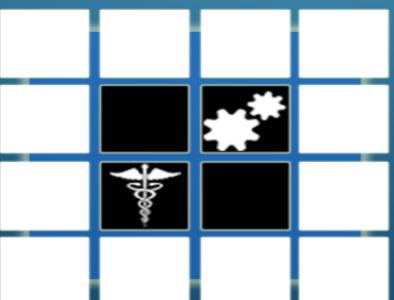


Improving surgical motor skill assessment and acquisition via neuromodulation, neuroimaging, and machine learning

Yuanyuan Gao

Committee members:

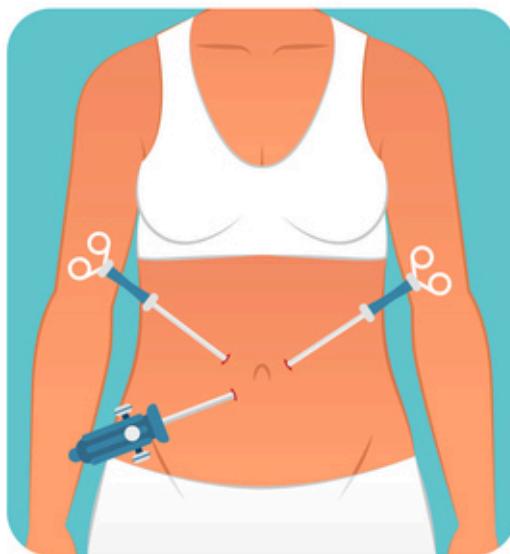
Dr. Suvranu De, Co-Chair
Dr. Xavier Intes, Co-Chair
Dr. Pingkun Yan
Dr. Lucy T. Zhang
Dr. Emily Liu



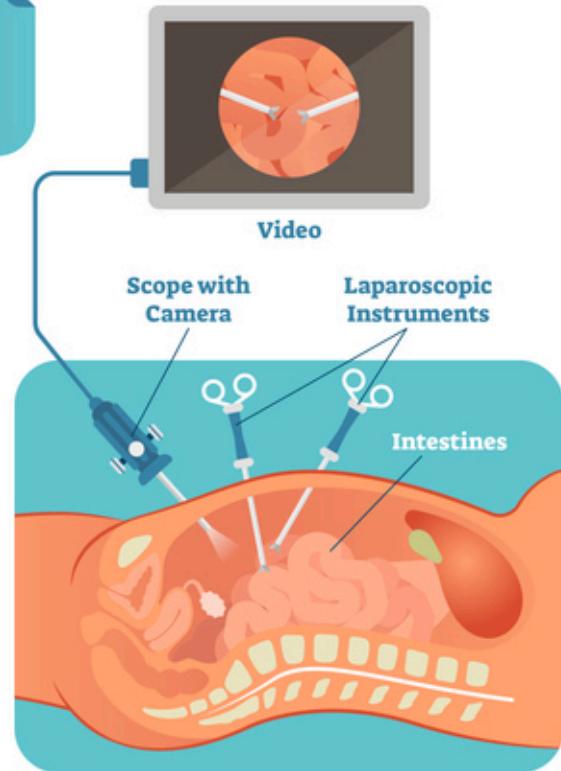
CeMSIM
THE CENTER FOR MODELING, SIMULATION
& IMAGING IN MEDICINE

Context – Modern surgical technique

LAPAROSCOPIC SURGERY



Patient Front



Patient Side View

craigrancho.com

- + Minimal incision
- + Reduced pain
- + Shorter recovery time.
- Complex bimanual motor skills and hand-eye coordination
- Variable adverse event rate¹
- Most errors during the learning phase

1. Flum DR, Koepsell T, Heagerty P, Sinanan M, Dellinger EP. Common Bile Duct Injury During Laparoscopic Cholecystectomy and the Use of Intraoperative Cholangiography: Adverse Outcome or Preventable Error? *Arch Surg.* 2001;136(11):1287–1292.

International accredited program

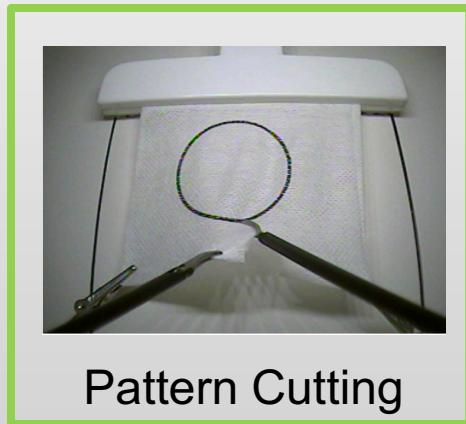


Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)

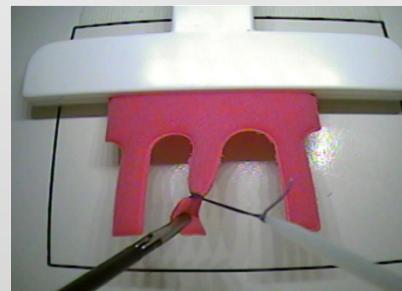
- **Fundamentals of Laparoscopic Surgery (FLS)** is a pre-requisite for **Board certification** to every general and Ob/Gyn surgeon².
- Two components – cognitive (high stakes exam) + psychomotor (trainer box)
- FLS trainer box is effective in teaching technical motor skills².
- FLS score = $f(\text{completion time, performance error})$;
- FLS score: 0-300 (higher score -> more skilled)



Peg Transfer



Pattern Cutting



Ligating Loop



Intracorporeal & Extracorporeal Suture

(www.flspogram.org)

Motivations

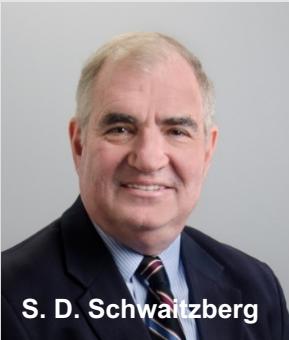
Fixed training protocol

Training Customization

Skill assessment

Skill training

Collaborator:



Professor and Chairman -
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**Former chair of the FLS
committee**

S. D. Schwartzberg

Challenges in learning curve prediction:

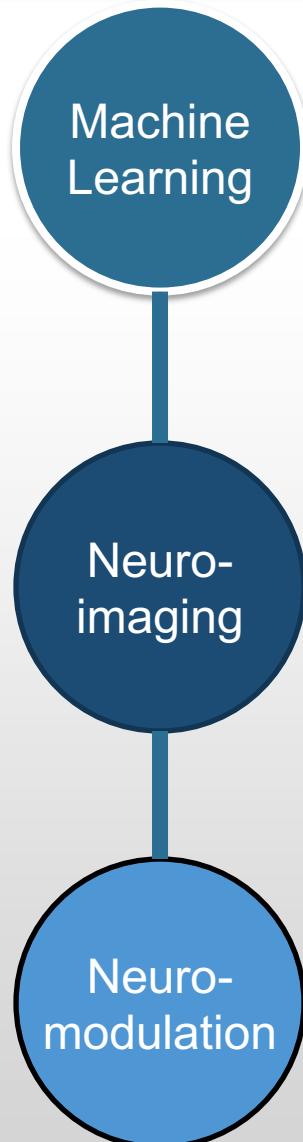
- Skill acquisition procedure is analyzed post-hoc.
 - Learning curve factors could not be predicted before the completion of the training.
 - Impede training protocol customization.

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- FLS score is manually calculated by proctor (www.flaprogram.org).
 - Time consuming- two to three weeks;
 - Labor intensive – trained proctor needed.

Challenges in surgical training:

- The training protocol relies on repetition.
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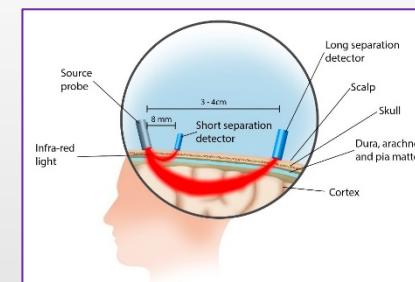
Challenges in learning curve prediction:

Specific aim 1 : to predict learning curve features in the early stage of training.

- Supervised: KPLS (Kernel partial least squares)
- Unsupervised: KPCA (Kernel principal component analysis) and k-means

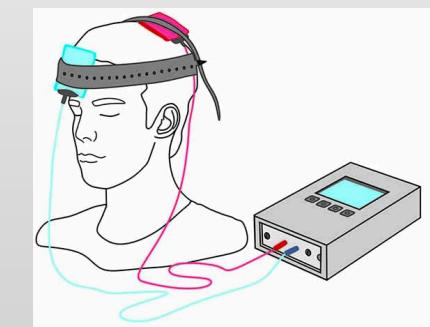
Challenges in skill assessment:

Specific aim 2 : to predict FLS scores via neuroimaging



Challenges in surgical training :

Specific aim 3 : to investigate whether surgical skill acquisition, retention, and transfer can be enhanced via neuromodulation.



S. A. 1: to predict learning curve features in the early stage of training.

Previous work:

- Graph or table displaying
- T-test, ANOVA to grouped data split by practice number
- Curve fitting
- Cumulative summation (CUSUM).

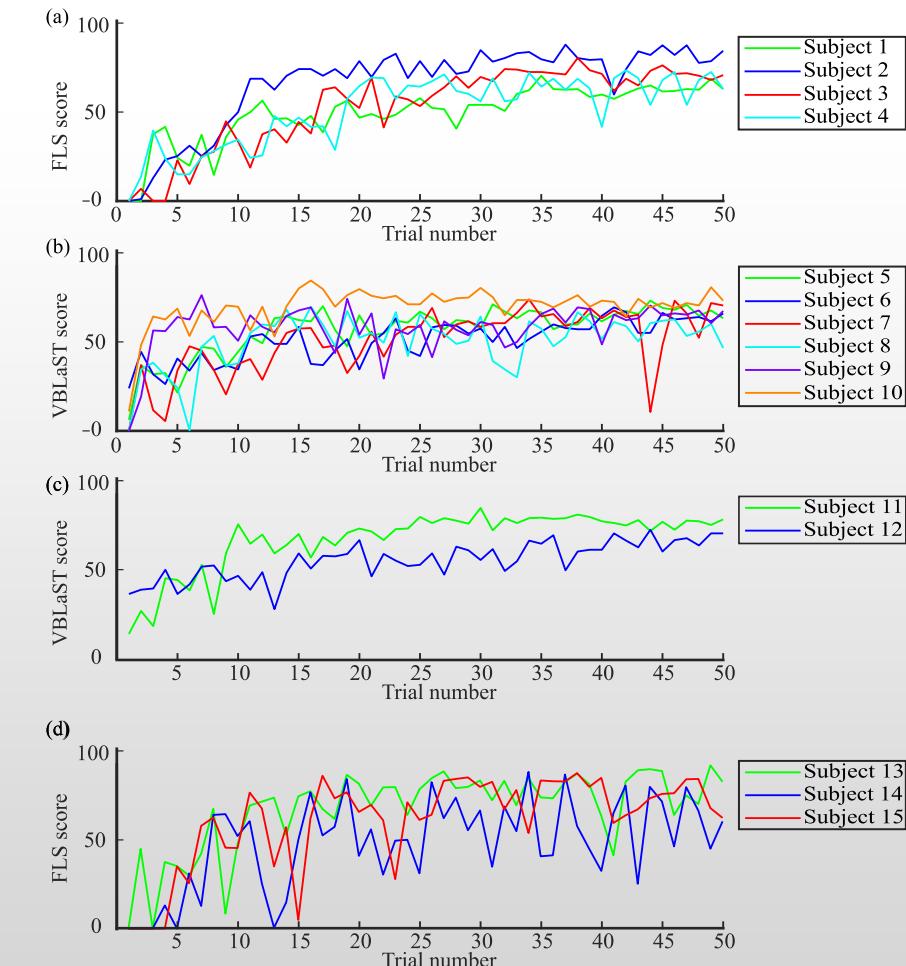
Drawback:

- Post-hoc analysis

Goal: predict learning curve features from beginning

Data:

Study	Platform	Motor task	No. of learning curves
Nemani et al. 2017	FLS	Pattern cutting	4
Nemani et al. 2017	VBLaST	Pattern cutting	6
Linsk et al. 2017	VBLaST	Pattern cutting	2
Fu et al. 2019	FLS*	Suturing	3
Total			15

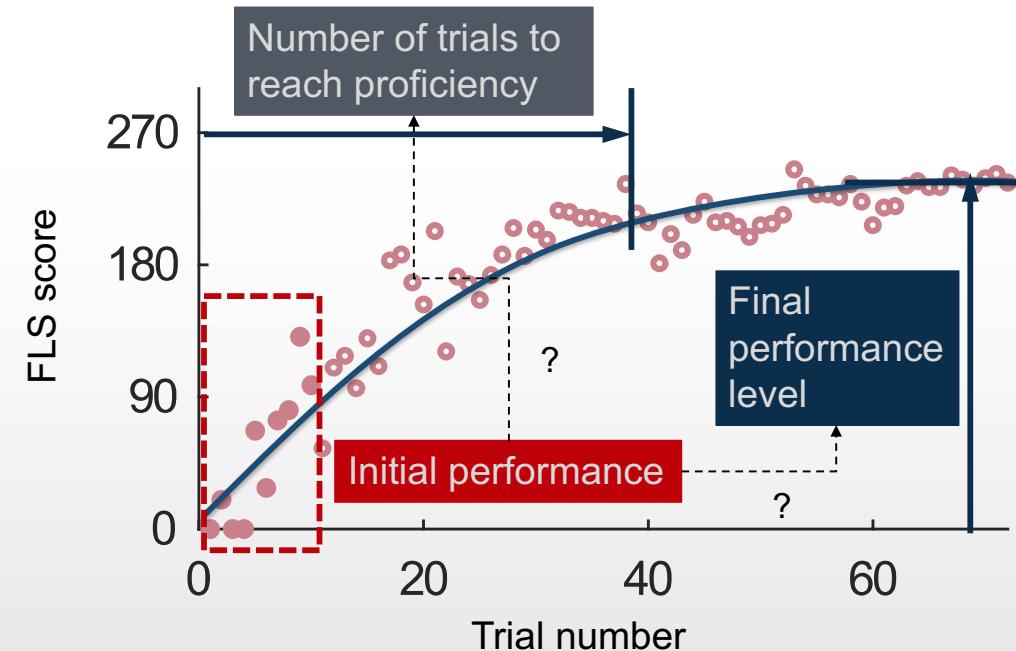


Hypothesis #1:

- The initial performance of a trainee can predict the number of trials required to achieve proficiency and the final proficiency level.

Algorithm:

- Kernel Partial Least Squares (KPLS)
 - Small sample size
 - High dimensional variables
- Cross-validation: leave-one-out



Prediction	KPLS	Log-linear model
Initial performance → Number of trials to reach proficiency	$R^2 = 0.72$	$R^2 = -109.55$
Initial performance → Final performance level	$R^2 = 0.89$	$R^2 = -3.36$

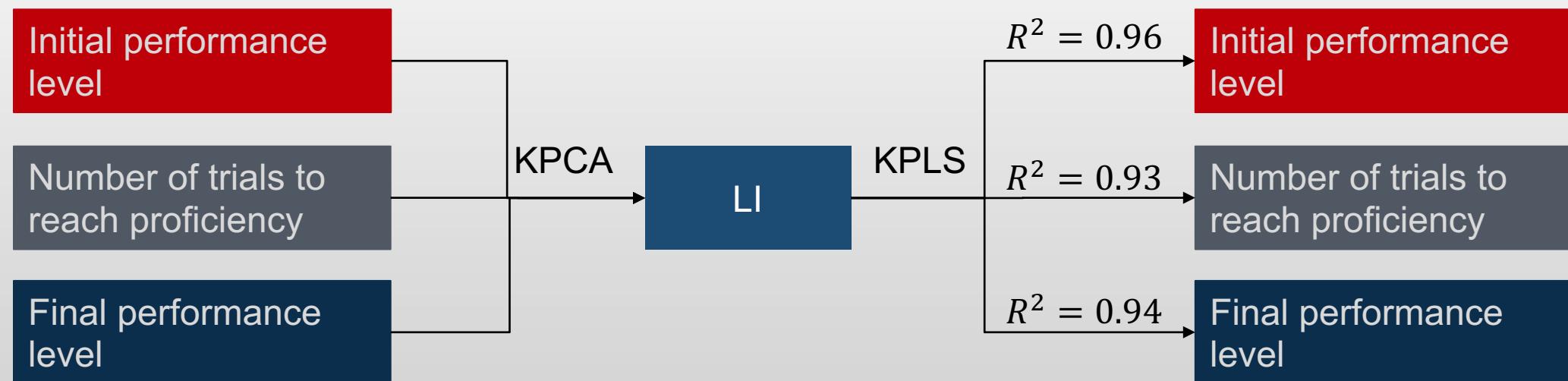
Gao, Y., Kruger, U., Intes, X., Schwartzberg, S. and De, S., 2020. A machine learning approach to predict surgical learning curves. *Surgery*, 167(2), pp.321-327.

Hypothesis #2:

- A single factor can describe the learning curve factors.

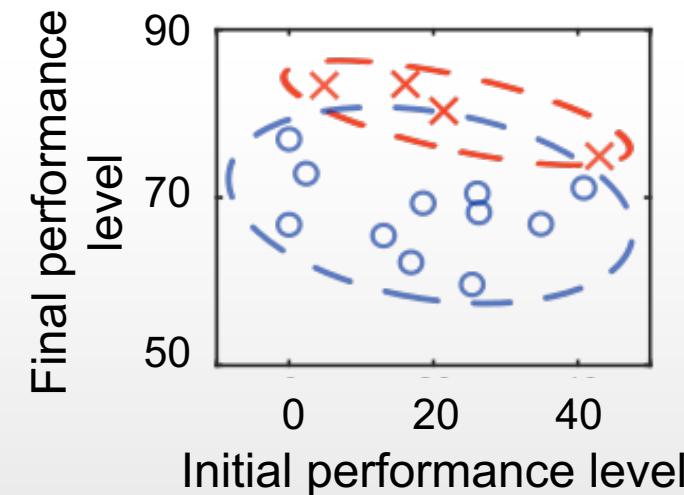
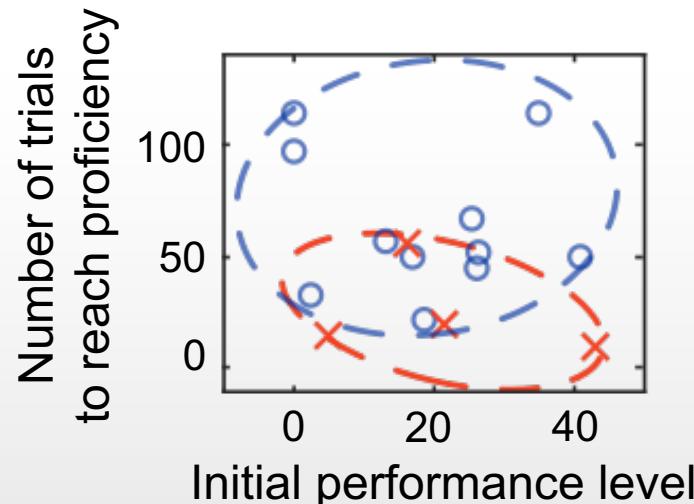
Algorithm:

- Kernel Principle Component Analysis (KPCA)
 - Small sample size
 - High dimensional variables
- Cross-validation: leave-one-out

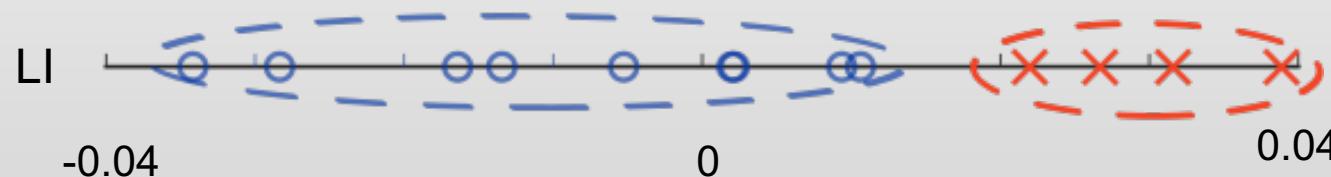


S. A. 1: Is learning curve information embedded in one factor

- K-means grouping results
 - Using the learning curve factors



- Using the extracted LI value



- The extracted single factor is enough to classify the learners

Specific aim 1

“.. is to predict learning curve features in the early stage of training”

We established that:

- Learning curve factors can be predicted from the initial performance;
- Single factor can represent the learning curve factors.

