Update on Longitudinal Monitoring Project and Sleep Project

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Background

- The prevalence of Parkinson's disease is increasing
- Clinician availability is limited
- Evaluate a model for longitudinal monitoring of individuals living with PD that:
  - Integrates seamlessly with patients' lifestyles
  - Provides the data physicians need to make better clinical decisions
- Focus on the development of algorithms to analyse the large amount of data collected

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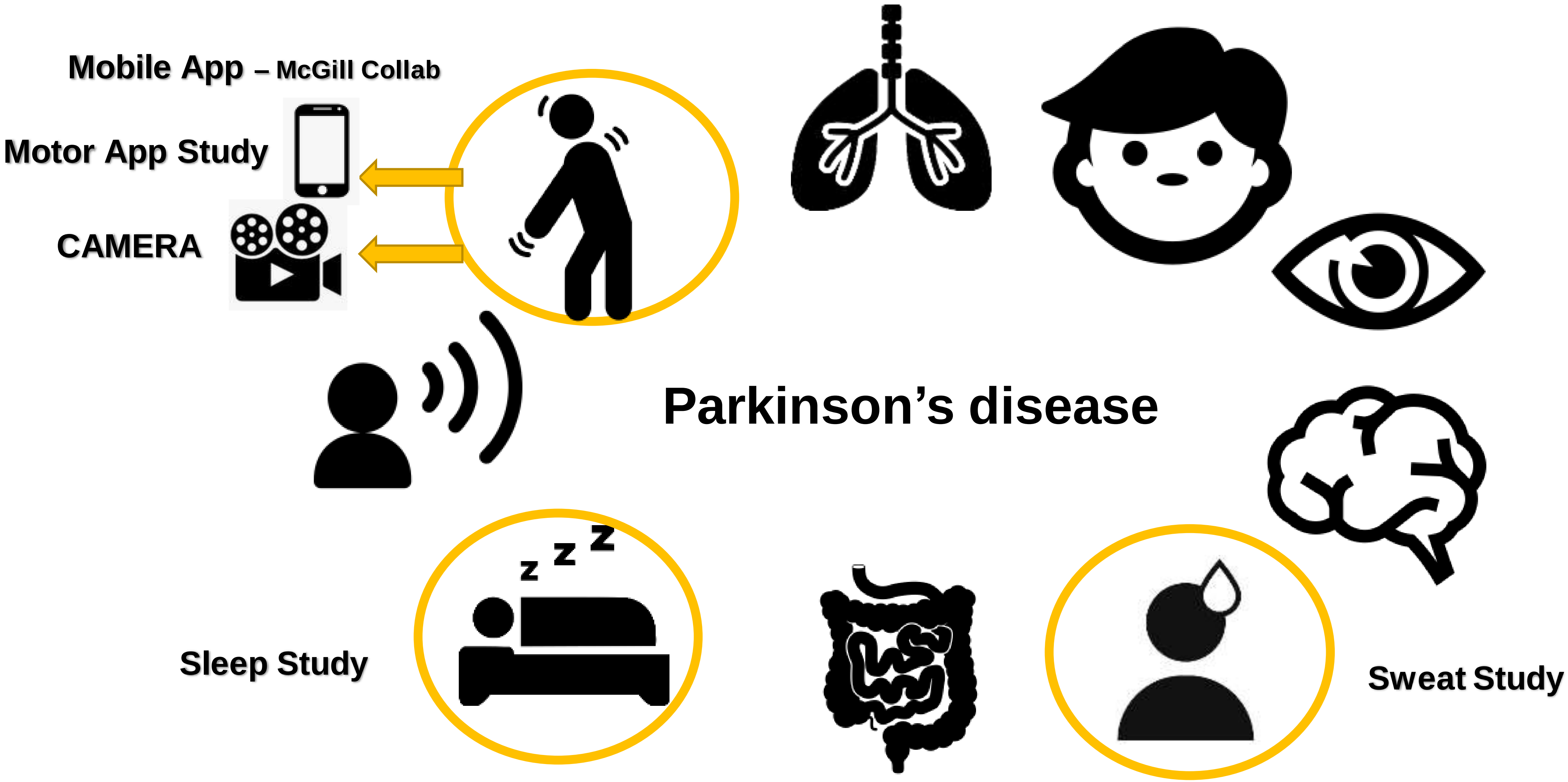

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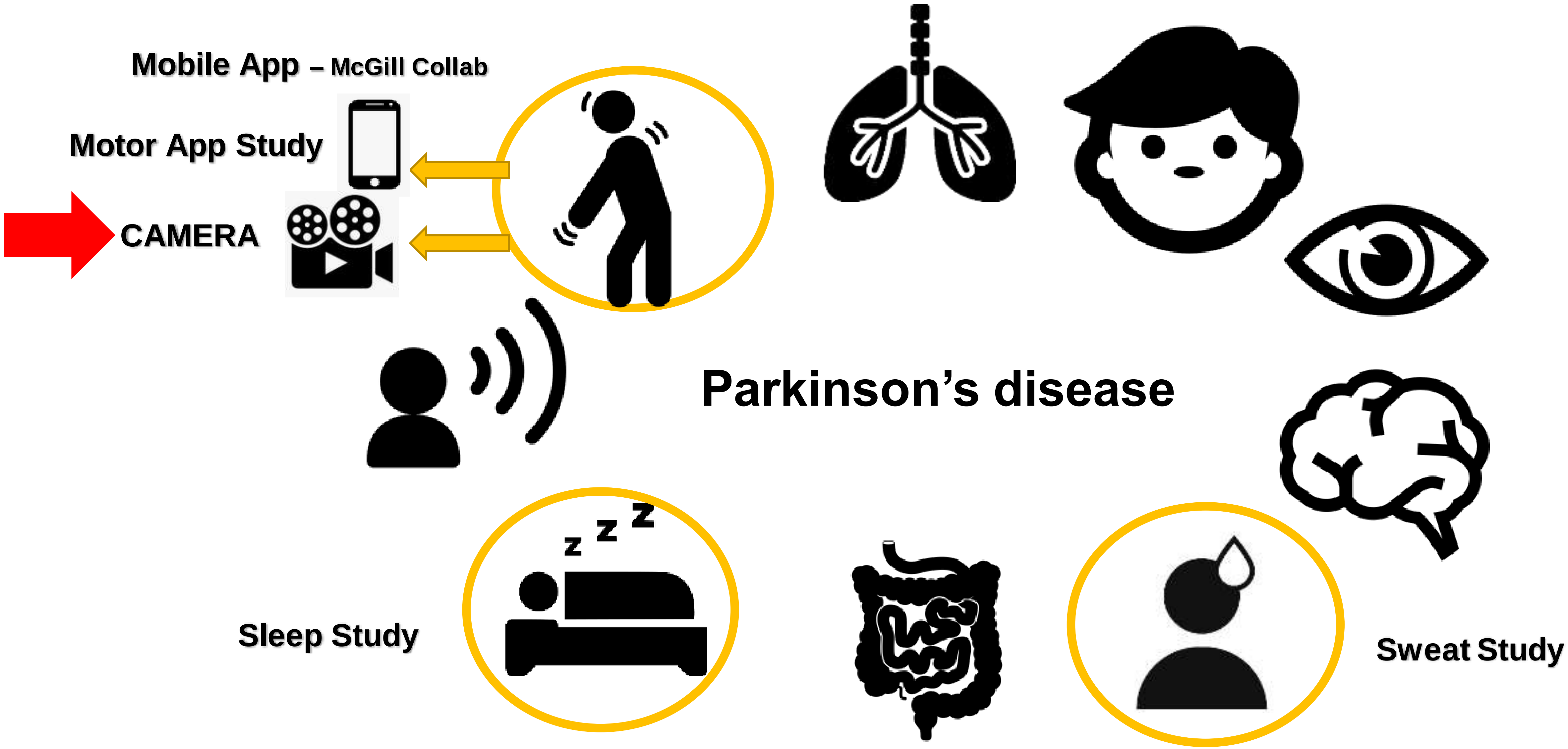

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CAMERA STUDY

Focus Group

Confidential Automatic Monitoring, Examination, and Recognition of disease Activity (CAMERA): Application to Parkinson (and Alzheimer) Diseases

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Background

- Assessments of Parkinson's symptoms are only performed once a year

- Monitoring cameras and patient-worn sensors currently available have many disadvantages
  - Only measure a limited number of disease aspects, such as falls
  - Not specifically developed for individuals with Parkinson's
  - Places a burden on the user
  - Create privacy concerns

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Goal of the Study

- Our goal is it to develop a novel monitoring tool:
  - Specifically developed to monitor Parkinson's symptoms
  - Immediately anonymizes the data via stick figures
  - Does not store or transmit data

- The tool may provide physicians with an ongoing report on the progression of the disease

3 Study Visits Overview

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Focus Group Visit

Subjects will be able to express their views, ideas and concerns regarding the monitoring tool for the in home facial expression and gait analysis

- Subjects will be asked to partake in a semi-structured focus group (guided by a clinical ethicist) to provide feedback on the goals and aims of this project, share their needs and wants regarding monitoring tools, and address potential implementation issues

- The focus group will be audio-recorded and transcribed (either by one of our study team members, or a professional service called Transcript Heroes)

- The entire visit lasts up to 2 hours

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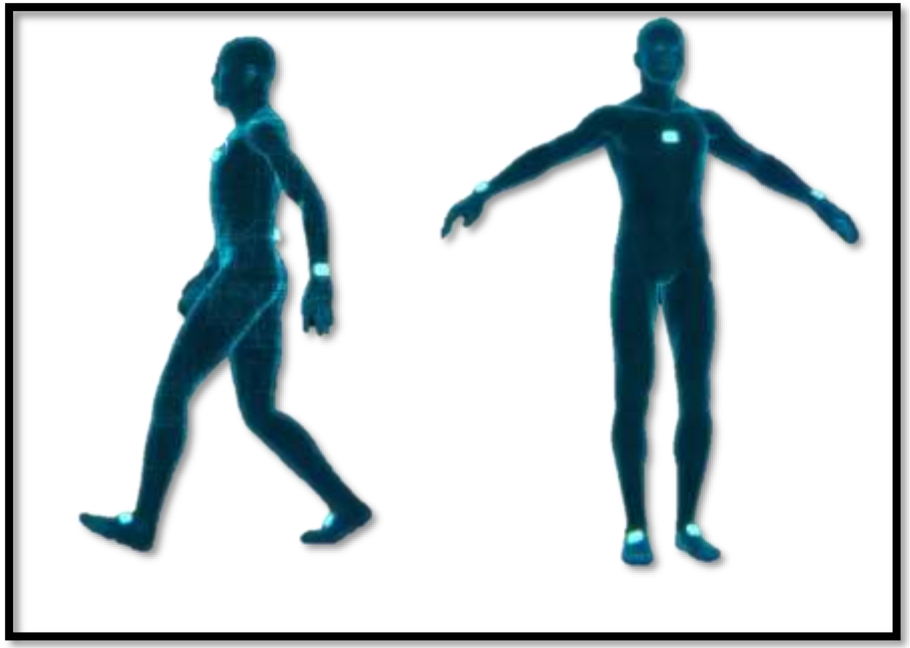
Mobility Visit

Subjects will be fitted with sensors designed to record information about their body movement. They will then be asked to perform various gait and balance tasks and a video of these activities will be recorded.

