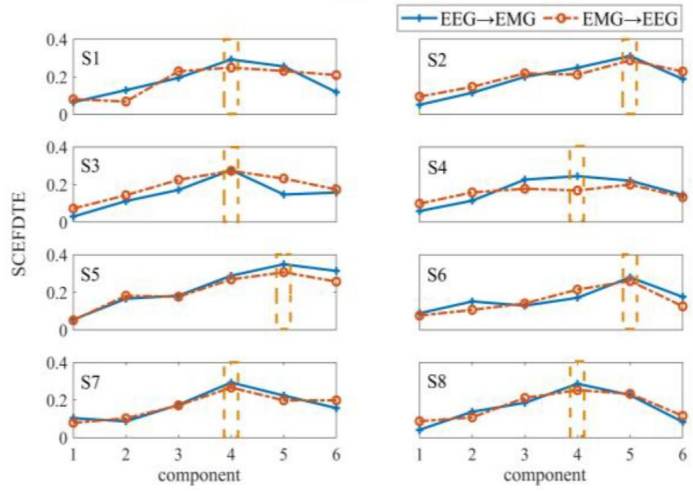
Method:

- 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)





Z. Shi, Y. Li, H. Lin and F. Zhu, "Coupling Analysis of EEG and EMG Signals Based on Transfer Entropy after Consistent Empirical Fourier Decomposition," *2022 8th International Conference on Control, Automation and Robotics (ICCAR)*, Xiamen, China, 2022, pp. 436-441, doi: 10.1109/ICCAR55106.2022.9782665.

Literature review for Coherence

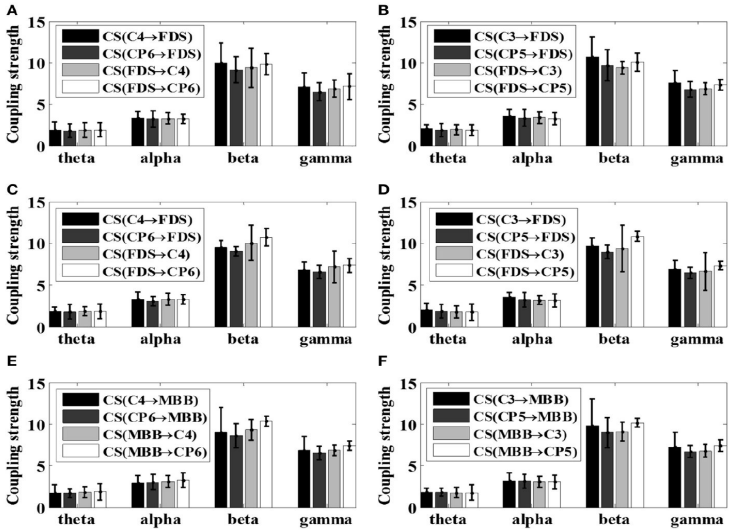
[10] Electroencephalogram–Electromyography Coupling Analysis in Stroke Based on Symbolic Transfer Entropy

- 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

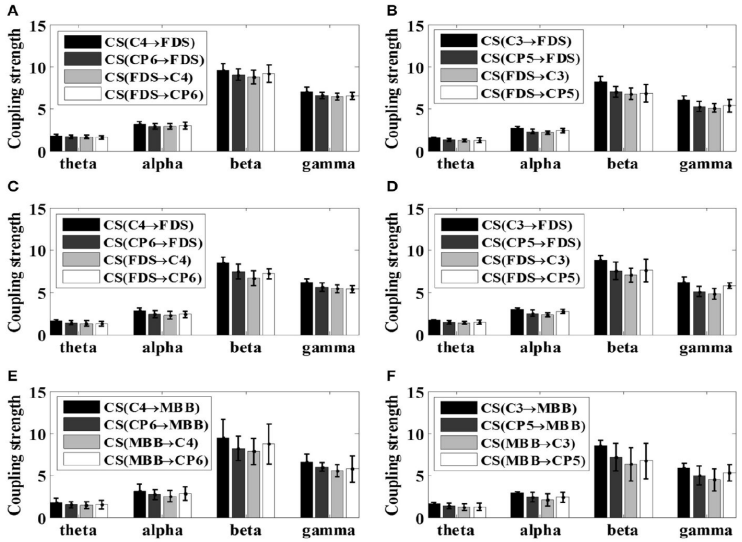
Method:

- 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



Patient group: (A) Left 5 kg; (B) right 5 kg; (C) left 10 kg; (D) right 10 kg; (E) left elbow flexion; (F) right elbow flexion.



Cpntrol group: (A) Left 5 kg; (B) right 5 kg; (C) left 10 kg; (D) right 10 kg; (E) left elbow flexion; (F) right elbow flexion.