Impact:

- We are the first to suggest predict learning curve from the early learning stage;
- It is a vital step towards surgical training remediation;
- Understanding of different learning abilities: the importance of training remediation

Motivations

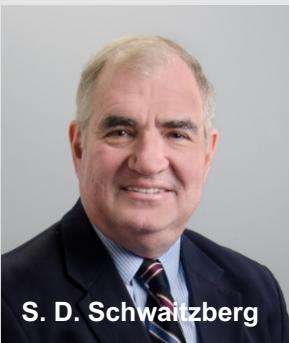
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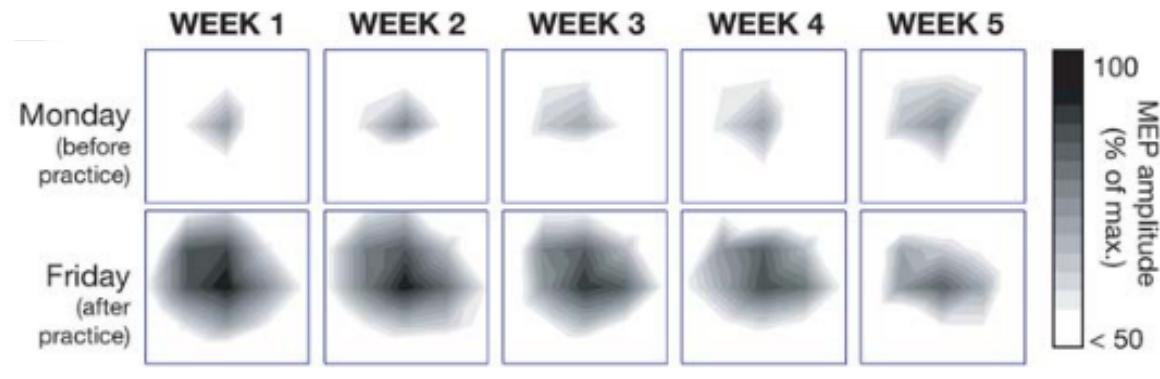
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Neural basis of motor learning

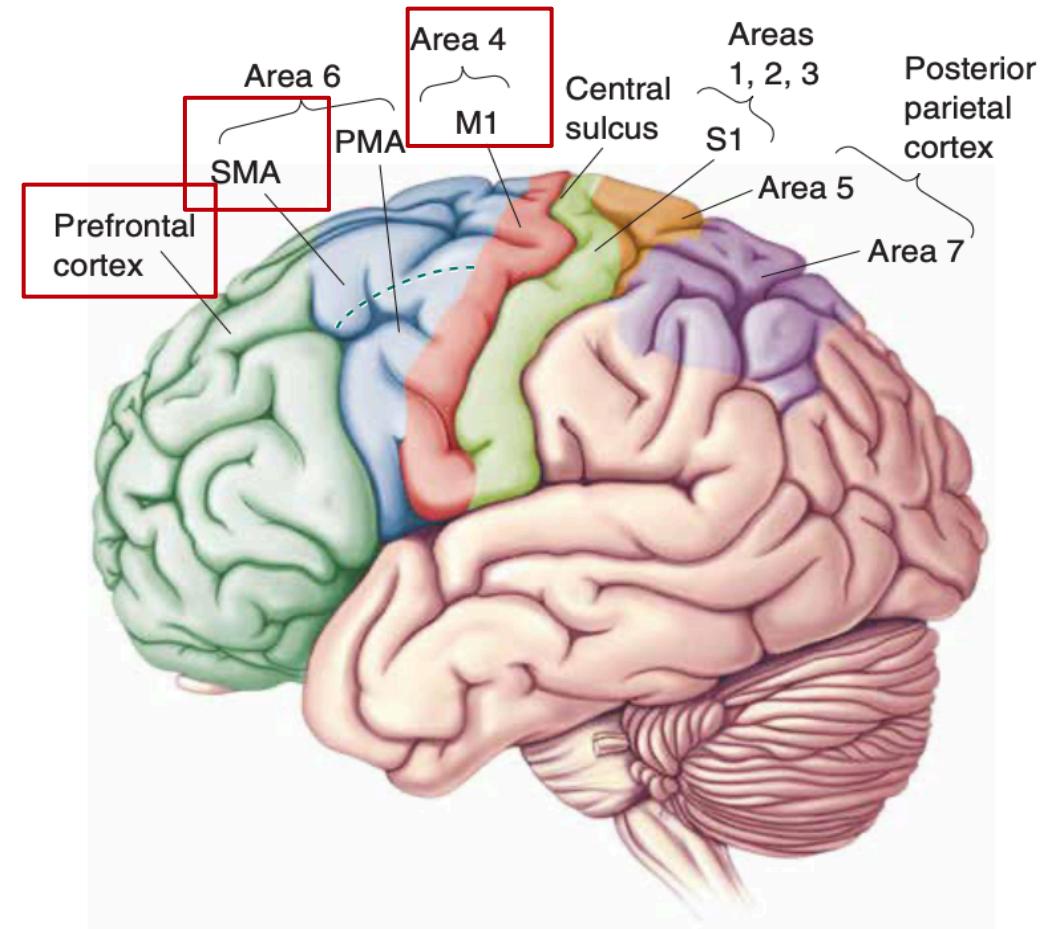
- Neuroplasticity



Two steps:

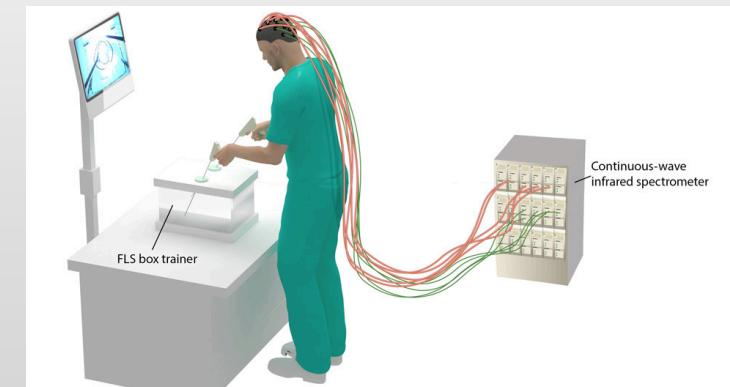
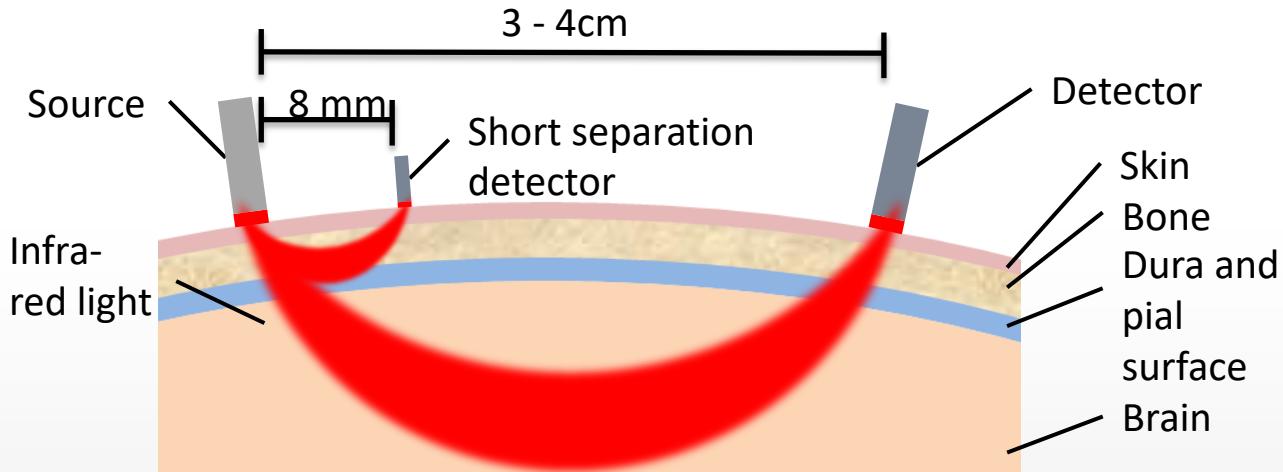
- Rapid reinforcement of preestablished organic pathways;
- Later formation of new pathways

- Cortex areas



Background

- Functional Near infrared spectroscopy (fNIRS)
 - Non-invasive imaging technique
 - Delivers infrared light on the surface of the scalp via source probes.
 - Infrared light scatters through turbid tissue and the backscattered light is detected
- Since attenuated light is related to functional chromophores (such as oxy-HbO₂ and deoxy-HbO₂), the relative concentration of these chromophores can be determined and finally be correlated with brain activity.
- Why should we use NIRS to measure brain activity?
 - High temporal resolution (~ 100Hz)
 - High depth penetration (~1.5 cm)
 - Allows for complex tasks to be performed



Previous work- fNIRS in motor classification

- fNIRS data could classify motor tasks.
 - Simple vs. complex motor tasks (Holper and Wolf 2011).
 - Left vs. right hand motion (Fazli et al. 2012, Naseer and Hong 2013).
 - Arm lifting vs. knee extension (Shin and Jeong 2014).
- fNIRS data could classify surgical levels.
 - PFC correlation to surgical skill level (Leff et al. 2008; Ohuchida et al. 2009; James et al. 2011)
 - Surgical skill levels could be classified by fNIRS (Nemani et al. 2018 & 2019).

Question: Can fNIRS data predict FLS score?

Experiment setup and data collection

Population:

- 13 novice medical students;

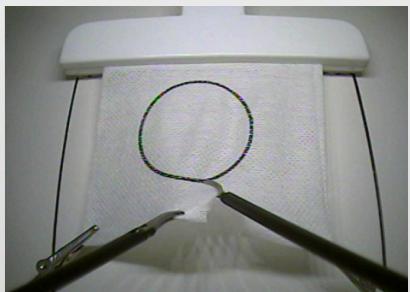
FLS task:

- Pattern cutting task

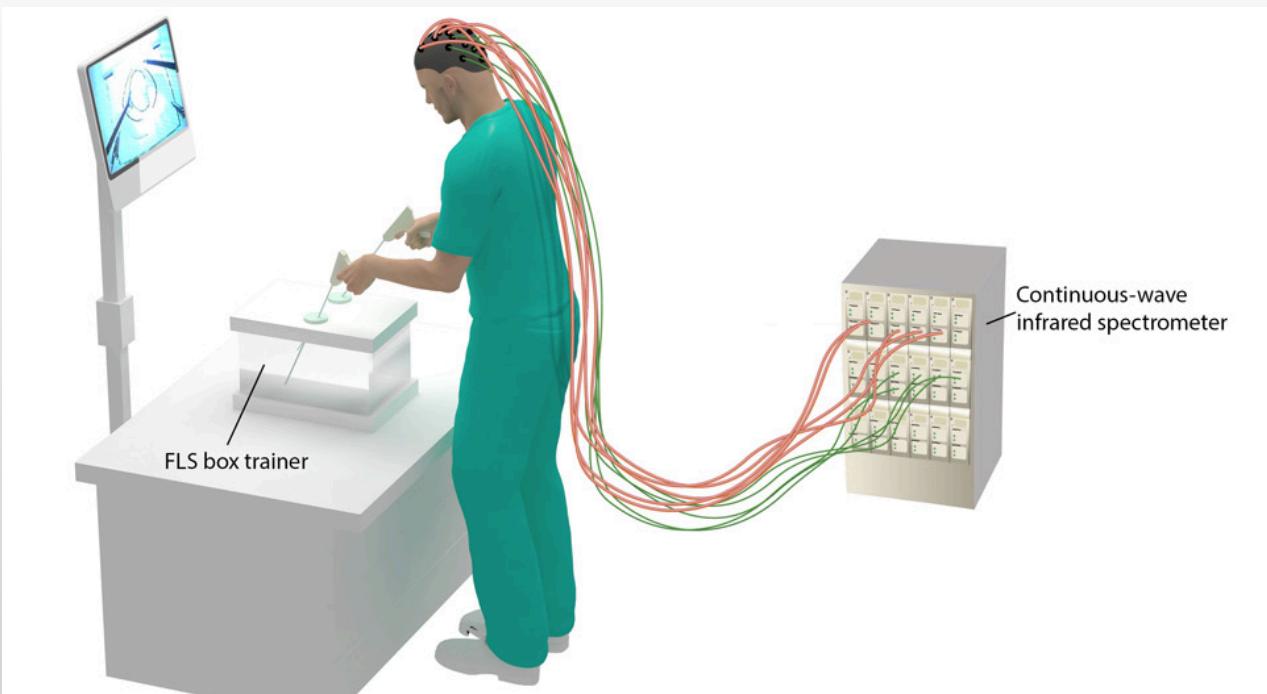
Instrumentation:

- TechEn CW6; continuous wave; 690&830 nm

HOMER2 software suite used for all infrared data processing

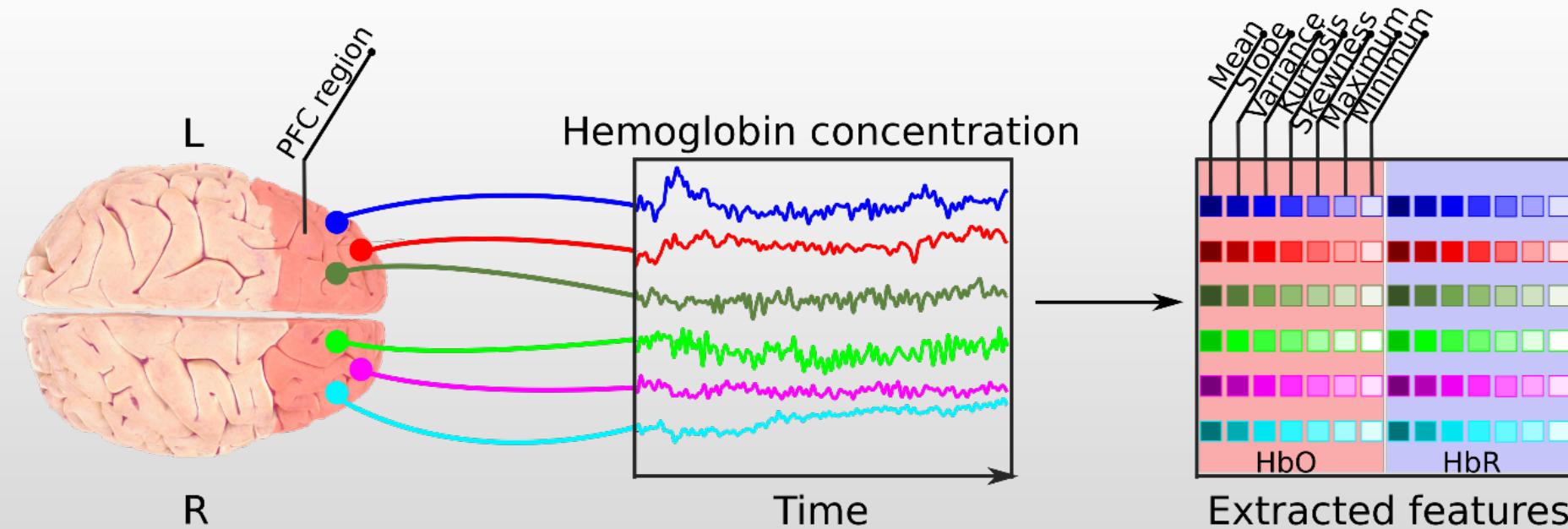


Pattern Cutting



Ease of use and implementation

- Restricted ourselves to PFC
- Data types → moments of temporal HbO₂ and Hb traces



Prediction models

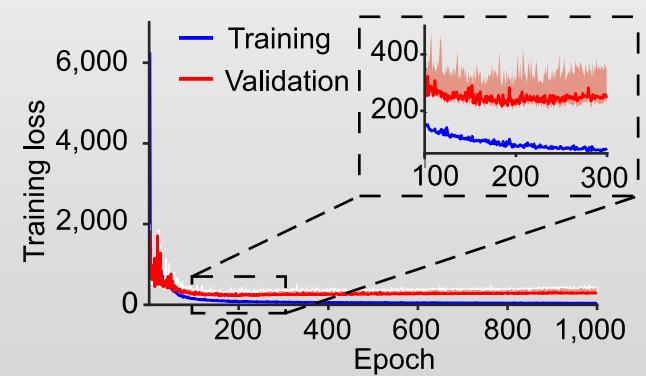
1. Machine Learning: Random Forest (RF), Kernel Partial Least Squares (KPLS), Support Vector Regression (SVR)
2. Deep Learning: **Brain-NET**

Simple Architecture

- 1D convolutional kernels along the feature direction;
- 1D convolutional kernels along the PFC location direction;
- Flatten layer;
- Two fully connected layers.

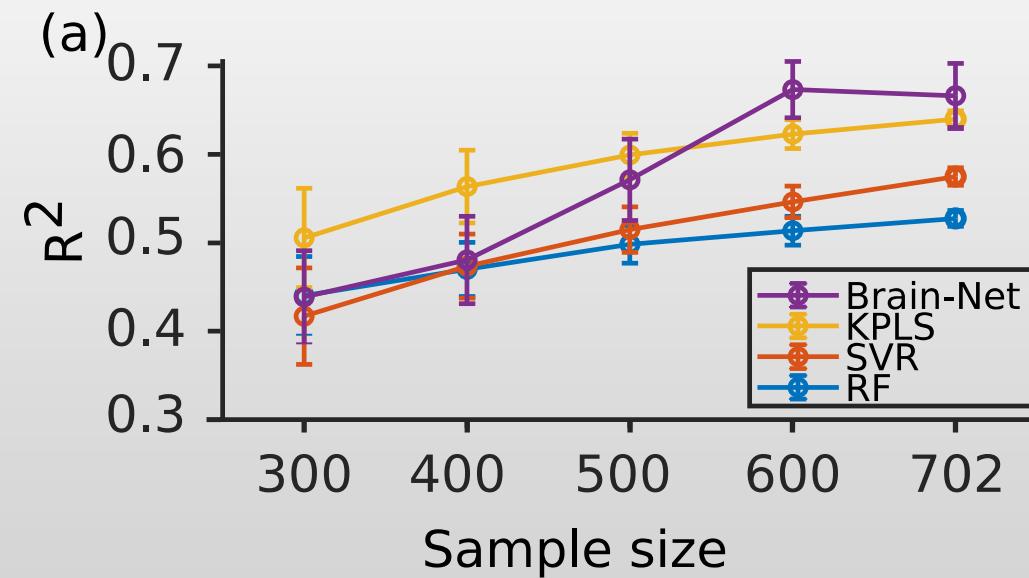
Robust training

30 rounds of ten-fold cross validation using randomly shuffled samples for each round



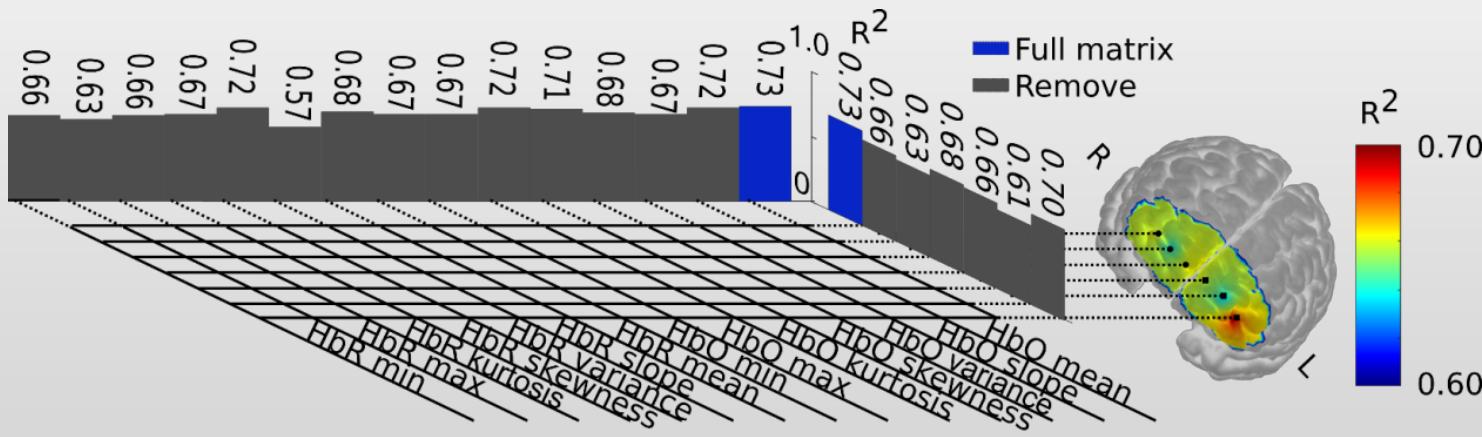
What is the effect of sample size?

- **Sample size:** 13 medical students; 1000 raw data; 700 processed data (due to motion artifacts)
- **Metric:** R^2 value
- ML>DL for small sample sizes (<600)
- DL>ML when #samples >600



What data type is important?

