طراحی و متدولوژی تحقیق در مطالعات نقشه برداری مغز با تمرکز بر پژوهش های longitudinal

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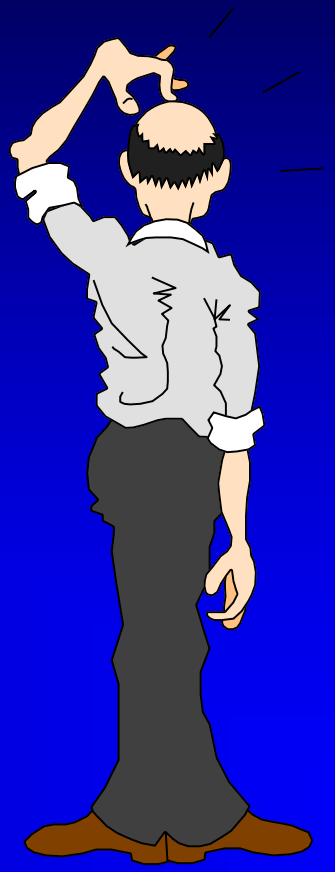
آزمایشگاه ملی نقشه برداری مغز ۱۳۹۹

ENGINEERING

- **Modeling**
  - **Predication**
    - **Control**



Neural Engineering

Neu

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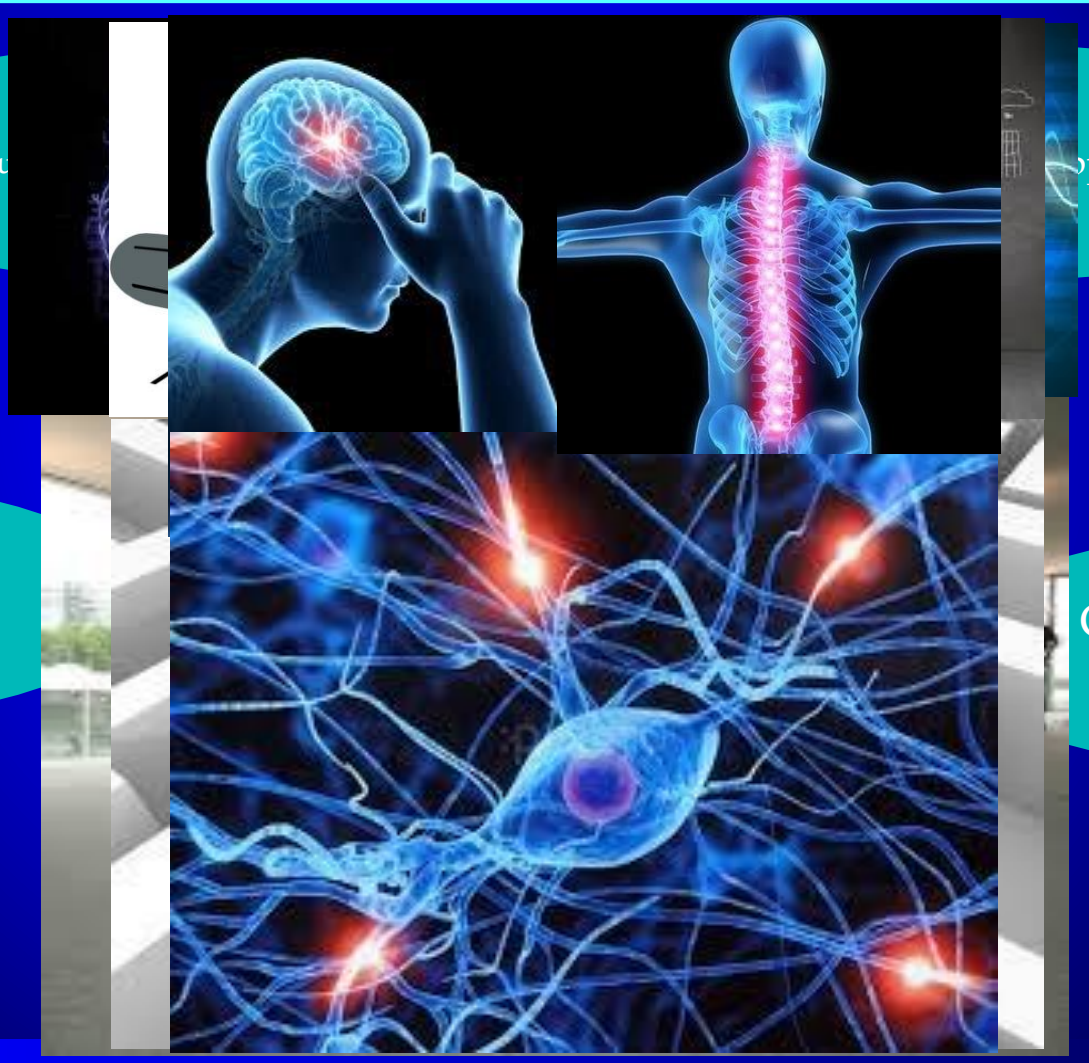


Decision Making

Computational Neuroscience

Experimental Protocol Design

- One time measure
  - Feature extraction
  - Classification
  - Comparison
- Repeated measures
  - Time course of changes
  - Natural history
  - Predication

Longitudinal studies

One Time Measure

- Feature extraction
  - Independent of each other
  - Sensitive
  - High Intra-subject reliability
  - Low Inter-subject variability

Appropriate for Longitudinal studies

Longitudinal Studies

- Diagnosis
  - Development of disease
- Treatment
  - Progress of treatment

Clinical Significance

Longitudinal Studies: Pre-Post Measures

- Inaccuracy
  - Possible outliers
  - Ignoring patterns
  - Can misguide
- Group-averaged results
  - Inadequate information
  - Can misguide

Repeated measures

→ recovery patterns

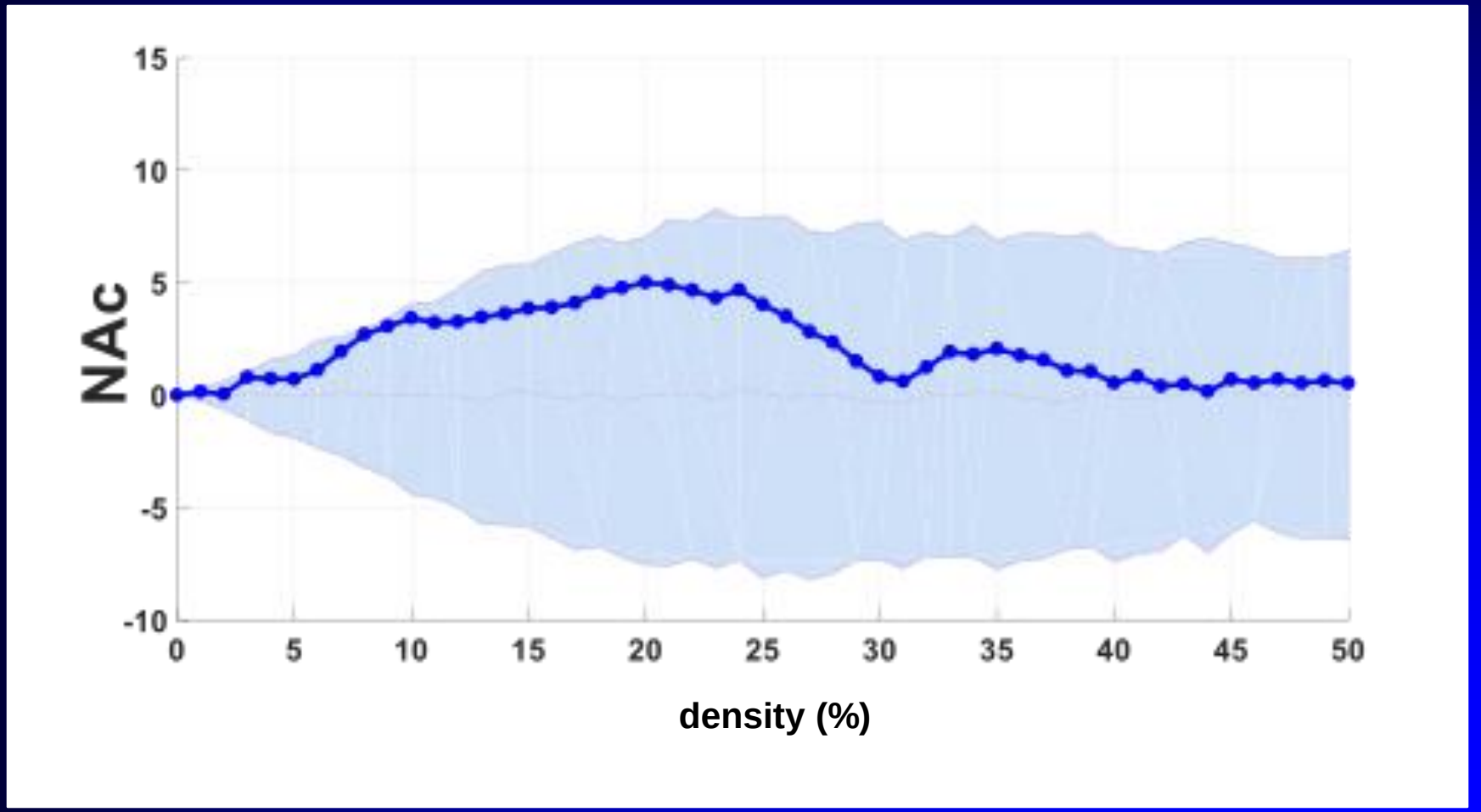
Identification of Recovery Patterns

- Address Pre-Post measures deficit
  - Eliminate outliers→ improve accuracy
  - Sufficient information → identify sub-groups
  - Reduce inter-subject variability → detect significant alteration

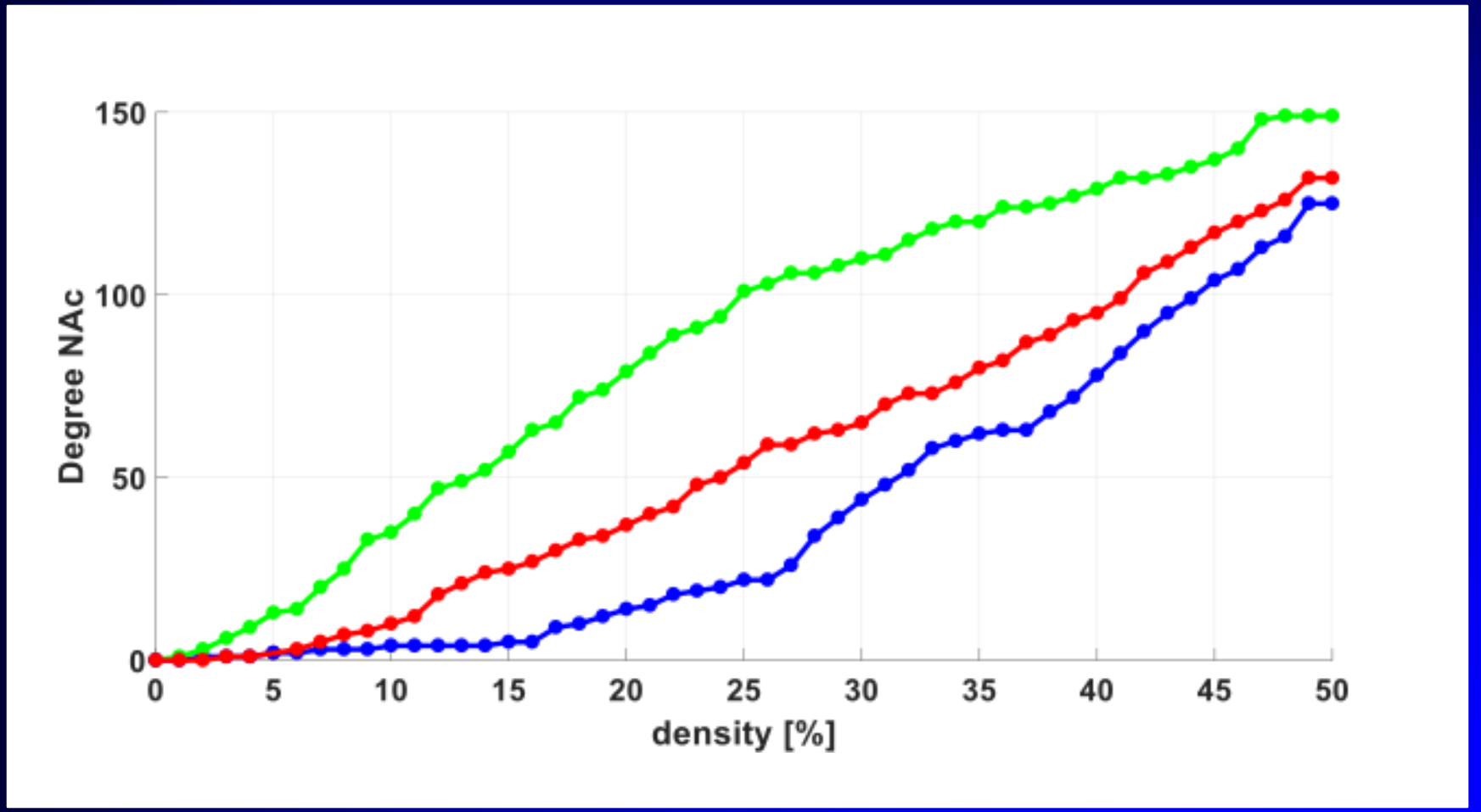
Recovery patterns

→ Prediction

Difference in Nodal Degree (MDD-HC)