Gao Y, Ren L, Li R and Zhang Y (2018) Electroencephalogram– Electromyography Coupling Analysis in Stroke Based on Symbolic Transfer Entropy. Front. Neurol. 8:716. doi: 10.3389/fneur.2017.00716

Literature review for Coherence

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

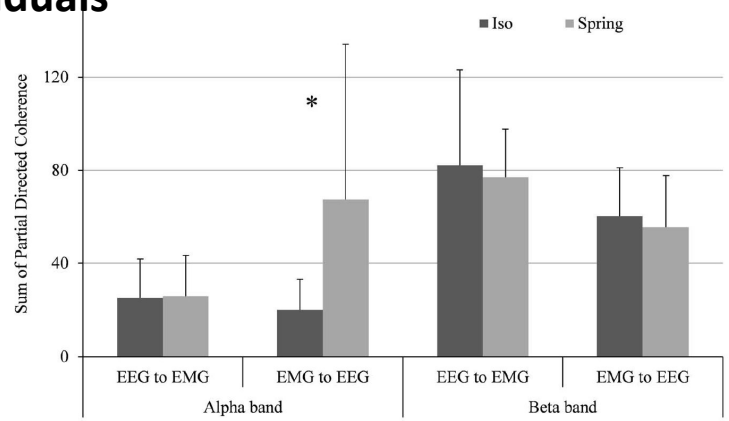
- Considering CMC in alpha band by inducing artificial tremor, given the absence of it in healthy people
- 13 volunteers, biceps brachii (BB) muscle EMG, C3, C5, FC5, FC3, CP5 and CP3 EEG
- Elbow flexor against a spring load and isometric condition of 20% of Maximal Voluntary Isometric Contraction (MVIC)

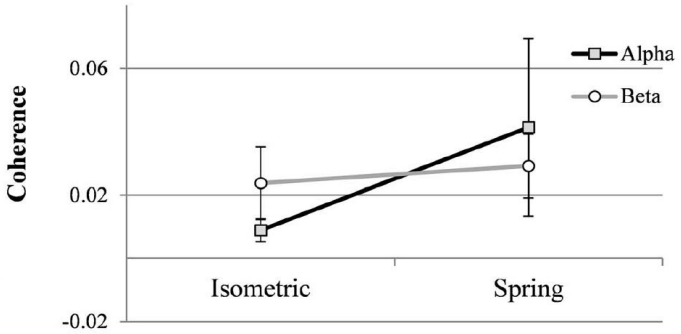
Method:

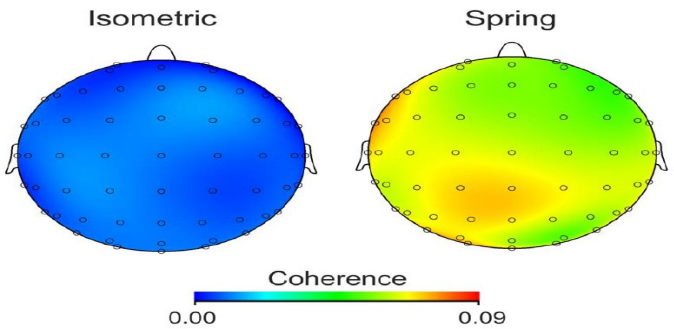
- Partial directed coherence using vector autoregressive

Result:

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







Budini F, McManus LM, Berchicci M, Menotti F, Macaluso A, et al. (2014) Alpha Band Cortico-Muscular Coherence Occurs in Healthy Individuals during Mechanically-Induced Tremor. PLOS ONE 9(12): e115012. https://doi.org/10.1371/journal.pone.0115012

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)

Introduction
Literature Review cleaning
Cleaning Methods
Literature Review coherence
Coherence Methods
Result of Coherence
Quick Glance to The future
questions

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)

Introduction
Literature Review cleaning
Cleaning Methods
Literature Review coherence
Coherence Methods
Result of Coherence
Quick Glance to The future
questions

Result of coherence : spectral coherence

Plots of some Significant difference in:

- Contralateral:
  - Figure1: (C3-right vas), intensity 50, beta band (p-value = 0.0062)
- Ipsilateral:
  - Figure 2: (C3-left vas), intensity 60, alpha bans (p-value = 0.0052)