APDM Sensors



Sensors on Subject

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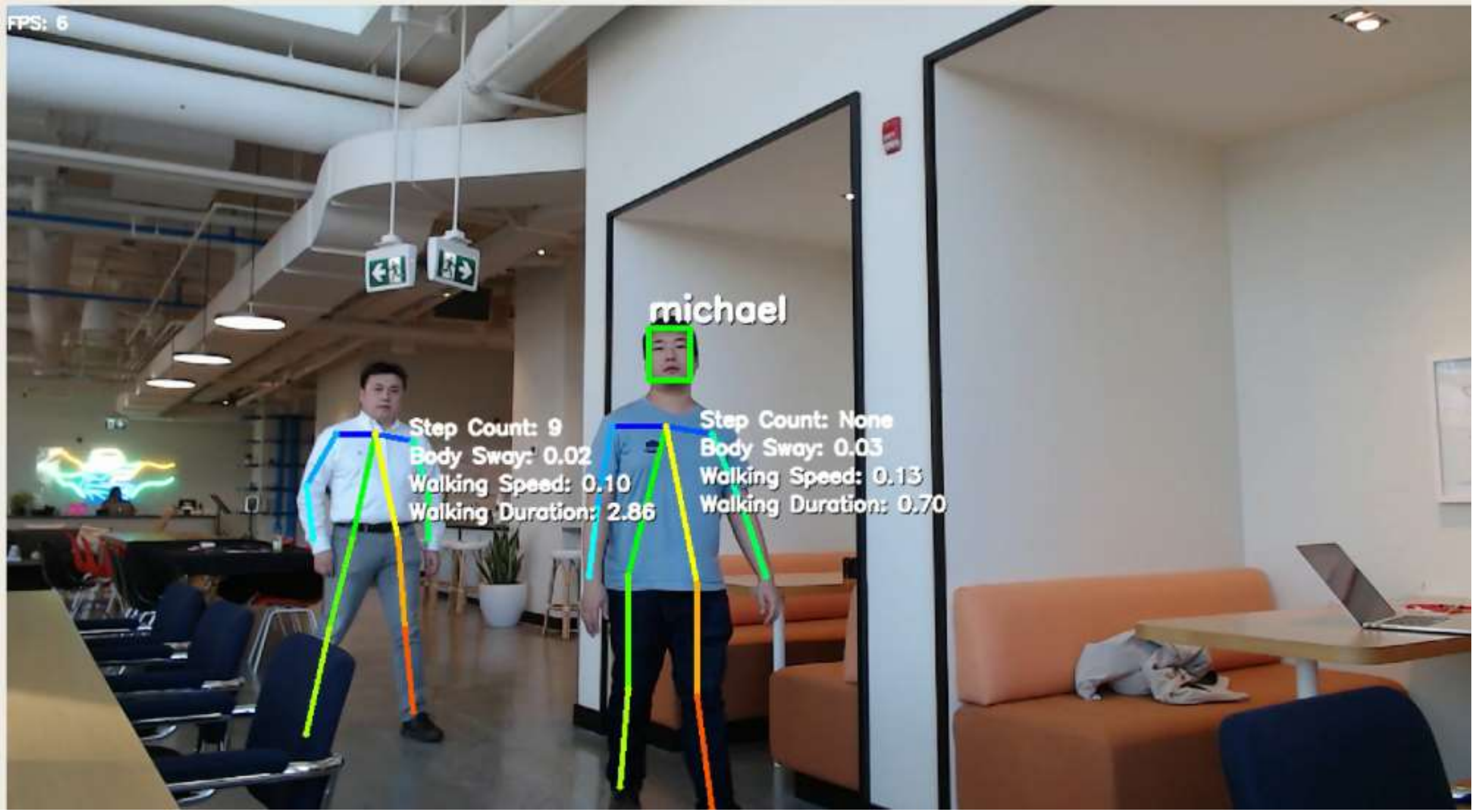
Mobility Visit Demo-Raw Video

Testing Stage Demo



Facial Expression Visit

View images while your facial expression is recorded by a video camera. After viewing each image, you will be asked to report your emotional response.

- Obtain video recordings of participants' facial expressions while they sit and watch 60 pictures displayed on a computer screen

- Pictures will be selected from the International Affective Picture System (IAPS) and include 20 pleasant pictures (romantic couples, food, erotica, vacation destinations), 20 unpleasant pictures (mutilations, threatening animals, human violence), and 20 neutral pictures (household items). An additional eight pictures will be selected for use in a practice trial

- Each picture will be displayed for 6 seconds and followed by a black screen during which the participant will record their subjective rating via an emotion rating scale

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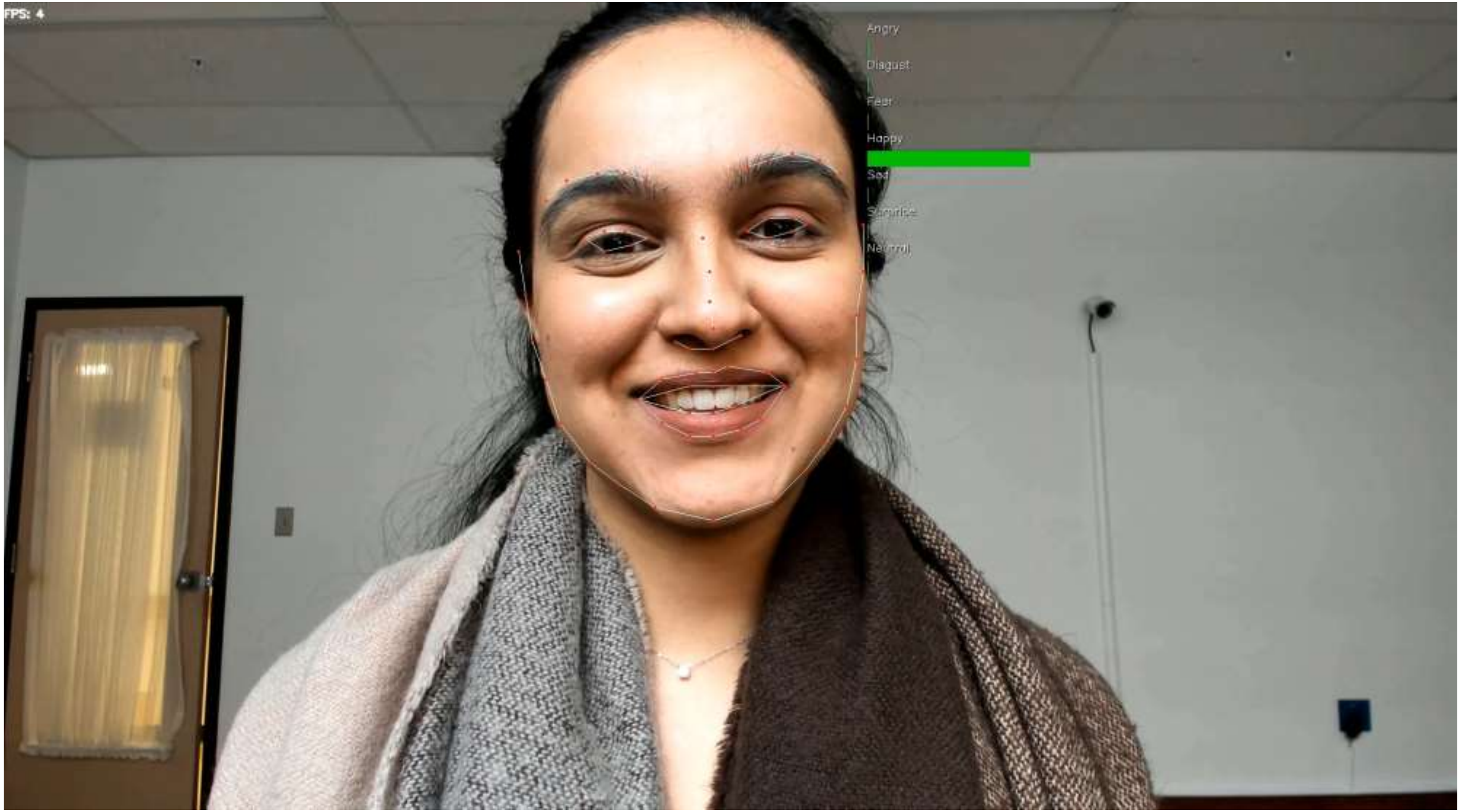
Facial Expression Visit Demo



Progress

Focus Group Visit

- 1 Focus Group has been successfully completed
- 6 PD Subjects and 2 Healthy Controls were included

Mobility Visit

- 20/50 PD Mobility Visits Completed
- 1/50 Healthy Control Visits Completed

Facial Expression Visit

- In the final stages of developing and recruiting for this visit

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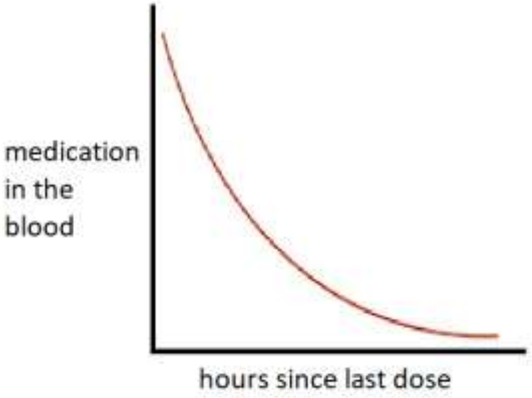
Dr. Devavrat Nene

Sweat:

How EDA acts as a marker for PD Motor Fluctuations?



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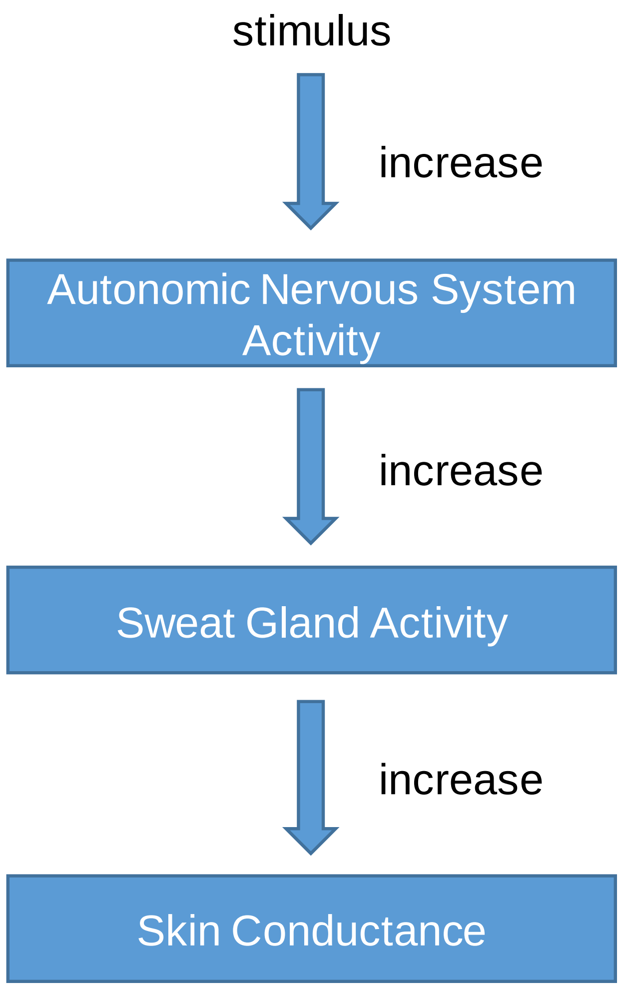
Sweat

- PD affects the autonomic nervous system
- Electrodermal activity (EDA) or skin conductance and heart rate variability (HRV) are indirect evaluations of the autonomic nervous system activity variability
  - EDA refers to electrical characteristics of the skin
  - HRV is the variation in the time interval between consecutive heartbeats in milliseconds



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Sweat

- Wrist sensors can measure EDA and HRV over long periods

- EDA is measured by passing a minuscule amount of current between two electrodes in contact with the skin

Sweat

- **The goal is to identify whether there is an association between fluctuations in EDA and HRV and motor fluctuations**
  - **Can we predict OFF/ON status based on EDA and HRV?**
  - **Can we predict time to next dosage? Or time since last dosage?**
- **Participants are asked to:**
  1. **Complete collection of clinical questionnaires to establish severity of Parkinson's symptoms**
  2. **Wear wrist sensor for 24 hours**
  3. **Keep diary of activity**

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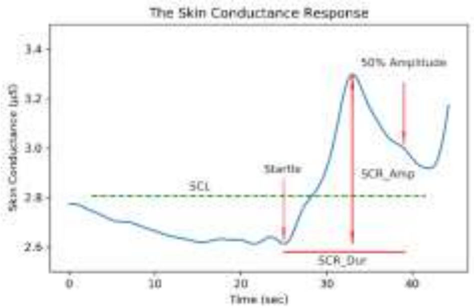
The Data