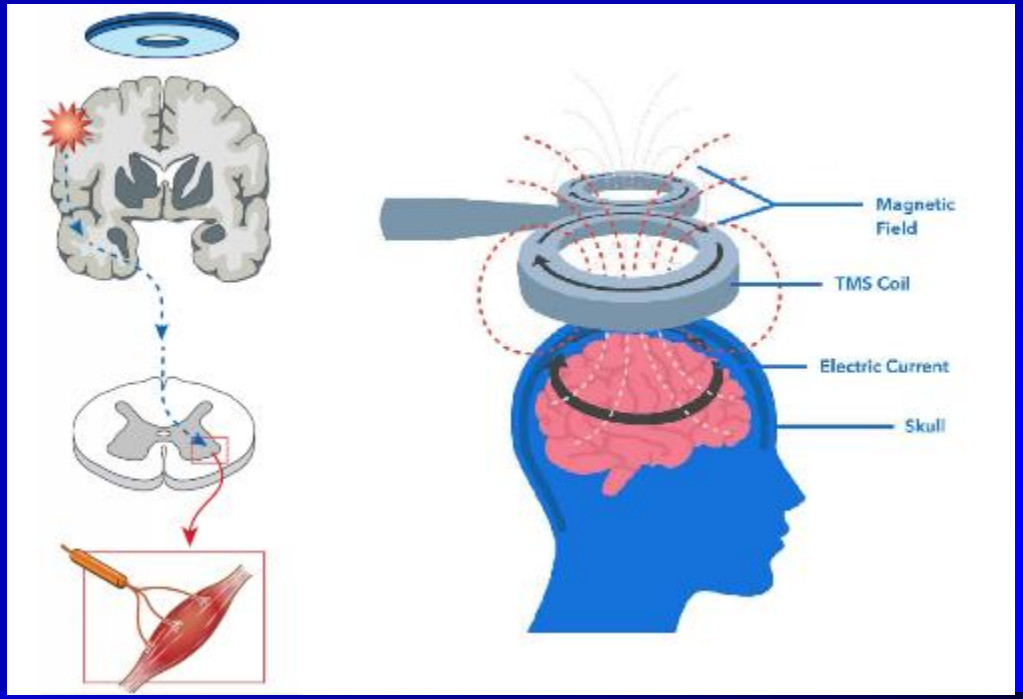


INTER-SUBJECT VARIABILITY

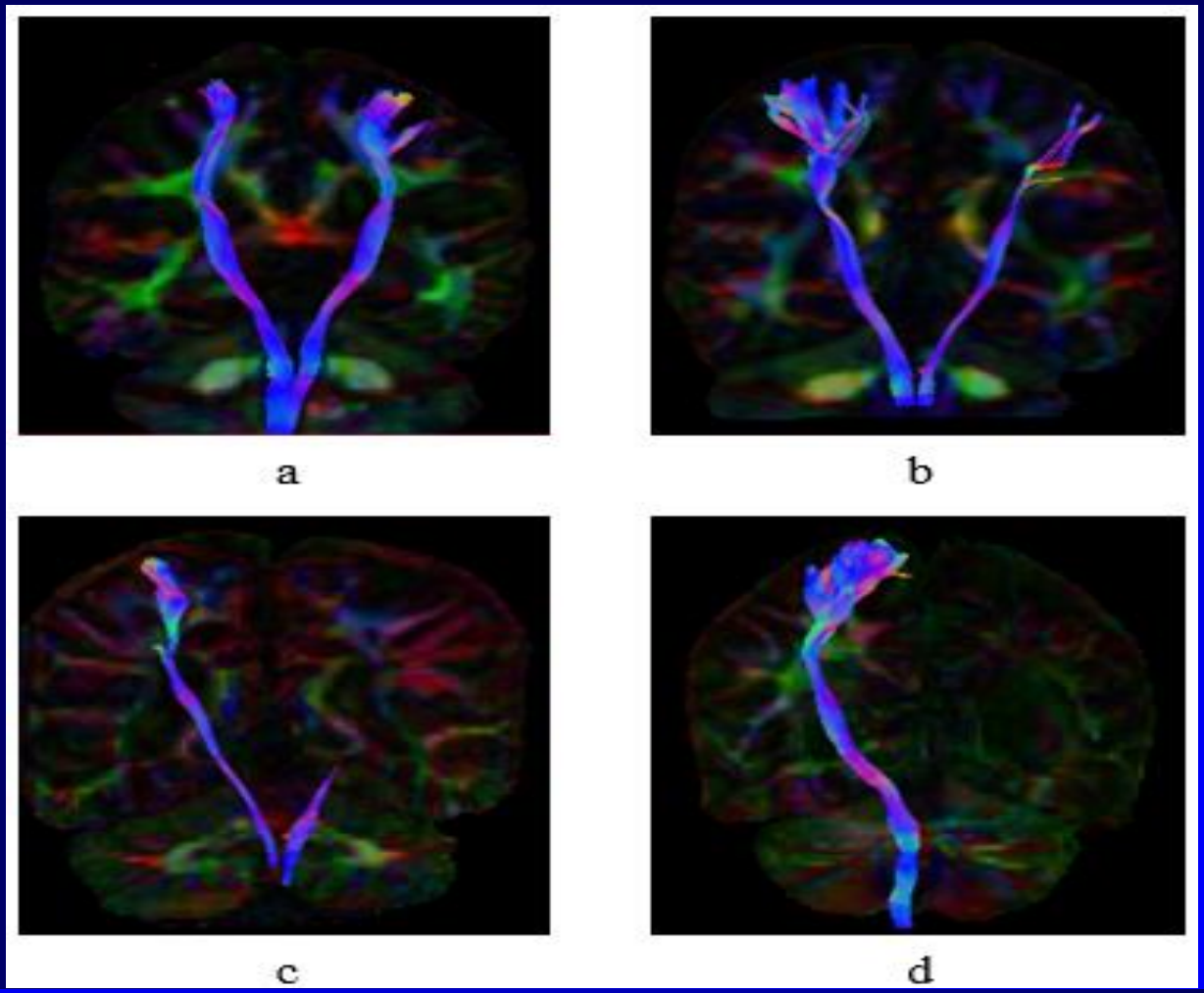


Evaluation of CST's structure and function

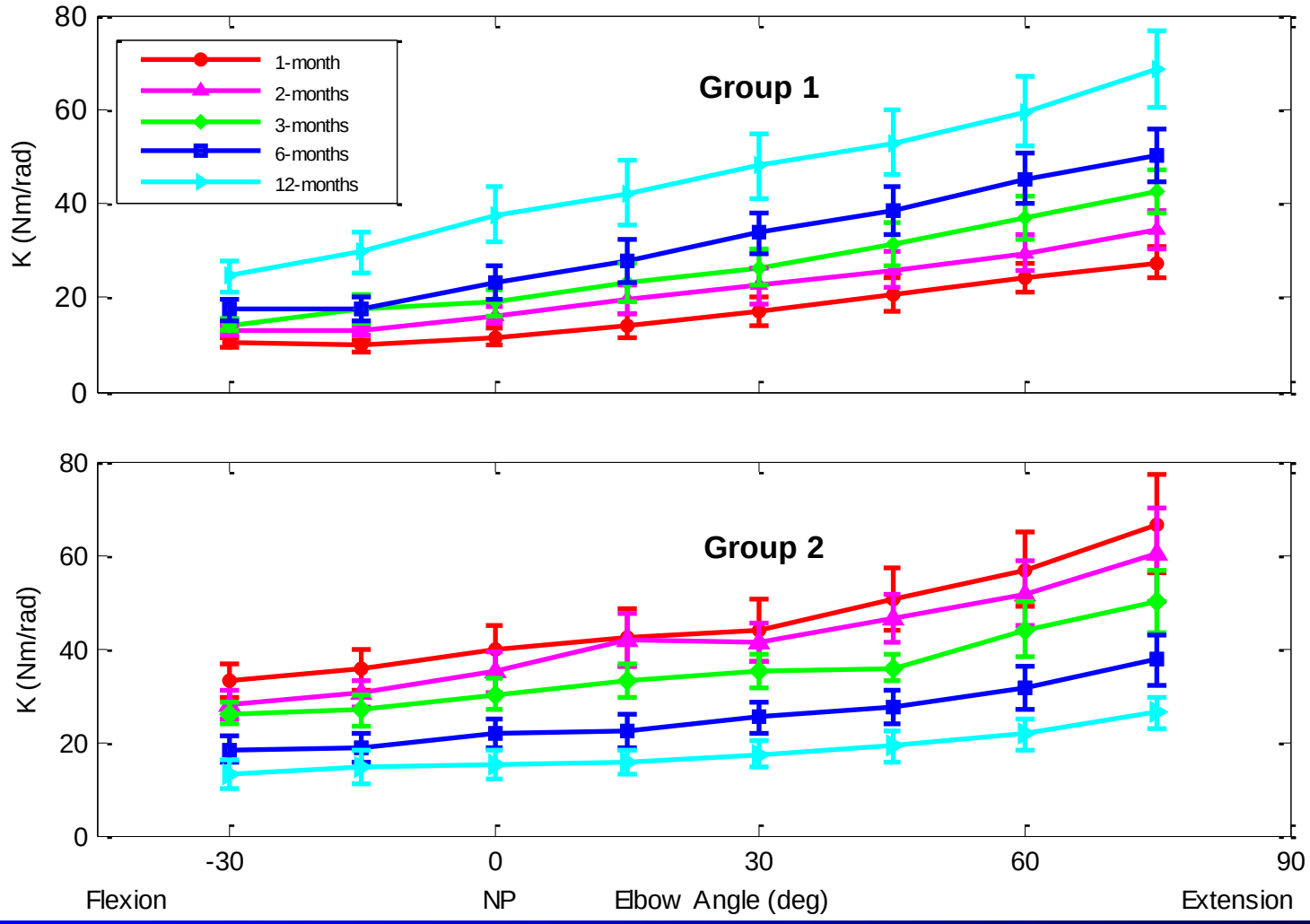
- Two neuroimaging methods including:
  - Transcranial Magnetic Stimulation (TMS)
  - Diffusion Tensor Imaging (DTI)