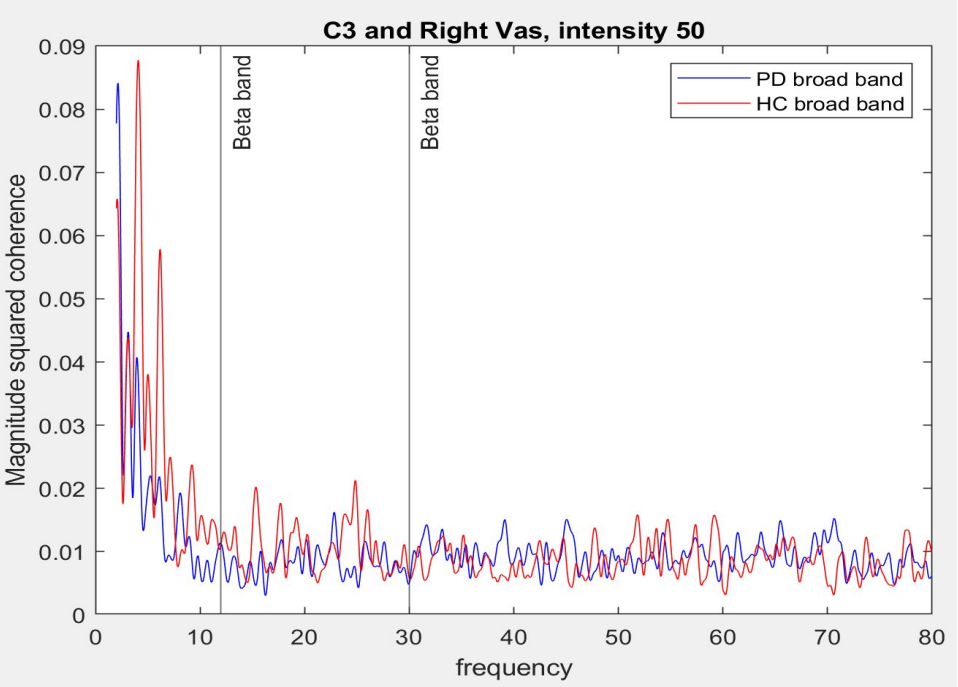


Figure 1

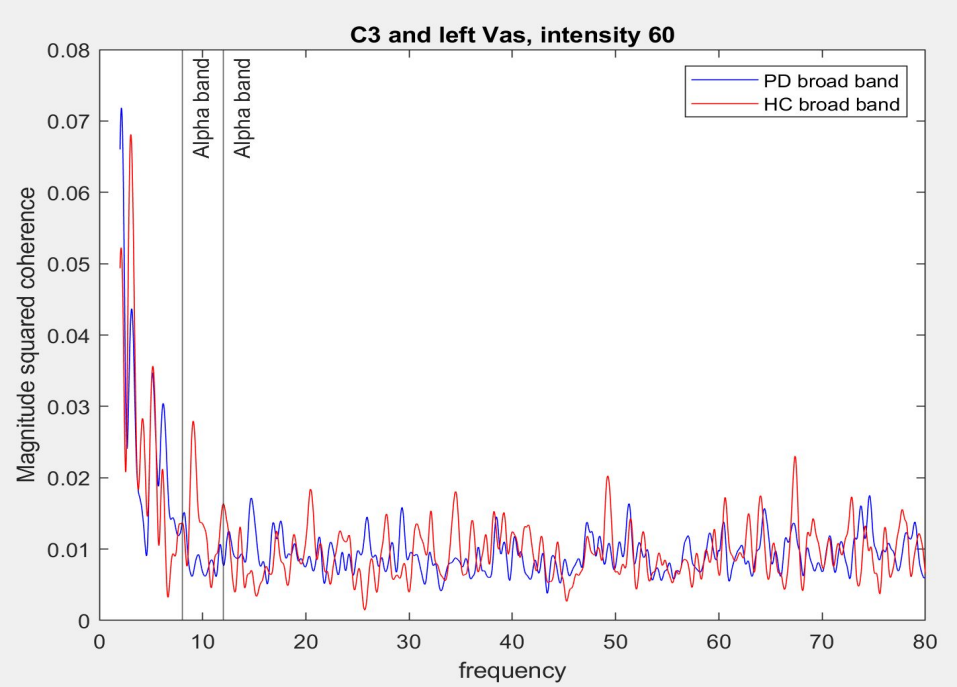


Figure 2

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)

Result of coherence : wavelet coherence

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

Introduction
Literature Review cleaning
Cleaning Methods
Literature Review coherence
Coherence Methods
Result of Coherence
Quick Glance to The future
questions