- We have raw EDA data and diaries of 20 different patients for 24 hours

  Diaries include:
    - On/Off: subjective feeling about when they are On or Off medication
    - Time of taking their medications
    - Activities at each hour



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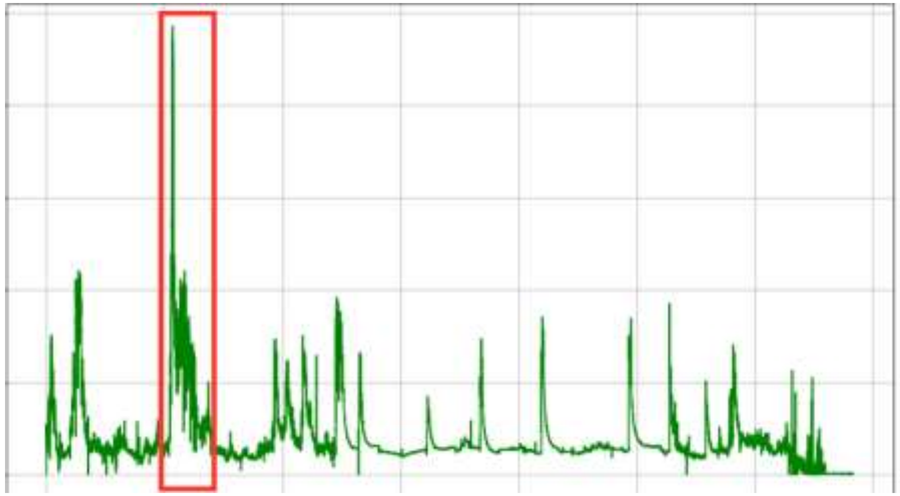
Invalidation Process

- Most initial models were poor- due to abundance of ‘bad data’ (for example, patient showers, swims, or exercises, causing fluctuations in skin conductance)
- Employed a Simple, Transparent, and Flexible Automated Quality Assessment Procedures for Ambulatory Electrodermal Activity Data (Ian R. Kleckner et al.)



- We use Kleckner’s algorithm to remove bad epochs based on value, steepness of slope, and the temperature
- We used this algorithm (“strict invalidation”) as well as a weaker version of the algorithm (“relaxed invalidation”)

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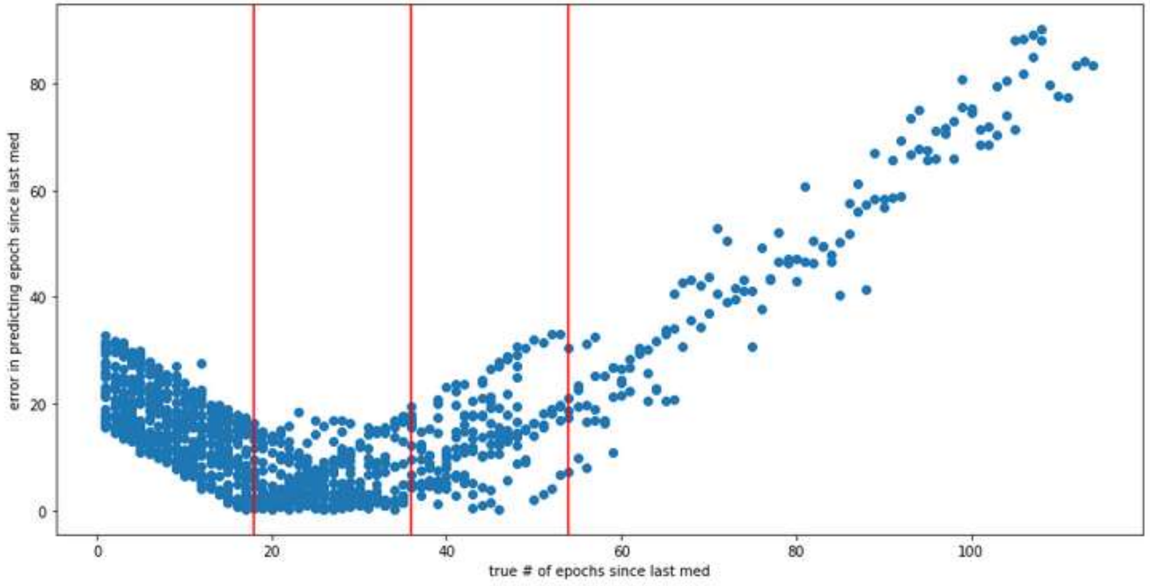
Results

- Support Vector Machine (SVM) classifier used to to differentiate on/off states
  - With strict invalidation, we can guess on/off with up to 82% accuracy
  - With relaxed invalidation, we can still guess with up to 70%



Error in prediction based on time since medication

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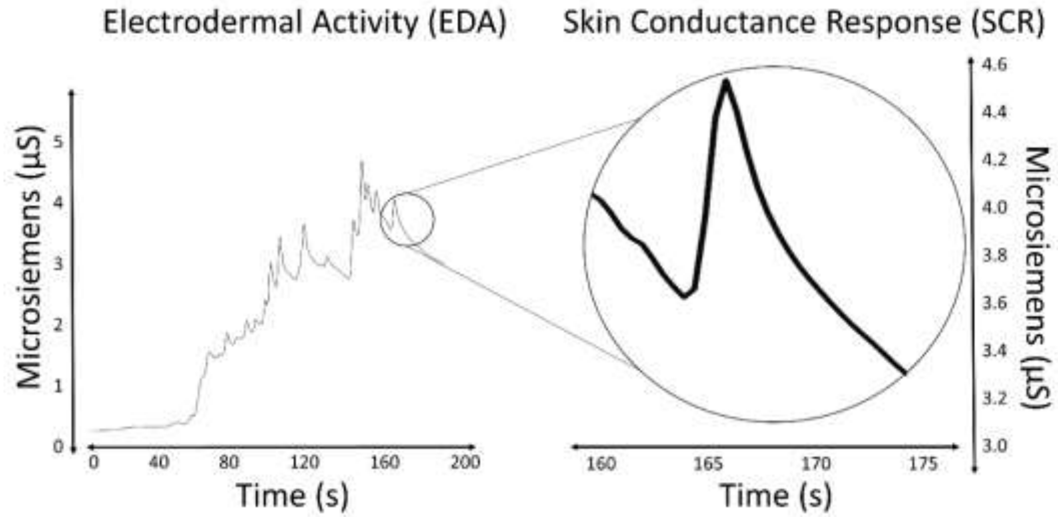
Next Steps

- Predict the **time to next dosage** accurately to alert the patient to take the medication before they are actually OFF



Take your medication before you really feel OFF!

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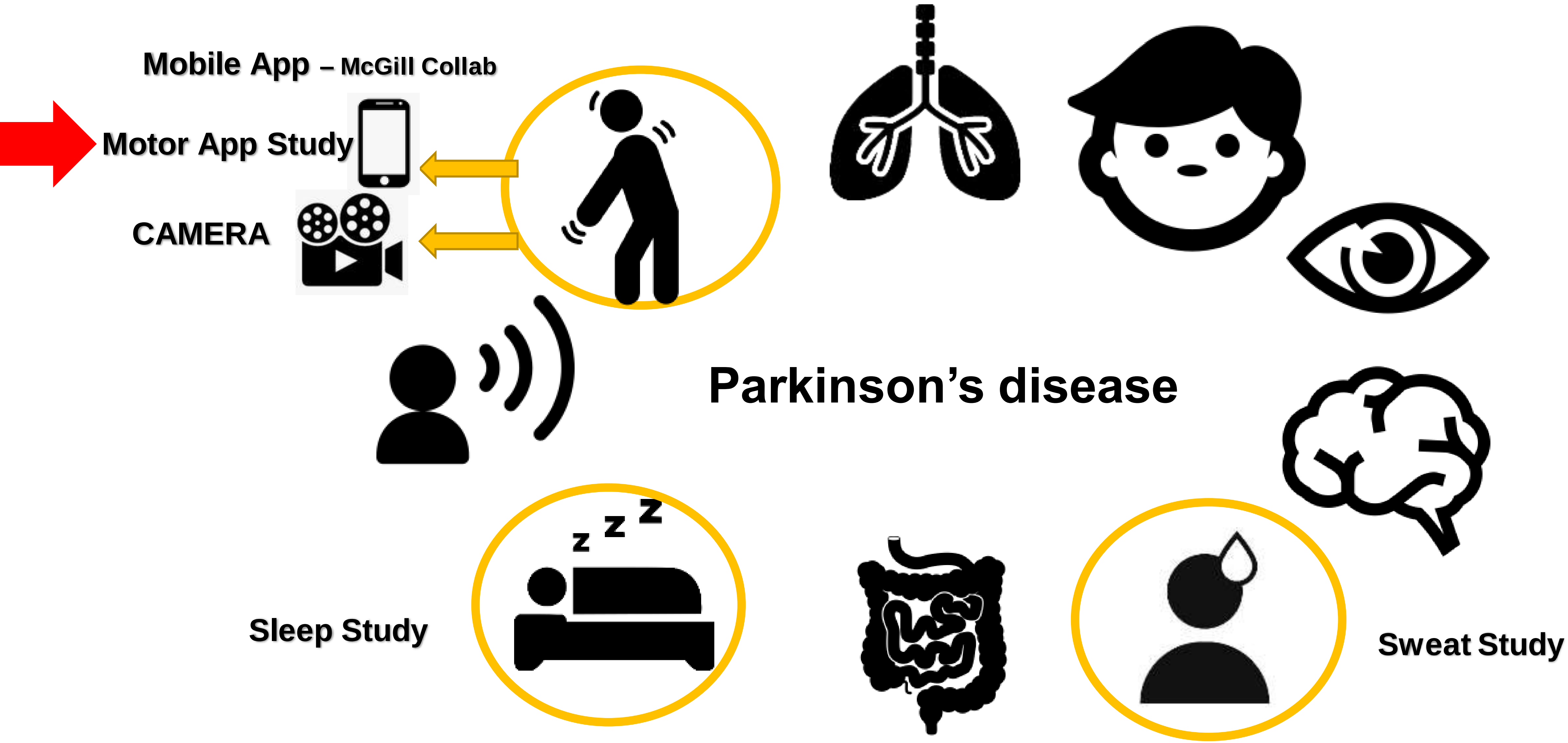

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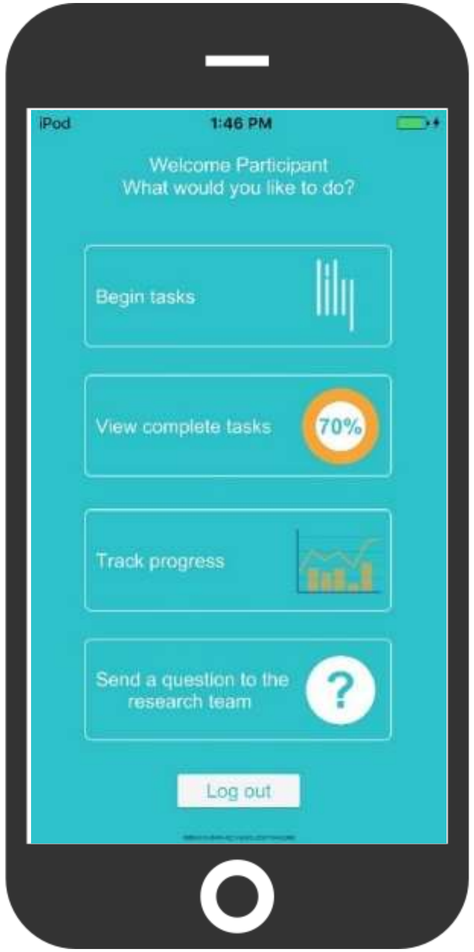
Motor App

- Develop a smartphone application to assess motor symptoms in home setting
  - Finger tapping, kinetic, resting, and postural tremor, gait, arising from a chair, heel tapping
- 2 phase approach
  - In-clinic study → Participants completed the smartphone application in person and the UPDRS
  - In-home study → Participants will complete the smartphone app at home for three weeks