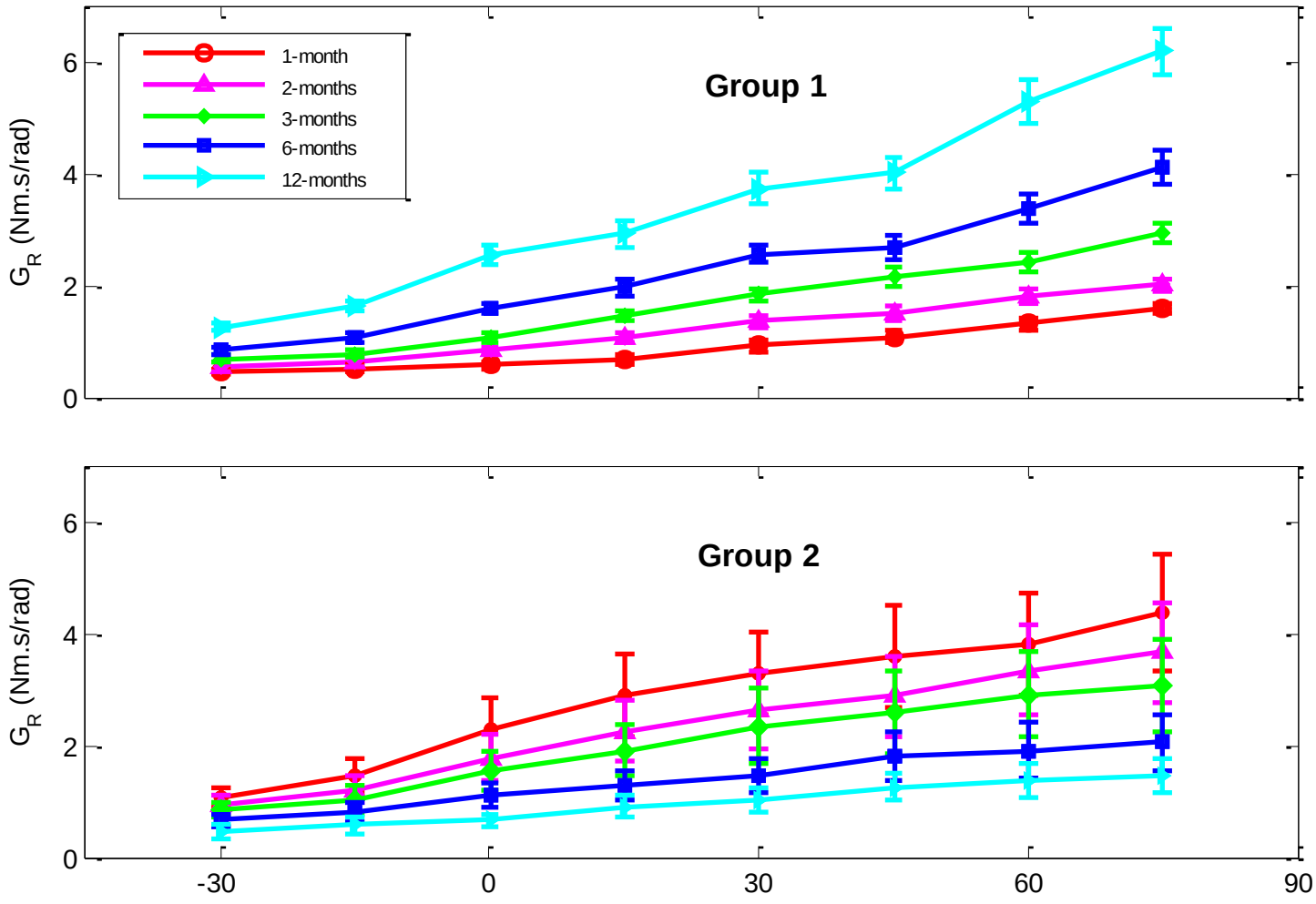
CST Pattern in CP



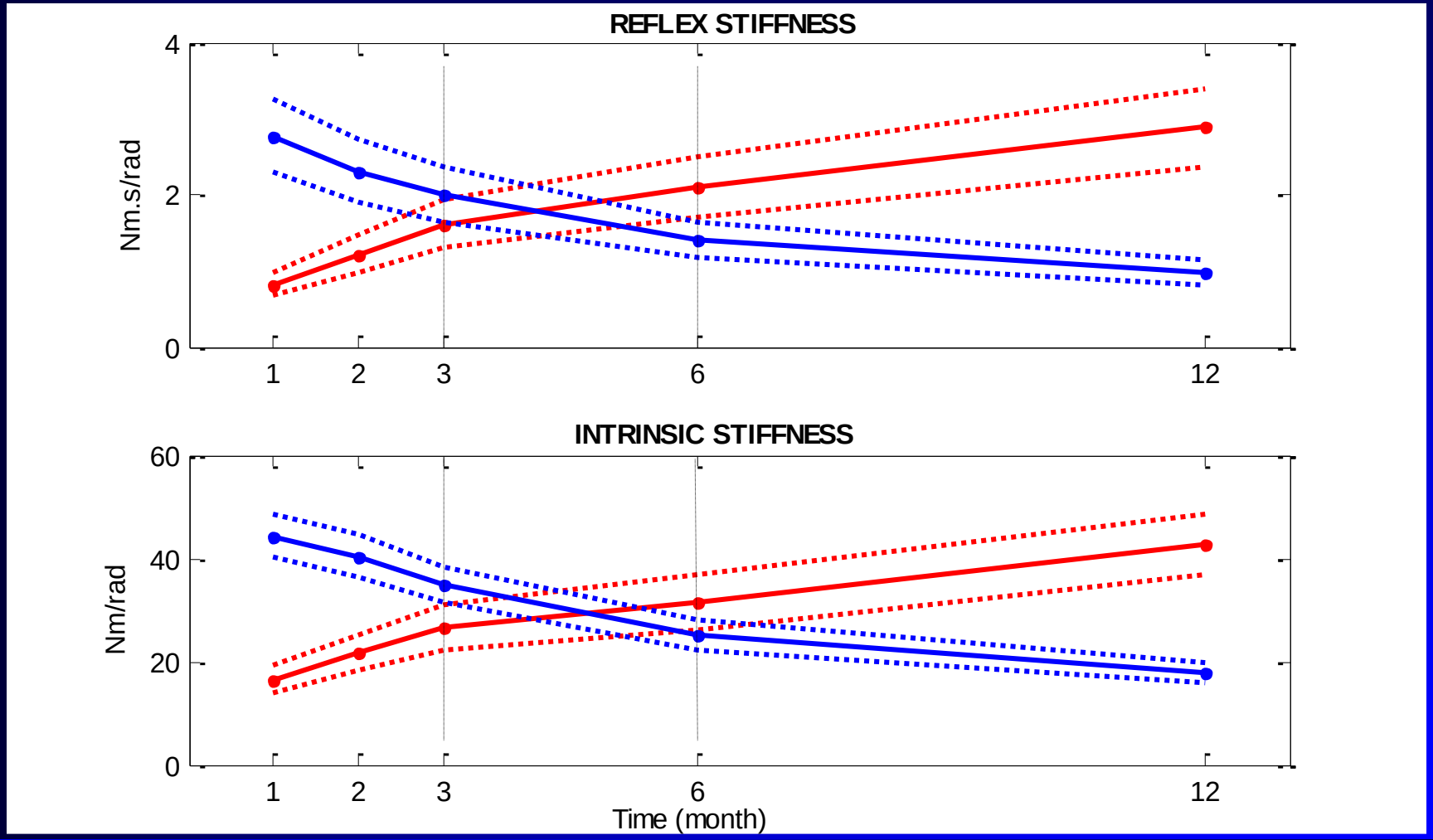
Time-course of Changes in Intrinsic Stiffness



Time-course of Changes in Reflex Stiffness

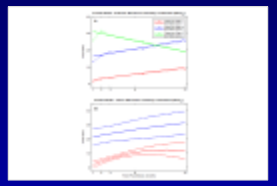


Recovery Patterns of Intrinsic and Reflex Stiffness



Prediction of Recovery Patterns

- Prognosis
  - Predictors
  - Bio-markers

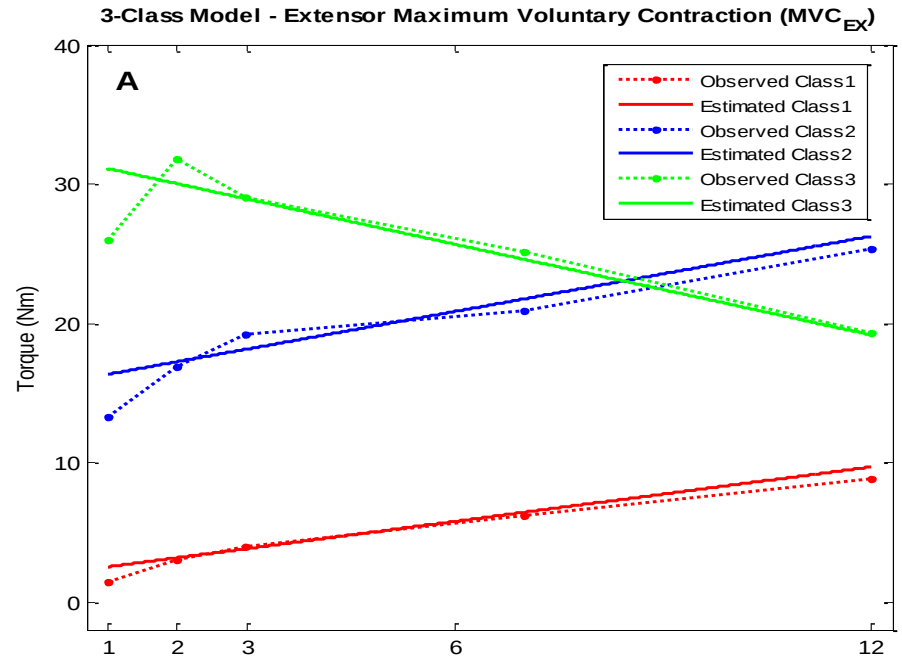


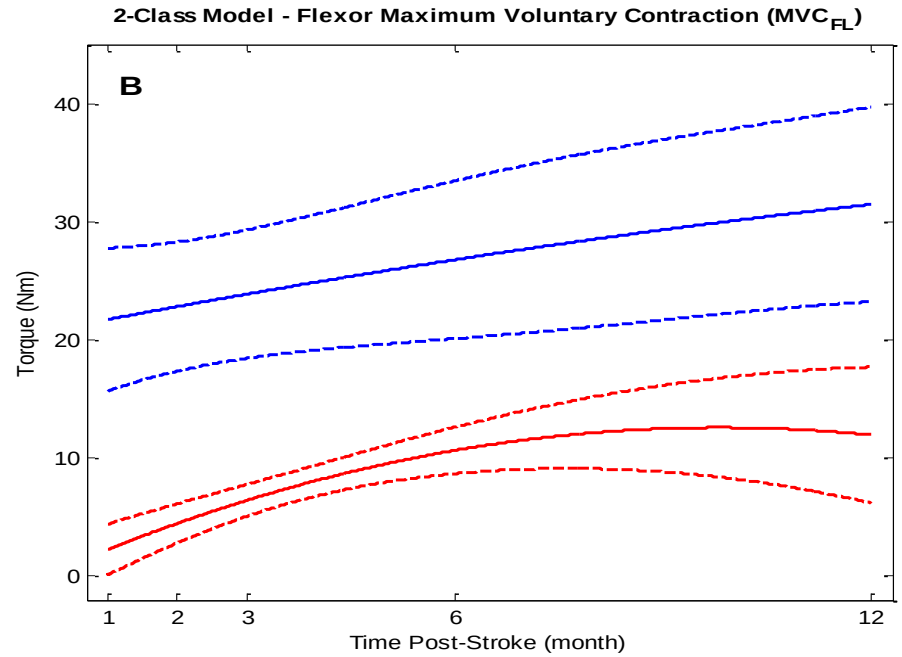
- Treatment protocol
  - Individualizing treatment

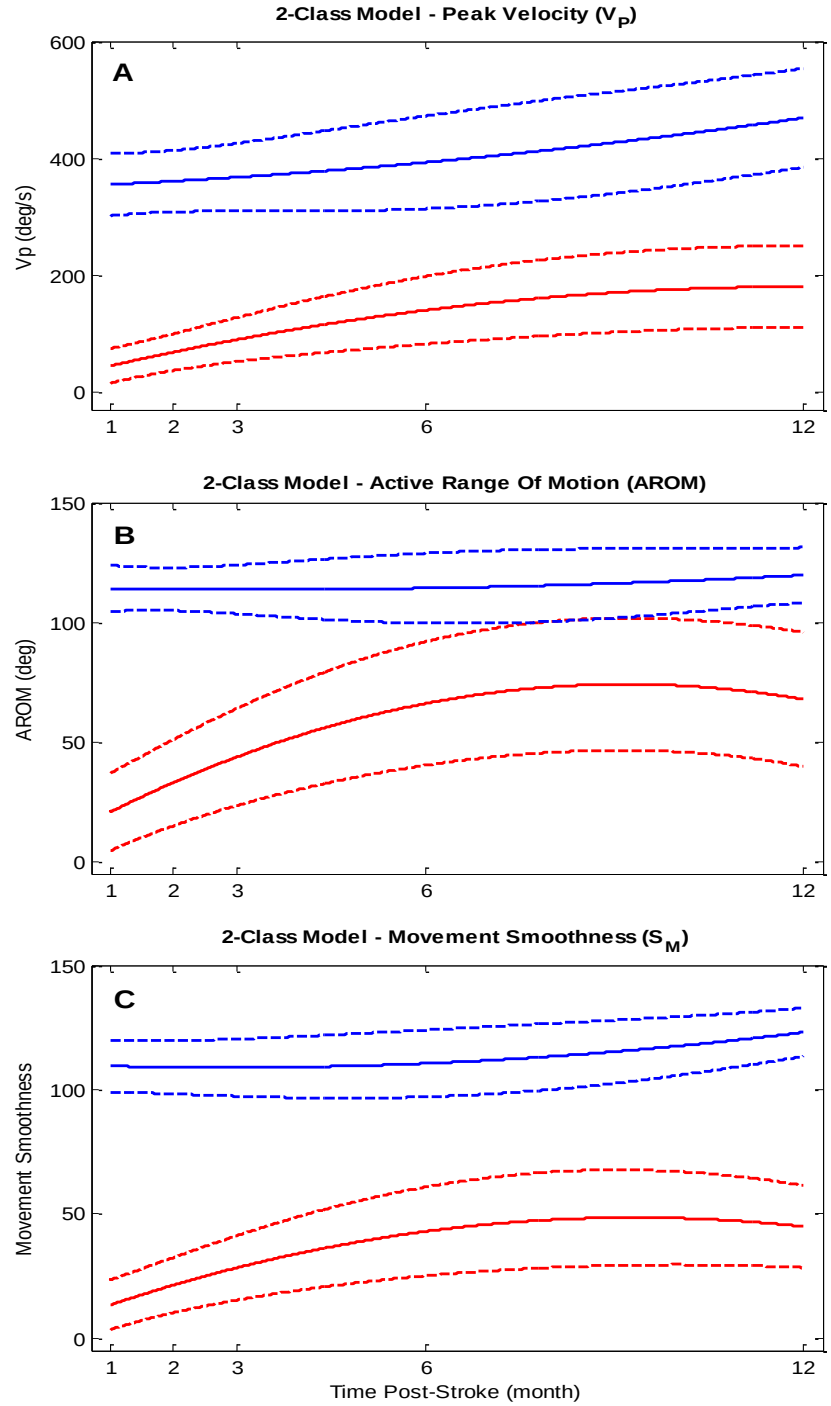
- Underlying mechanisms
  - Time course of changes in key features
  - Interactions between the key features
  - Relationships between outcome measures and features