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

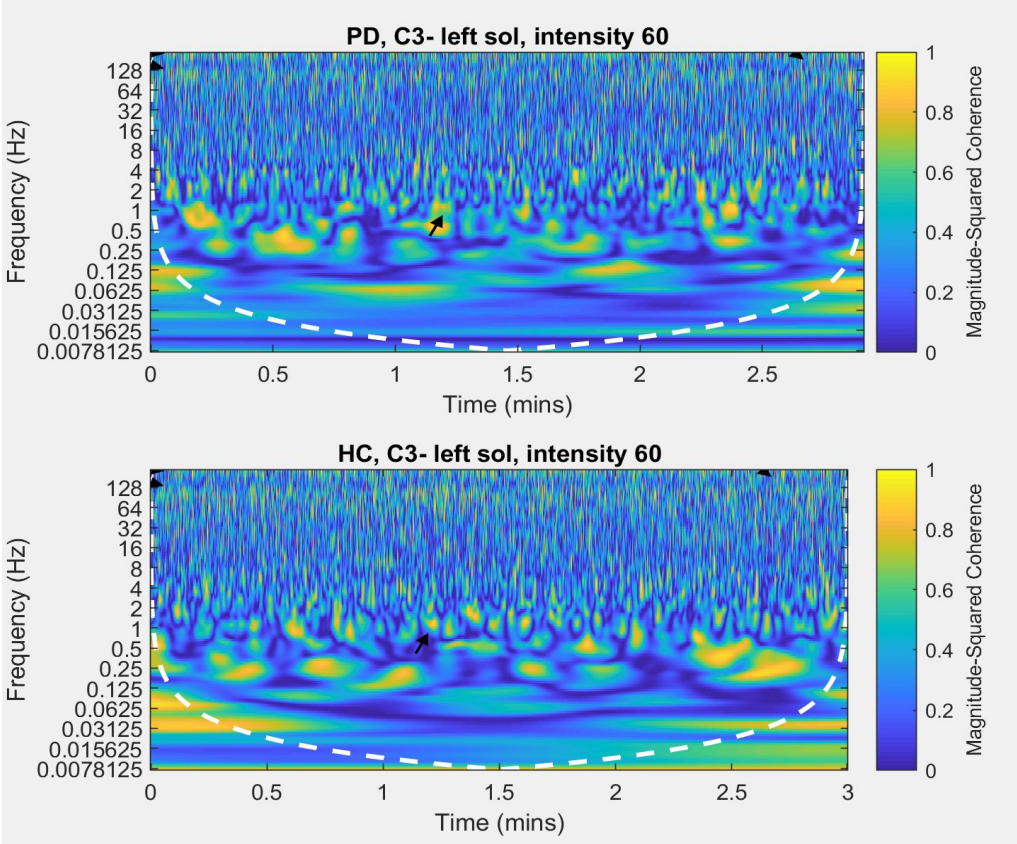


Figure 1

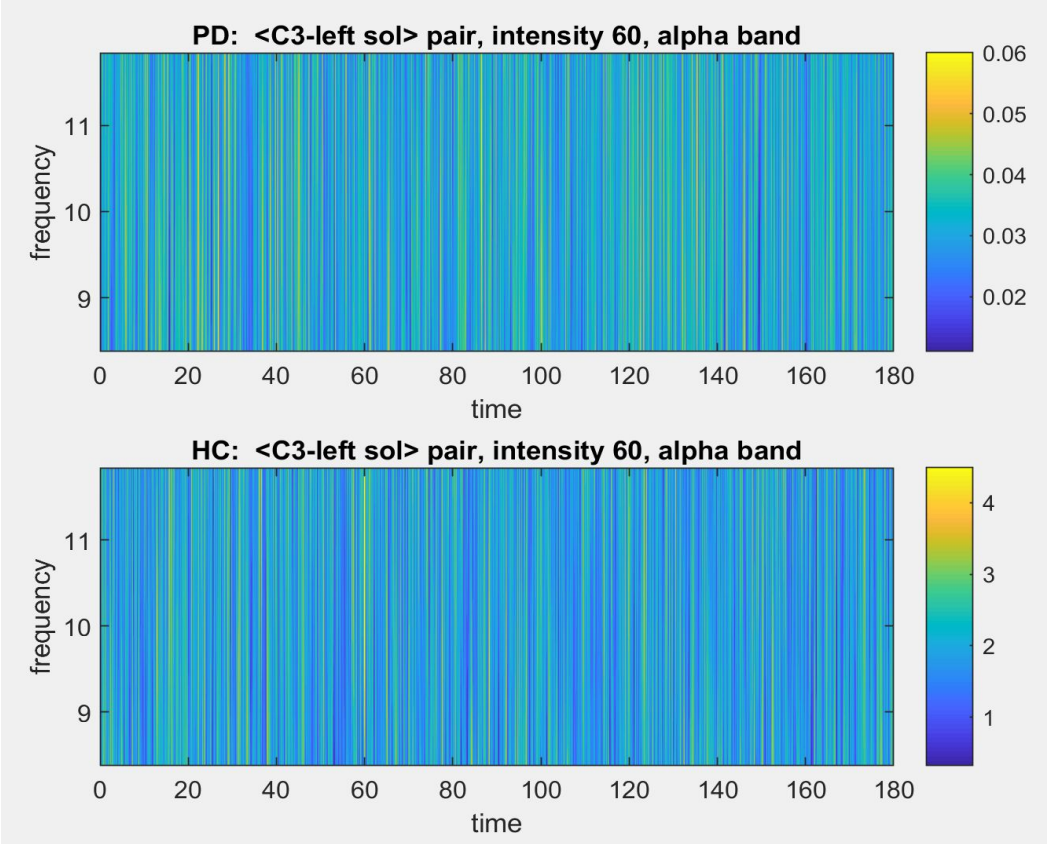


Figure 2

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