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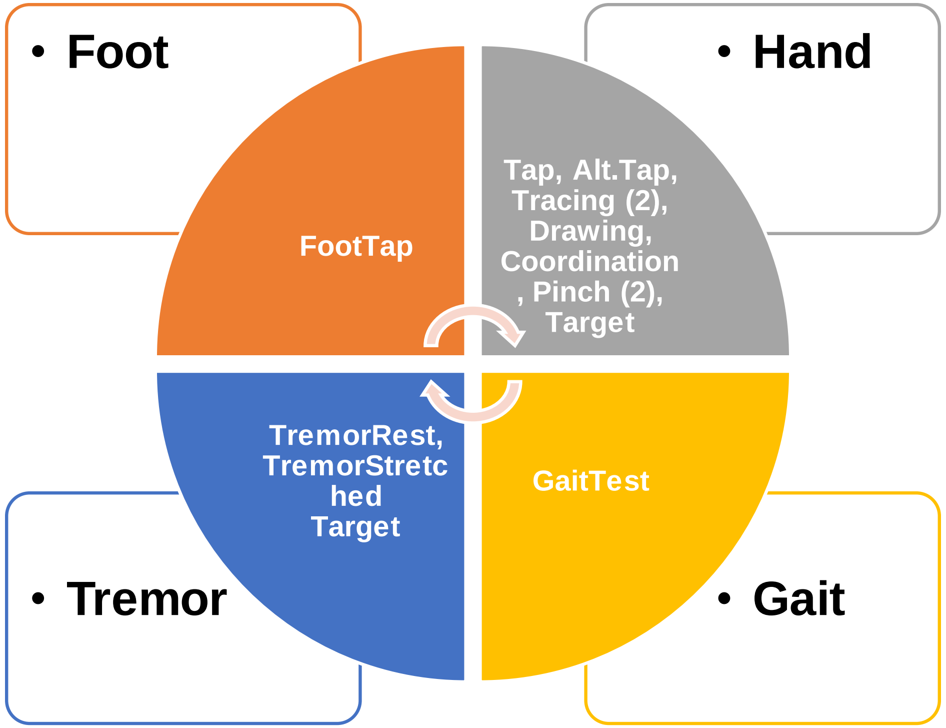
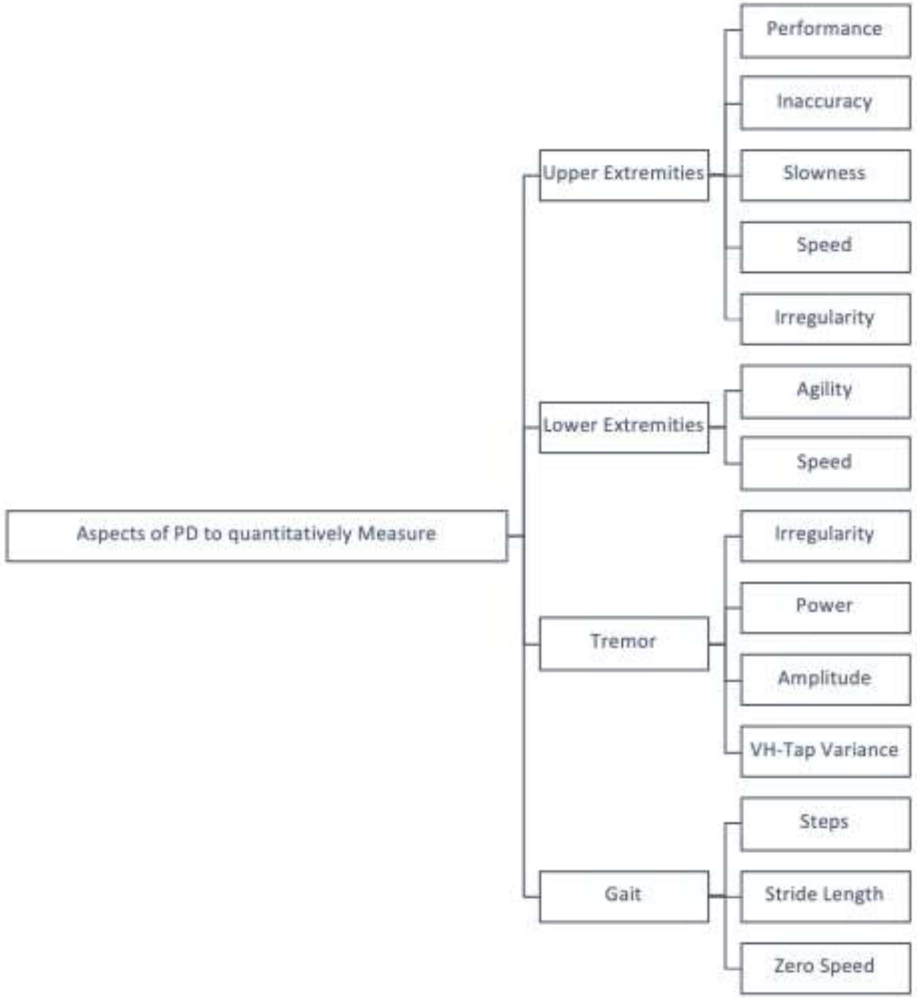
Motor App





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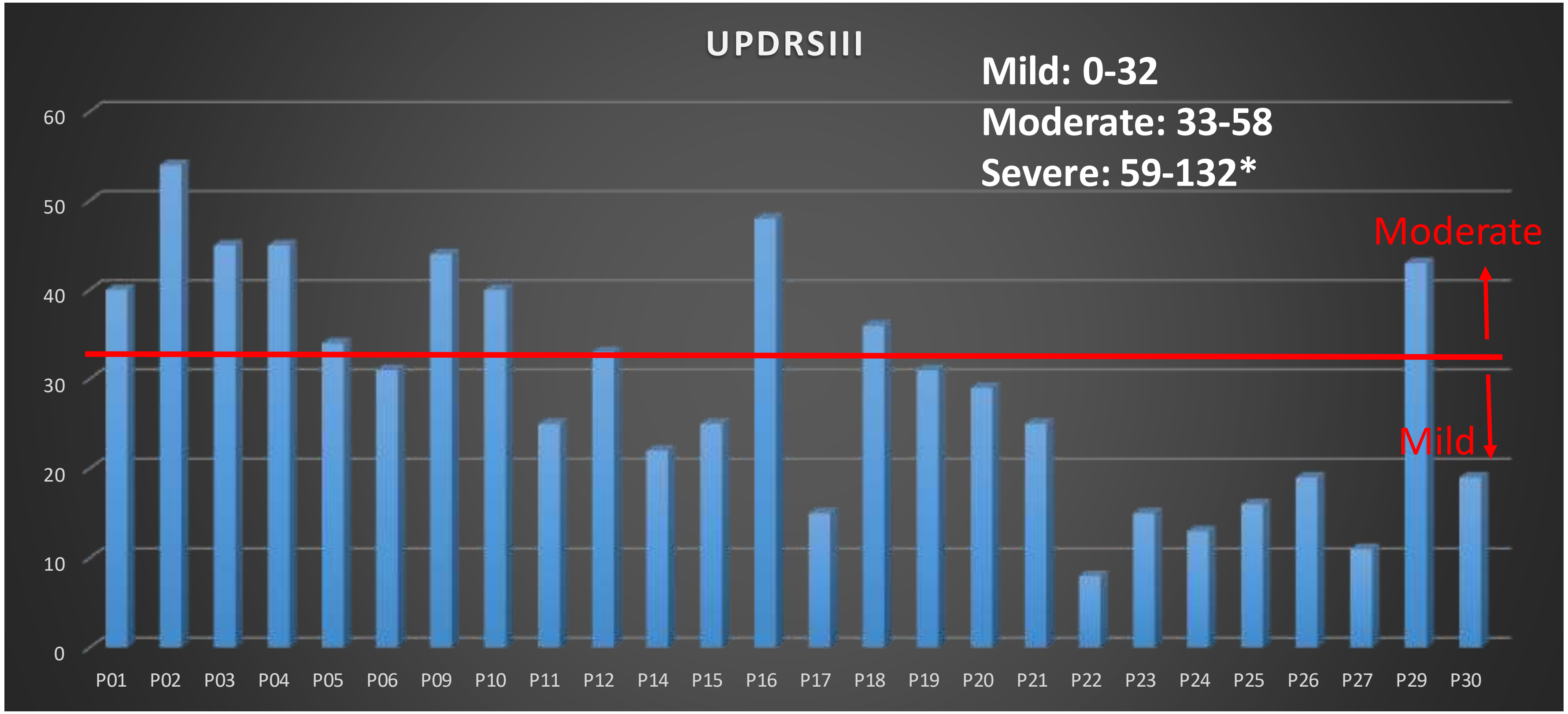
Partitioning the patients according to UPDRSIII score



By using 4 metrics calculated out of the App data, we can reliably discriminate Moderate vs. Mild
Amplitude of tremor (unit *9.81 m/s^2)
Irregularity of tremor (sec)
Slowness of taps (tap/sec)
Tap variance (cm^2/sec)

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Conclusion

- It is possible to estimate disease severity with performance on an app

- The app may assist clinicians in decision-making and in remote monitoring

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Future Steps

- Adding time of medication info from Smart Pillbox
  - Try the App, Take medication, Try the app
    - which motor-related features are robust? which are affected the most?

- Combining with Sweat study:
  - We can ethically make patients stressful (by trying the App tasks) and try looking at EDA signal and effects at motor fluctuations.

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PD Mobile App – McGill Collaboration

- McGill initiated study
- One-year multi-site longitudinal biomarker study
- Objective: determine the reliability and validity of remote patient monitoring using a smartphone app which combines active testing with passive monitoring to detect
- Participants will be asked to complete a number of active tests every morning for one year and carry the phone with them throughout the day
- Recruitment target:
  - n=50 idiopathic RBD patients
  - n=150 PD patients
  - n=30 healthy control (HC) participants

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PD Mobile App

Progress to date

- McGill has submitted the ethics application
  - Ethics board is having many questions with regard to data sharing, which is causing a major delay
- Vancouver is waiting for McGill to get ethics approval
- Planned to start summer 2020

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Sleep Project: long story short!

(Visual)

Sleep

- Data collection initiated with Cognionics

Headband + PSG

- **Very valuable data collected with AD group at PPRC**

Algorithms to clean the data + Algorithms to automatically stage the sleep

Paper 1: Polysomnography validation of a portable two-channel EEG headband for assessing sleep in the home environment

HeadBand quality very Poor!

- **Unsupervised Algorithm to stage sleep**

Paper 2: Semi-unsupervised Sleep Scoring identifies novel sleep signatures associated with REM Sleep Behavior Disorder", submitted (Dec.2019) for publication in Journal of Biomedical and Health Informatics.

Capstone Project

- **Design a new head wear with custom-manufactured electrodes at UBC**

Micro-needle electrode

Sleep Project: long story short!
(Textual)

- We started the project with Cognionics headband.
- With collaboration of AD group, we collected very valuable data
  - Simultaneous recording from Headband and Polysomnogram
- Dr. Jason Velario (neurologist and sleep expert) investigated the headband data and found that the quality is rather poor
- What have we done since then?
  - First, we designed an algorithm to remove the artifacts from the headband data and make the headband and PSG data synchronized.
  - Then, we designed an algorithm to automatically stage the sleep data with least use from the labels provided by the sleep expert
    - It is called _S_tep-wise _C_lustering in Stage-based _D_iscriminative _S_ubspaces (SCDS)
    - It is an unsupervised methods => can capture novel patterns of sleep profile
    - A technical journal paper titled "Semi-unsupervised Sleep Scoring identifies novel sleep signatures associated with REM Sleep Behavior Disorder", submitted (Dec.2019) for publication in Journal of Biomedical and Health Informatics.
  - We have tried this algorithm on 6 PD sleep data recorded by Cognionics and generated corresponding hypnograms
  - We did Polysomnography validation of a portable two-channel EEG headband for assessing sleep in the home environments
    - You will see some detailed results.
  - We decided to work on preparing a new headband with our colleagues at UBC
    - We are currently running a Capstone design project to create a “Novel Sleep Monitoring System”

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Sleep Monitoring: traditional way

While you sleep, a technologist monitors your:

- Brain waves (EEG)
- Eye movements
- Heart rate
- Breathing pattern
- Blood oxygen level
- Body position
- Chest and abdominal movement
- Limb movement
- Snoring and other noise you may make as you sleep

http://homesleepmonitoring.com.au/

Full Polysomnography Test - Greater Montreal Sleep Clinic

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Manual Sleep Scoring….