Optimizing the treatment protocol

→ Minimizing time, effort and cost


3-Class Model - Extensor Maximum Voluntary Contraction (MVC$_{EX}$)
A
Observed Class1
Estimated Class1
Observed Class2
Estimated Class2
Observed Class3
Estimated Class3
Torque (Nm)
0
10
20
30
40
1
2
3
6
12


2-Class Model - Flexor Maximum Voluntary Contraction (MVC$_{FL}$)
B
Torque (Nm)
0
10
20
30
40
1
2
3
6
12
Time Post-Stroke (month)


2-Class Model - Peak Velocity (V_P)
A
Vp (deg/s)
600
400
200
0
1
2
3
6
12
2-Class Model - Active Range Of Motion (AROM)
B
AROM (deg)
150
100
50
0
1
2
3
6
12
2-Class Model - Movement Smoothness (S_M)
C
Movement Smoothness
150
100
50
0
1
2
3
6
12
Time Post-Stroke (month)

Growth Mixture Model

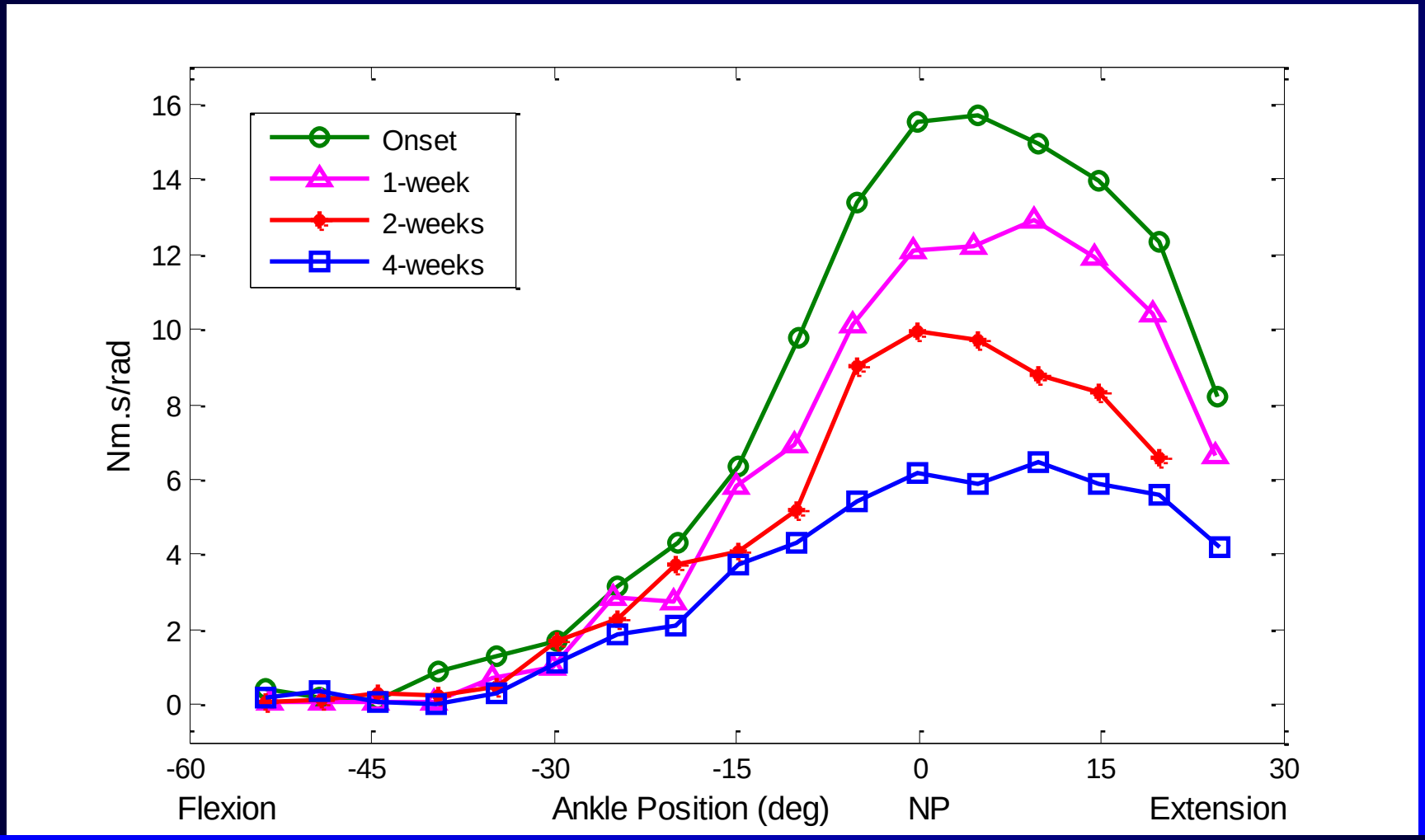
- The growth mixture model can used to extract the recovery pattern (class) for outcome measures during the required time.
- The model assumes that the population can be divided into several latent classes.
- The growth mixture modeling allows the membership of the latent classes to be associated with a group of baseline factors, via a multinomial logistic regression model.
- Estimation of the model parameters is based on maximizing the likelihood function via the Expectation-Maximization algorithm.
- In the fitted growth mixture model, the multinomial logistic regression are used to characterize the association between the membership and predictors.
- To predict the membership for each subject, the probability of the subject's data lying in each of the potential subclasses is calculated, and the membership as the class with the highest predicted probability is identified.
- This procedure helps explore the association of predictors at baseline with outcome measures class membership in the growth mixture model.

	No. Subjects	% Sample-size	Growth Mixture Model			The logistic regression		FMS	entropy
			Intercept	Slope	Quadratic	Coefficient Intercept	Coefficient FMS		
MVC_{EX}									
Class 1	11	55%	2.515 (p=0.005)	0.653 (p=0.001)	---	6.533 (p=0.009)	-0.167 (p=0.021)	<= 35	0.992 (0.986)
Class 2	6	30%	16.333 (p=0.001)	0.902 (p=0.008)	---	1.140 (p=0.697)	-0.009 (p=0.876)	>35	
Class 3	3	15%	31.121 (p=0.001)	-1.087 (0.006)	---	the reference			
MVC_{FL}									
Class 1	9	45%	2.245 (p=0.042)	2.346 (0.001)	-0.133 (p=0.001)	classes do not overlap based on FMS		<= 11*	1.0 (0.997)
Class 2	11	55%	21.714 (p=0.001)	1.118 (p=0.287)	-0.021 (p=0.763)	classes do not overlap based on FMS		> 11	
V_P									
Class 1	11	55%	44.705 (p=0.003)	24.685 (p=0.001)	-1.122 (p=0.04)	classes do not overlap based on FMS		<= 35**	0.999 (0.990)
Class 2	9	45%	355.687 (0.001)	5.235 (p=0.64)	0.466 (p=0.573)	classes do not overlap based on FMS		> 35	
AROM									
Class 1	9	45%	20.644 (p=0.012)	13.079 (p=0.001)	-0.799 (p=0.001)	classes do not overlap based on FMS		<= 11*	1.0 (0.988)
Class 2	11	55%	114.183 (p=0.001)	-0.389 (p=0.881)	0.081 (p=0.7)	classes do not overlap based on FMS		> 11	
S_M									
Class 1	10	50%	13.267 (p=0.009)	8.461 (p=0.001)	-0.508 (p=0.001)	5.358 (p=0.001)	-0.196 (p=0.001)	<= 27	1.0 (1.0)
Class 2	10	50%	109.438 (p=0.001)	-0.647 (p=0.691)	0.171 (p=0.196)	the reference		> 27	

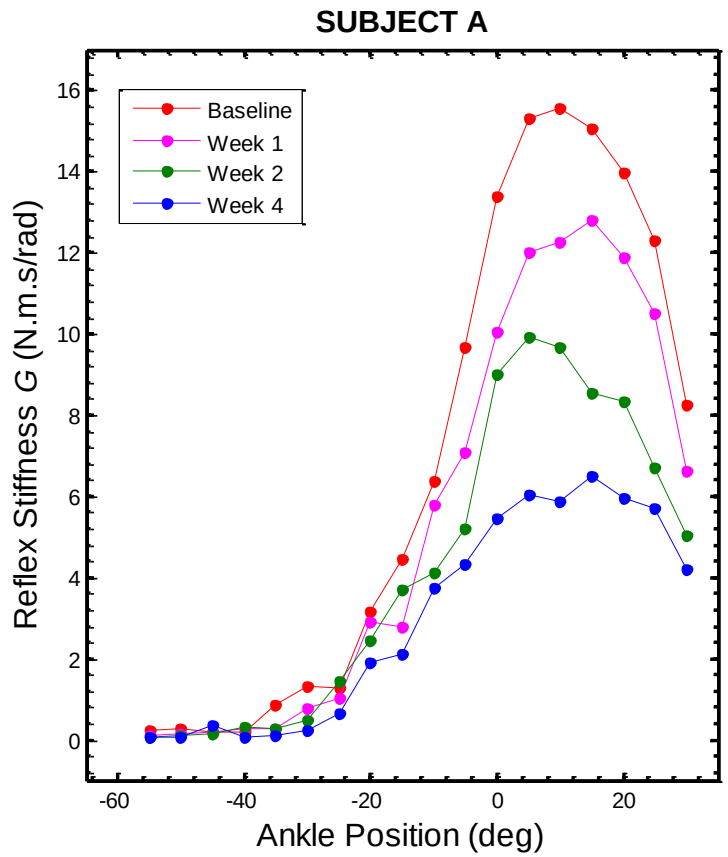
Prediction of Arm Movement Recovery

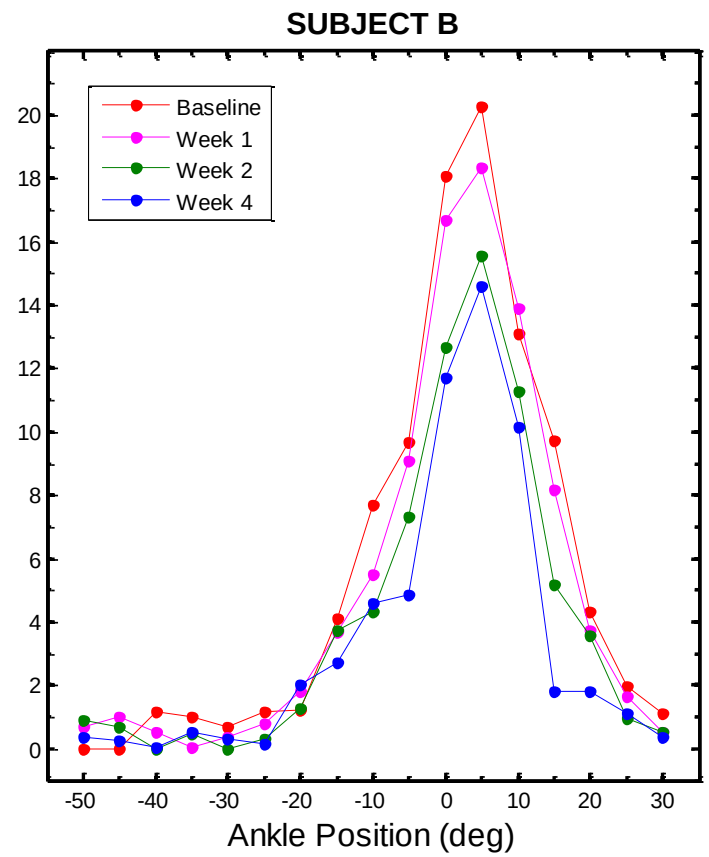
Fugl-Meyer Score (FMS)	AROM	MVC_{FX}	S_M	MVC_{EX}	V_P, V_a, A_P
36-65					
28-35				●	●
12-27			●	●	●
0-11	●	●	●	●	●