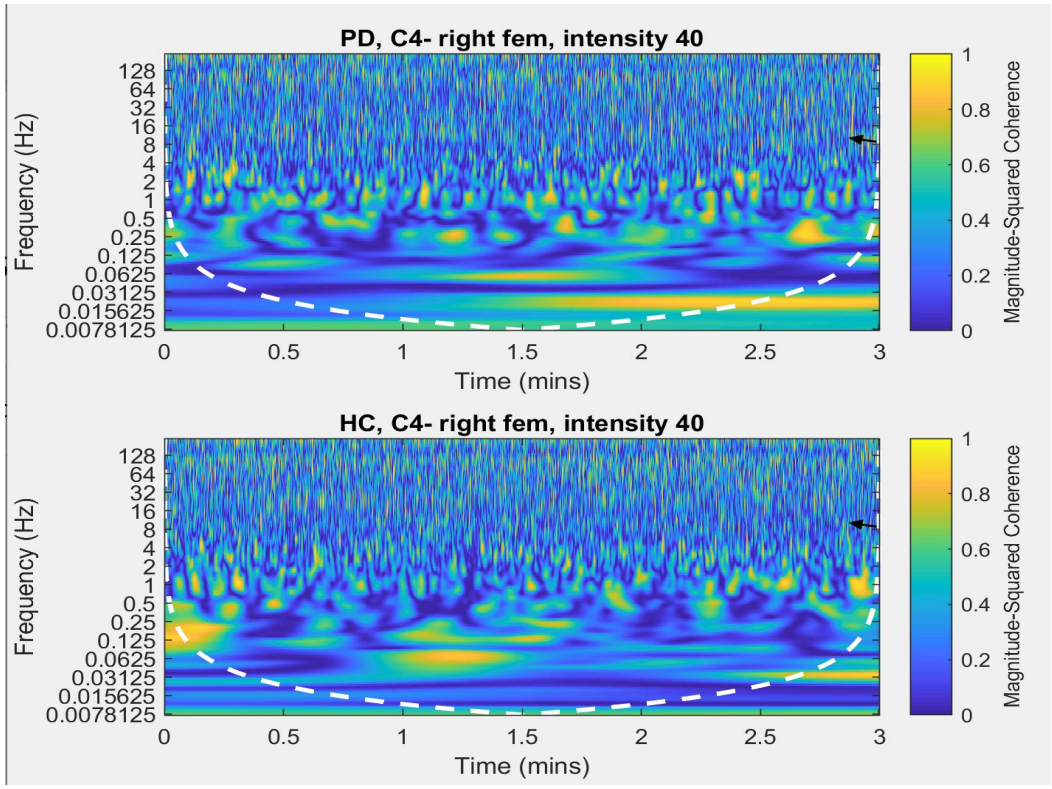


Figure 1

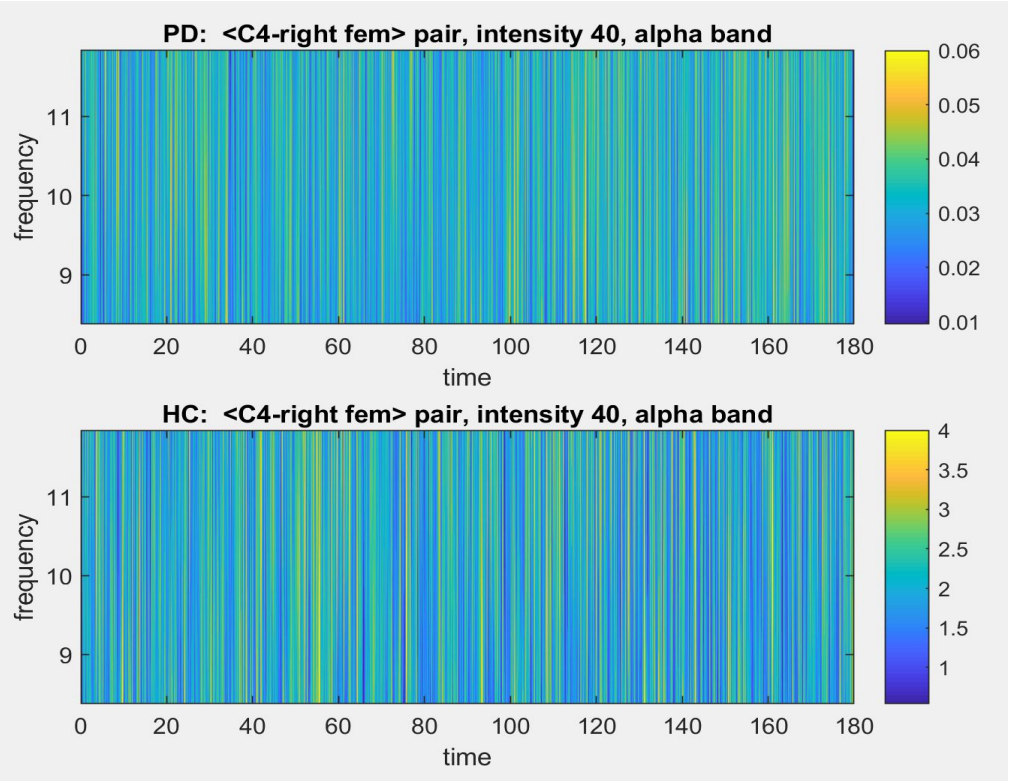


Figure 2

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 group> 0.05)
- Figure 1: MI of PD and control group in a