- Done using PSG recordings include multiple signal channels visually examined by an expert
  - is expensive when you hire an expert or bring patient to the lab
  - is prone to human error
  - is tedious and time consuming as a high-dimensional visualization task
    - EEG, EMG, ECG, EOG
  - High Inter-observer variability
  - is usually performed in a hospital setting with an unfamiliar environment for patients → uncomfortable which also affects the patient's sleep efficiency

From Garcia Molina at EUSIPCO 2015

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Automatic Sleep Staging:

Cost reduction for diagnosis, treatment, and research

- Required when trained experts are not available to produce a human-level scoring
  - Or when the recording device is unfamiliar to experts!
- Reduces the workload for technician.
  - Requires validation from human experts.
  - Decreases the time demand for the clinicians
- Improves the analytical accuracy
  - improves the diagnosis and treatment of sleep disorders
  - Provides reproducible results

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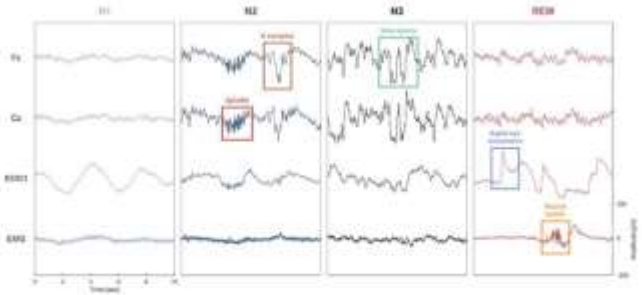
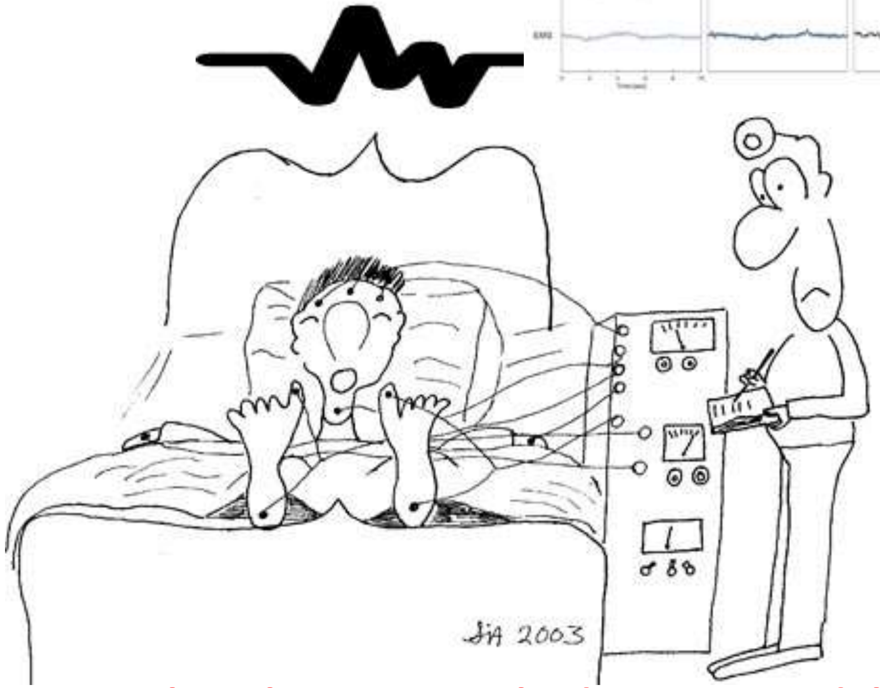
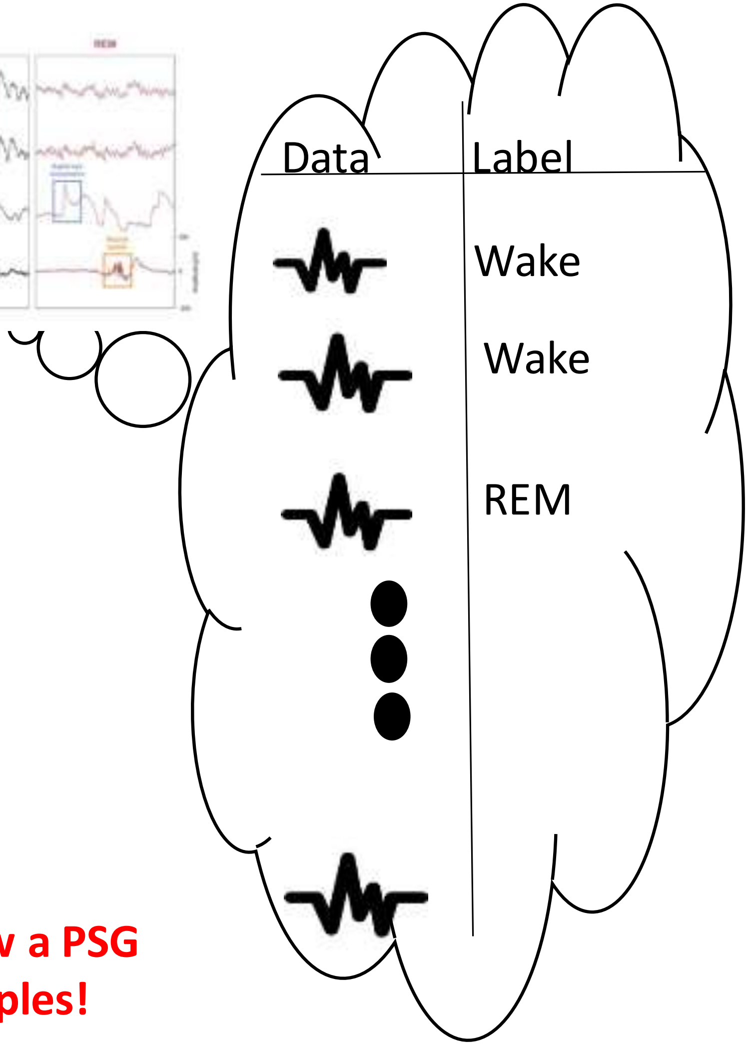
What do we mean by "Automatic"?



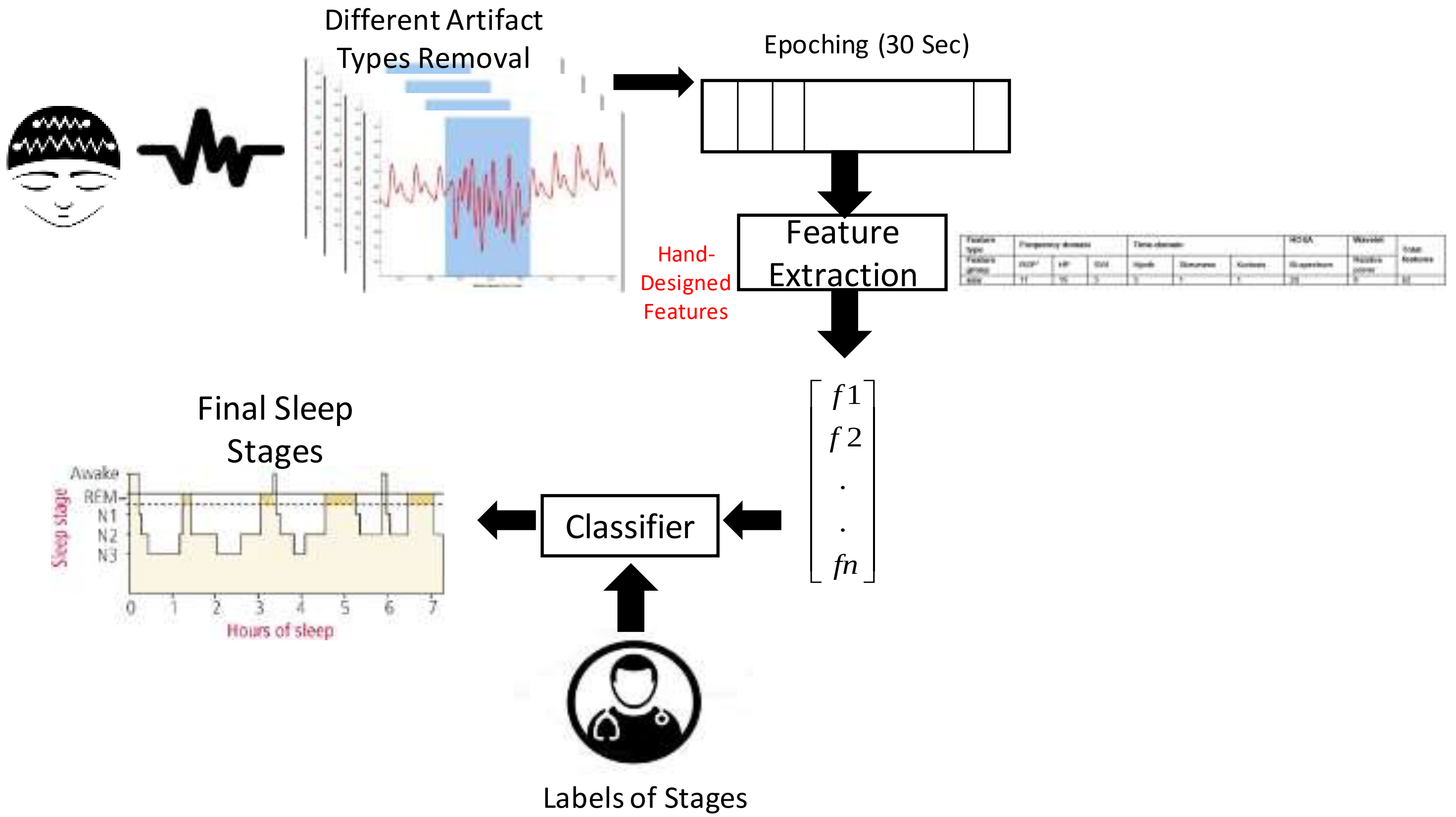




A machine learning method tries to model how a PSG expert tags the data by observing enough samples!

How it works?

- Cleaning of the headband data
  - Artifact removal
  - Synchronization with PSG data
- Epoching to 30 sec and Feature Extraction
- Training a model and validation
- Testing on new patients