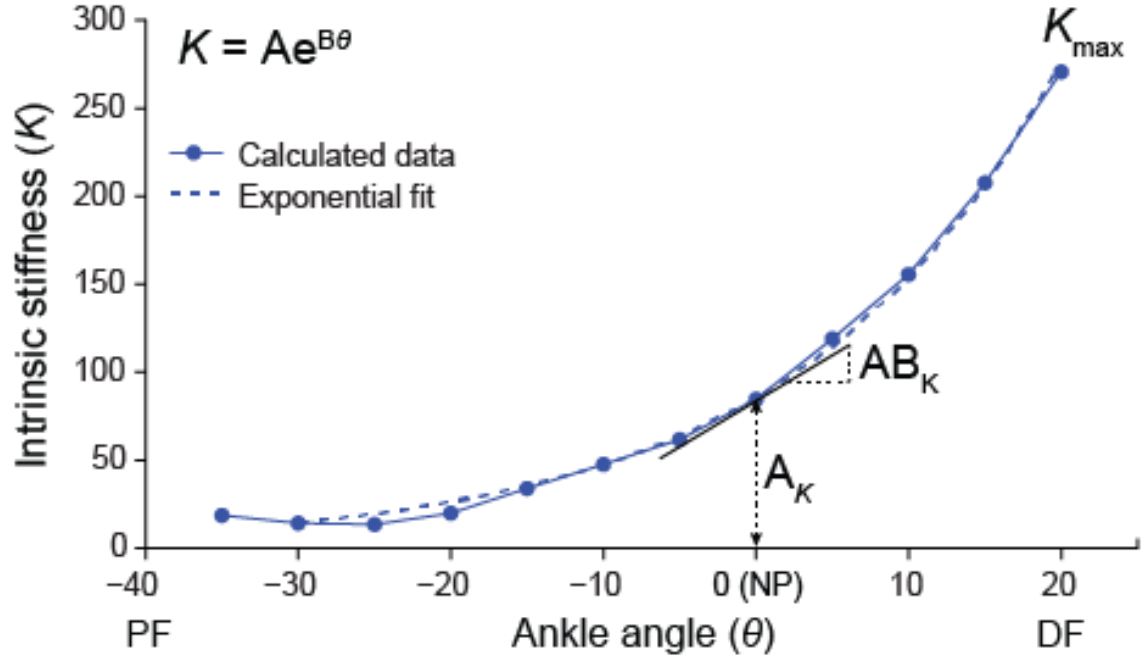
LOKOMAT Effects on Reflex Stiffness

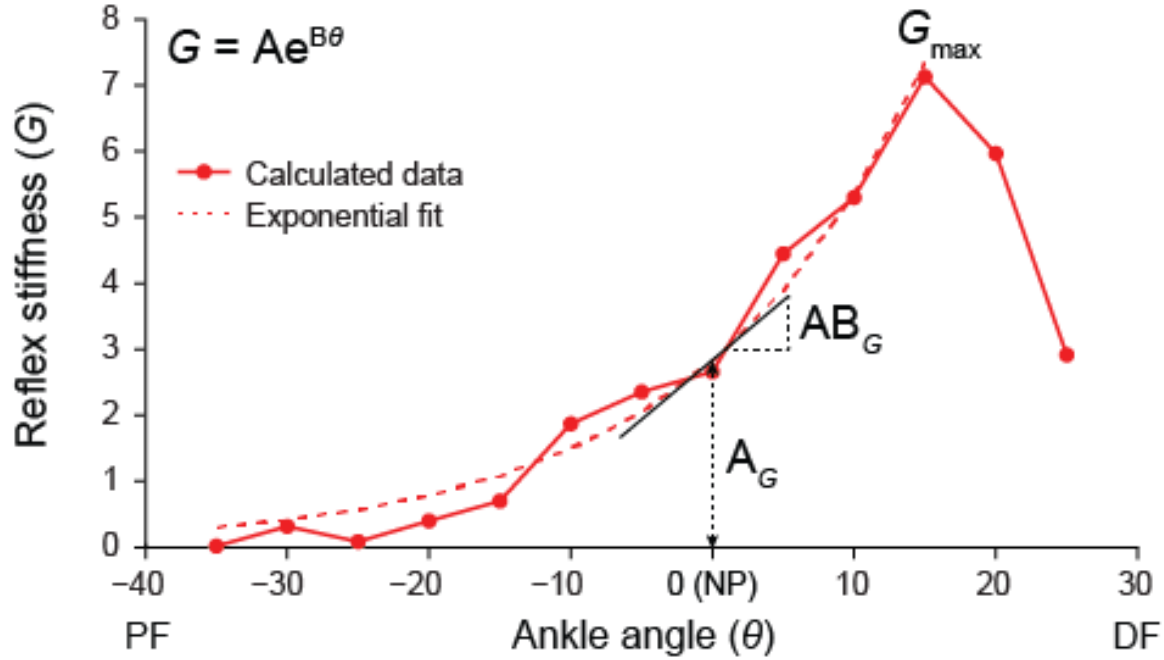


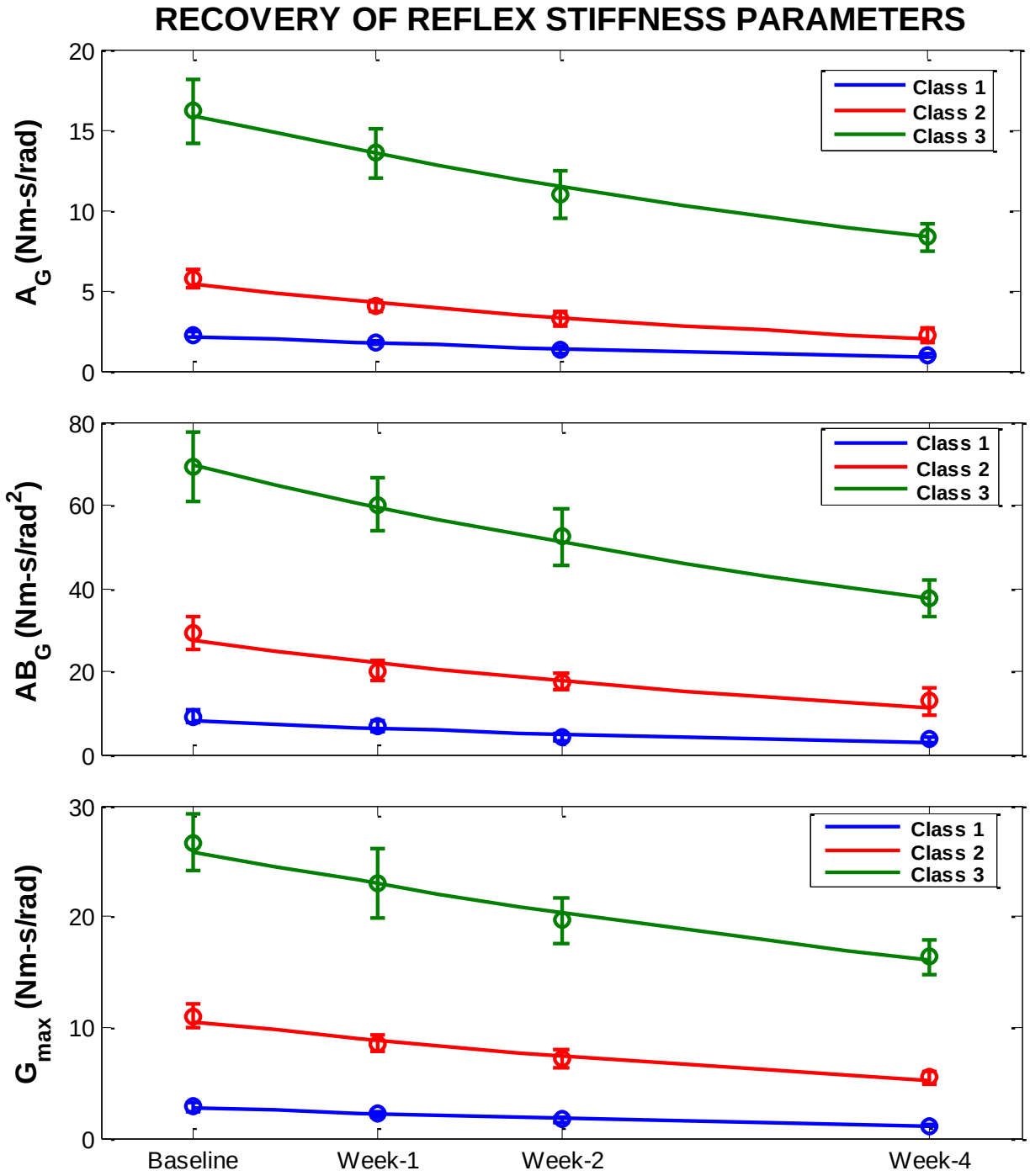
LOKOMAT Effects on Reflex Stiffness

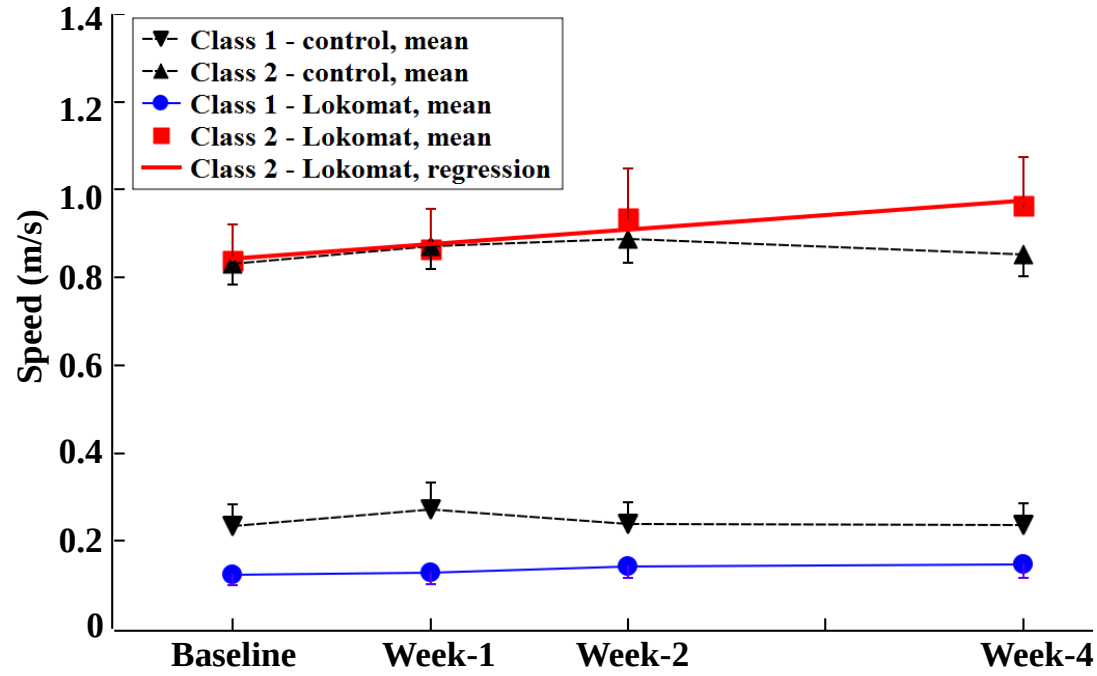


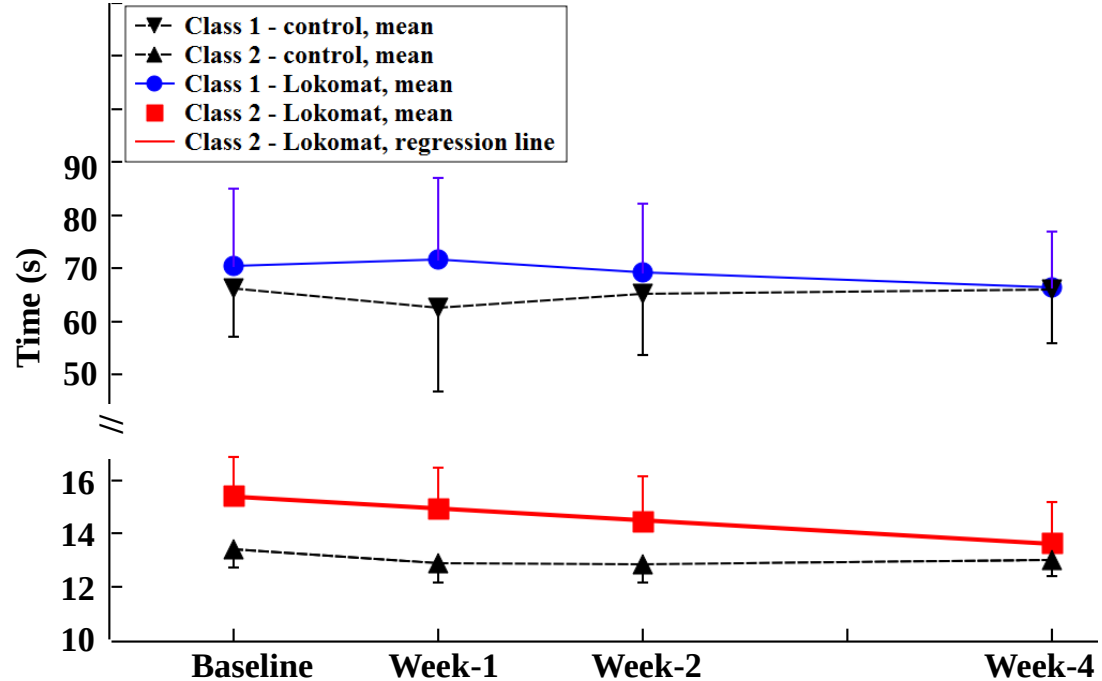


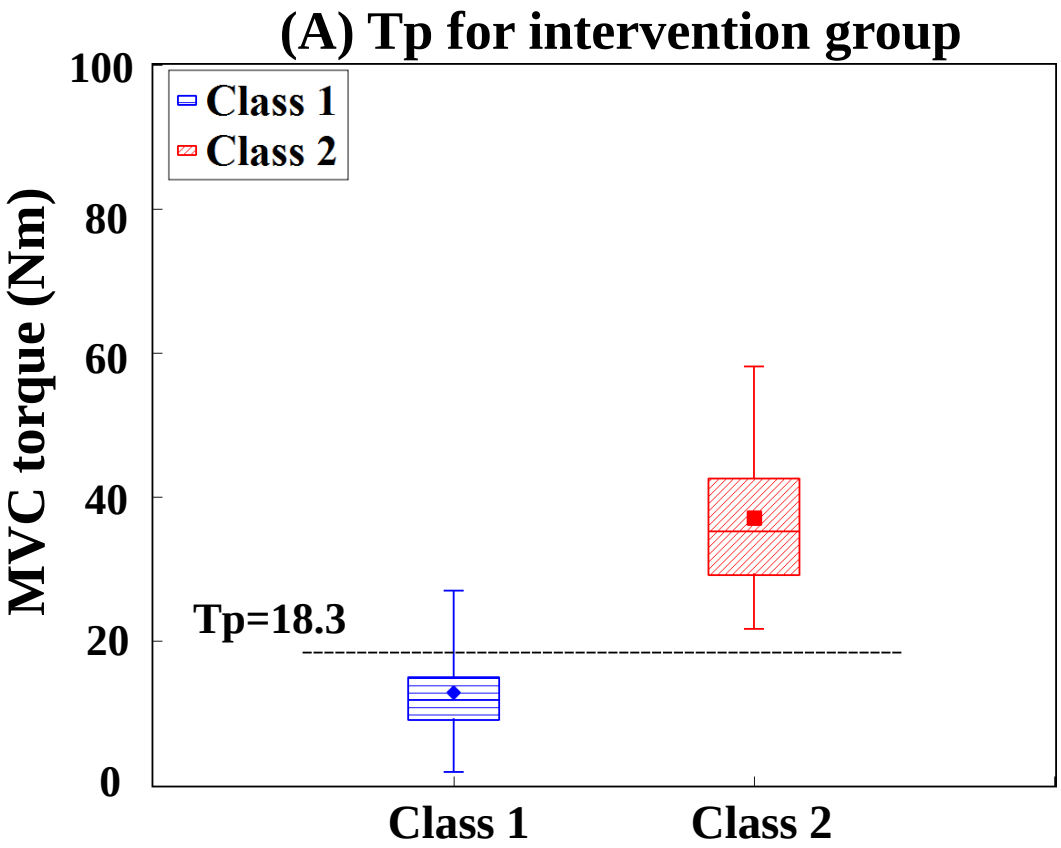

$K = Ae^{B\theta}$
K_{max}
Calculated data
Exponential fit
AB_K
A_K
Intrinsic stiffness (K)
300
250
200
150
100
50
0
−40
−30
−20
−10
0 (NP)
10
20
PF
Ankle angle (θ)
DF

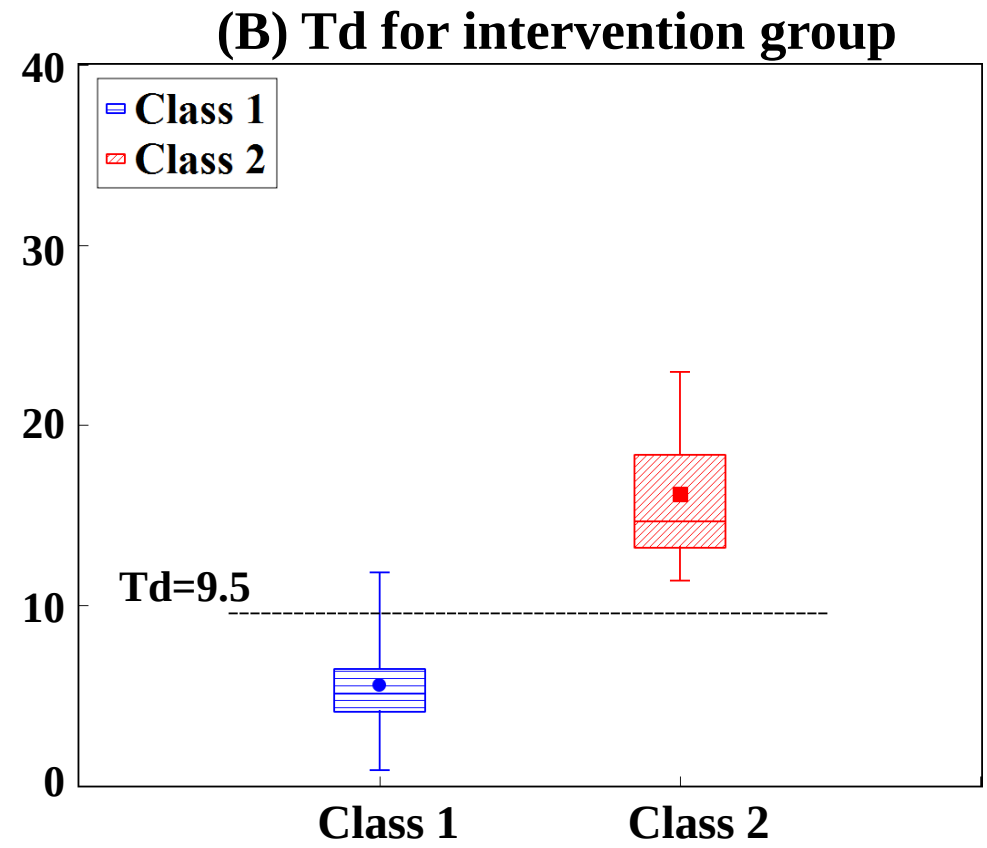

$G = Ae^{B\theta}$
G_{max}
Calculated data
Exponential fit
AB_G
A_G
Reflex stiffness (G)
8
7
6
5
4
3
2
1
0
−40
−30
−20
−10
0 (NP)
10
20
30
PF
Ankle angle (θ)
DF

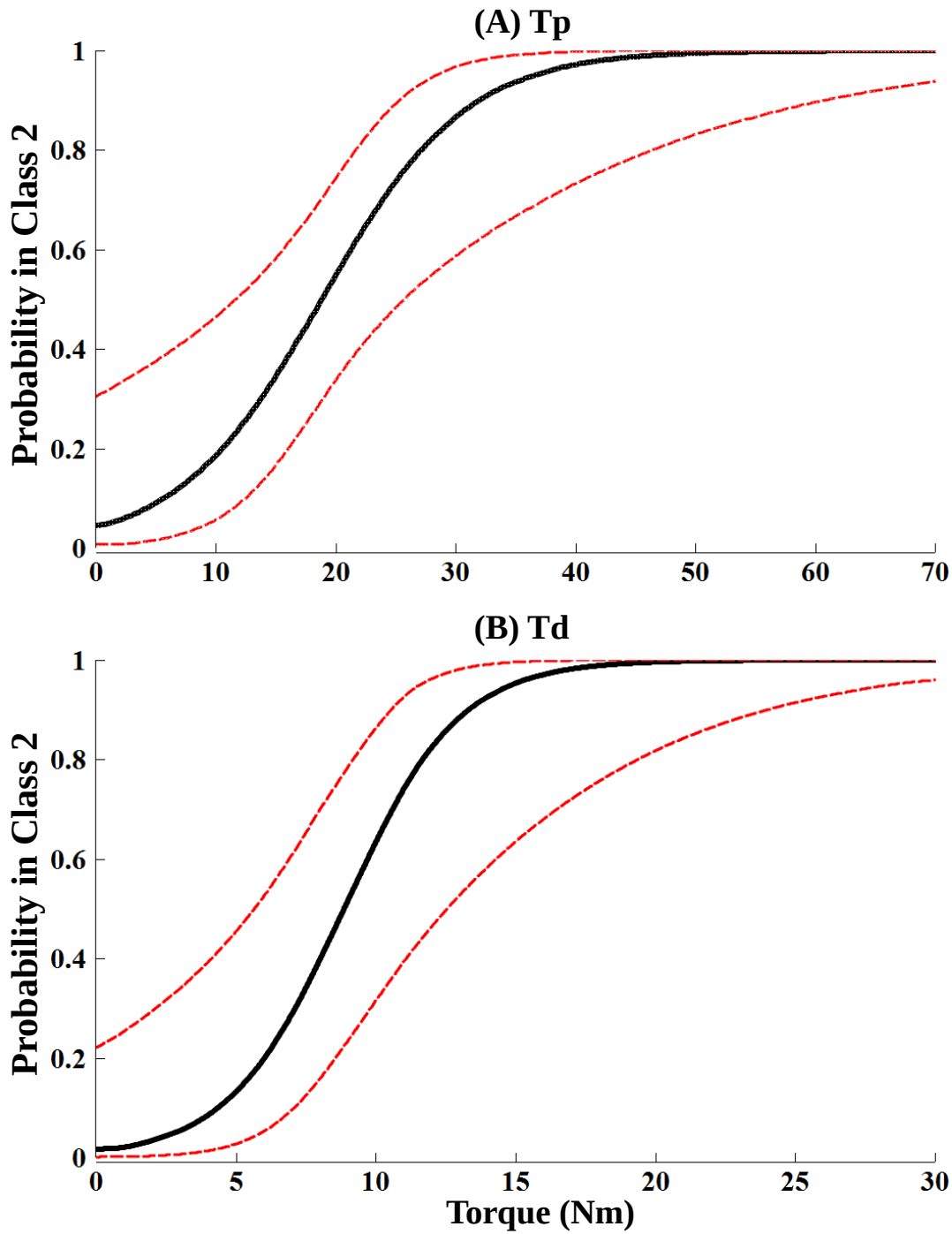

RECOVERY OF REFLEX STIFFNESS PARAMETERS
A_G (Nm-s/rad)
AB_G (Nm-s/rad^2)
G_{max} (Nm-s/rad)
Class 1
Class 2
Class 3
0
5
10
15