- Full dataset: 702 samples
- **Methodology:** Remove-one-component scheme
- Feature: Removing the **HbR slope** produces the lowest R^2 ;
- Region: Removing the **left middle PFC region** produces the lowest R^2
- Overall: Best R^2 obtain with **7 features of the 2 regions**



Component removed	R^2
None	0.73
Rightmost PFC	0.66
Second right PFC	0.63
Medial right PFC	0.68
Leftmost PFC	0.70
Second left PFC	0.61
Medial left PFC	0.66

Component removed	HbO	HbR
None	0.73	
Mean	0.72	0.68
Slop	0.67	0.57
Variance	0.68	0.72
Skewness	0.71	0.67
Kurtosis	0.72	0.66
Max	0.67	0.63
Min	0.67	0.66

Is the model robust to new participants?

- Of particular interests
- Cross-validation: ten-fold and Leave-One-User-Out
- An additional experiment: 6 new participants

Model	10-fold	LOUO
Brain-NET	0.67 ± 0.04	0.61
KPLS	0.64 ± 0.01	0.34
SVR	0.58 ± 0.01	0.26
RF	0.53 ± 0.01	0.31

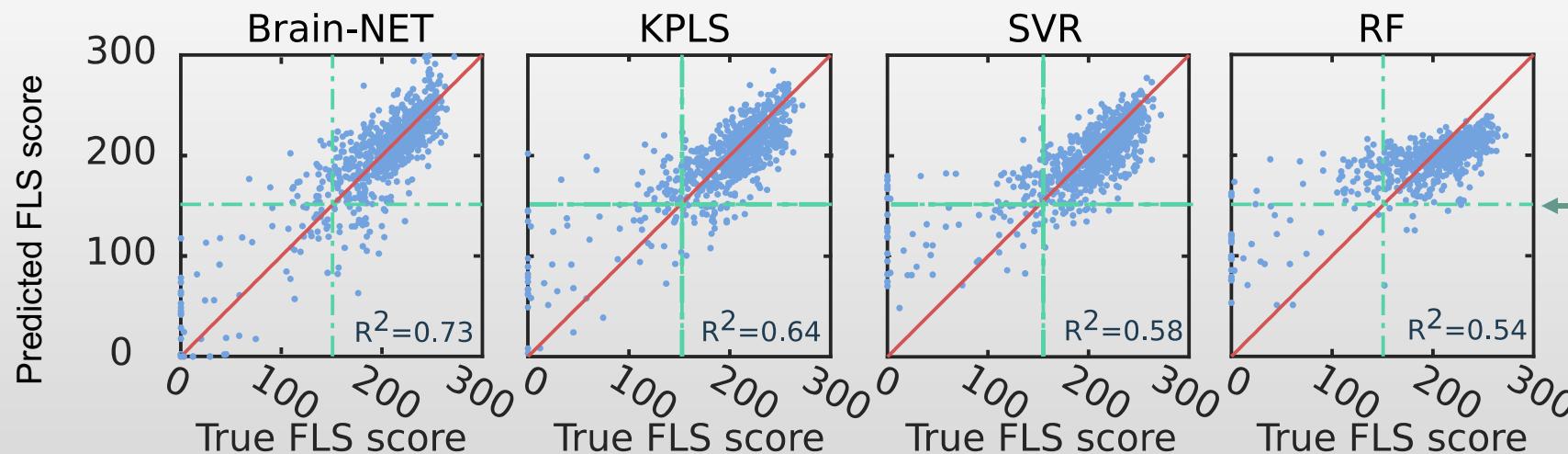
Subject No.	Total trials	True score	Predicted score	Absolute error
1	10	163	147	16
2	10	180	162	18
3	5	121	133	12
4	9	185	174	11
5	5	238	240	2
6	10	207	216	9

Prediction accuracy

- KPLS – Kernel partial least squares
- SVR – Support vector regression
- RF – Random forest

High stake:

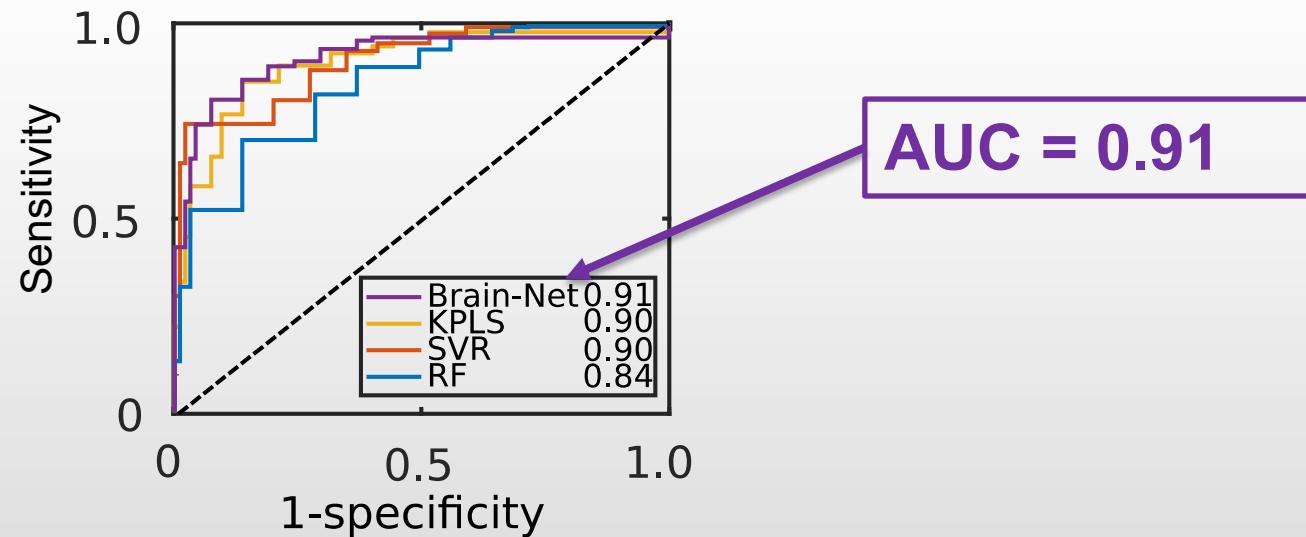
- Every surgeon
- 1 trial



FLS score
threshold for
pass/fail

Board certification accuracy?

- AUC value of the ROC curve (Hajian-Tilaki et al. 2013)
- Conventional for medical test accuracy: above 0.90 indicates good classifier.



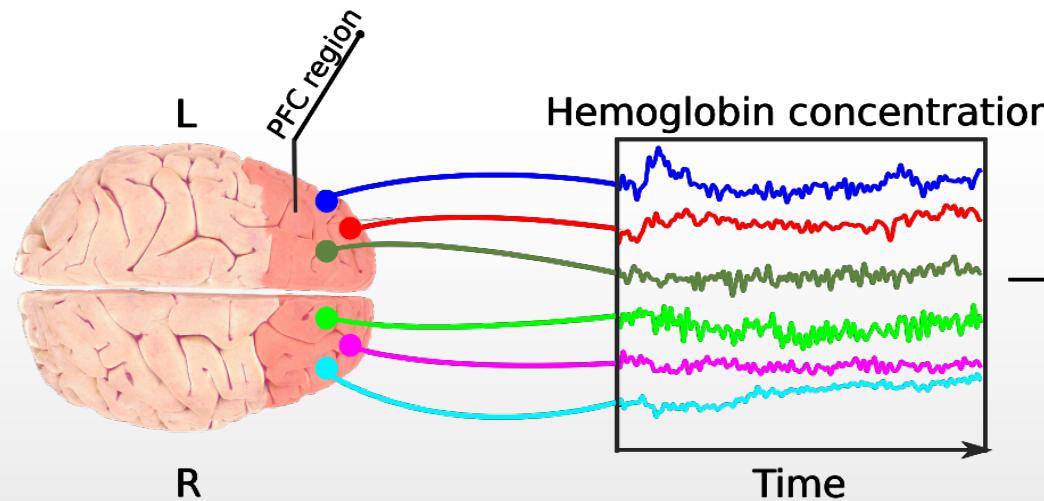
Conclusion

- Brain-NET demonstrate good prediction accuracy of FLS score.

Limitations

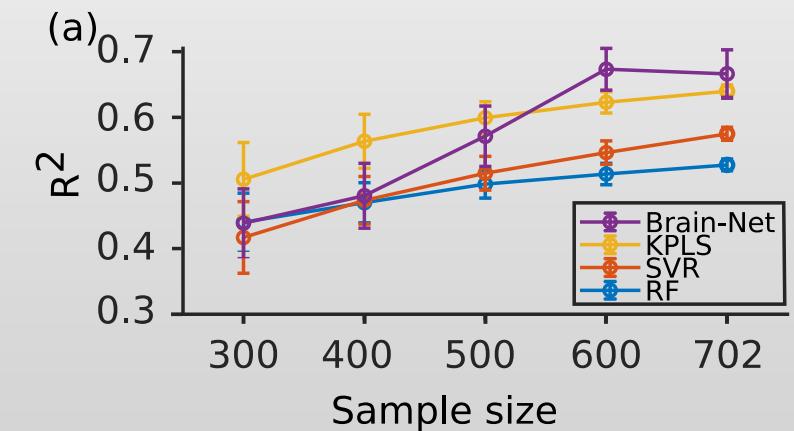
Limitations:

1. Feature extraction is required.



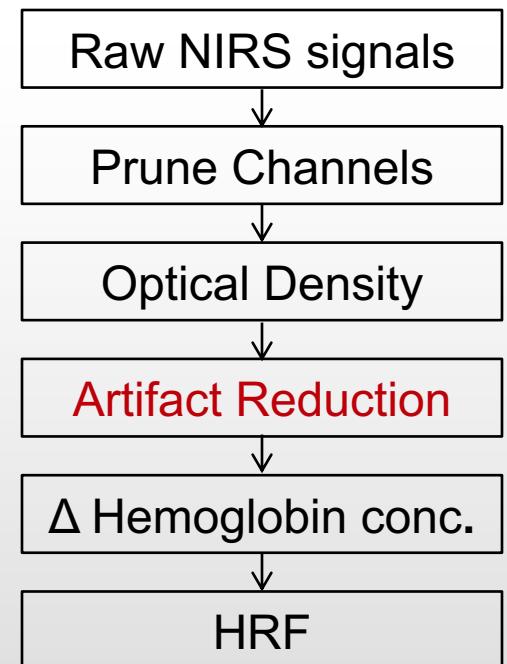
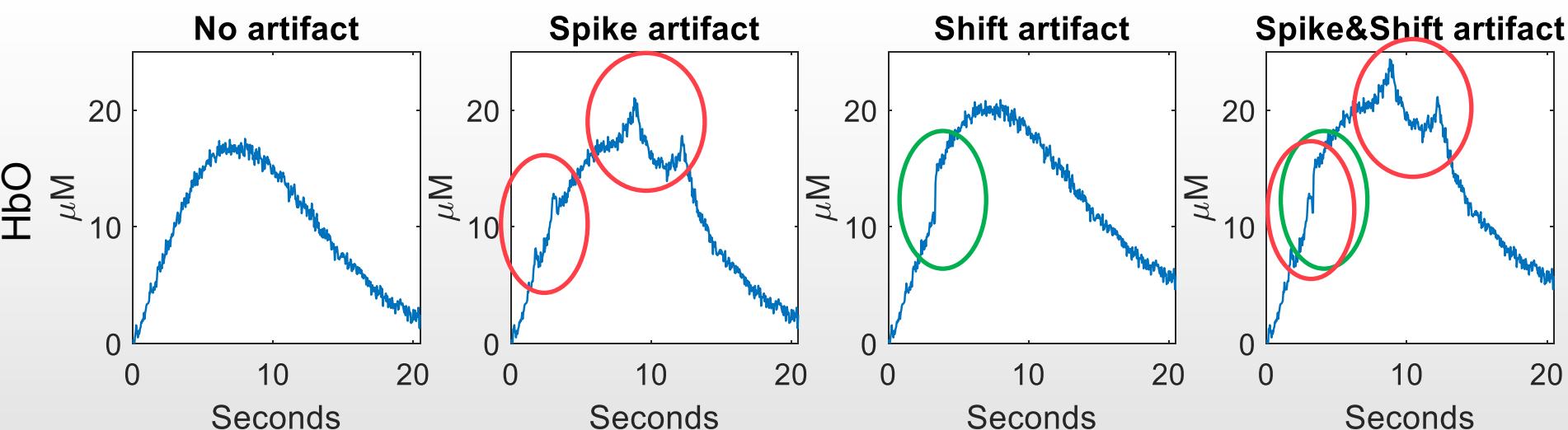
2. Limited sample size
 - Recruitment of specific cohort
 - Trial discard due to **motion artifacts** (300 in 1000 discarded)

	Brain-NET	Timeseries
R^2	0.67 ± 0.04	-1.98 ± 1.40



The impact of motion artifacts

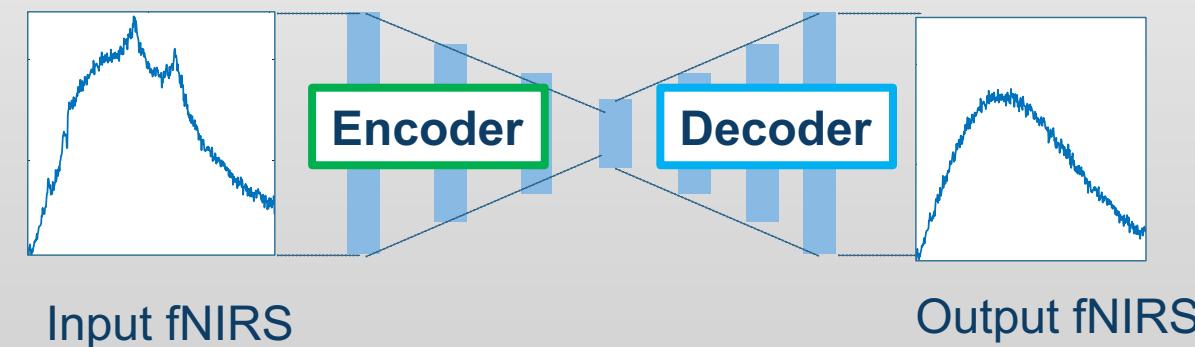
- What is motion artifacts?
- fNIRS data processing flow



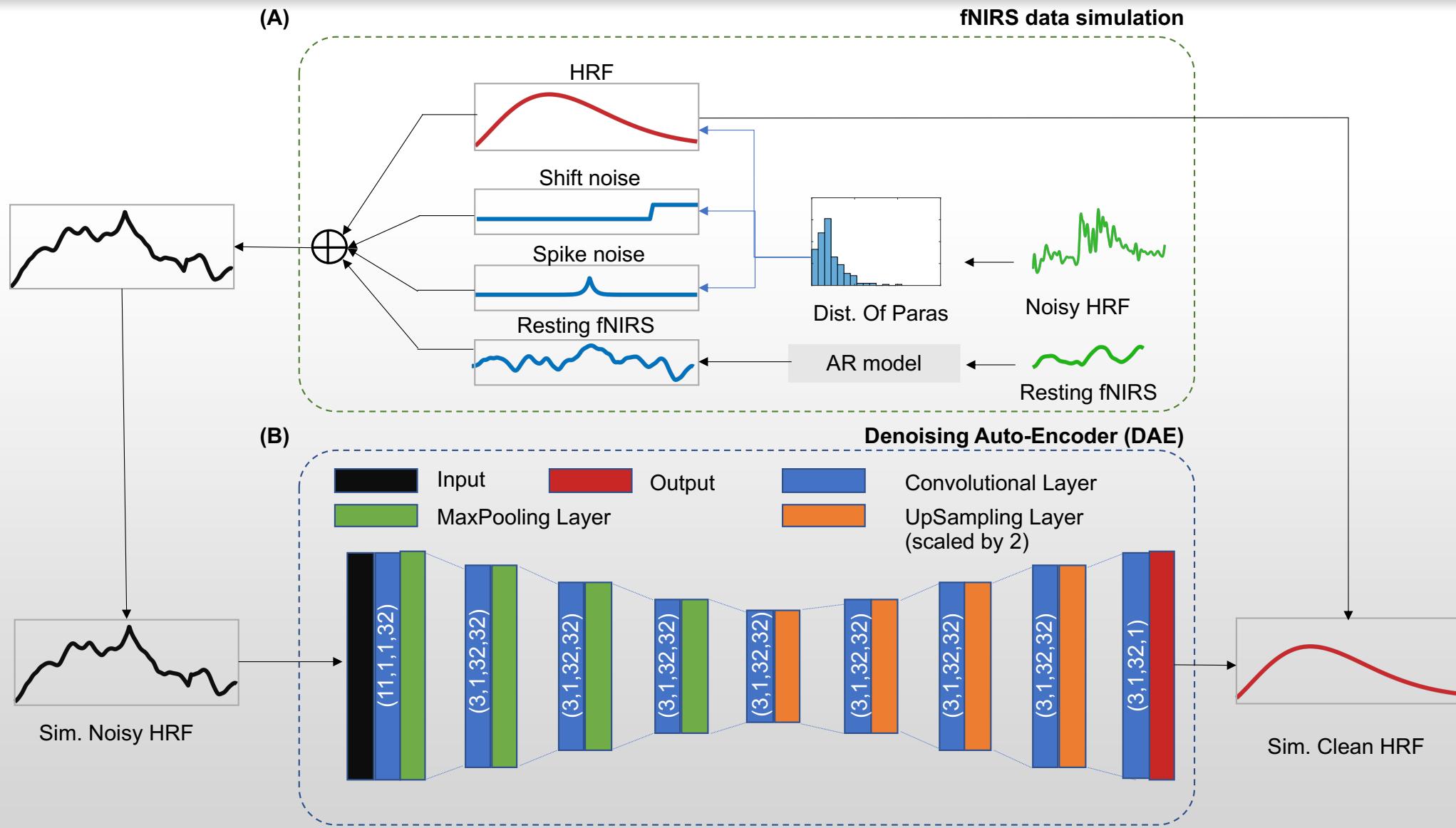
- Efficient removal of motion artifacts could save trials and increase the accuracy of the information.