c3-left sol pair, alpha band, intensity 30

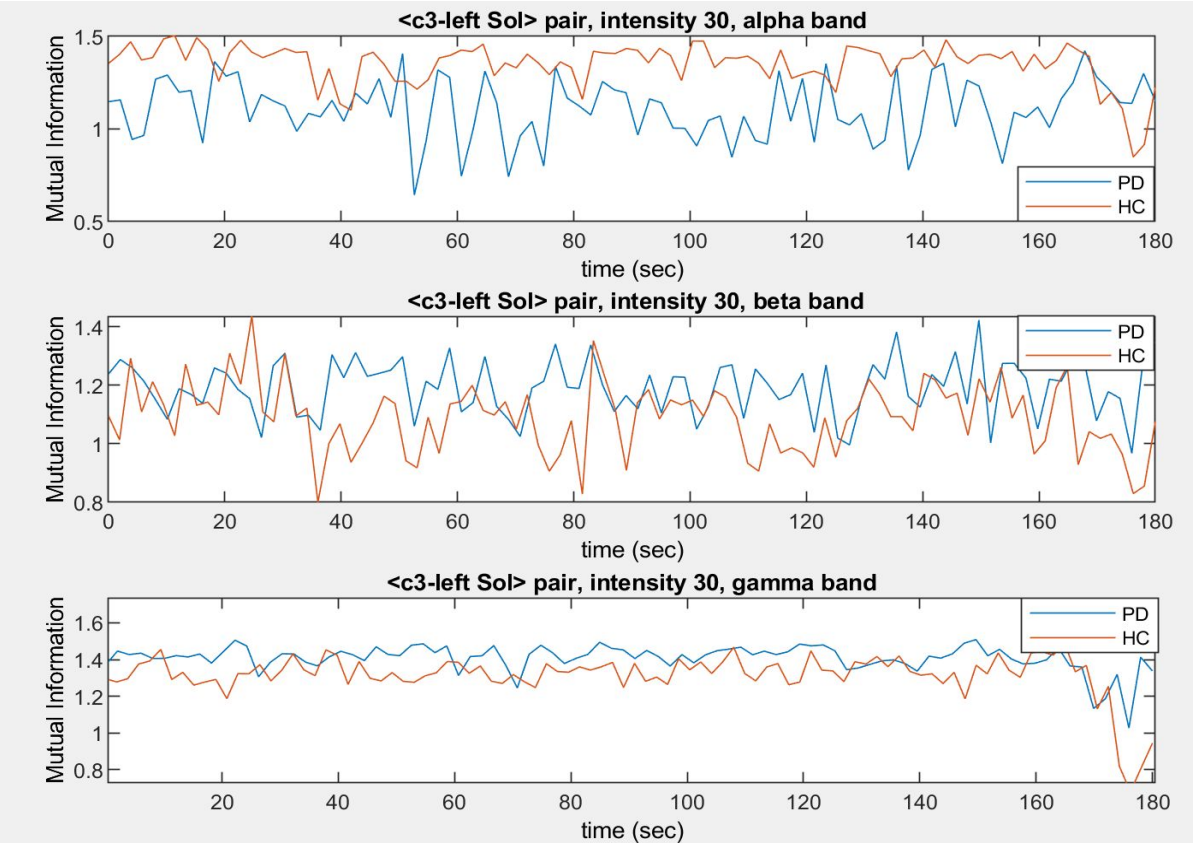
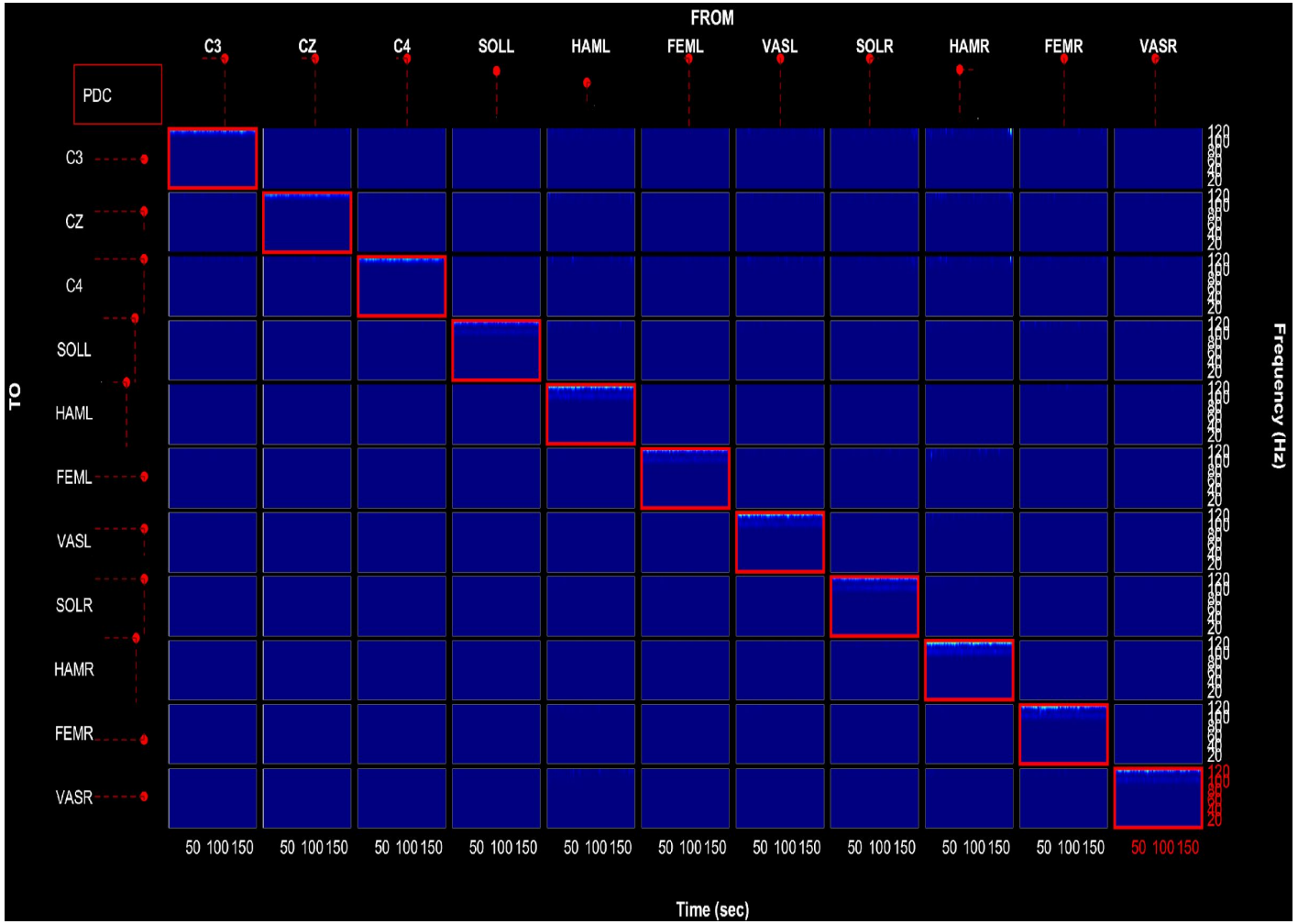