20
0
20
40
60
80
0
10
20
30
Baseline
Week-1
Week-2
Week-4


Class 1 - control, mean
Class 2 - control, mean
Class 1 - Lokomat, mean
Class 2 - Lokomat, mean
Class 2 - Lokomat, regression
Speed (m/s)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
Baseline
Week-1
Week-2
Week-4


Class 1 - control, mean
Class 2 - control, mean
Class 1 - Lokomat, mean
Class 2 - Lokomat, mean
Class 2 - Lokomat, regression line
Time (s)
90
80
70
60
50
16
14
12
10
Baseline
Week-1
Week-2
Week-4


(A) Tp for intervention group
MVC torque (Nm)
100
80
60
40
20
0
Class 1
Class 2
Tp=18.3
Class 1
Class 2


(B) Td for intervention group
40
30
20
10
0
Class 1
Class 2
Td=9.5
Class 1
Class 2

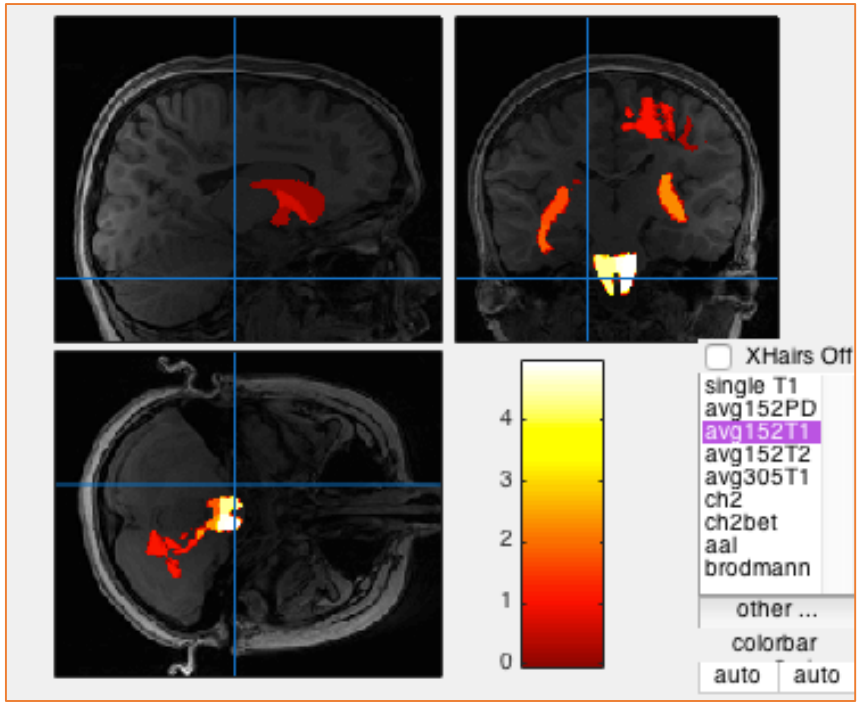

(A) Tp
Probability in Class 2
0
0.2
0.4
0.6
0.8
1
0
10
20
30
40
50
60
70
(B) Td
Probability in Class 2
0
0.2
0.4
0.6
0.8
1
0
5
10
15
20
25
30
Torque (Nm)