Current gold-standard methods

- Motion artifact removal methods in fNIRS
 - Spline (Scholkmann et al, 2010)
 - Kalman (Izzetoglu et al. 2010)
 - Wavelet (Molavi and Dumont 2012)
 - PCA (Zhang et al. 2005)
 - Cbsi (Cui et al. 2010)
- Drawbacks
 - Depend on assumptions to describe motion artifacts
 - Subjective selection of associated tuning of parameters
- Goal: A model that does not rely on assumptions or require subjective fine-tuning
- Propose: **Deep learning (denoising autoencoder structure (DAE))**
 - Have been shown superior in denoising of medical images
- Motivation:



In-silico training



- First loss: mean squared error (MSE) loss

$$L_{mse} = \frac{1}{n} \sum_i (y_i - \hat{y}_i)^2$$

- Second loss: the total variation of the predicted signal

$$L_{var} = \frac{1}{n} \sum_i (\hat{y}_i - \hat{\mu})^2$$

- Third loss: the number of motion artifacts

- the standard deviation (std) exceeds the standard deviation threshold

$$L_{std} = \frac{1}{N_{std}} \sum_{i=1}^T \sum_{j \in \{j | \Delta_i dc_j > m\}} \Delta_i dc_j$$

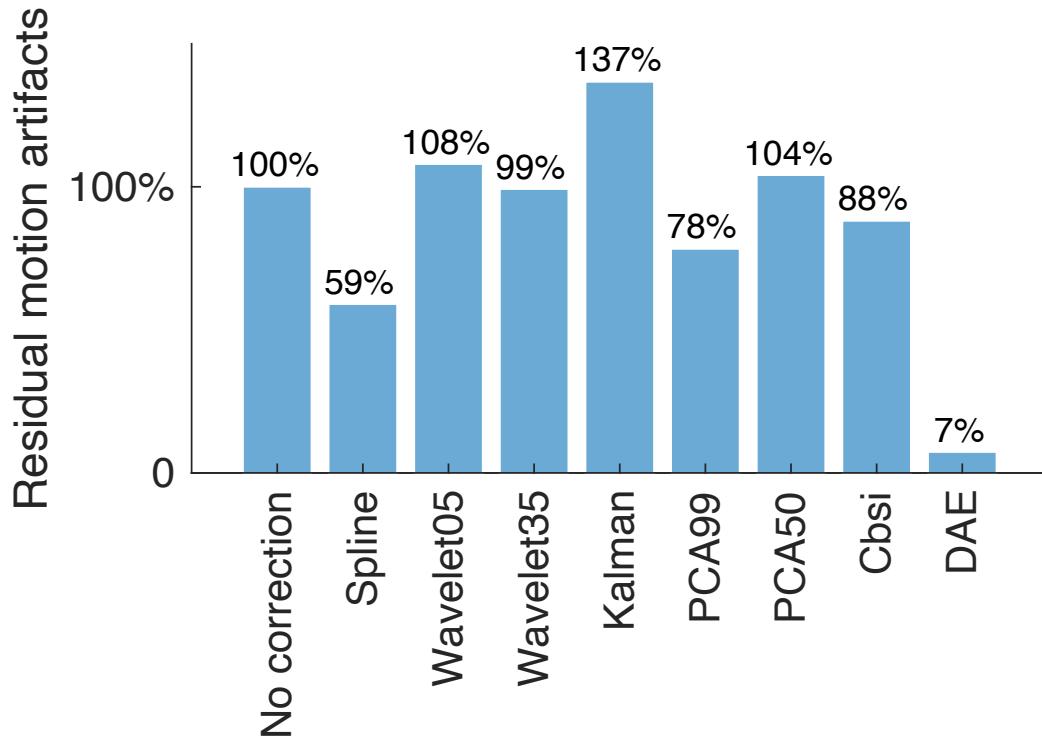
- the amplitude change (amp) exceeds the amplitude threshold

$$L_{amp} = \frac{1}{N_{amp}} \sum_{i=1}^T \sum_{j \in \{j | \Delta_i dc_j > c_{amp}\}} \Delta_i dc_j$$

- Loss function: weighted sum of the above losses

$$\text{Loss} = L_{mse} + \theta_1 \times L_{var} + \theta_2 \times L_{std} + \theta_3 \times L_{amp}$$

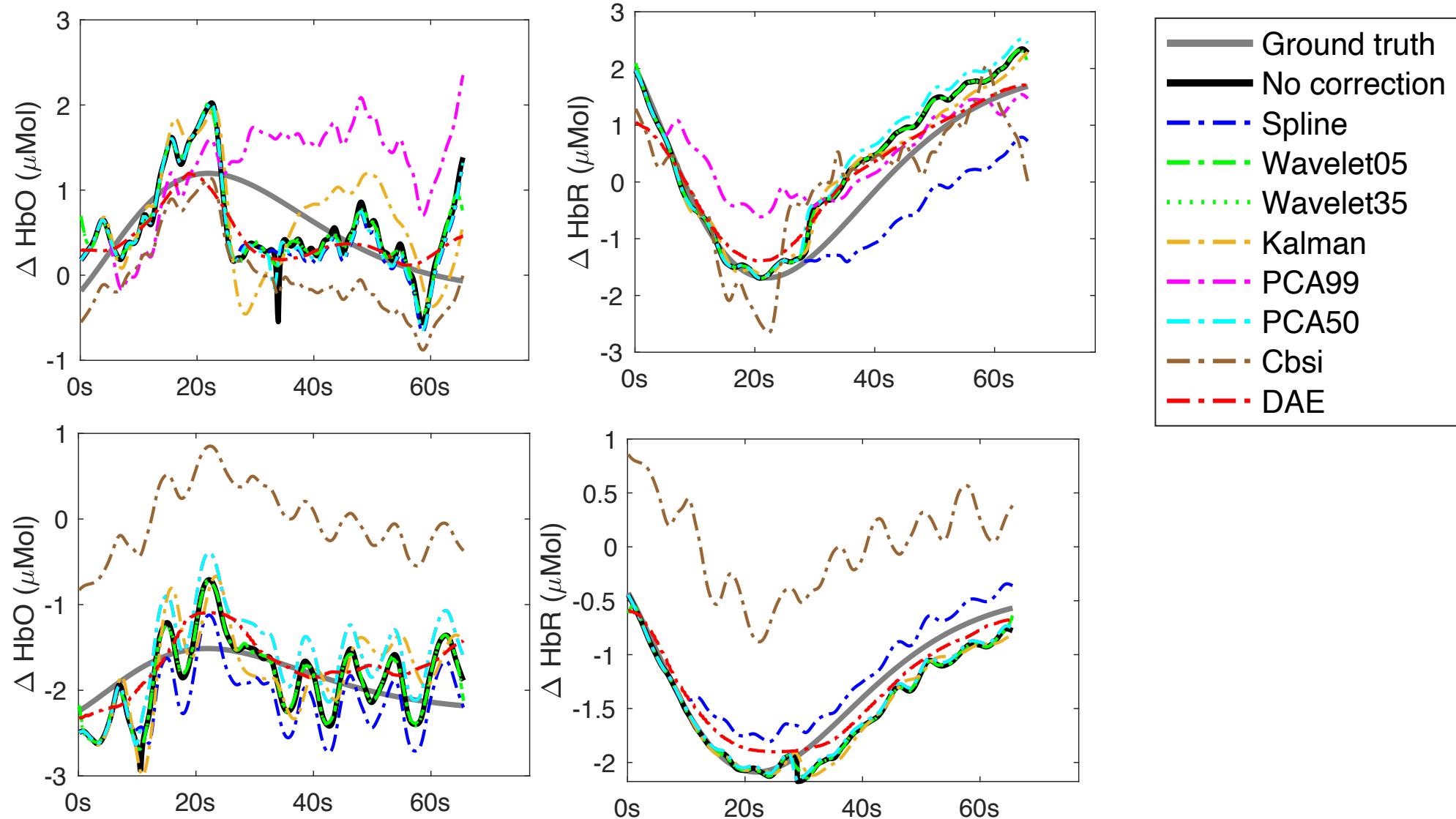
Denoise performance on simulation data



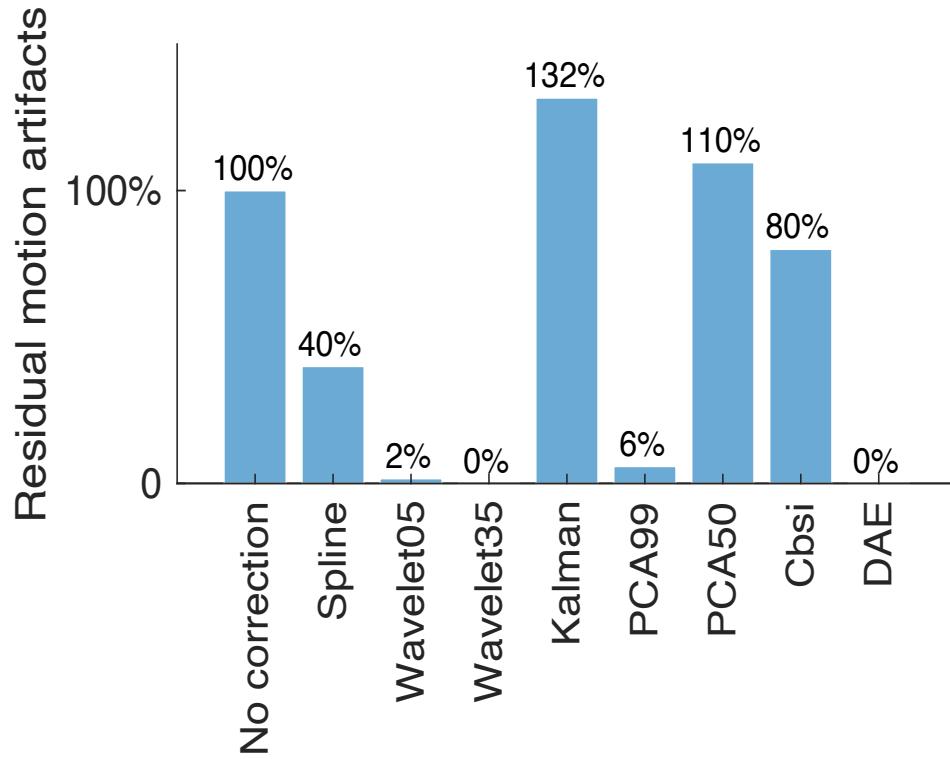
	Mean (std)	MSE ($\mu M o l^2$)	CNR
No correction		0.49 (0.69)	5.30 (4.69)
Spline		0.47 (0.90)*	5.47 (4.55)*
Wavelet05		0.44 (0.67)*	6.17 (6.22)*
Wavelet35		0.45 (0.67)*	6.04 (6.00)*
Kalman		0.48 (0.66)*	5.37 (5.02)
PCA99		0.81 (2.14)*	5.09 (4.98)*
PCA50		0.55 (0.93)*	5.48 (5.21)*
Cbsi		5.03 (10.31)*	6.49 (4.94)*
DAE		0.35 (0.53)*	5.51 (4.43)*

*: significantly different from 'No correction' by t-test ($p < 0.05$)

Denoise performance on simulation data

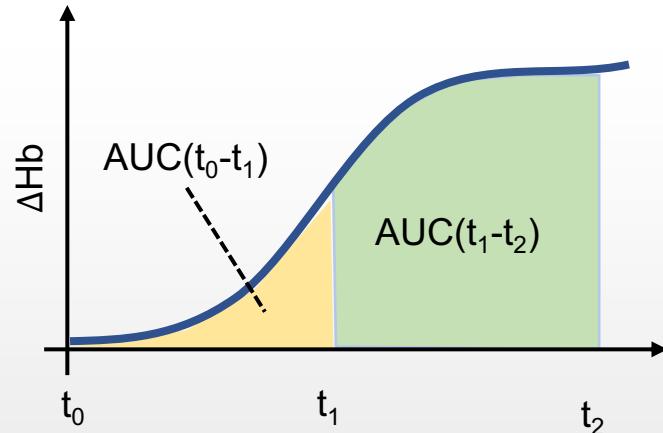


Denoise performance on experimental data



Model	Computation time (s)
Spline	0.44
Wavelet05	81.22
Wavelet35	85.92
Kalman	1.48
PCA99	0.27
PCA50	0.18
Cbsi	0.03
DAE	0.19

Denoise performance on experimental data



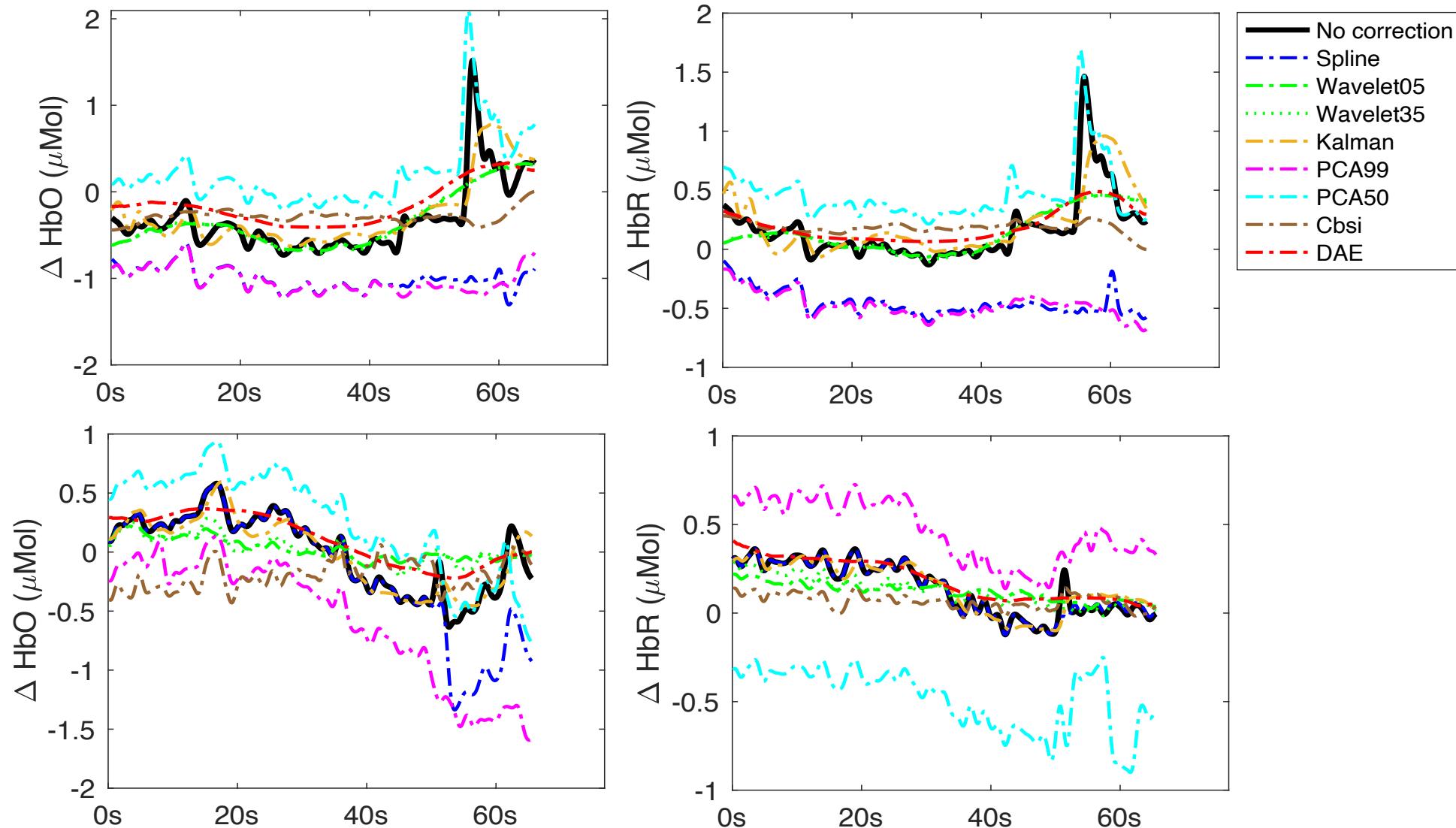
$$\text{AUCratio} = \frac{\text{AUC}(t_1-t_2)}{\text{AUC}(t_0-t_1)}$$

Model	AUC0-2 ($\mu\text{Mol} * s$)	AUCratio
No correction	0.13 (0.21)	26.60 (98.54)
Spline	0.09 (0.13)*	64.75 (271.01)*
Wavelet05	0.03 (0.03)*	33.49 (86.91)
Wavelet35	0.05 (0.05)*	23.85 (43.85)
Kalman	0.17 (0.22)	22.74 (48.73)
PCA99	0.11 (0.15)*	85.24 (482.75)
PCA50	0.17 (0.25)*	54.69 (277.42)
Cbsi	0.07 (0.10)*	57.88 (205.15)
DAE	0.02 (0.03)*	98.26 (686.87)

*: significantly different from 'No correction' by t-test ($p < 0.05$)

Brigadoi, Sabrina, et al. "Motion artifacts in functional near-infrared spectroscopy: a comparison of motion correction techniques applied to real cognitive data." *Neuroimage* 85 (2014): 181-191.

Denoise performance on experimental data



Brain-NET

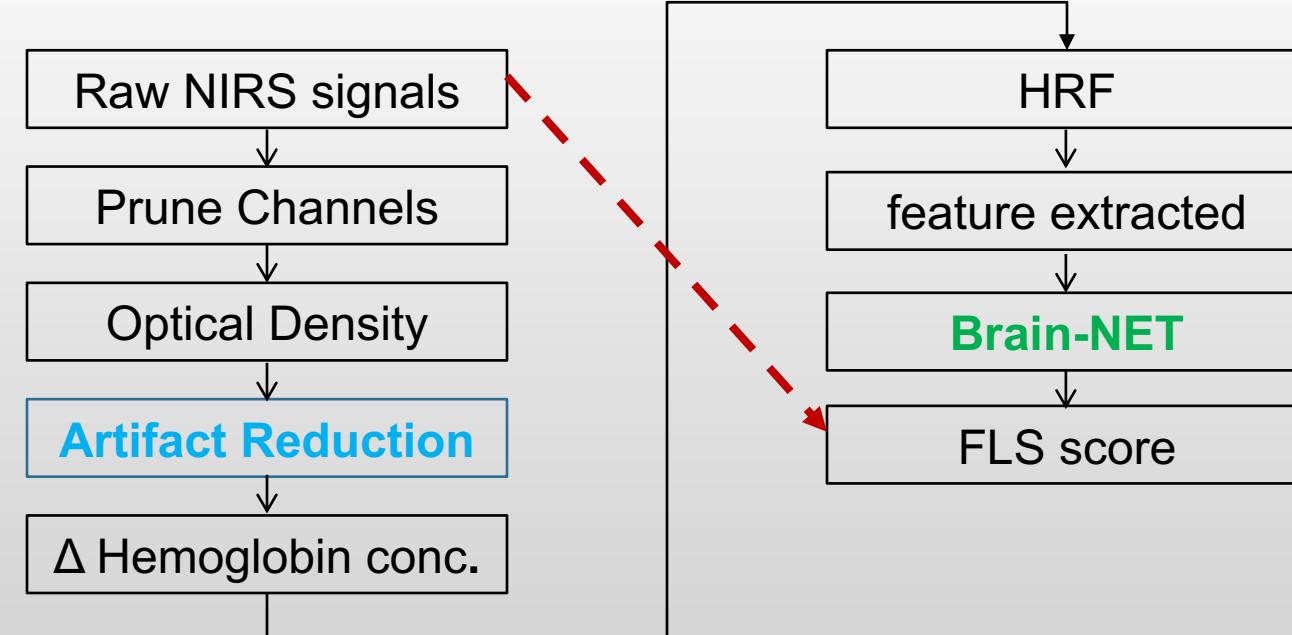
- Provide a fast, accurate, and robust method to assess FLS score.

DAE

- Provide an assumption-free and effective method to remove fNIRS motion artifact.

Significance:

- A step toward real time skill assessment;
- Impact the training



Motivations

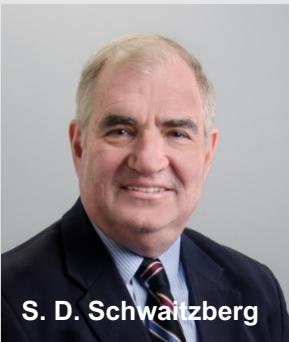
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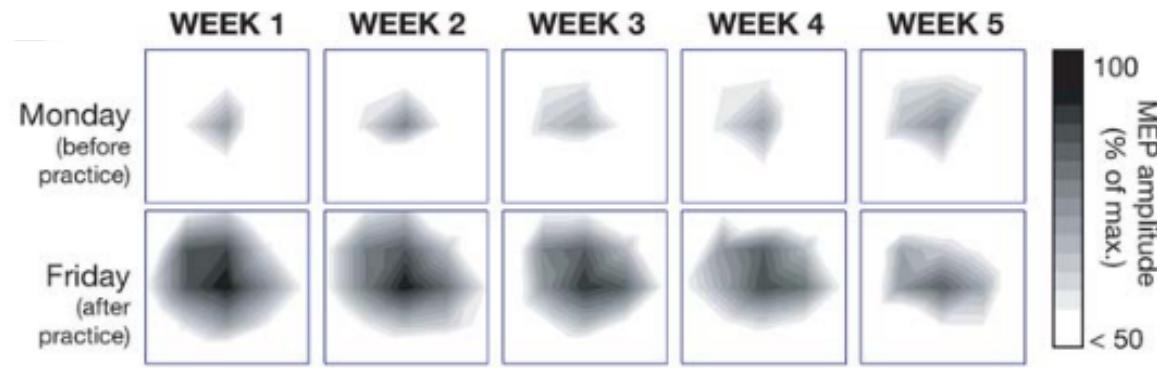
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Neural basis of motor learning

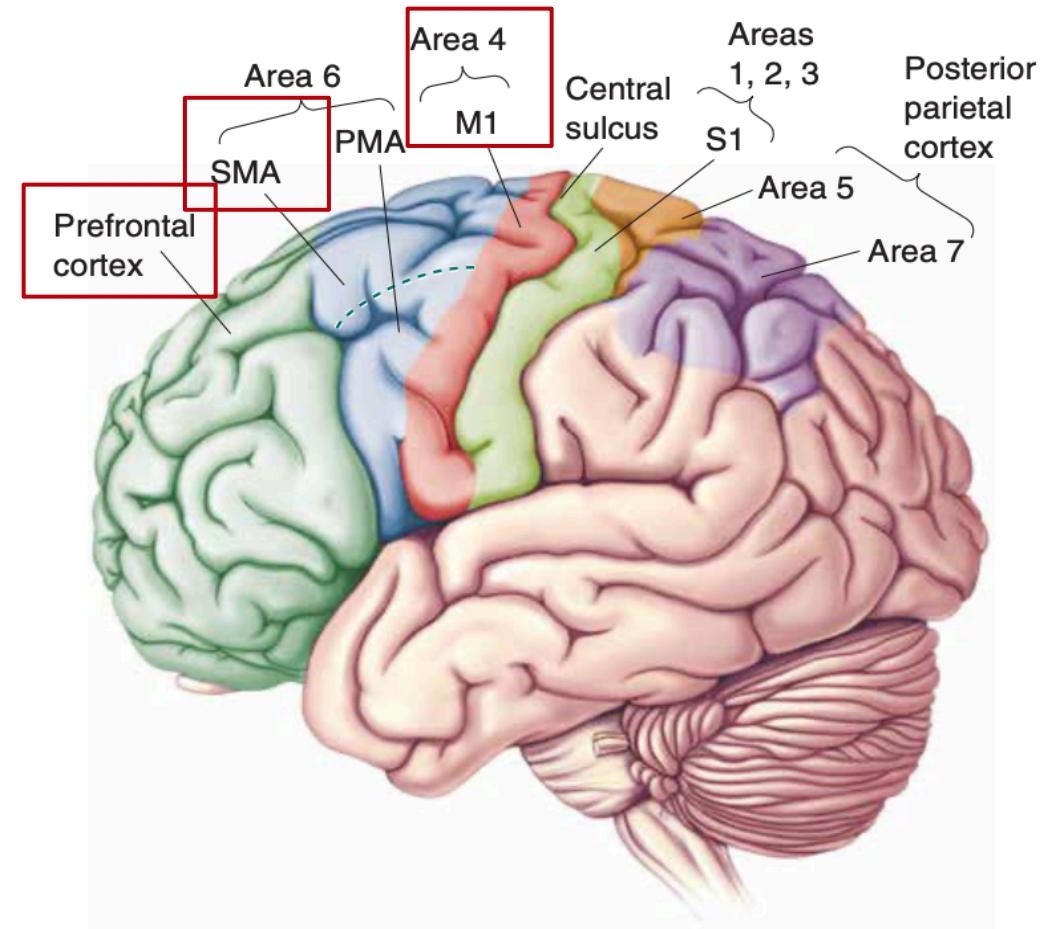
- Neuroplasticity



Two steps:

