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3. **V. Sharma** – Exploring the Frequency-Mediated Dynamic Repertoire of Brain Activity Following Stroke
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12. **S. Konik** – Characterise disturbances in the perception of the affected upper limb following stroke with the new Affected Limb Perception Questionnaire (ALPQ)
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15. **B. Favre-Bulle** – Efficacy of a new virtual reality-based serious game for the rehabilitation of unilateral neglect in patients with acquired brain injury
16. **Z. Rotach** – Exploring attention recovery and cerebral modulation following a new virtual-reality training in patients with stroke
17. **D. Zeugin** – Analyzing Attentional Deficits and Spatial Neglect Through Reinforcement Learning and Deep Neural Networks

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Intra- and inter-hemispheric effective connectivity and automatic classification of ischemic stroke using reservoir computing causality

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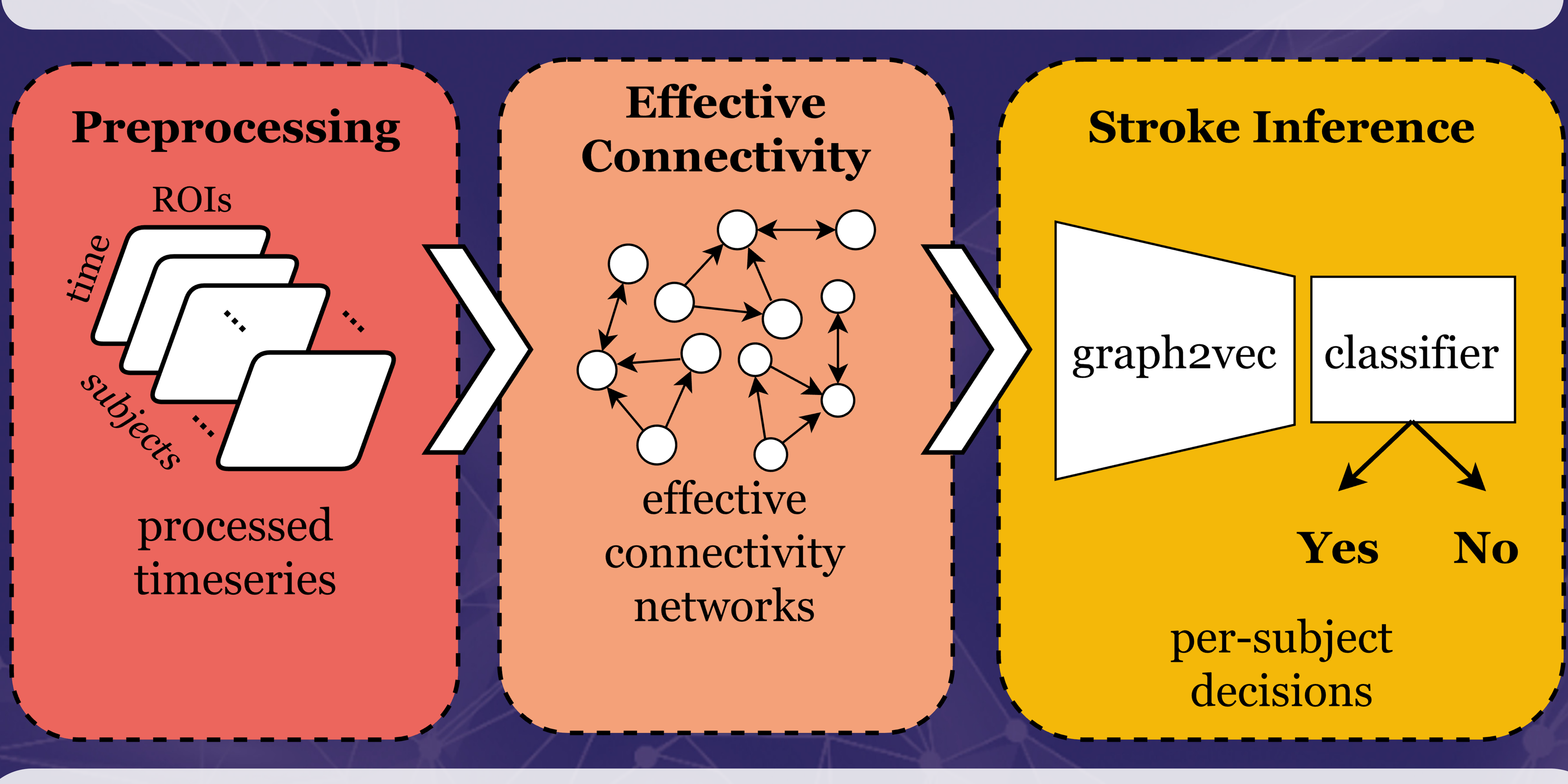
Introduction