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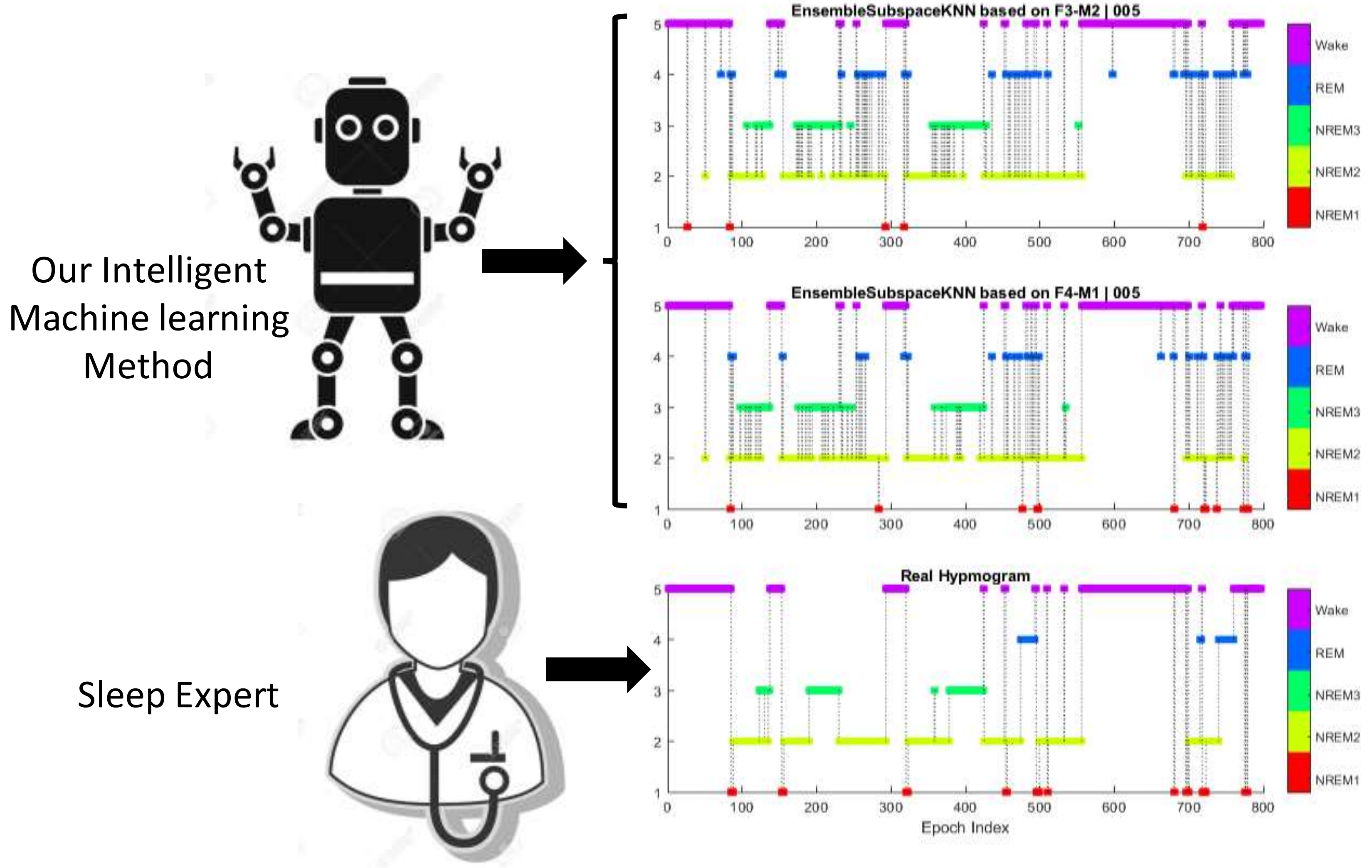
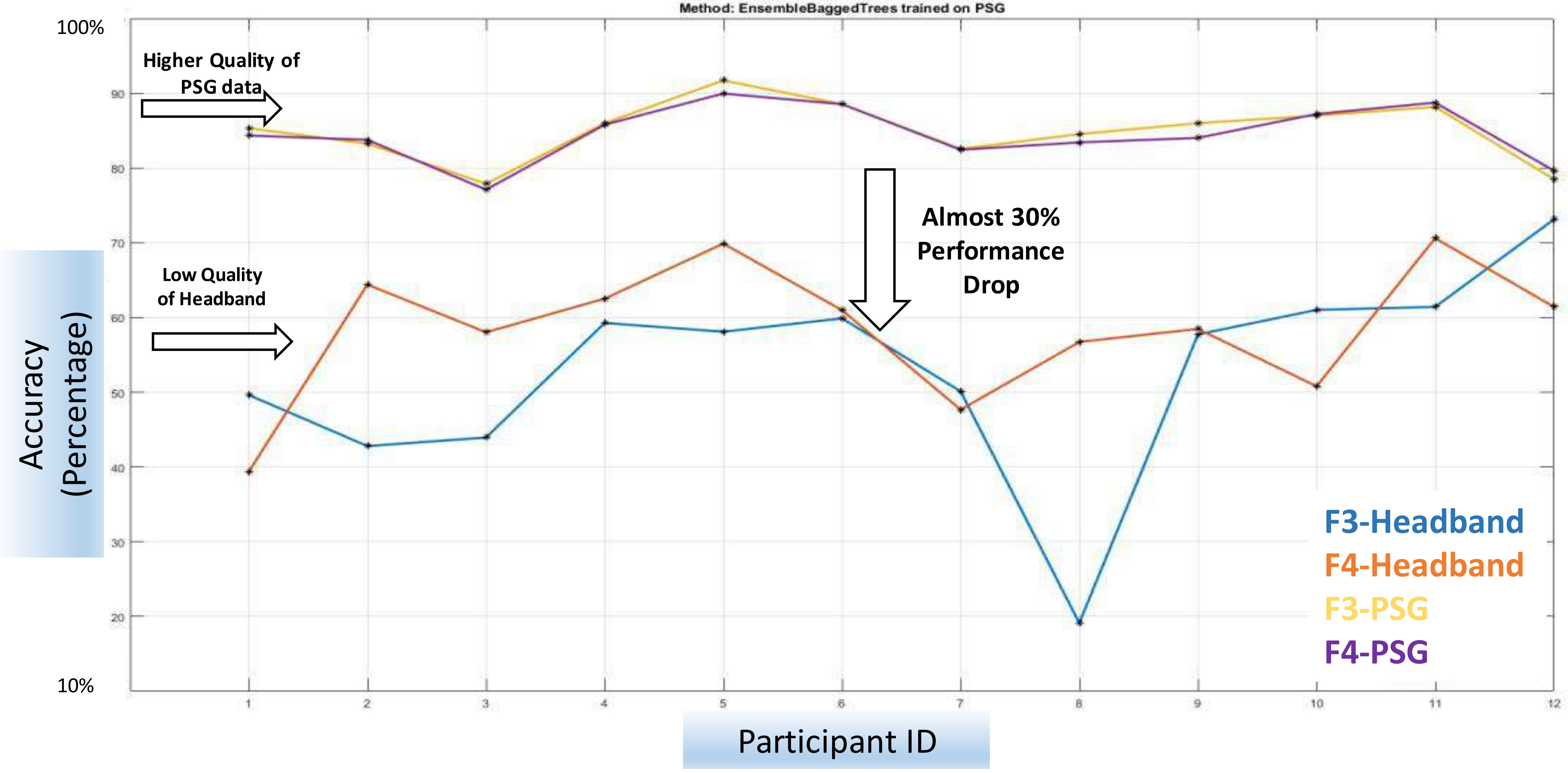
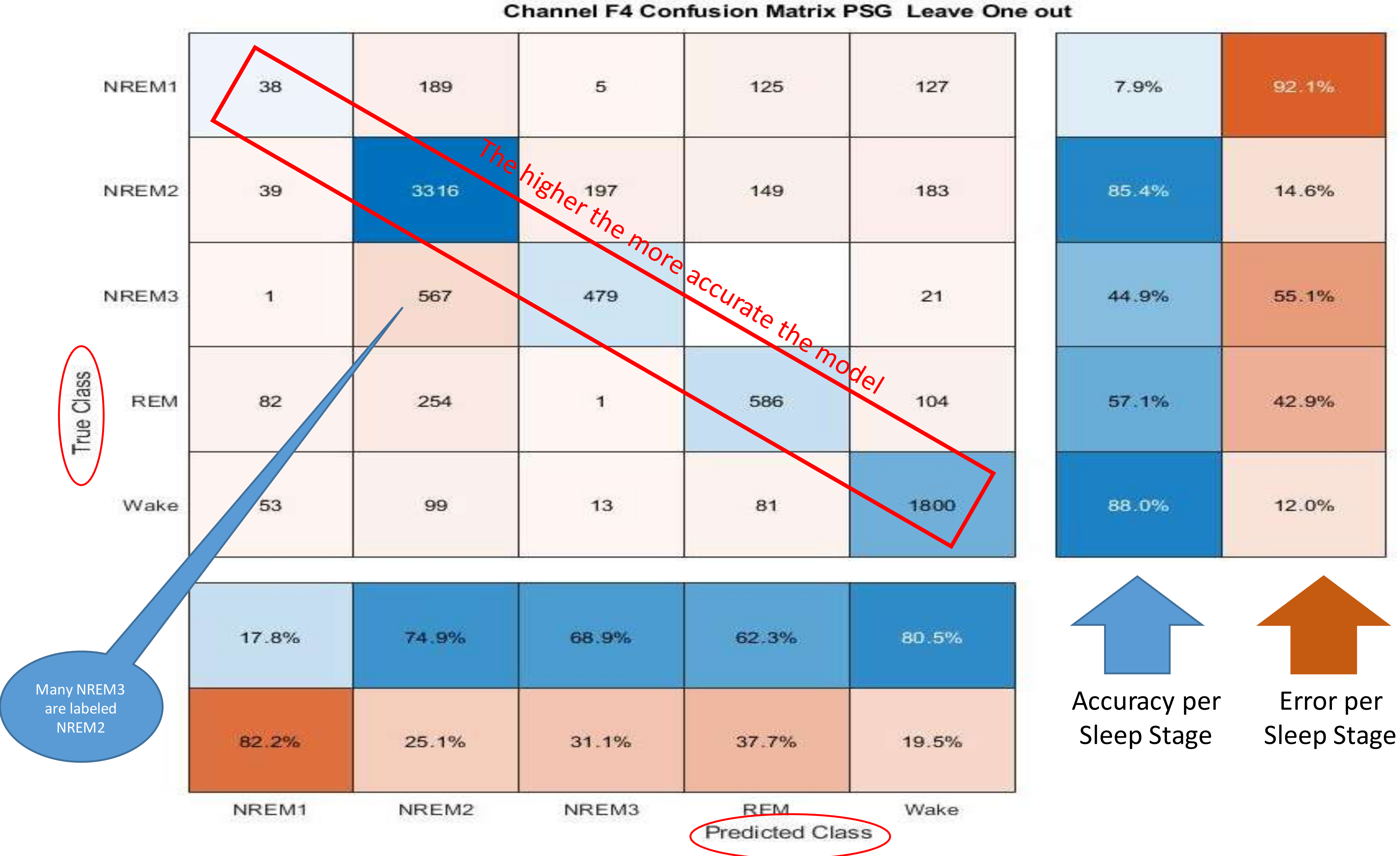


Our Intelligent Machine learning Method
Sleep Expert
EnsembleSubspaceKNN based on F3-M2 | 005
EnsembleSubspaceKNN based on F4-M1 | 005
Real Hypmogram
Epoch Index
Wake
REM
NREM3
NREM2
NREM1

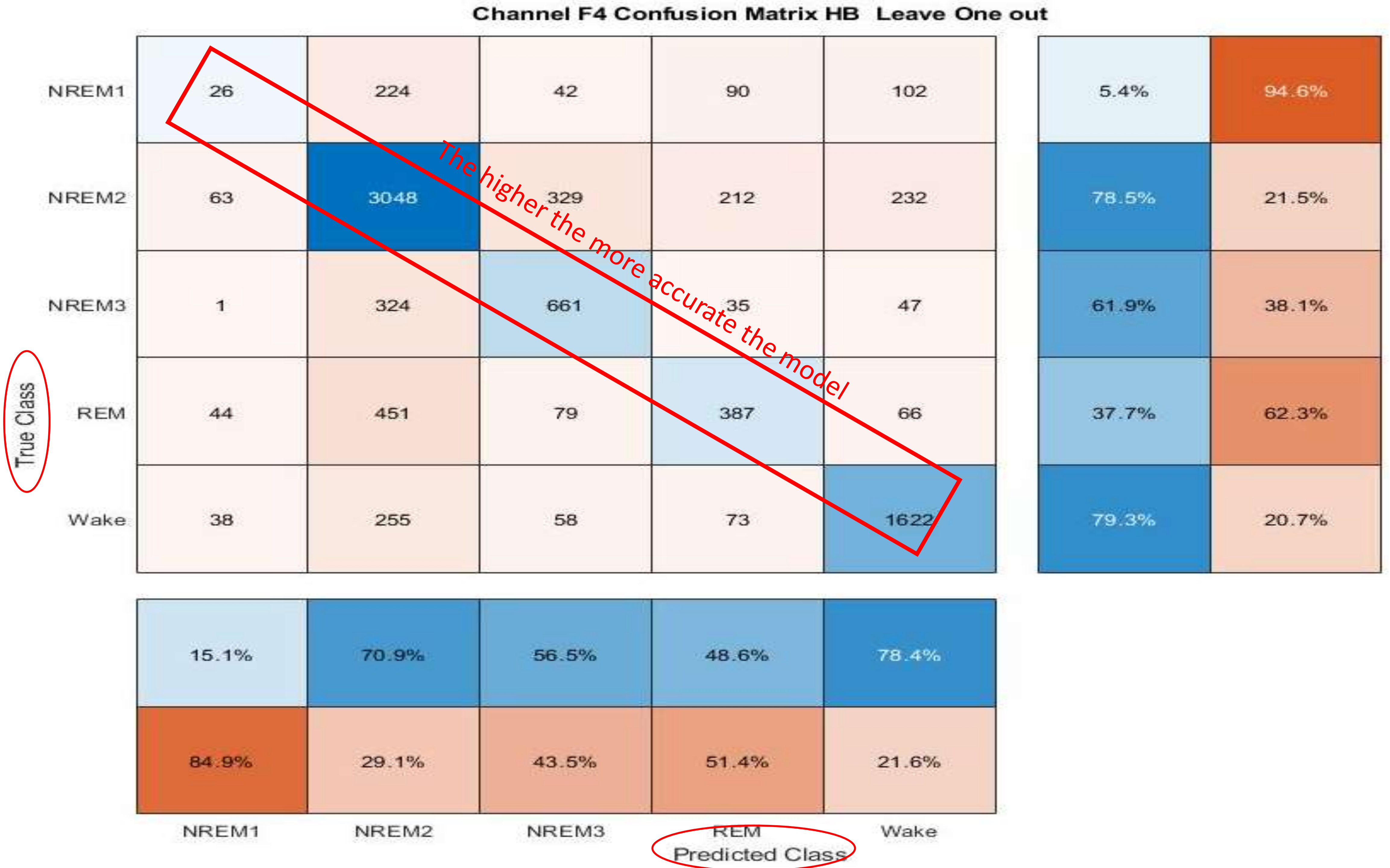
Accuracy of the best performing model* for each participant