Figure 1: MI of PD and control subject

Result of coherence: PDC

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

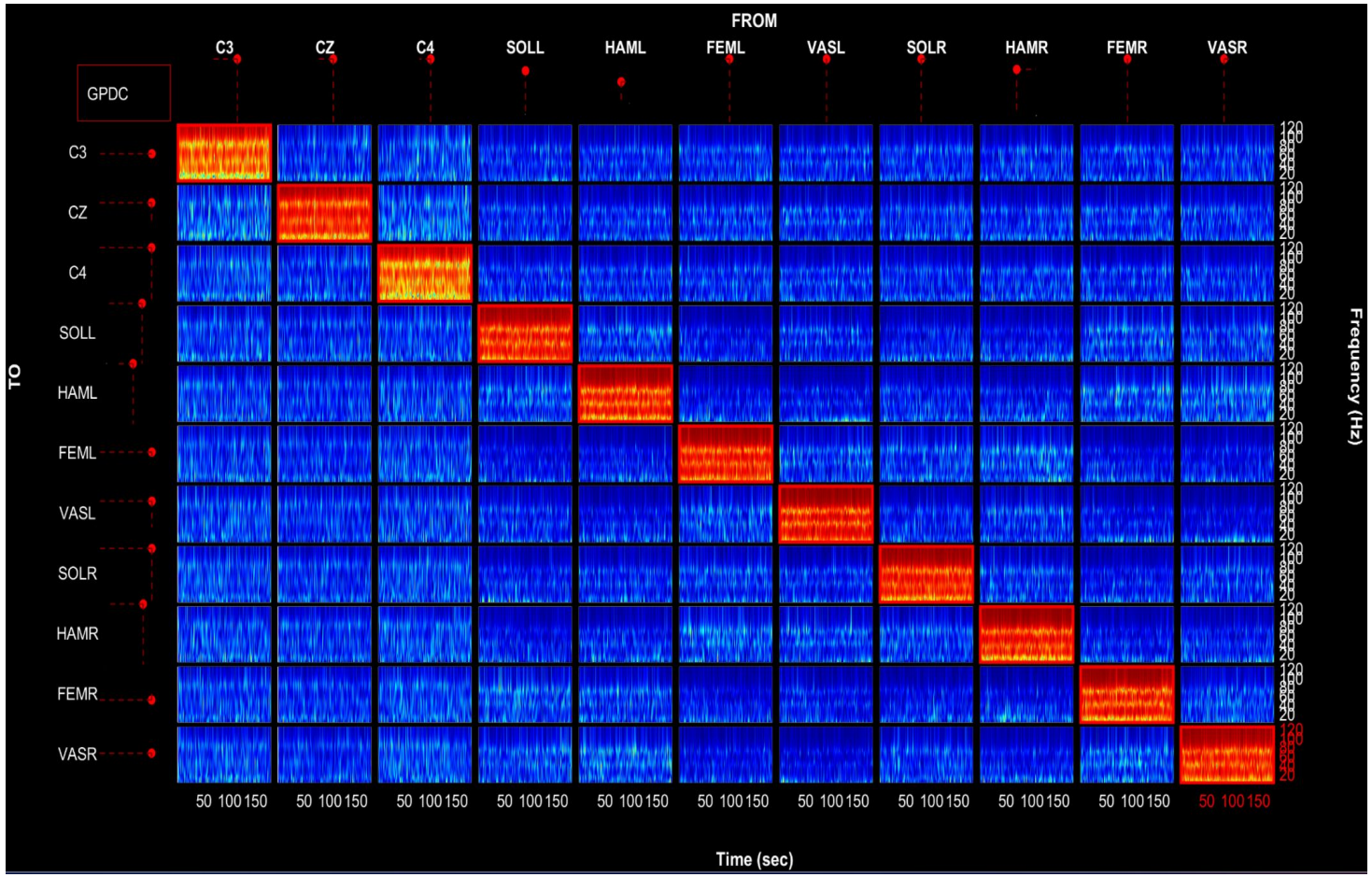


Figure 1: GPDC for subject 1

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

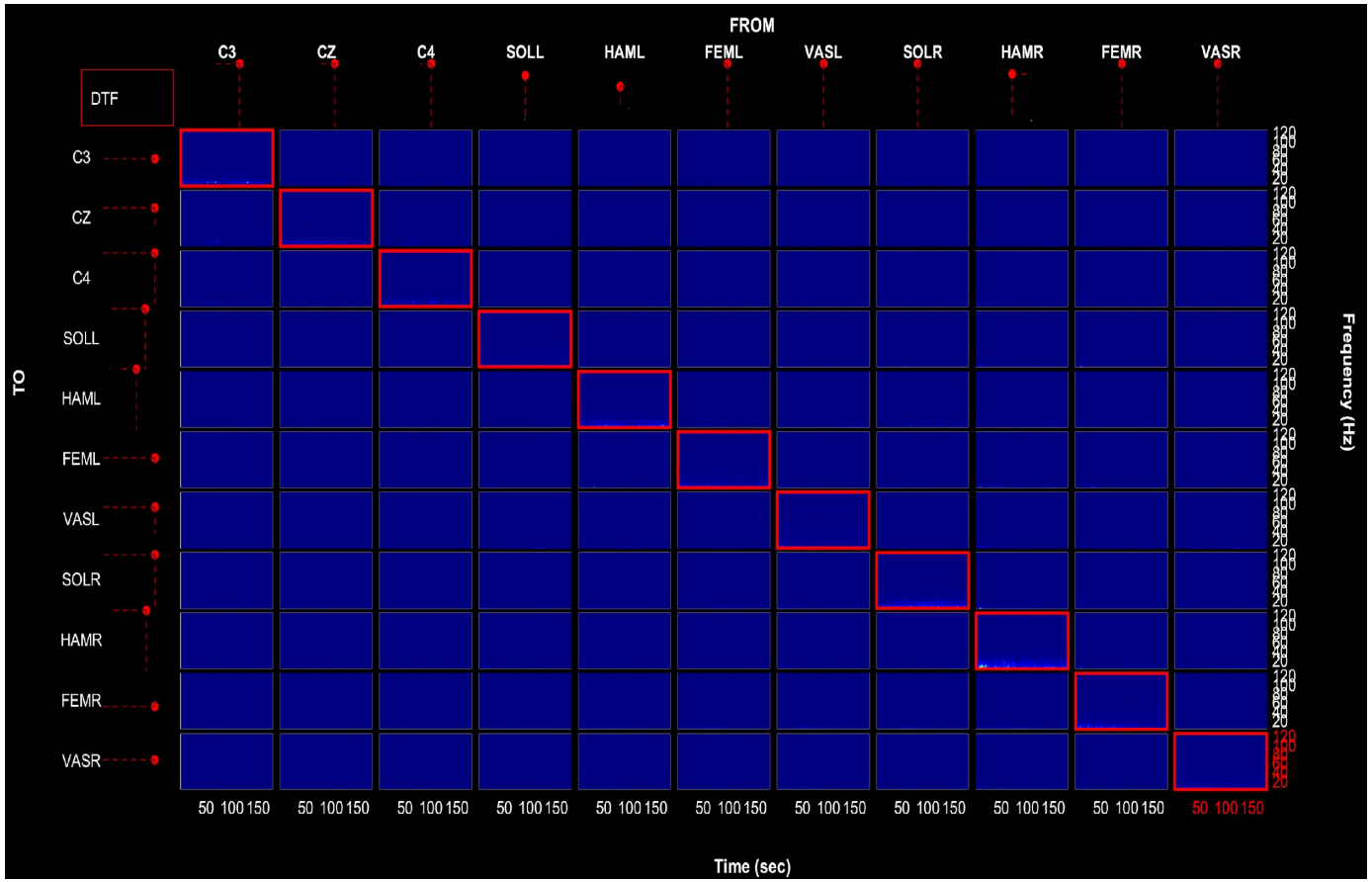
Significant difference in:

- 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)

Introduction
Literature Review cleaning
Cleaning Methods
Literature Review coherence
Coherence Methods
Result of Coherence
Quick Glance to The future
questions

Questions

Any question? ☺️

Introduction
Literature Review cleaning
Cleaning Methods
Literature Review coherence
Coherence Methods
Result of Coherence
Quick Glance to The future
questions

Thanks for your attention ☺️