Functional MRI unveils the intricate network disruptions caused by stroke. Directed interactions can hold more clinical insights than symmetric ones [1]. State reconstruction methods offer a novel approach [2] to infer causal relationships, with preliminary findings paving the way for clinical validation of this promising technique.

The Dataset

194 subjects scanned [3]

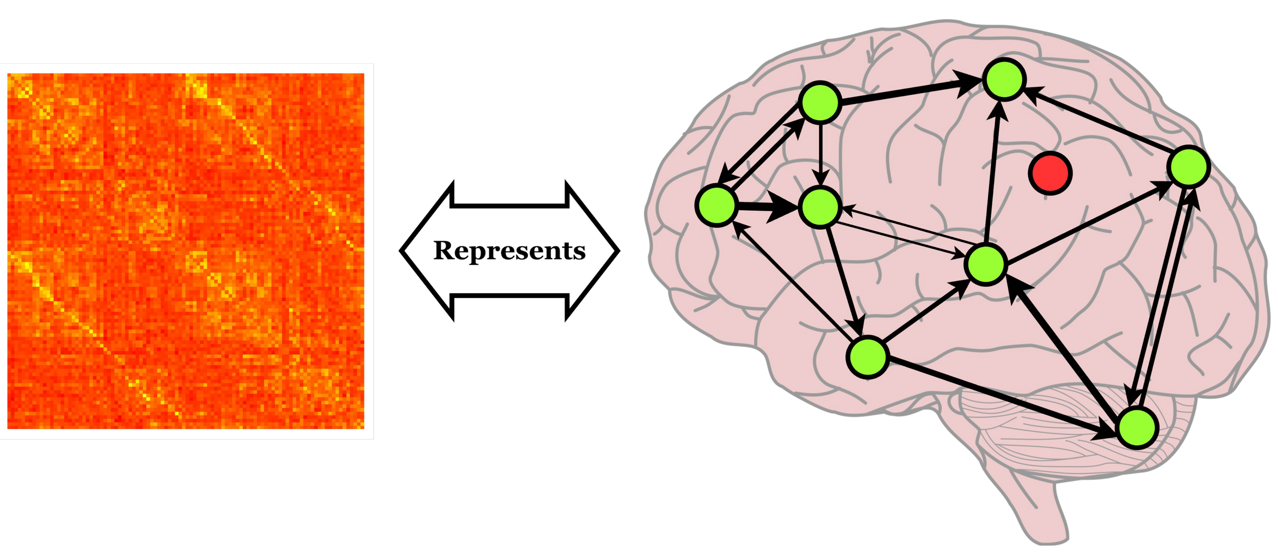
- Stroke 161 subj. (54±11 years) Control 33 subj. (55±12 years)
- Ischemic 128 subjects Hemorrhagic 25 subjects
- Left hemisphere 82 subjects Right hemisphere 79 subjects



Preprocessing Part

- fMRIPrep preprocessing
- XCP-D postprocessing
- Schaefer parcellation – 100 ROIS, 17 networks