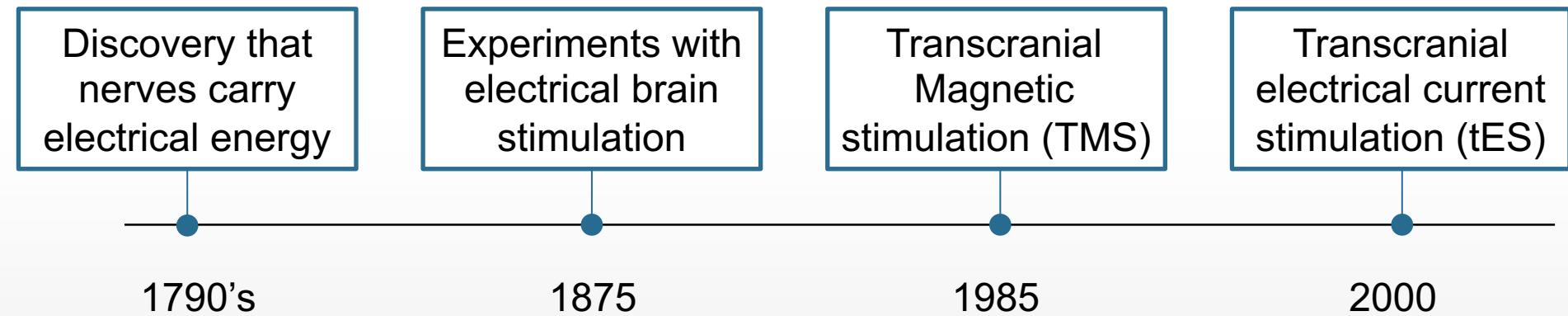
- Rapid reinforcement of preestablished organic pathways;
- Later formation of new pathways

- Cortex areas

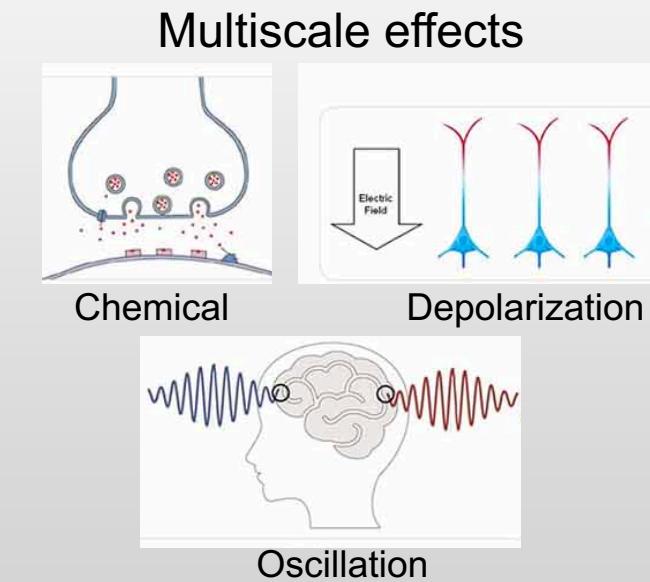
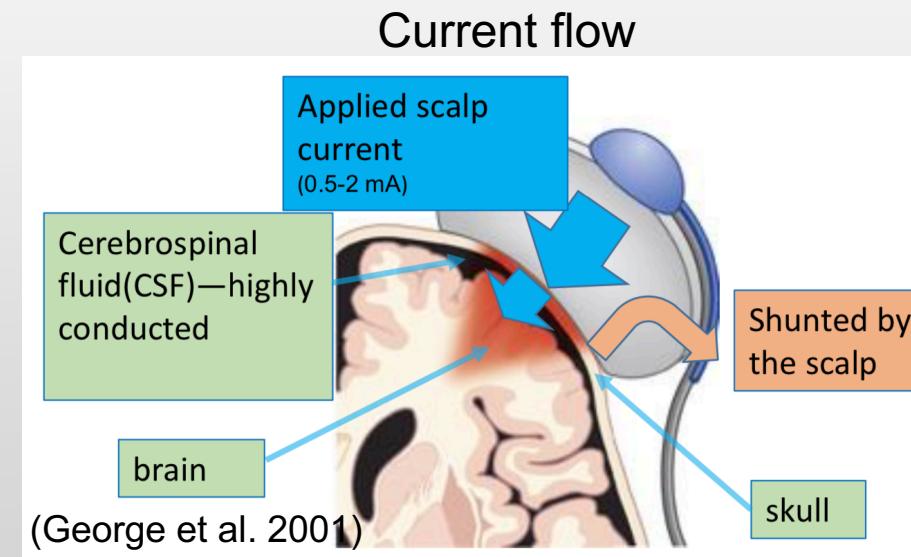
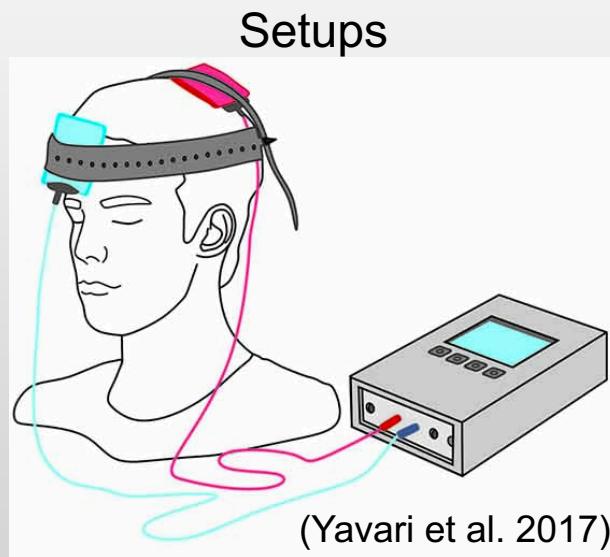


Noninvasive brain stimulation

- Noninvasive brain stimulation

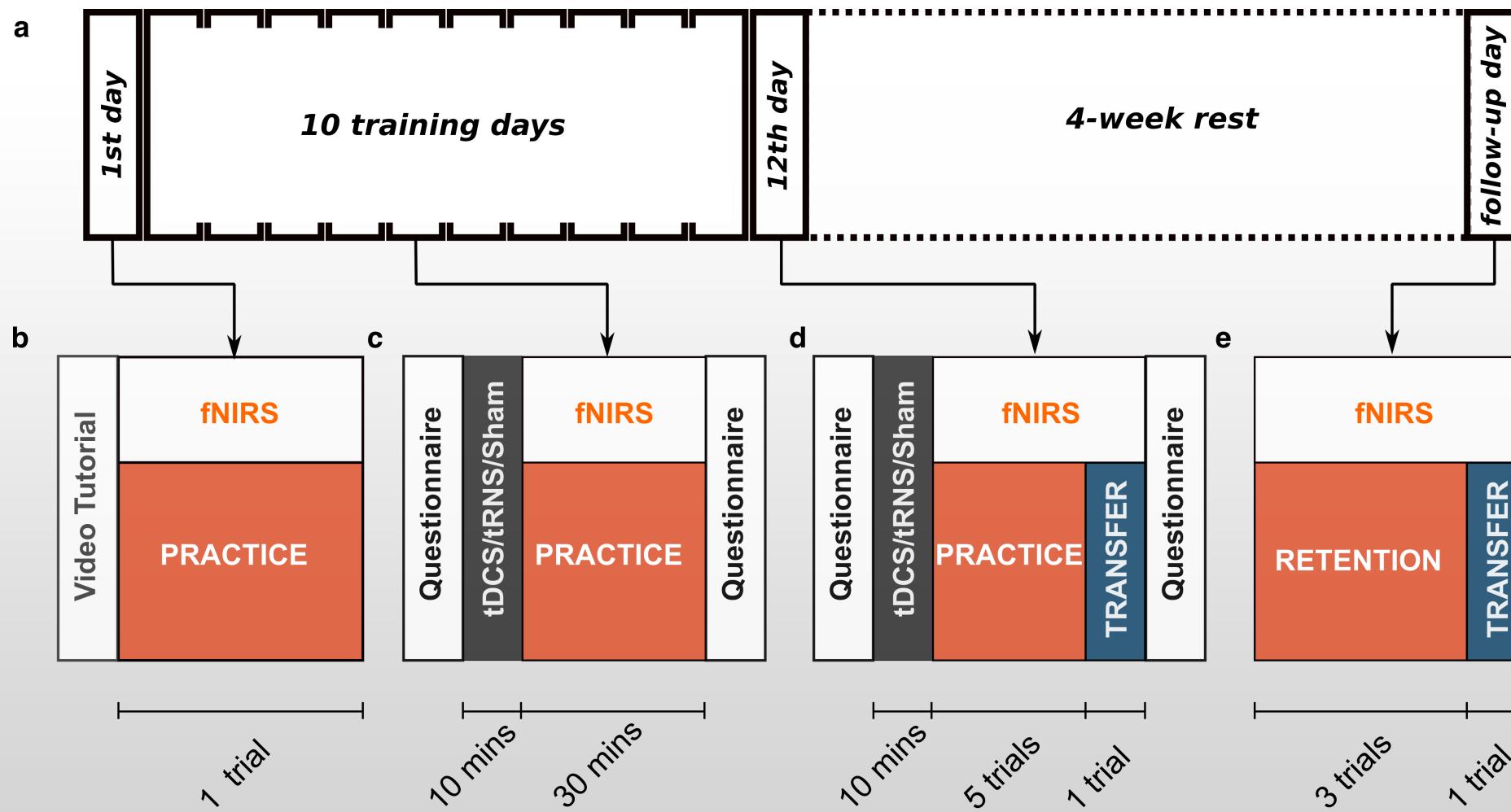


- tES



Experiment design

Hypothesis: tES (tDCS and tRNS) enhances the long-term acquisition, retention, and transfer of learning of the complex surgical skills.



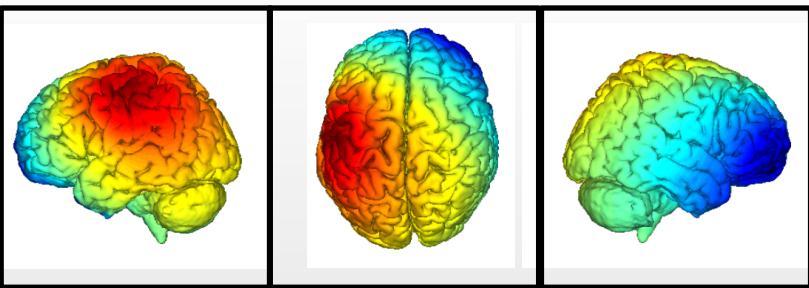
Motor task: Pattern cutting

N of trainees:

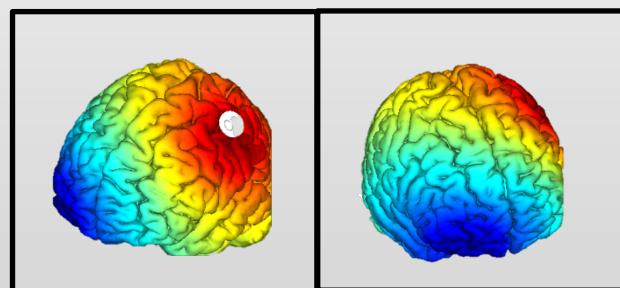
'tDCS group', n = 5;
'tRNS group', n = 5;
'Sham group', n = 7;

tES setup

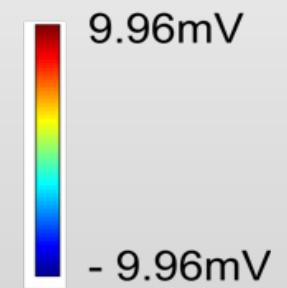
Commercial Instrument: StarStim 8



Left View Top View Right View



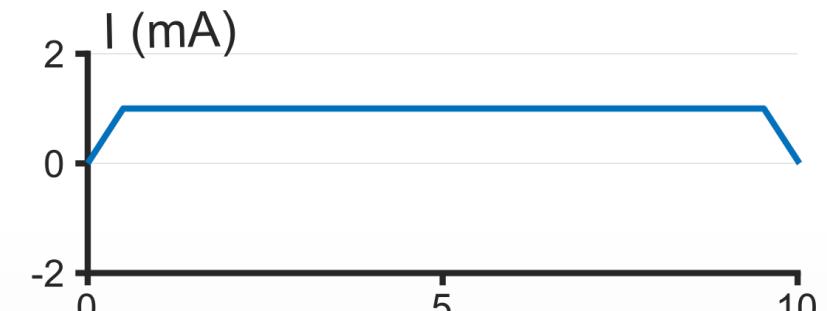
Top Left View Top Right View



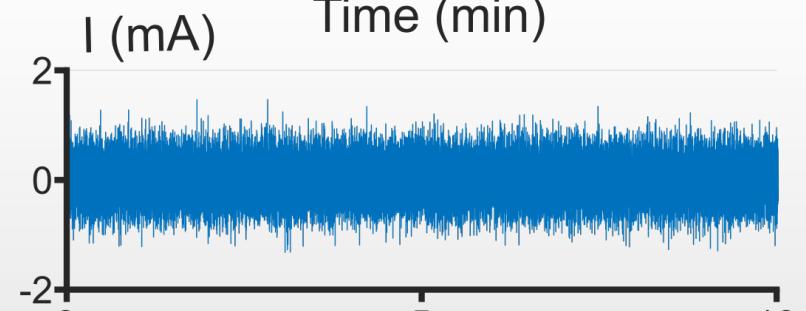
(Buch et al. 2017)