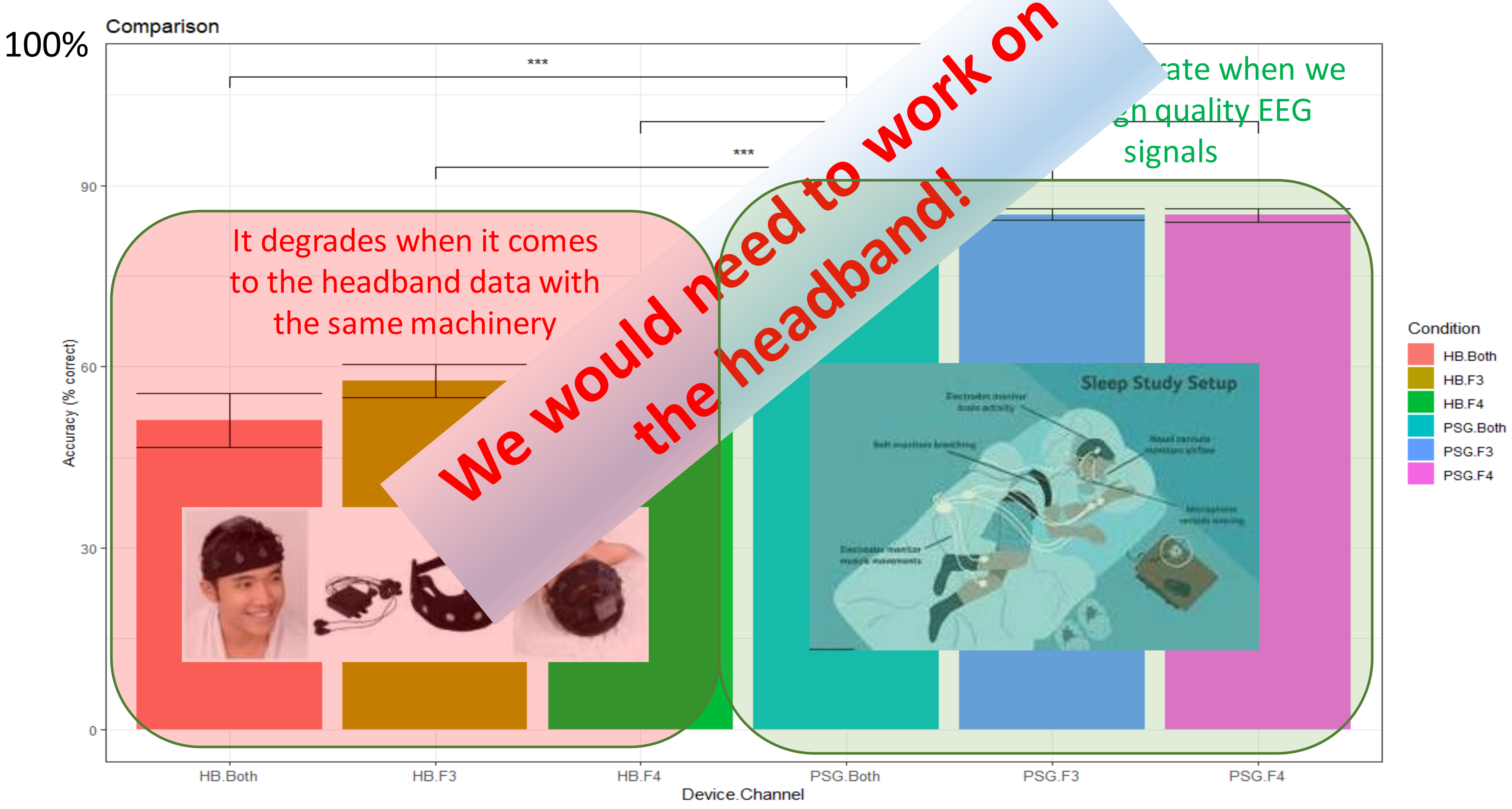
* We tried different classification methods. The best performance was gained by Ensemble Bagged Trees



Channel F4 Confusion Matrix PSG Leave One out
True Class
NREM1
NREM2
NREM3
REM
Wake
38
189
5
125
127
39
3316
197
149
183
1
567
479
21
82
254
1
586
104
53
99
13
81
1800
7.9%
92.1%
85.4%
14.6%
44.9%
55.1%
57.1%
42.9%
88.0%
12.0%
17.8%
74.9%
68.9%
62.3%
80.5%
82.2%
25.1%
31.1%
37.7%
19.5%
NREM1
NREM2
NREM3
REM
Wake
Predicted Class
The higher the more accurate the model
Many NREM3 are labeled NREM2
Accuracy per Sleep Stage
Error per Sleep Stage


Channel F4 Confusion Matrix HB Leave One out
NREM1
NREM2
NREM3
REM
Wake
True Class
26
224
42
90
102
63
3048
329
212
232
1
324
661
35
47
44
451
79
387
66
38
255
58
73
1622
5.4%
94.6%
78.5%
21.5%
61.9%
38.1%
37.7%
62.3%
79.3%
20.7%
15.1%
70.9%
56.5%
48.6%
78.4%
84.9%
29.1%
43.5%
51.4%
21.6%
NREM1
NREM2
NREM3
REM
Wake
Predicted Class
The higher the more accurate the model

How ACCURATE with our current headband?

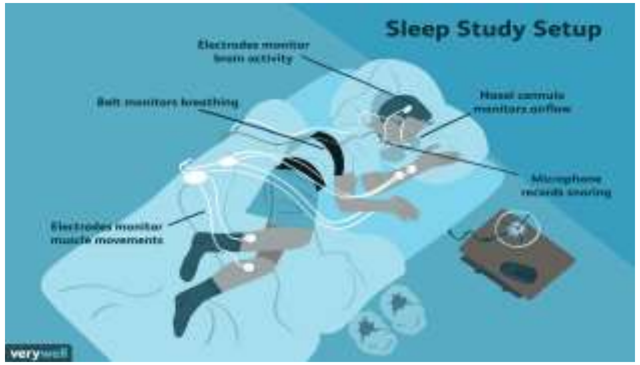


We defined a Capstone Design project* for UBC ECE undergrad students

* A capstone design project is a major component of engineering curriculum. They design a product/service of significance, and solve an open-ended problem in electrical or computer engineering.

inexpensive,
non-invasive,
but inaccurate

highly
accurate,
expensive, and
invasive



Capstone Design Project Goals

- To construct a system that does not require a trained technologist to apply but still is capable of recording EEG
- Reasonably accurate
- Challenges
  - Finding **comfortable ways to keep electrodes in place** during sleep and keeping good electrical contact during sleep
  - Dealing with **novel types of artifacts**
  - Statistical pattern recognition methods to do **sleep staging**

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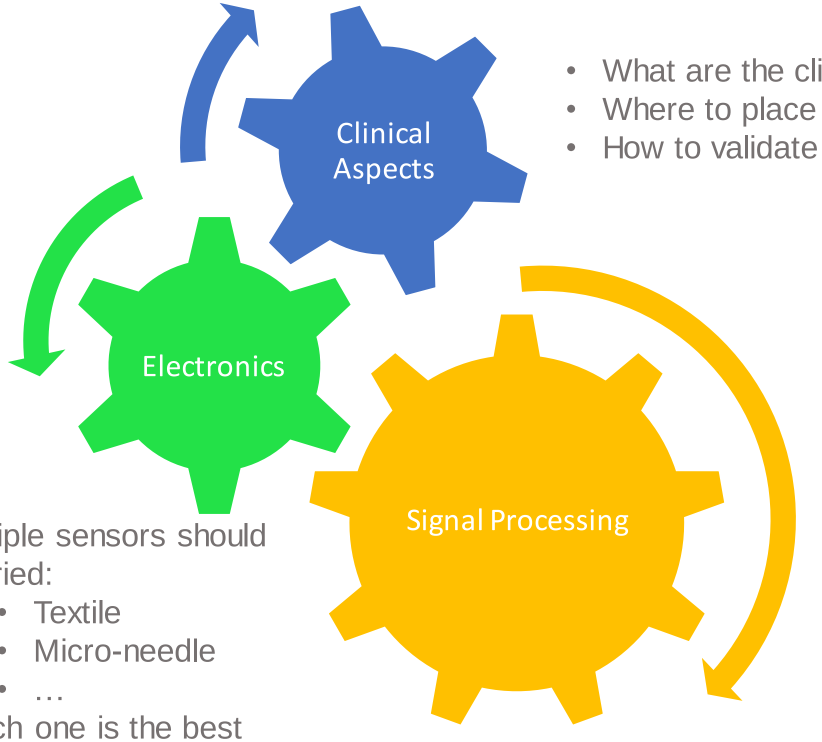
Why did the students choose our Capstone Project?

Capstone students:
Jasmine Ma, Kay Xi, Megan Hii, Sally Wang, Dhruval Shah, Rayhan Bosch