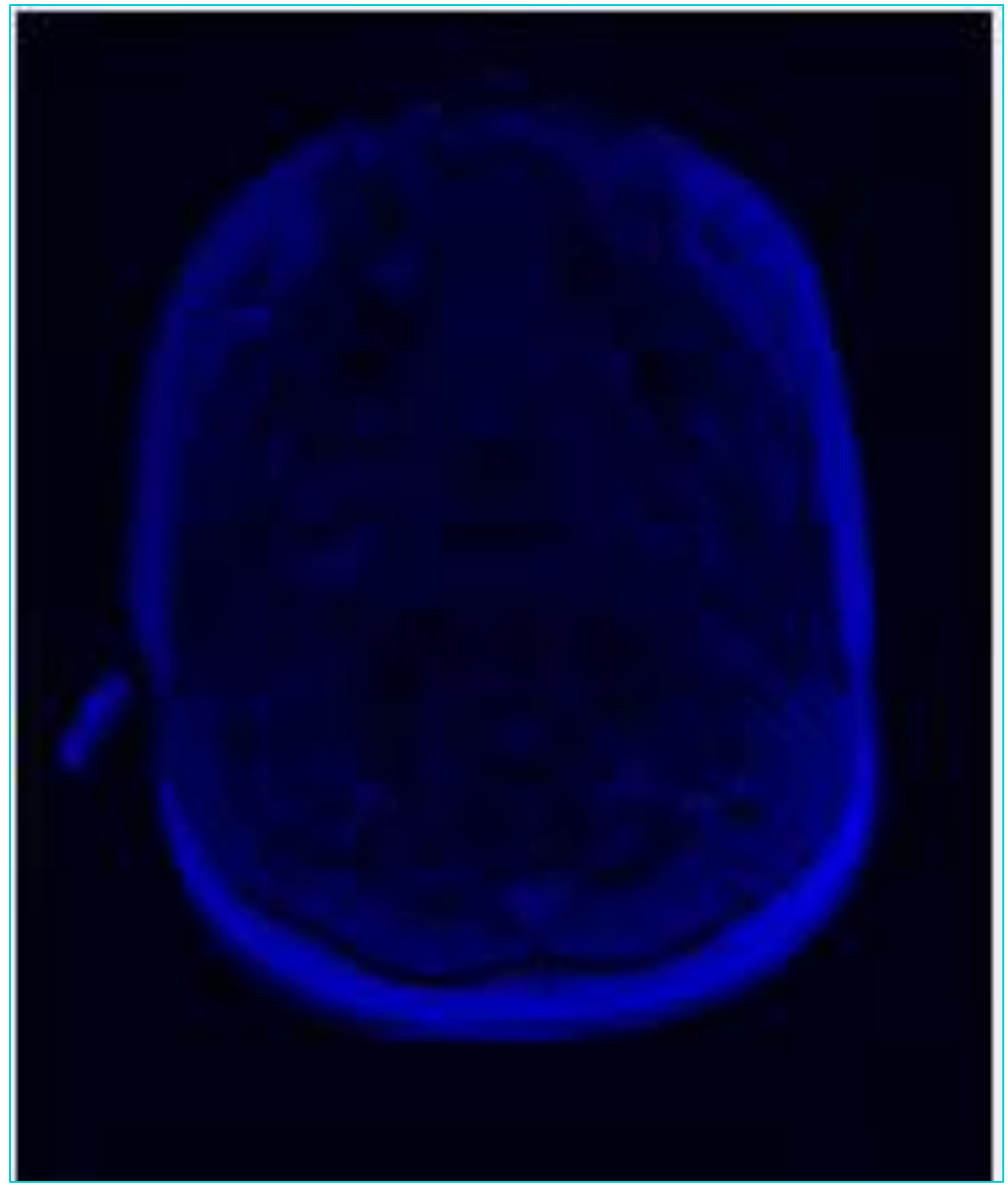
Brain Mapping Applications

- Prognosis
  - Alzheimer's disease
  - Parkinson's disease
  - Adrenoleukodystrophy (ALD)
  - Multiple Sclerosis (MS)
  - Stroke
  - Brain tumor
  - Epilepsy

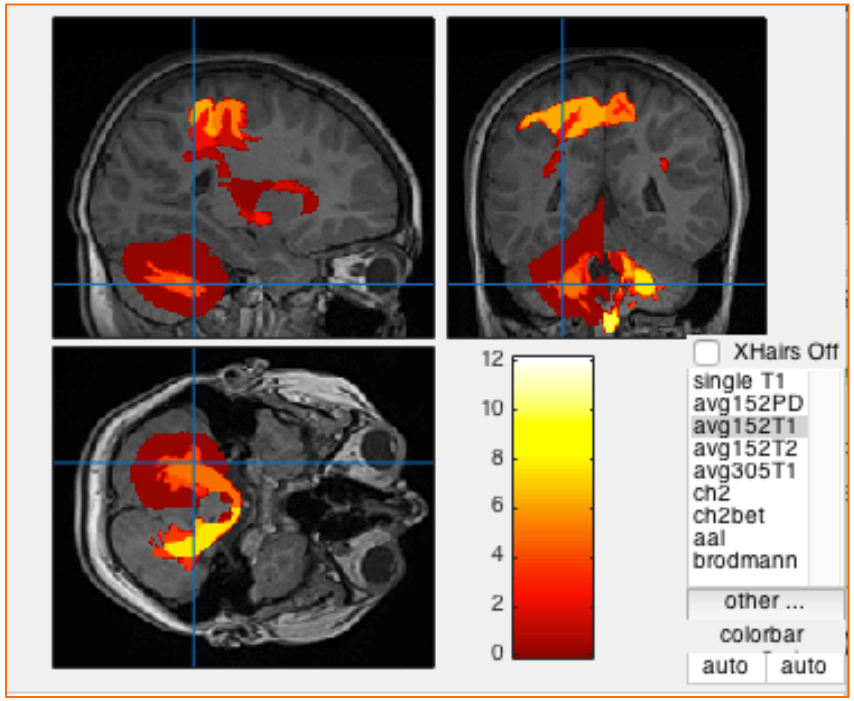
Brain Mapping Applications

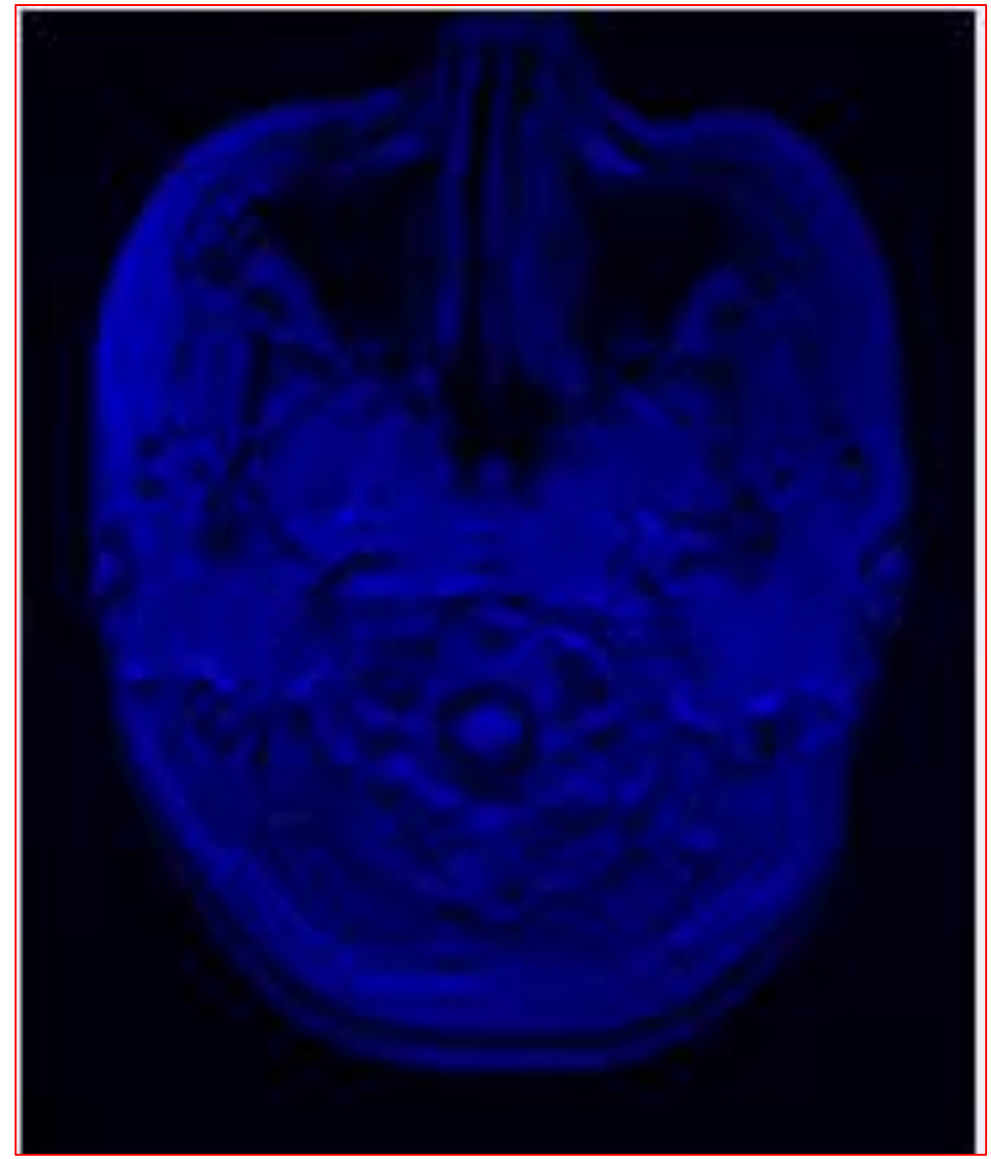
- Treatment
  - Neuroplasticity
  - Persistency