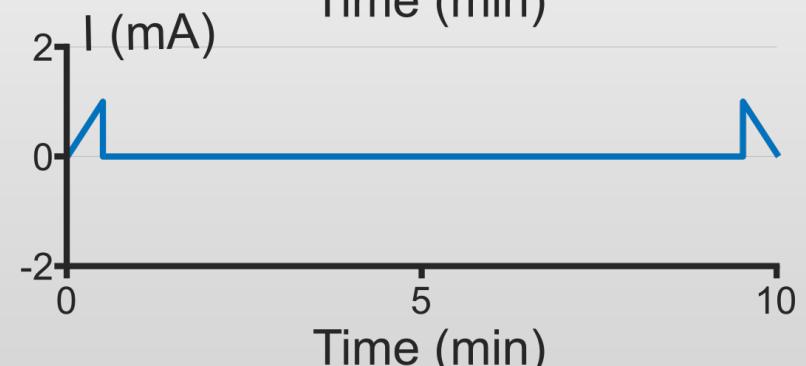
tDCS



tRNS



Sham

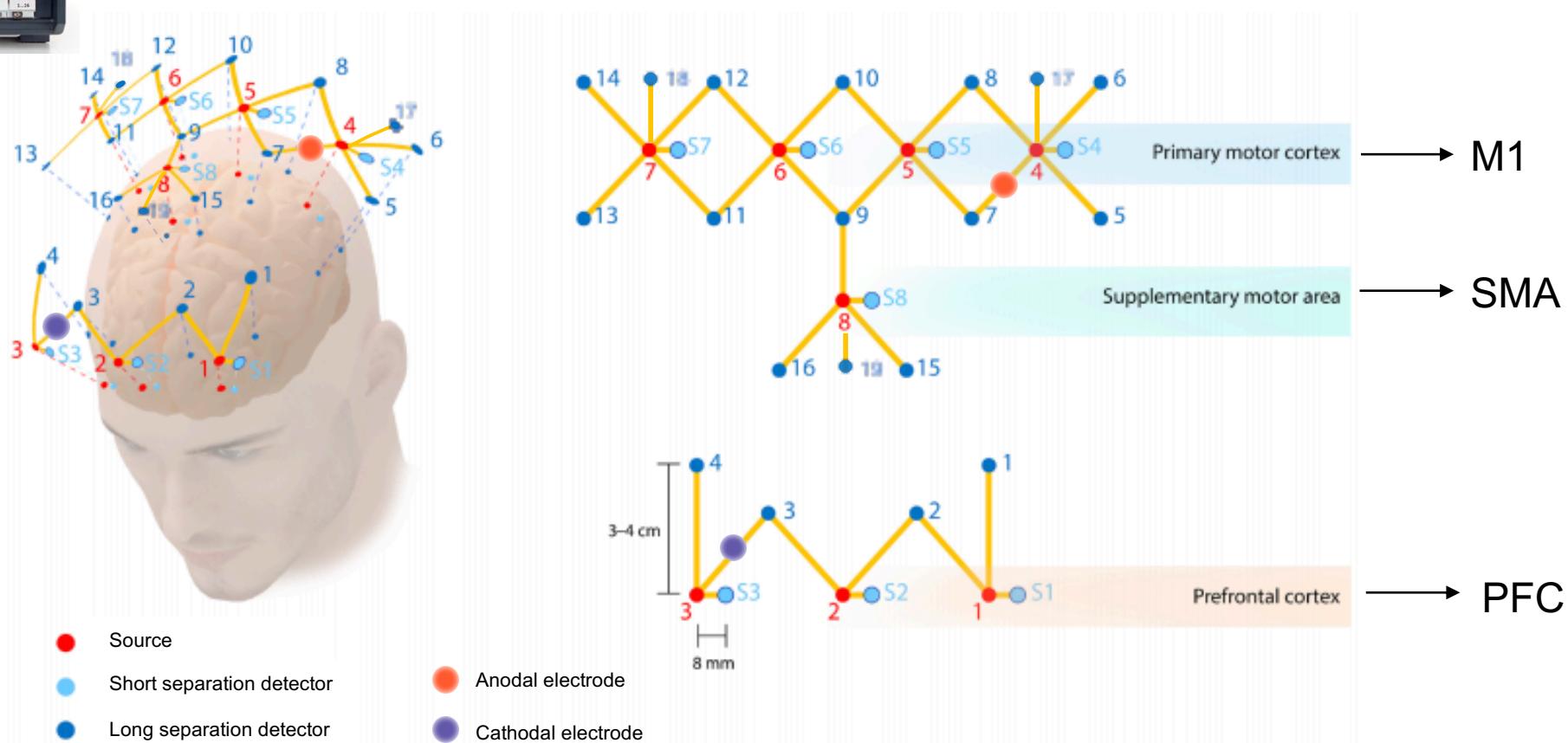


fNIRS setup

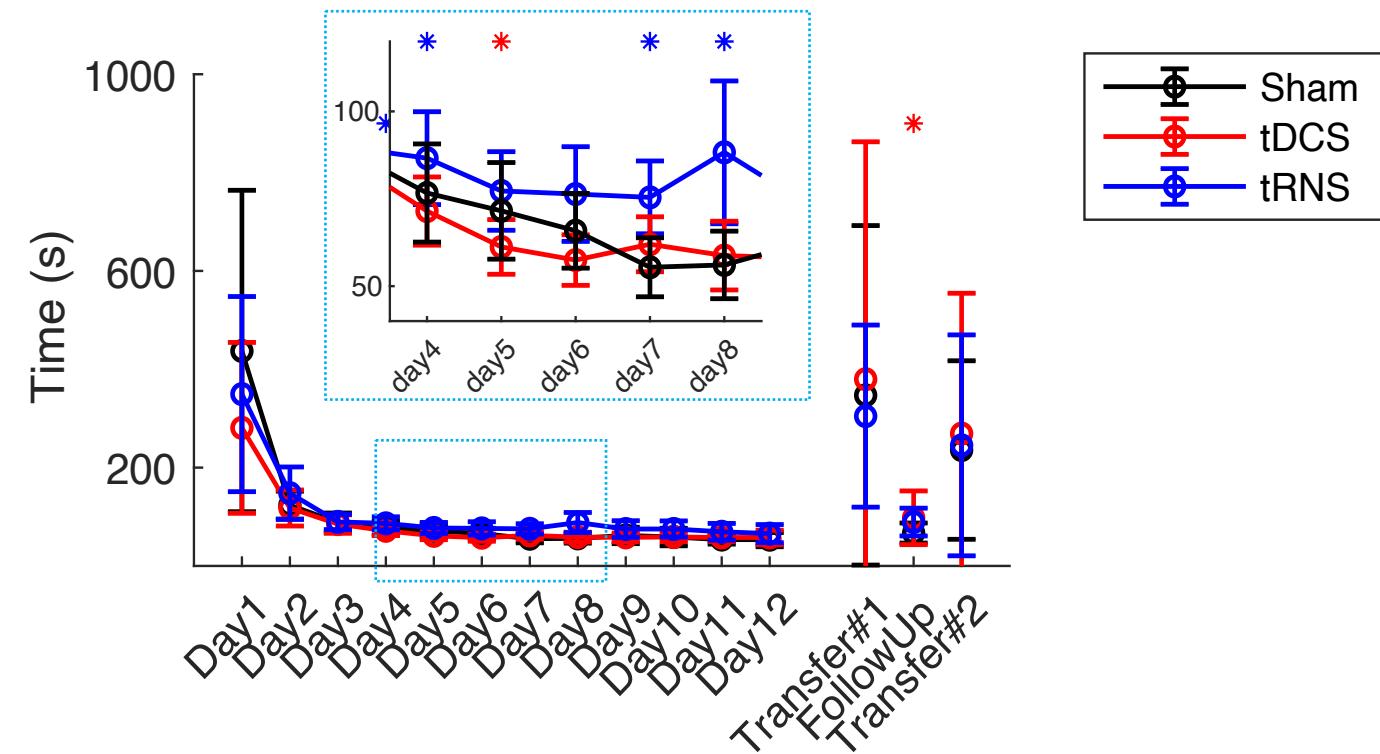
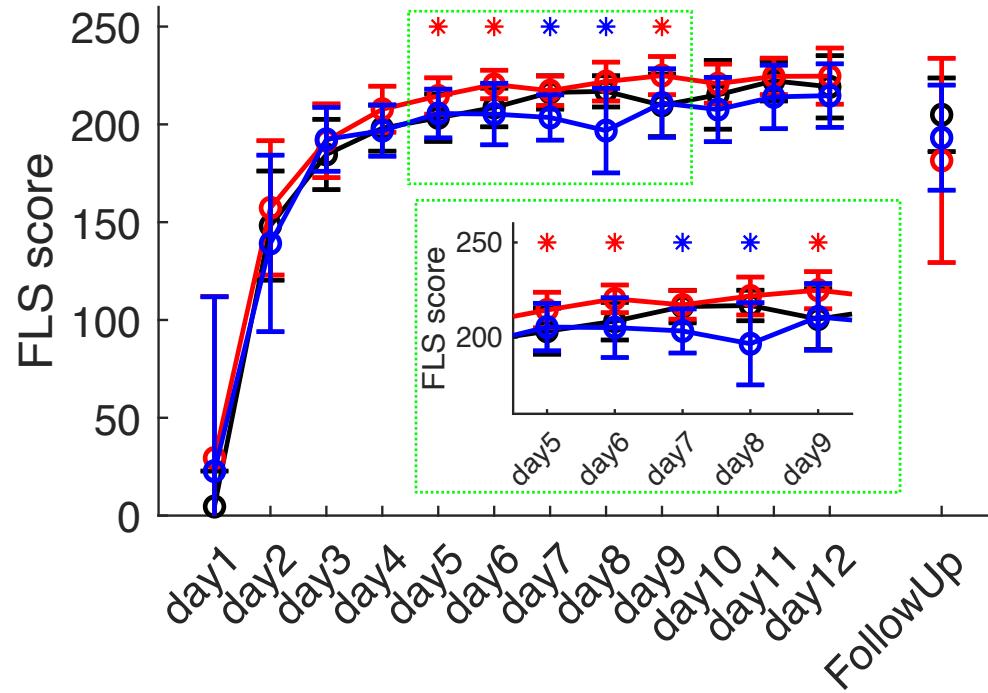


Commercial Instrument: Nirx

- LED 760&850nm

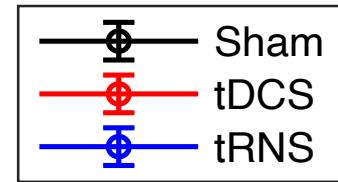
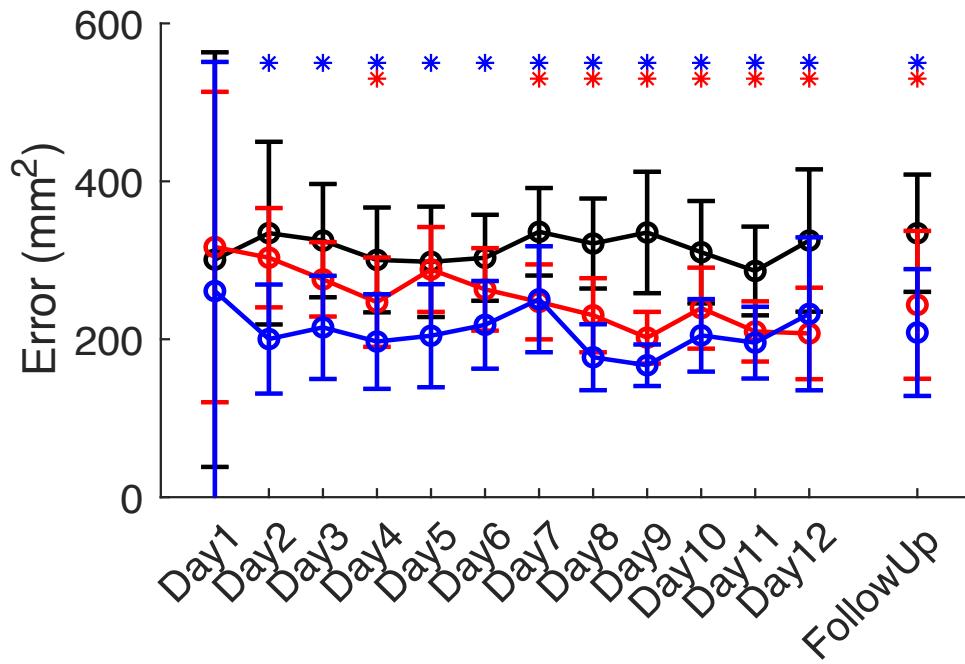


Behavioral Results – Time & FLS score

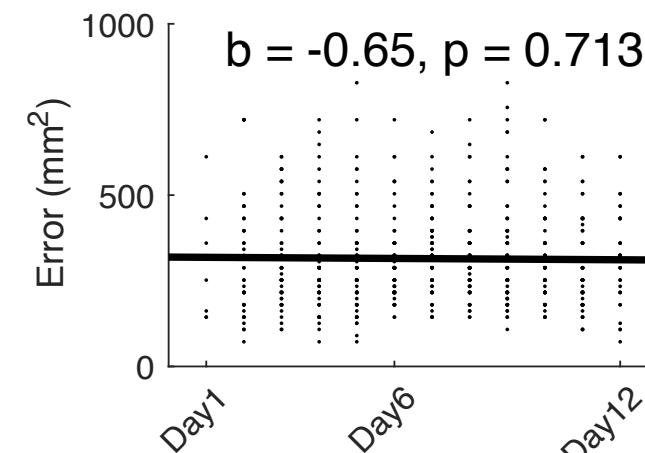
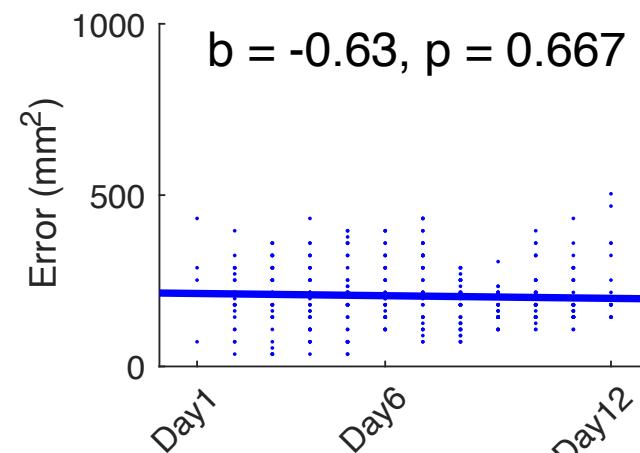
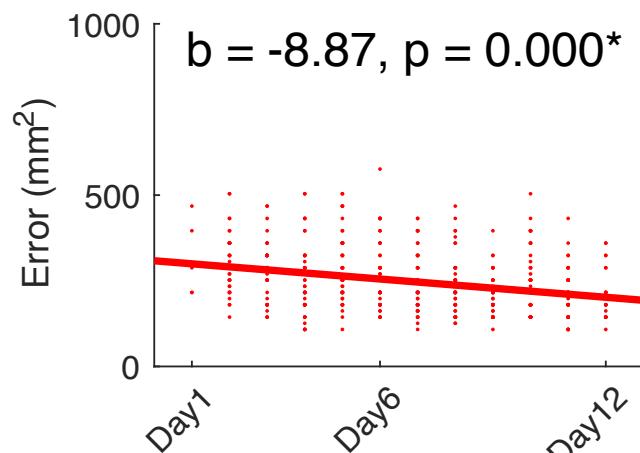


- No significant difference prior to training or at the end of the training

Behavioral Results - Error

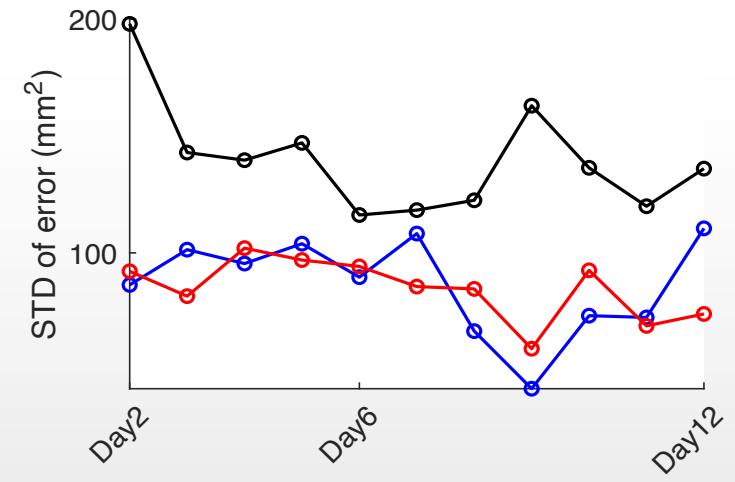
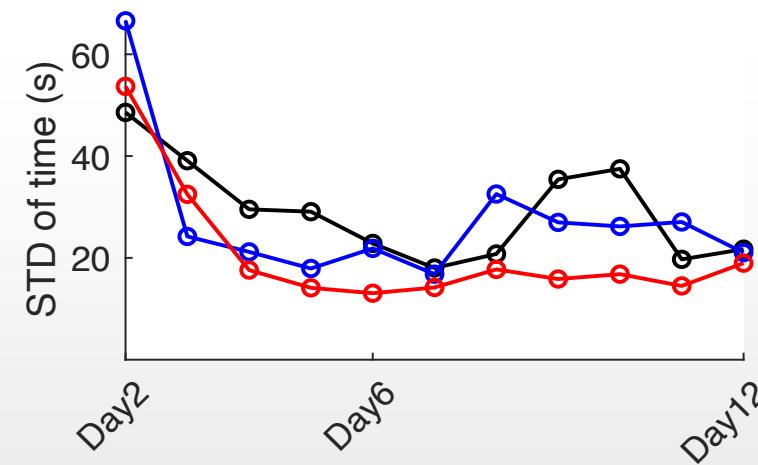
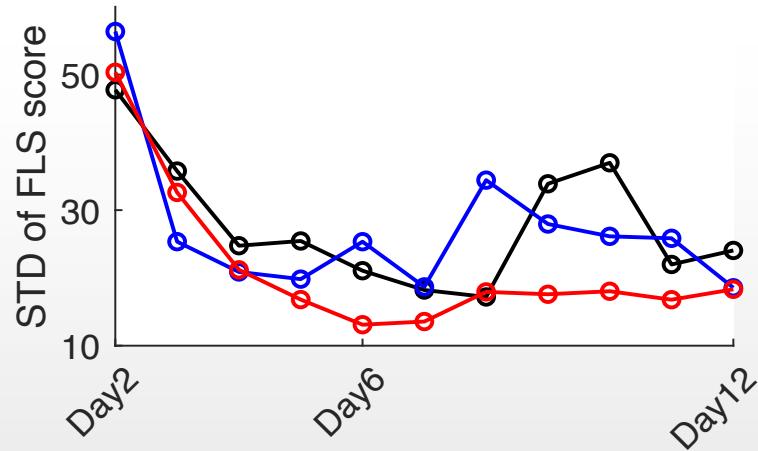


- No change in Sham
- tRNS ↓ error in the beginning than Sham
- tDCS ↓ error during the training than Sham



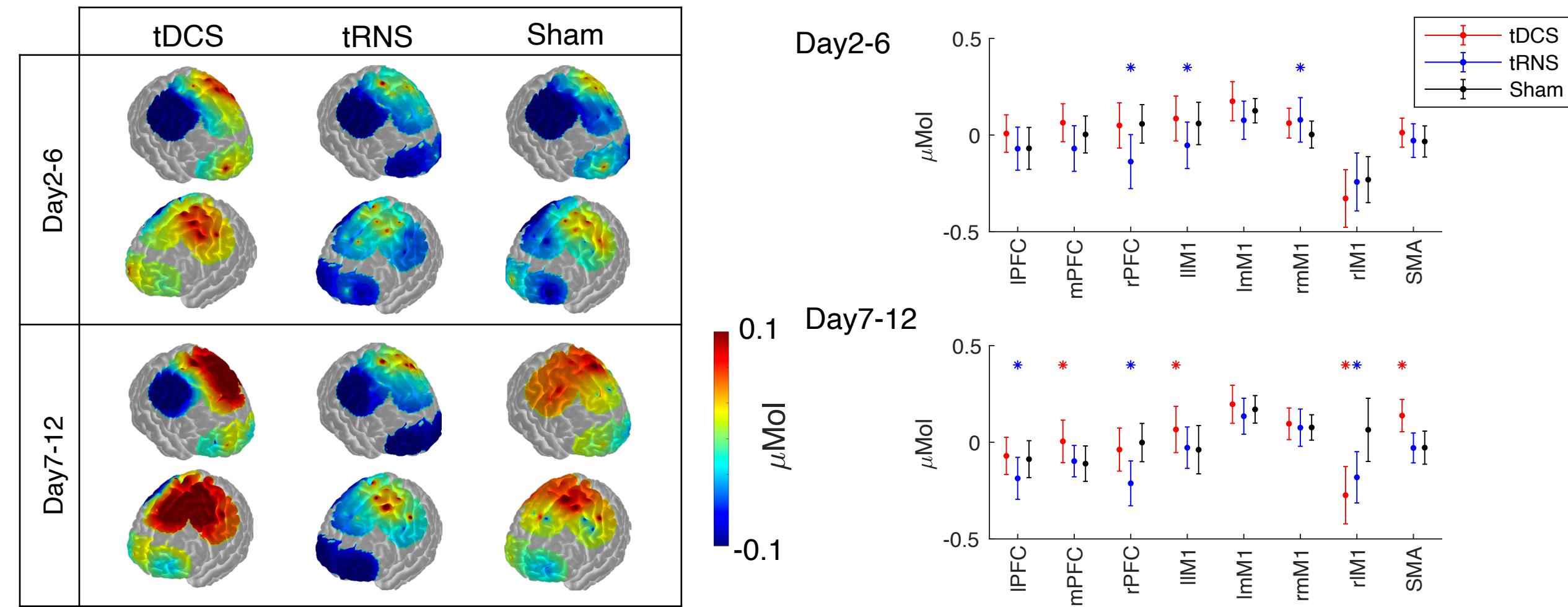
Variance analysis on performance

Standard deviation: the consistency of the behavioral output.



- **tDCS** ↓ the std of **FLS score and time** than **tRNS** and **Sham**
- **tDCS** and **tRNS** ↓ the std of **error** than **Sham**

Brain Activation Results



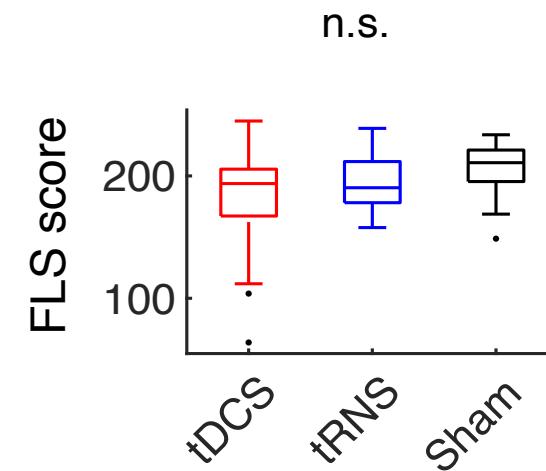
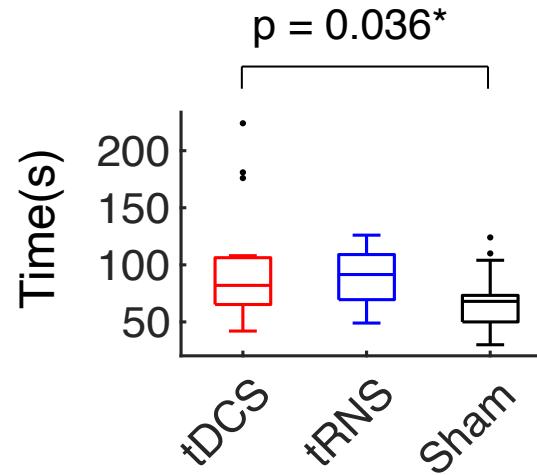
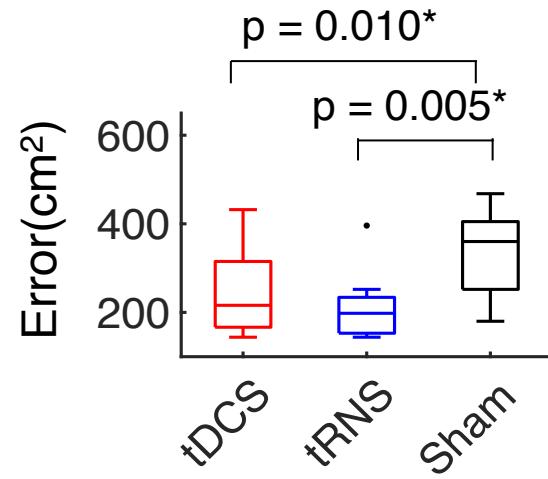
- Sham \uparrow M1 activation (Floyer-Lea et al. 2005; Ma et al. 2010)
- tDCS \uparrow M1 activation than Sham
- tRNS \downarrow total activation than Sham

Behavioral Results – retention

12 training days

4 weeks break

Retention task



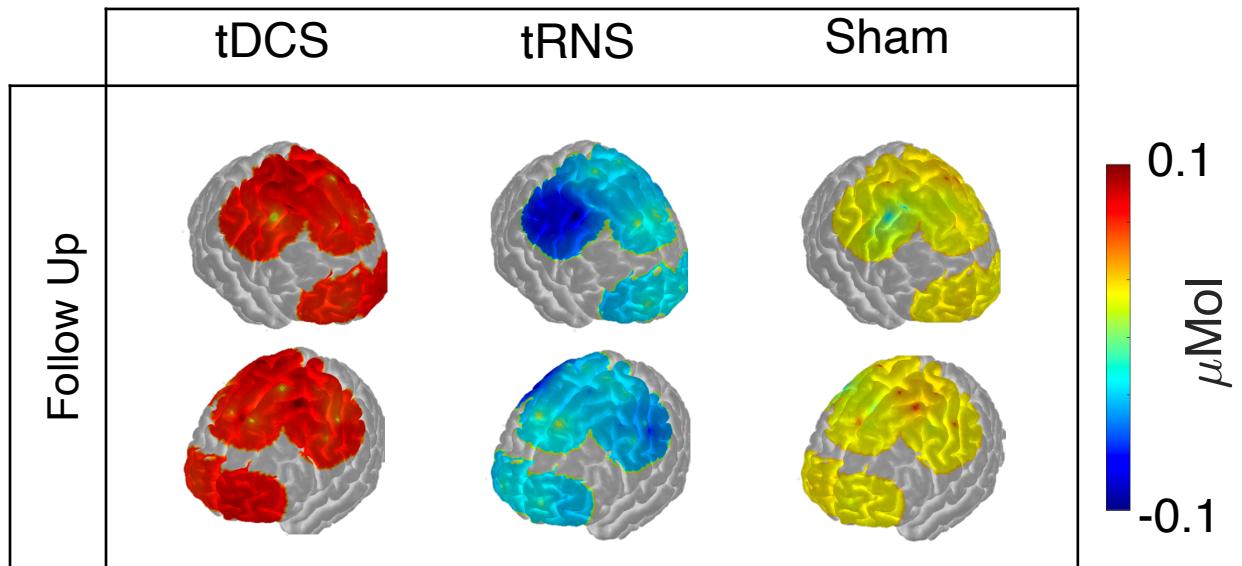
- tDCS and tRNS ↓ error than Sham
- tDCS ↑ time than Sham
- FLS score is not different