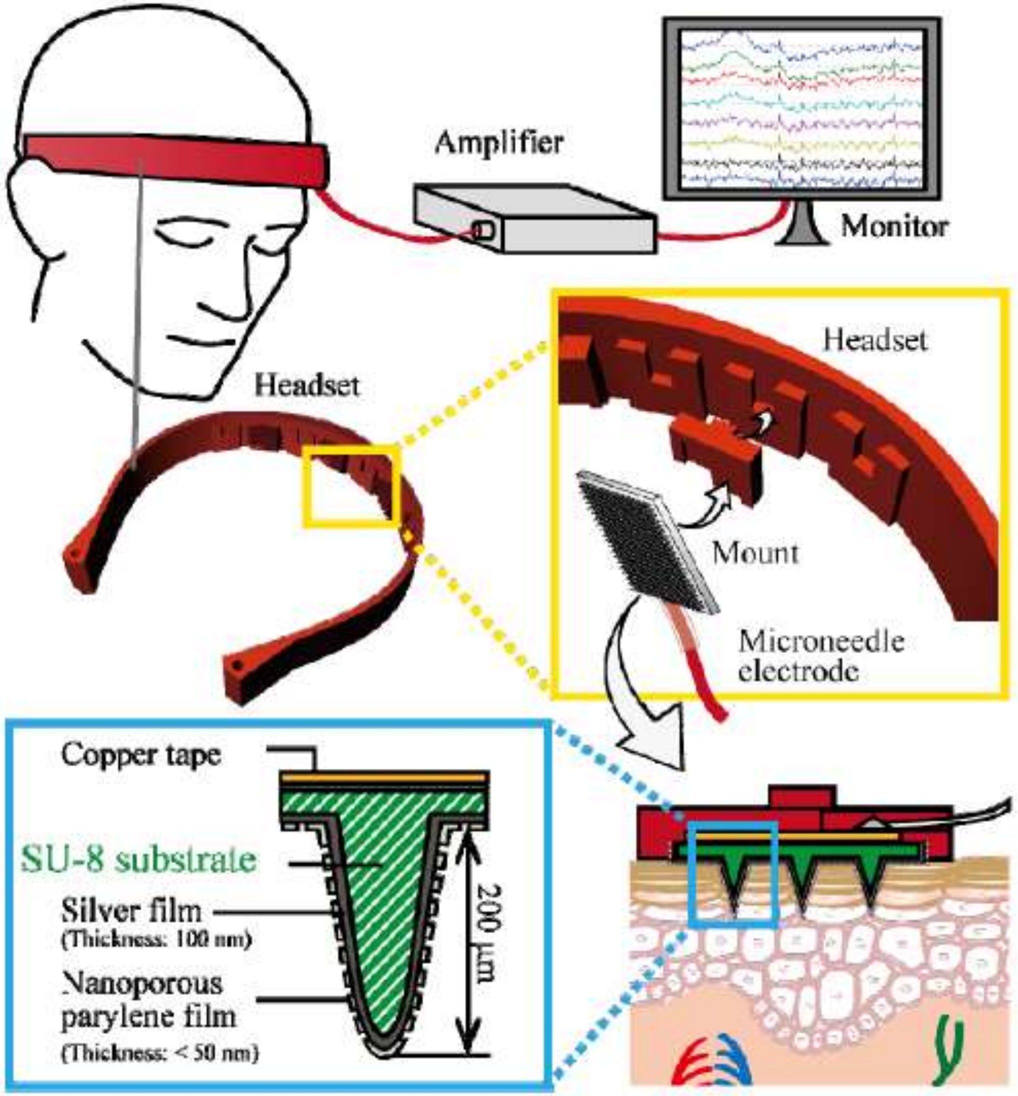
A novel system for sleep monitoring



- What are the clinical features to detect the sleep?
- Where to place the electrodes for most efficiency?
- How to validate the system in clinical settings?

- Multiple sensors should be tried:
  - Textile
  - Micro-needle
  - …
- Which one is the best option to measure scalp EEG?

- What types of artifacts emerge?
- Which technique best works for removing such artifacts?



M. Arai, Y. Nishinaka, and N. Miki, Polymer-based candle-shaped micro-needle electrodes for electroencephalography on hairy skin, Japanese Journal of Applied Physics, 2016.

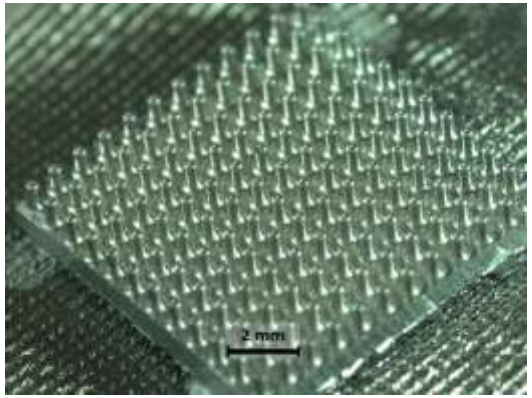
We ask Dr. Peyman Servati and Dr. Boris Stoeber to manufacture customized electrodes for us

Dr. Peyman Servati, ECE Professor, Director of Flexible Electronics and Energy Lab (FEEL)

Dr. Boris Stoeber, Tier 2 CRC in Microfluidics and Sensing Technology

Custom-Manufactured Electrodes by UBC Flexible Electronics and Energy Lab

4 types
Textile Electrodes
Brush Electrodes
Urchin Electrodes
Micro-Needle Electrodes



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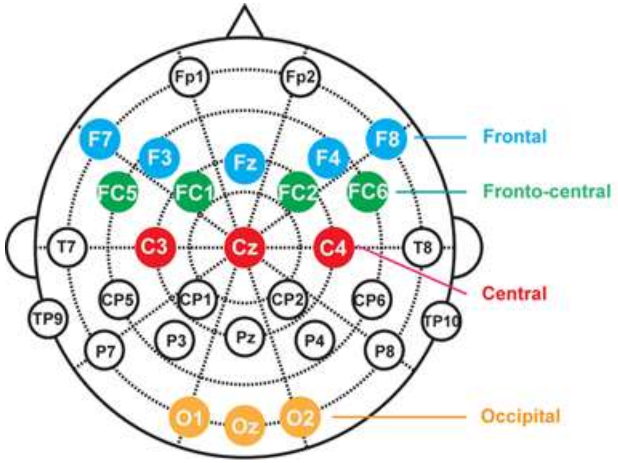
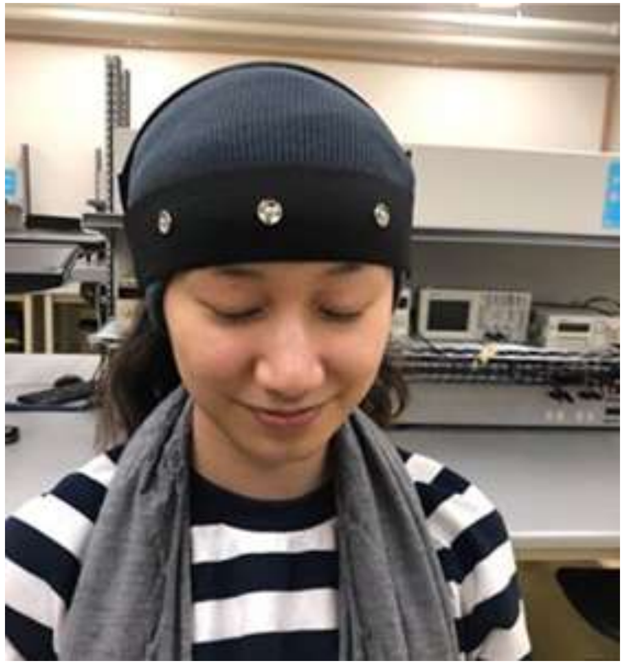
Primary Headwear Design

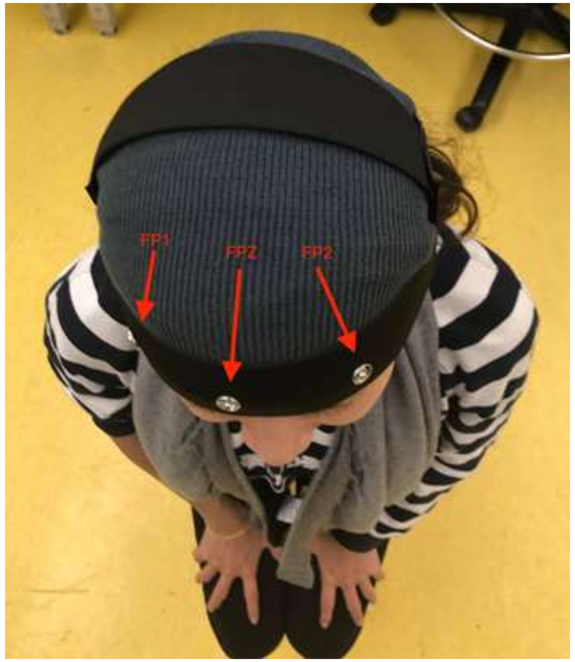
- Bandana + Elastic = 'Bandastic'
- 2 inches - Knit Elastic Bands
- 57 ± 4 cm
- Hook and Loop Strap (Adjustable)
- 8 Electrodes
  - Forehead (Fp1,Fp2,Fpz)
  - Frontal (F3,F4)
  - Central (C3, C4)
  - Ground electrode



Electrodes Placements



Front View



Top view

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Current Status of Capstone Design Project

- Students had designed a nice compact electronic board
- They are working on
  - mounting textile electrodes to the forehead part of the headwear
  - Attaching micro-needles to the parts that need to go through the hair
- They will start signal processing to see how the signal we receive can compare against a real EEG

Tasks	Details
Hardware	
Market Study	Sleep Monitoring device[5]
	Headwear (helmet/headband/Mask)
Headwear Material screening	Foam
	Soft Fabric
Prototype Headwear	Manufacturing (e.g 3D printing)
	Electrode Integration
Refinement/Commercialization	
Firmware	
Prototype Circuit Components	Analog Digital Converter
	Amplifier
	Microcontroller
	Power Source
Data Storage	
PCB Manufacturing	
Software	
Total	

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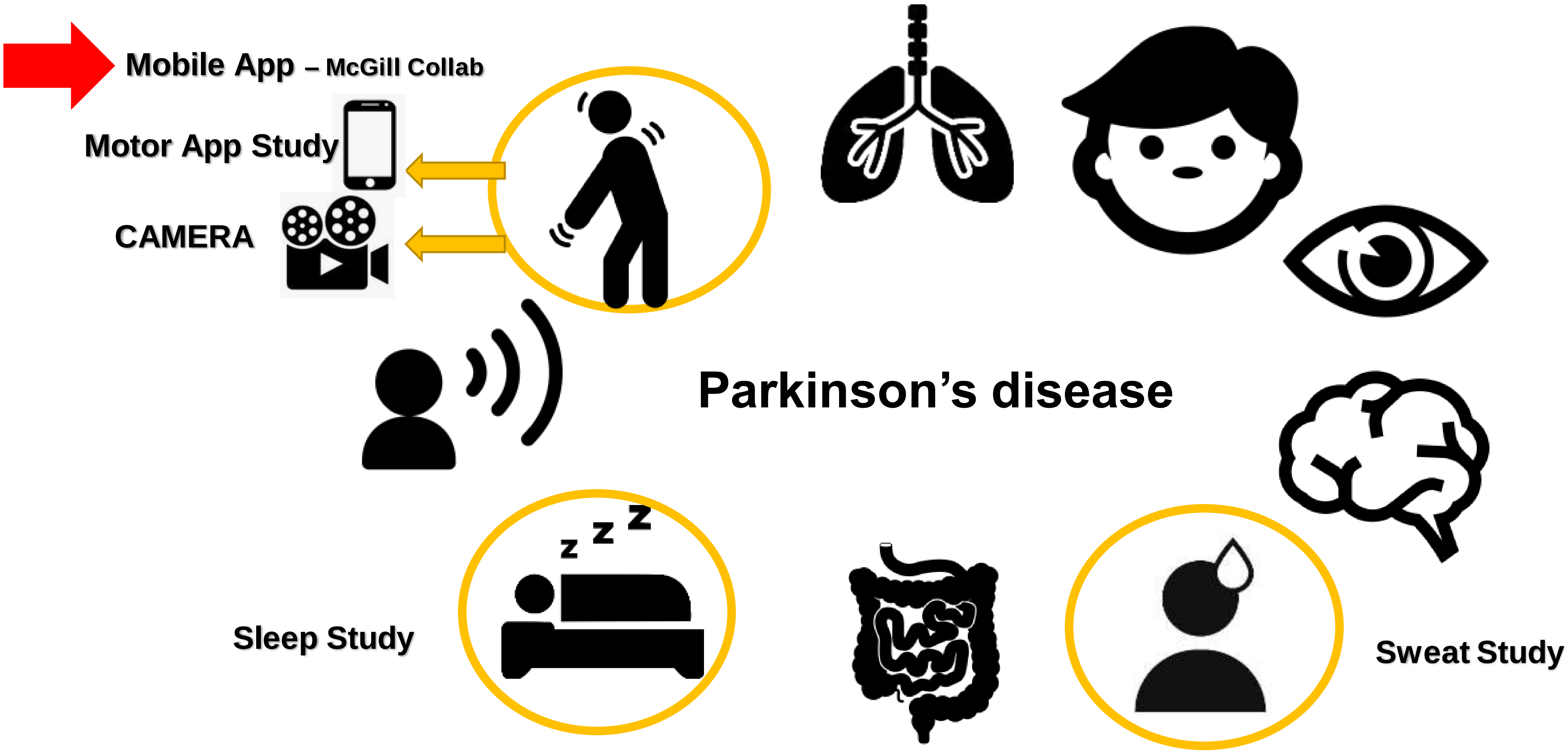

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Thank you

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