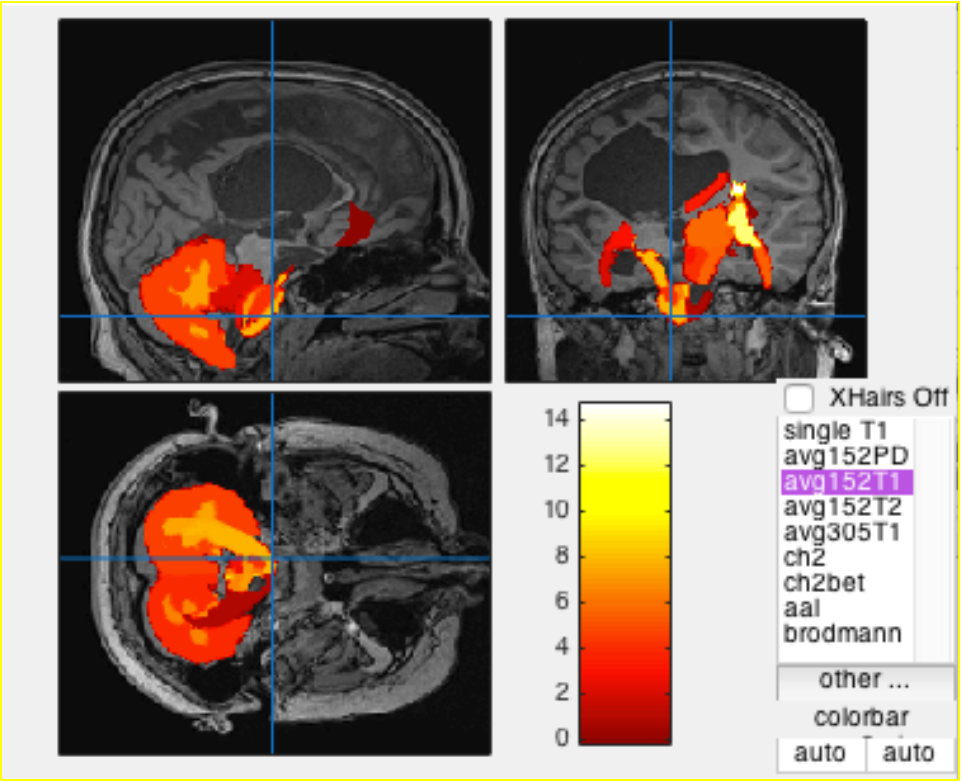


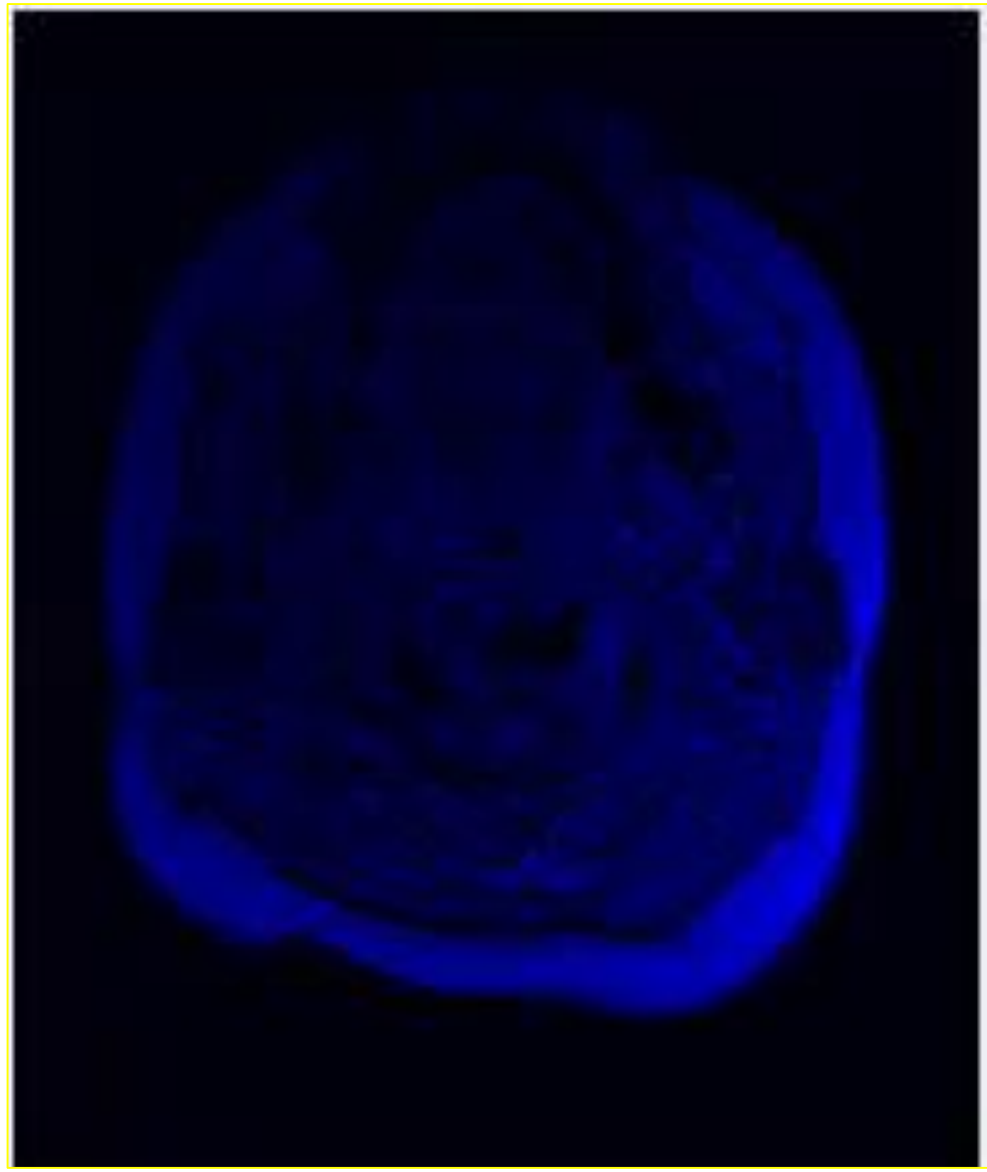
- Congenital CP
- Structural MRI (T1W): left periventricular leukomalacia
- Hemiplegia-Right Side
- FA changes: mostly affected side



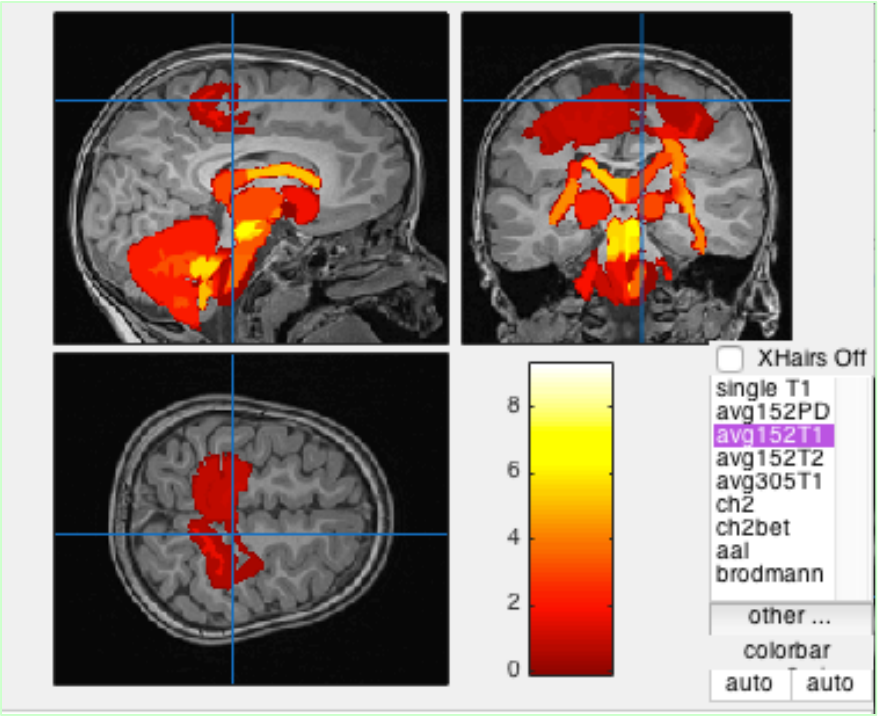


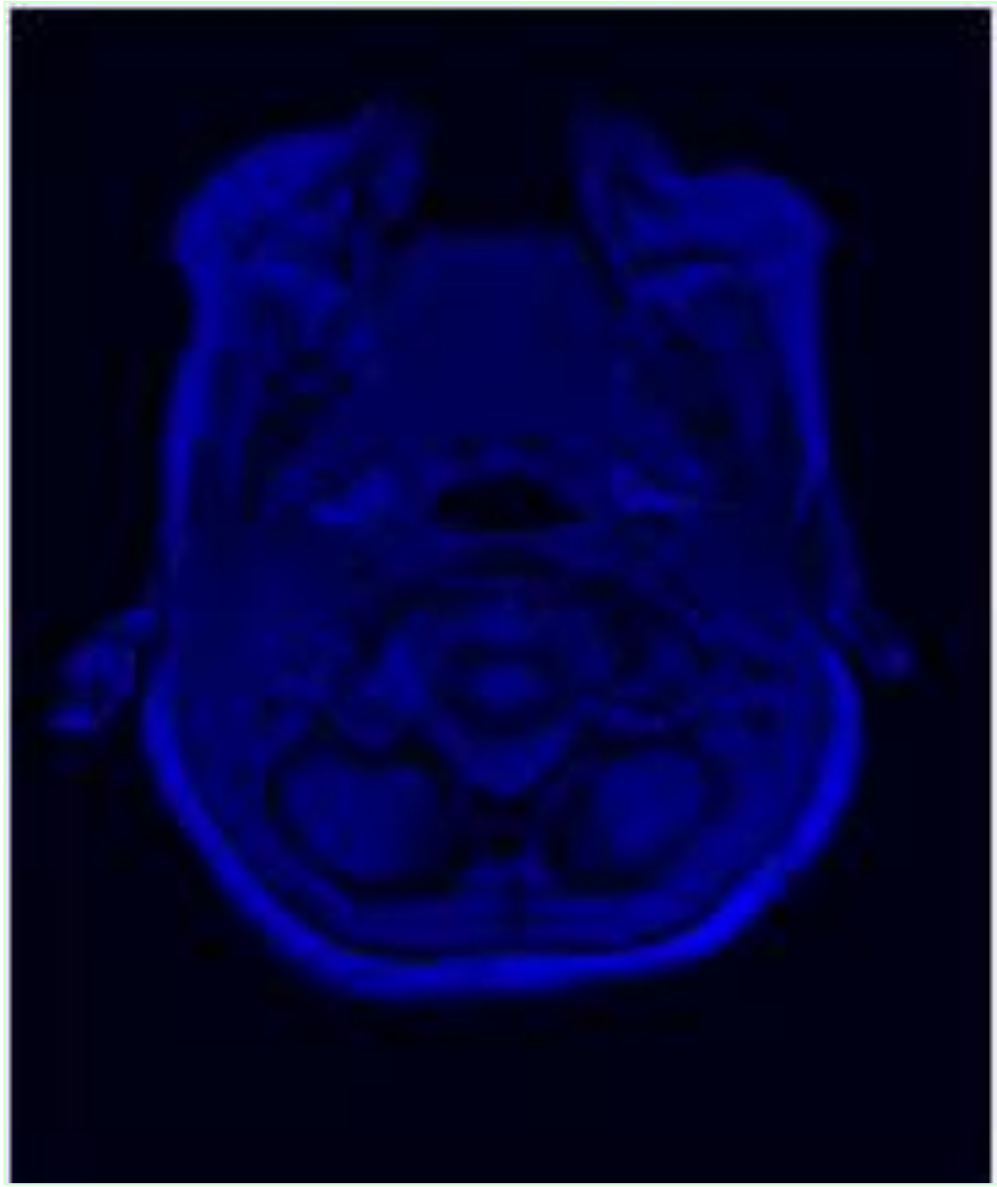
- Congenital CP
- Structural MRI (T1W): Normal
- Clinically Hemiplegia- Left Side
- Both brain sides FA changes





- Congenital CP-Seizure
- Hemiplegia- Left Side
- Both side Cerebellum FA Changes





- Hemiplegia- Left Side
- 4 years old- Control group
- Both side FA Changes

Brain Mapping Applications

- Underlying mechanisms
  - Depression
  - Stress and anxiety
  - Drug addiction
  - Obsessive-Compulsive disorder (OCD)
  - Cognitive issues
    - Autism disorder
  - Social behavior
    - Mapping social behavior-induced brain activation

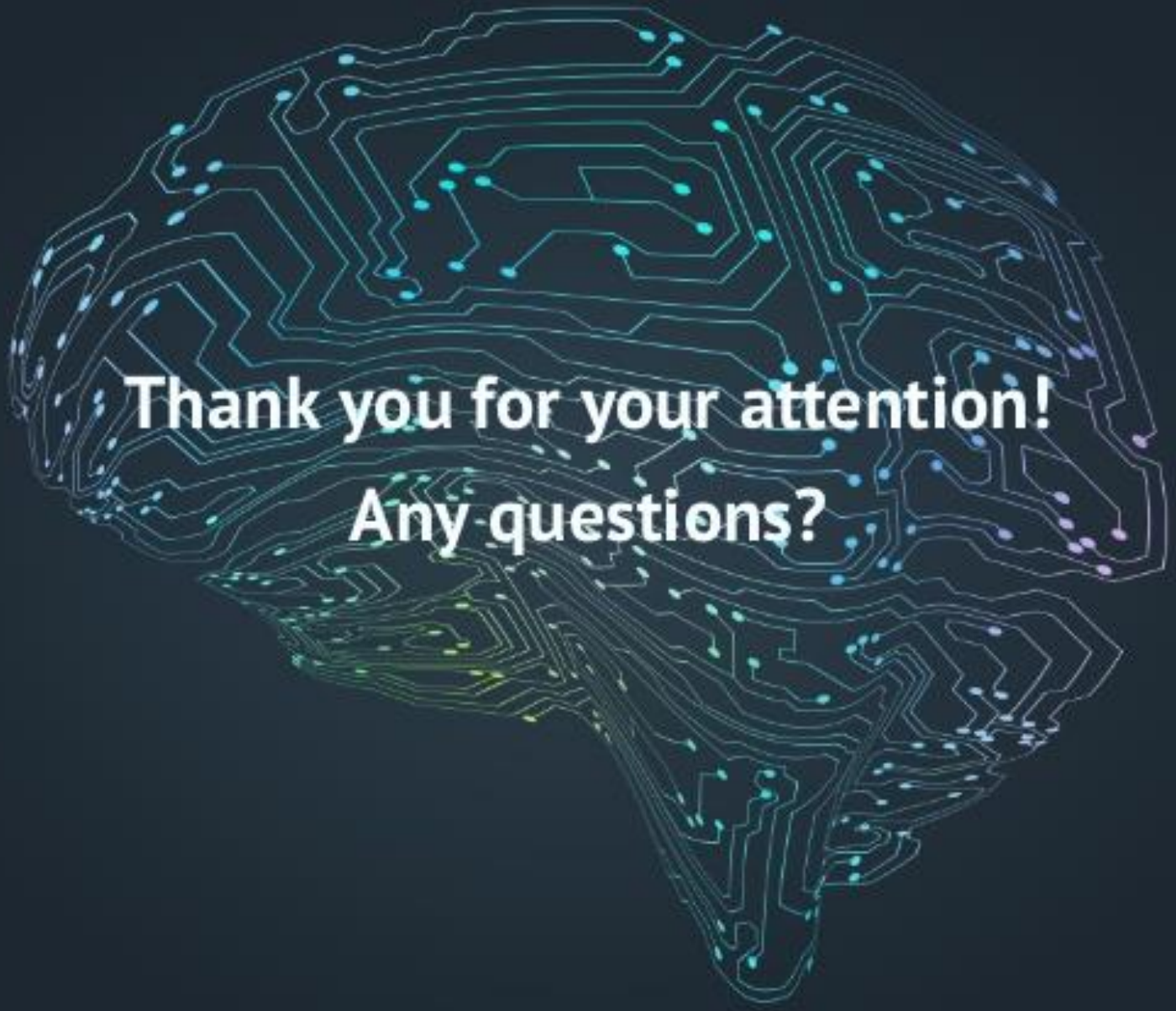
Designing Experimental Protocols

- Number of time points
  - Depends on the application
  - recovery patterns, at least 3 time points
  - Including persistency, at least 4 time points
  - Middle time points, strongly depend on the application

Designing Experimental Protocols

- Determining appropriate features
- Choosing appropriate clinical measures
- Identifying the recovery patterns
- Predicting the recovery patterns
- Identifying the interactions among the major features throughout the course of recovery
- Determining the associations of clinical measures and features

Individualized Treatment


Thank you for your attention!
Any questions?