Brain Activation Results – Retention

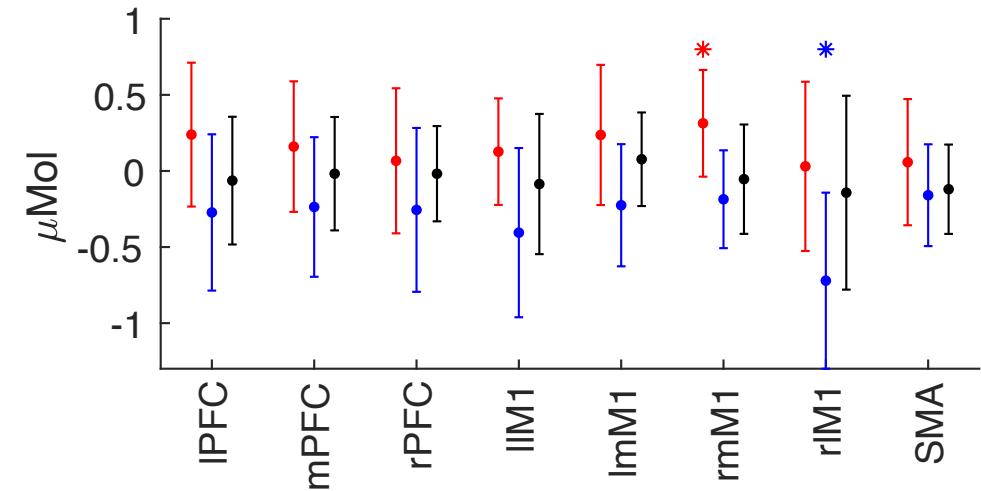
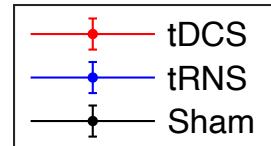
12 training days

4 weeks break

Retention task

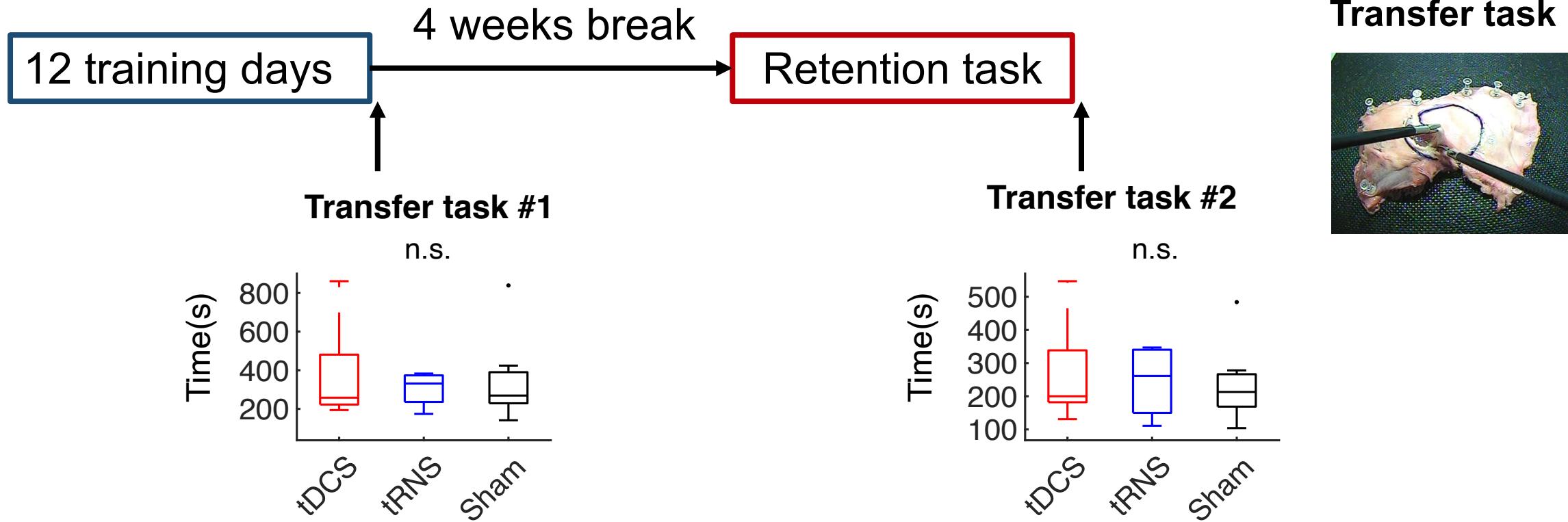


Follow Up



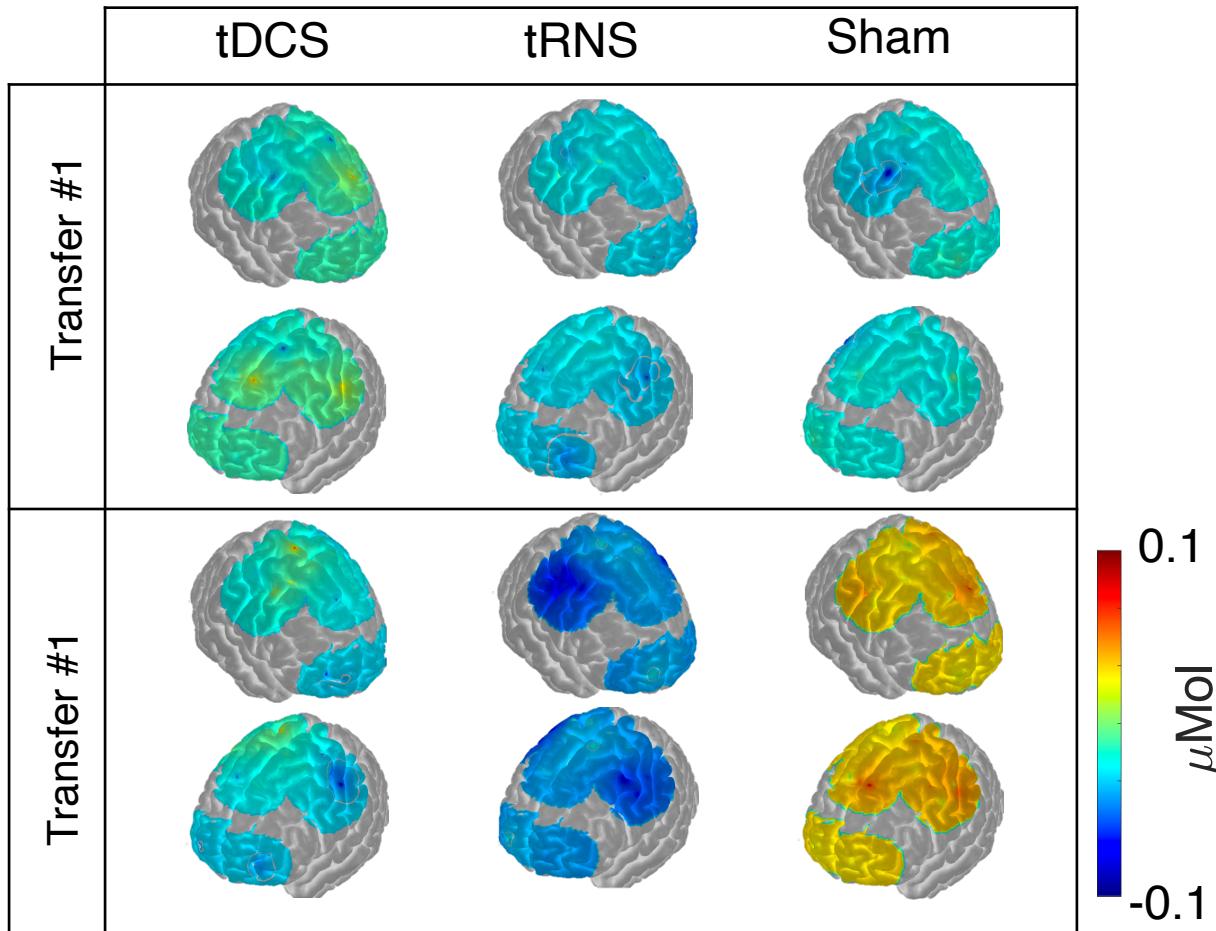
- **tDCS** ↑ brain activation than **Sham**
- **tRNS** ↓ brain activation than **Sham**
- brain activation is not concentrated in **M1** region

Behavioral Results – Follow Up & Transfer

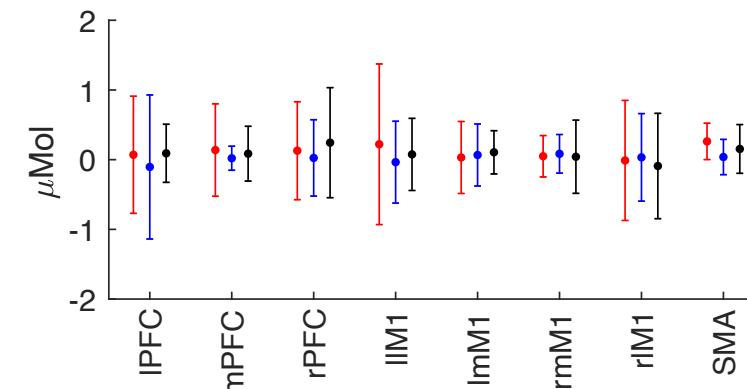


- There is **no significant difference** between the three groups

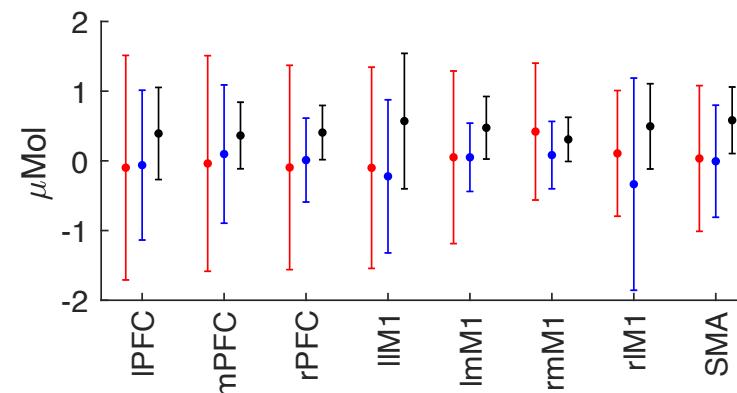
Brain Activation Results –Transfer



Transfer #1



Transfer #2



➤ There is **no significant difference** between the three groups

Specific aim 3 : to investigate whether surgical skill performance, acquisition, retention, and transfer can be enhanced via neuromodulation.

- Conclusion:
 - tDCS facilitated surgical motor learning by lowering the performance error.
 - The M1 cortex excitation was enhanced with tDCS.
- Impact:
 - Offers a tool to enhance surgical motor skills, especially decrease the surgical errors

Specific aim 1 : to predict learning curve features in the early stage of training.

- Learning curve features can be predicted from the initial performance;
- Single factor can represent the learning curve features;

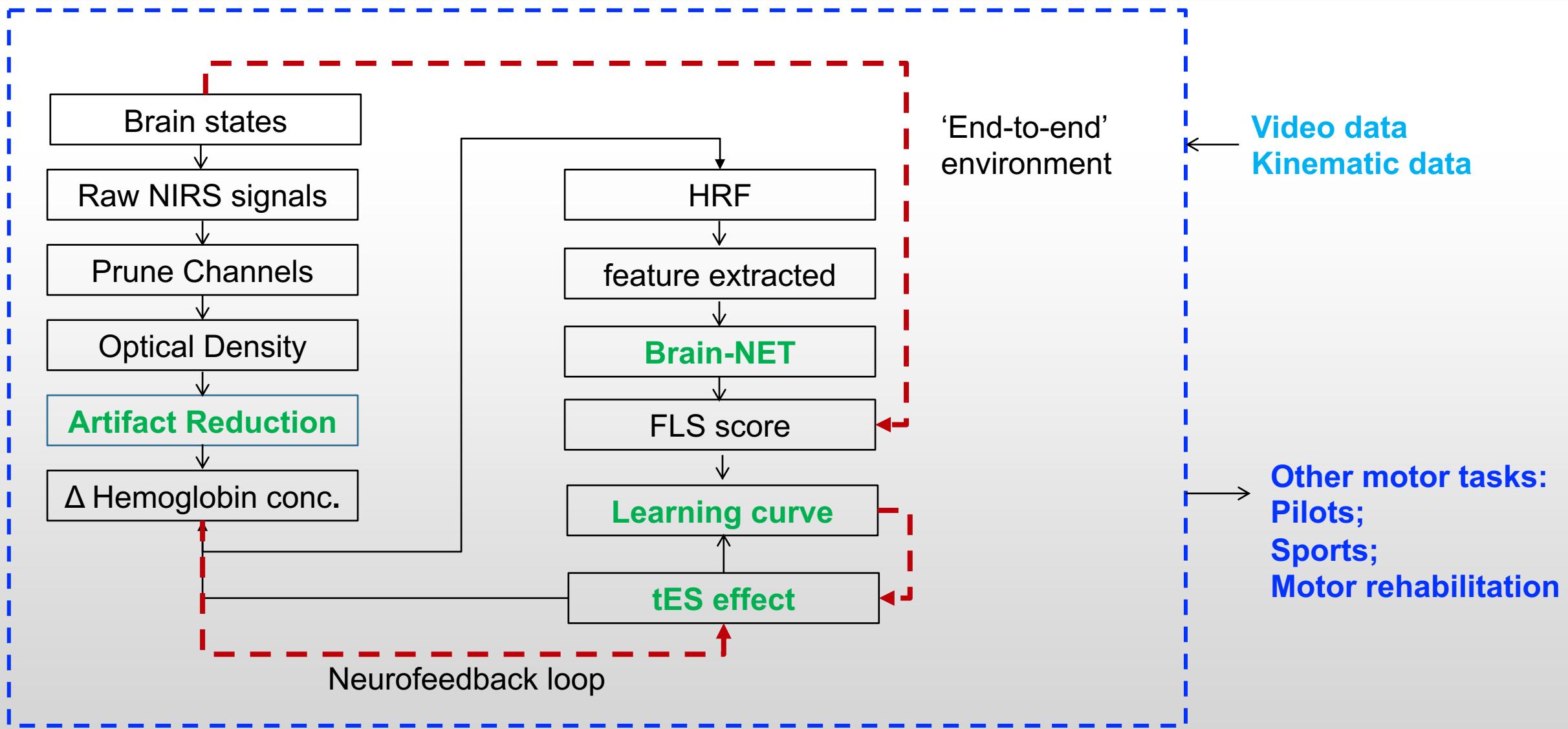
Specific aim 2 : to predict FLS scores via neuroimaging.

- Neuroimaging can predict FLS score;
- DAE model is superior in fNIRS motion artifact removal

Specific aim 3 : to investigate whether surgical skill performance, acquisition, retention, and transfer can be enhanced via neuromodulation.

- tDCS enhanced the lengthy learning procedure by reducing the performance error via strengthening brain activation in the M1 region.

Overview and Future Work



Journal papers

Published/Accepted:

Gao, Y., Kruger, U., Intes, X., Schwatzberg, S. and De, S., 2020. A machine learning approach to predict surgical learning curves. *Surgery*, 167(2), pp.321-327. **(S.A. #1)**

Gao, Y., Cavuoto, L., Schwatzberg, S., Norfleet, J., Intes, X. and De, S., 2020. The effects of transcranial electrical stimulation on human motor functions: a comprehensive review of functional neuroimaging studies. *Frontiers in Neuroscience*, accepted. **(review for S.A. #3)**

Under review:

Gao, Y., Yan, P., Kruger, U., Cavuoto, L., Schwatzberg, S., De, S. and Intes, X. 2020. Functional brain imaging reliably predicts bimanual motor skill performance in a standardized surgical task. *IEEE TBME*, under review. **(S.A. #2)**

Gao, Y., Chao, H., Cavuoto, L., Yan, P., Kruger, U., Norfleet, J., Makled B., Schwatzberg, S., De, S. and Intes, X., 2020. Deep learning-based motion artifact removal in functional near-infrared spectroscopy (fNIRS). *NeuroImage*, under review. **(S.A. #2)**

Journal papers (continued)

In Preparation:

Gao, Y., Cavuoto, L., Dutta, A., Kruger, U., Yan, P., Norfleet, J., Makled B., Silverstri, J., Schwatzberg, S., Intes, X. and De, S., 2020. tDCS-induced primary motor cortex activation diminishes errors in fine bimanual motor skill learning. *Nature biomedical engineering*, in polish. (S.A. #3)

A draft for the transfer learning is also under preparation (S.A. #3);

A Nemanic, **Gao, Y.**, M Yucel, D Gee, C Cooper, S Schwatzberg, X Intes and S De, “Functional brain connectivity distinguishes surgical skill dexterity in both physical and virtual simulation environments,” *Neuroimage*, in polish.

Conference papers

Yuanyuan Gao, Pingkun Yan, Uwe Kruger, Suvranu De and Xavier Intes, “Neuroimaging biomarkers for surgical skill level prediction”, *SPIE.bios, San Francisco, CA, February 2019.*

Yuanyuan Gao, Pingkun Yan, Uwe Kruger, Suvranu De and Xavier Intes, “fNIRS as a quantitative tool to asses and predict surgical skills”, *OSA Biophotonics Congress: Optics in the Life Sciences, Tucson, AZ, April 2019.*

Yuanyuan Gao, Lora Cavuoto, L., Pingkun Yan, Uwe Kruger, Steven Schwartzberg, Suvranu De, and Xavier Intes, “A deep learning approach to remove motion artifacts in fNIRS data analysis”. *In Optics and the Brain, Optical Society of America, 2020.*

Yuanyuan Gao, Lora Cavuoto, L., Pingkun Yan, Uwe Kruger, Jessica Silvestri, Steven Schwartzberg, Xavier Intes and Suvranu De, “Monitoring the effect of transcranial Electric current Stimulation (tES) during a bimanual motor task via functional Near-InfraRed Spectroscopy (fNIRS)”. *In Optics and the Brain, Optical Society of America, 2020.*

Yuanyuan Gao, Lora Cavuoto, L., Pingkun Yan, Uwe Kruger, Jessica Silvestri, Steven Schwartzberg, Jack E. Norfleet, Basiel A. Makled, Xavier Intes and Suvranu De, “Transcranial direct current stimulation speeds up surgical bimanual motor learning and increases functional activation ”, *In MHSRS, Young Investigator breakout session award paper, August 2020.*

Acknowledgements

- Committee members
 - Suvranu De, Xavier Intes, Pingkun Yan, Lucy Zhang, Emily Liu
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- NIH grant funding
- Tech support: TechEn (Dr. A. “Buzz” DiMartino), NIRx, NVIDIA corp.
- Collaborators:



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Rensselaer

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& IMAGING IN MEDICINE

UB University
at Buffalo

BU Neurophotonics Center



BA CNBS Berenson-Allen Center
For Noninvasive Brain Stimulation

HARVARD
MEDICAL SCHOOL



National
Institutes
of Health

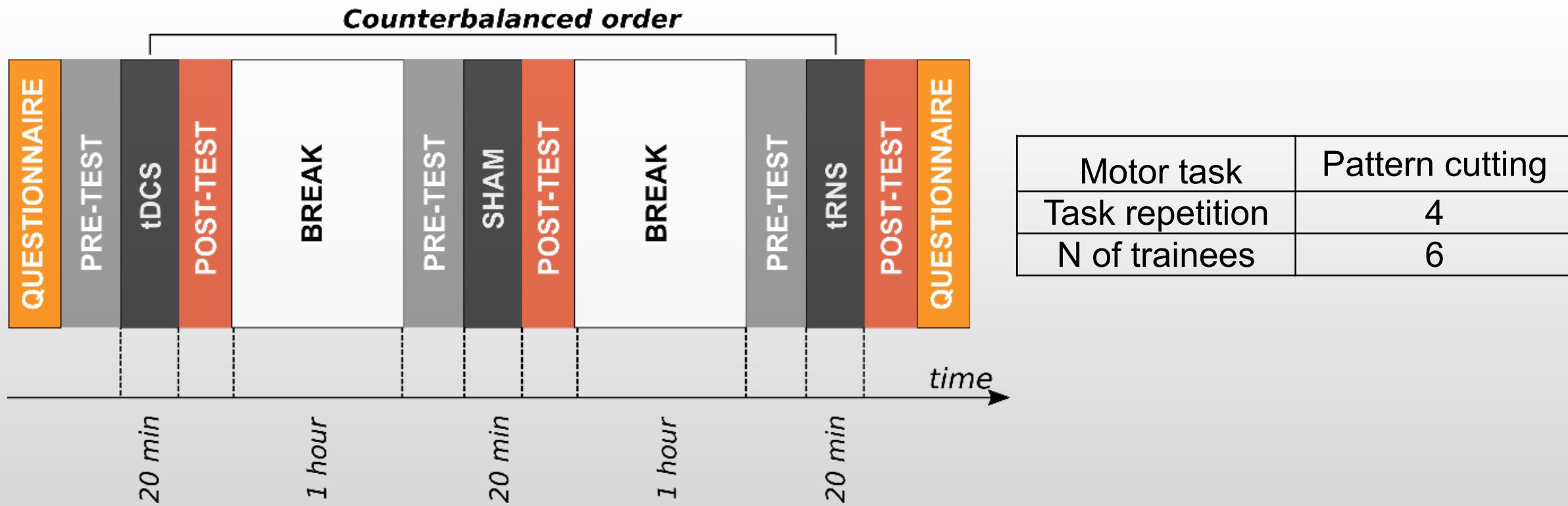
CeMSIM
THE CENTER FOR MODELING, SIMULATION
& IMAGING IN MEDICINE

Thank you!

Backups

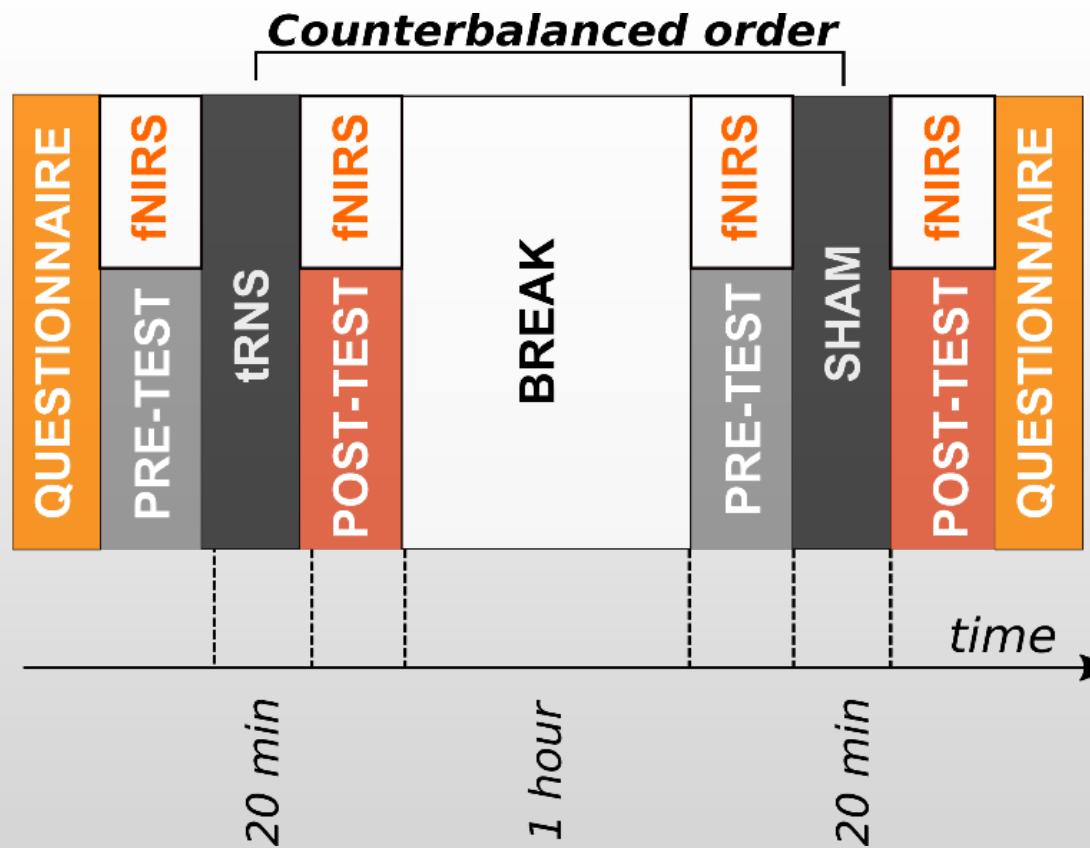
Pilot study

- **Hypothesis:** tES (tDCS and tRNS) enhances the surgical bimanual task performance in a short term.
- **Experimental design:**



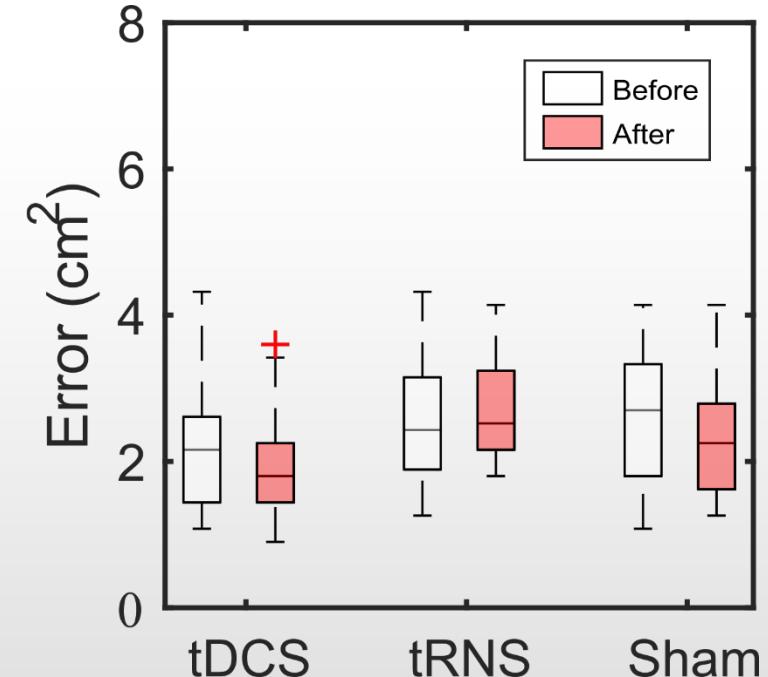
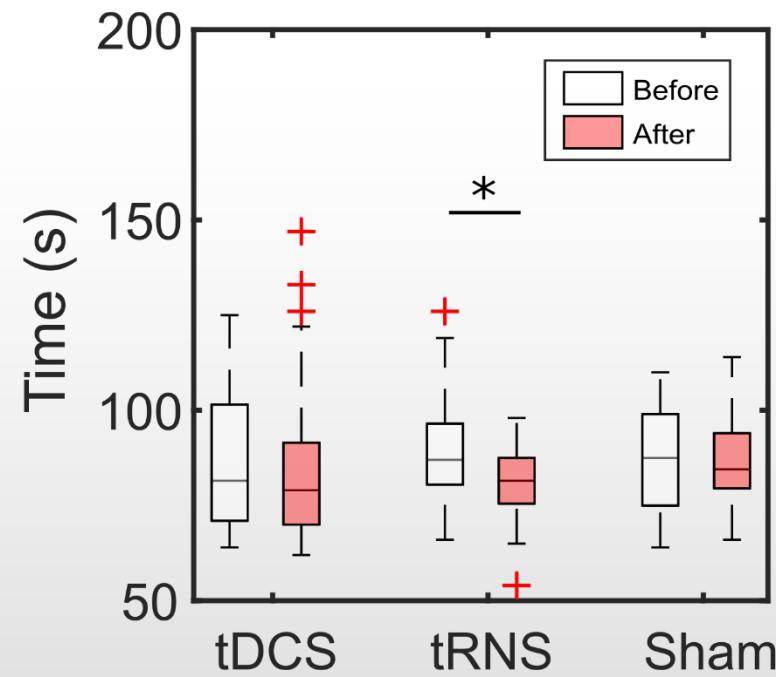
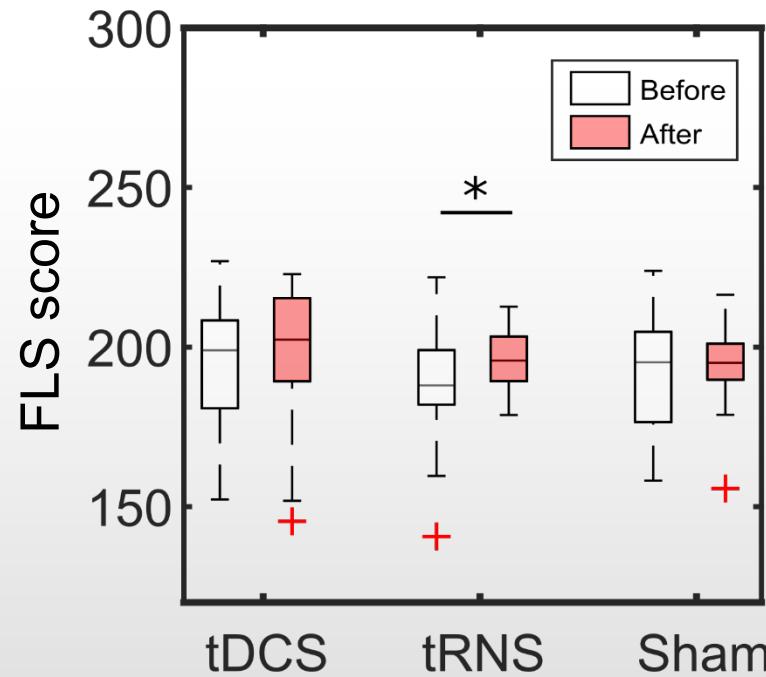
Experiment #1

- **Hypothesis:** tRNS enhances the surgical bimanual task performance in a short term and changes the brain activation.
- **Experimental design:**



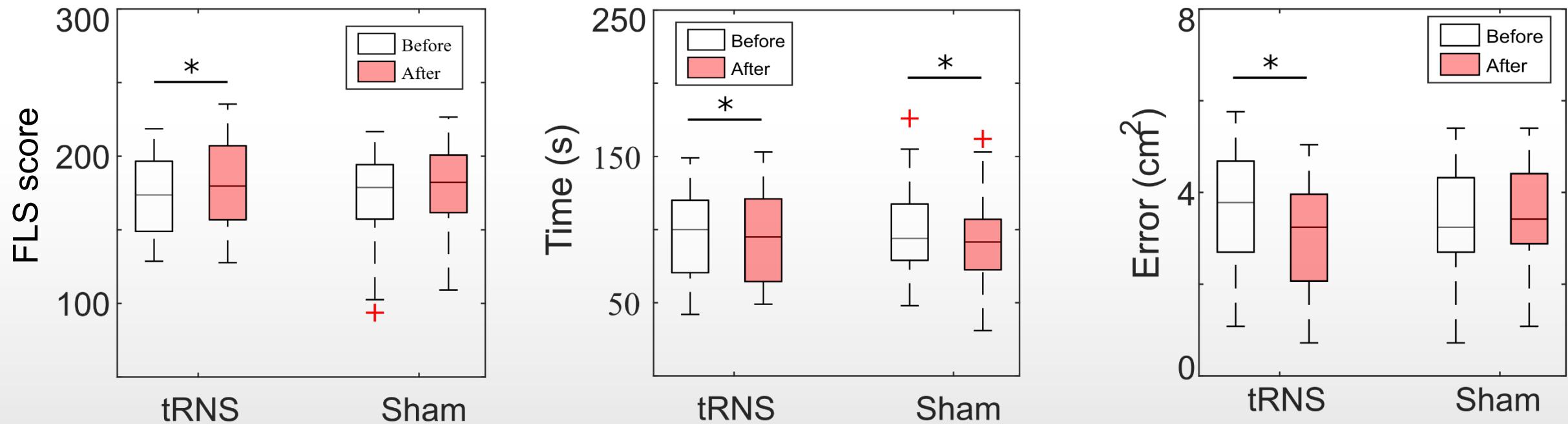
Motor task	Pattern cutting
Task repetition	4
N of trainees	12

Pilot study



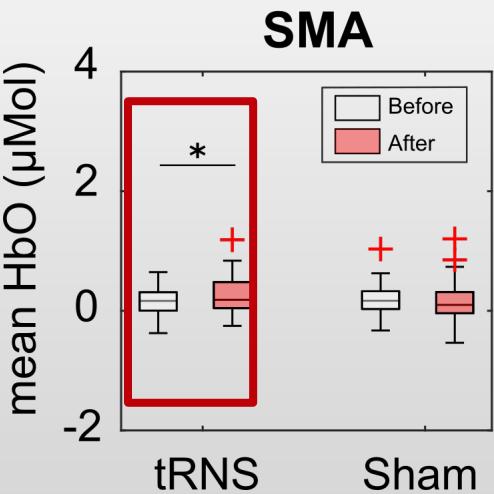
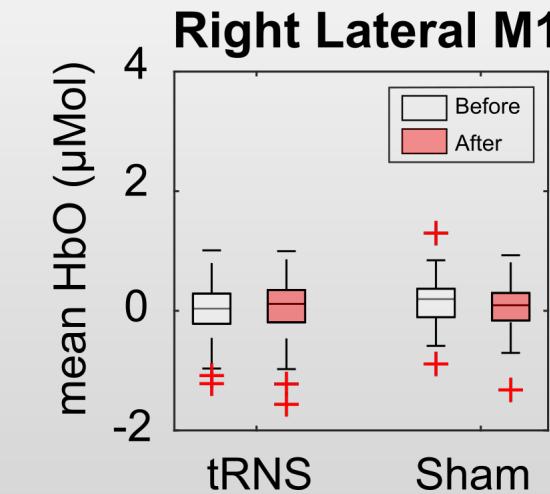
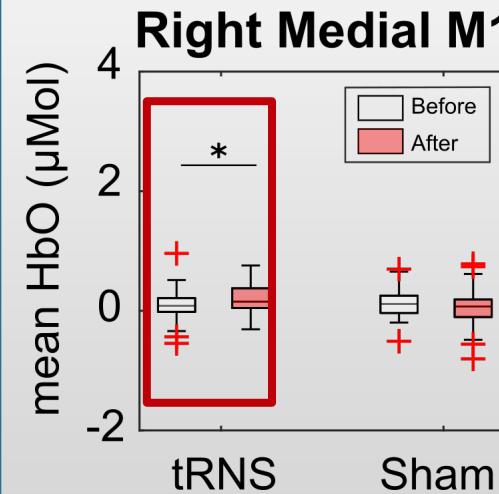
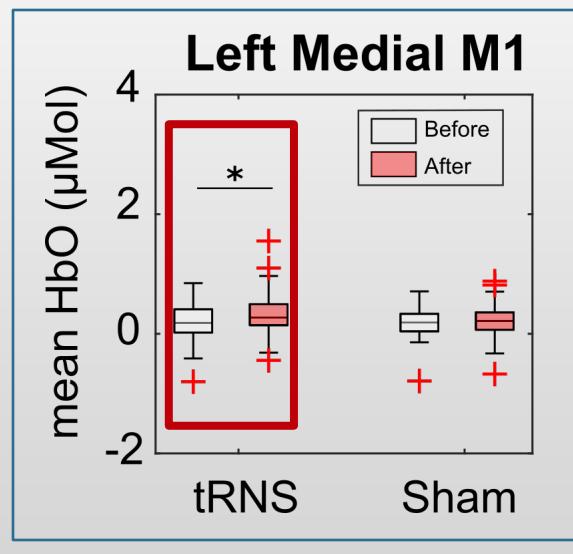
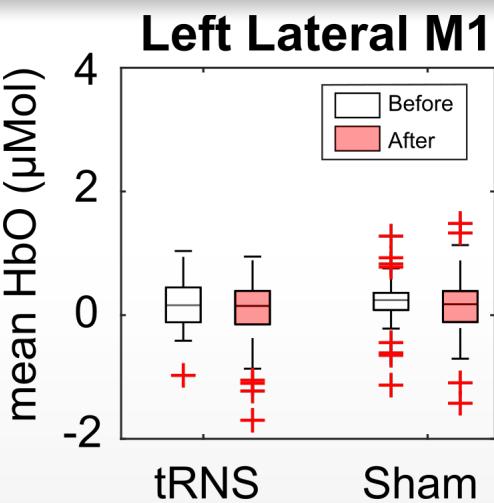
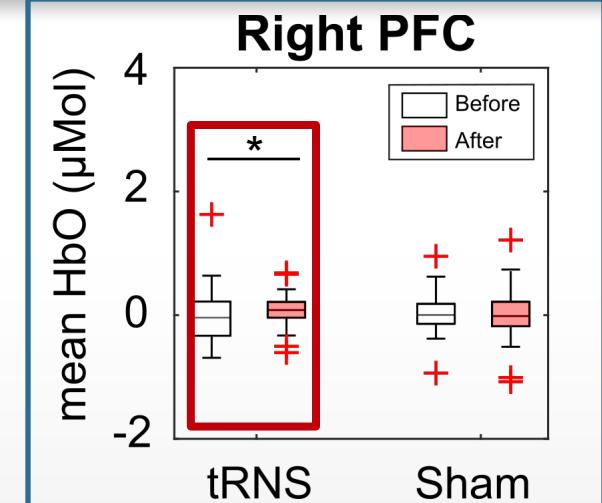
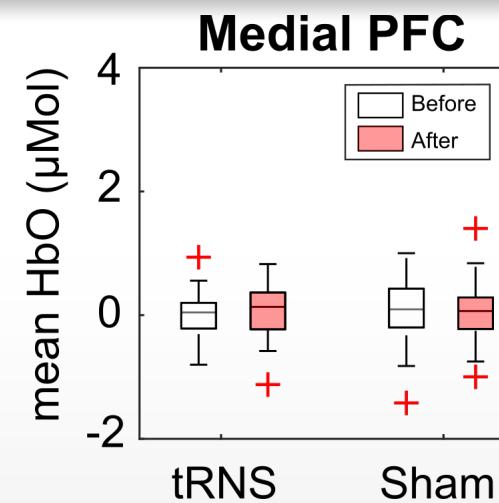
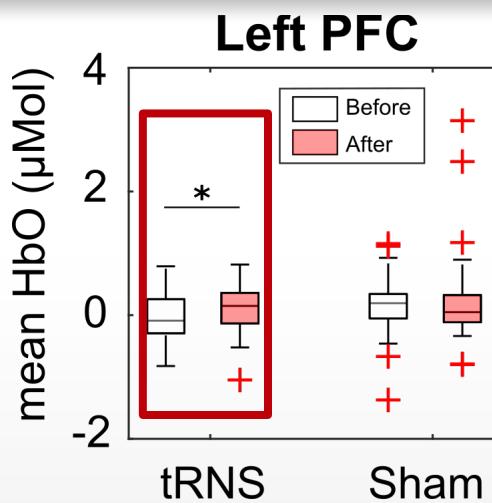
- The FLS score increased significantly under tRNS condition.

Experiment #1

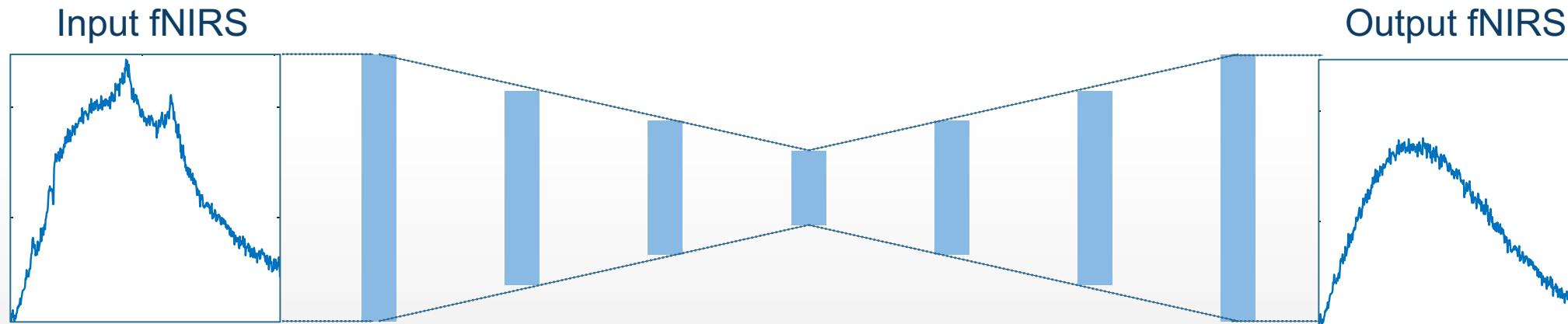


- The FLS score increased under tRNS condition;
- Time decreased for both conditions;
- Error decreased under tRNS condition.

Experiment #1



- ‘Denoising autoencoder’ (DAE)



- Preliminary results