Effective Connectivity Part



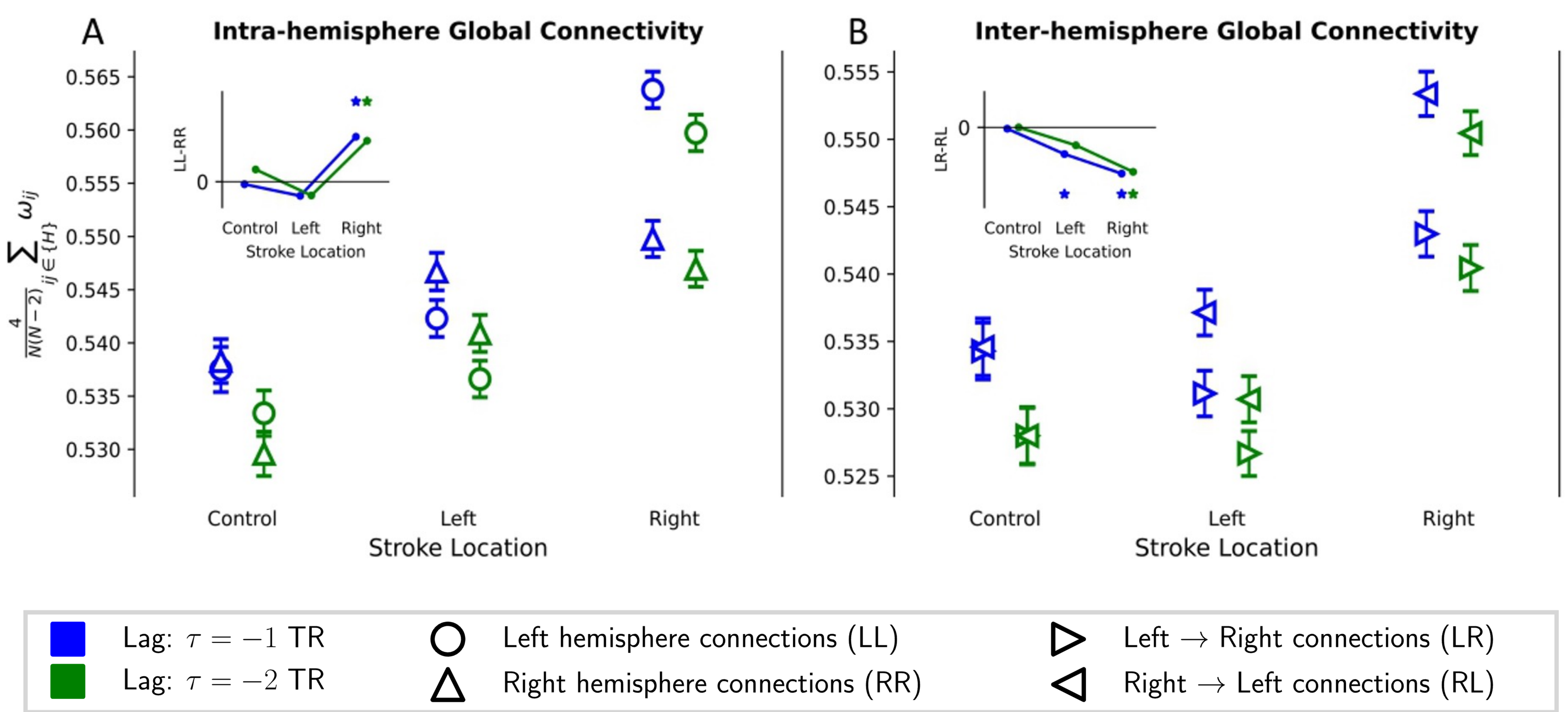
The averaged effective connectivity networks for Pathological subjects (left) and the directed network representation (right). The bottom equation describes the single connection as a sum of RCC scores for directional and bidirectional connections

$$A_\tau(x,y) = \delta_\tau^{\mathbf{x}\to\mathbf{y}} + \delta_\tau^{\mathbf{x}\rightleftarrows\mathbf{y}}$$

Stroke Inference Part

To determine whether a subject is a stroke victim, a directed graph representing the effective connectivity network was embedded using graph2vec [4] into a 16D vector. The final step was to use a binary classifier on that vector. We experimented with ridge regression, support vector machine and multi-layer perceptron

Effective Connectivity Results



For each lag, the mean effective connectivity of each group was further subdivided between intra- and inter-hemispheric connections; that is, *left-left*, *right-right*, *left-right*, and *right-left* connections.

Stroke Inference Results

Comparison of different models' performance in the final stroke inference part.

Classifier	AUC test score	Hyperparameters	Value
Ridge Regression	0.65	L_2	100.0
Support Vector Machine	0.60	C	0.2
		kernel	RBF
Multi Layer Perceptron	0.73	depth	1
		hidden nodes	64

Discussion

- Global intra- and inter-hemispheric effective connectivity affected by lesion laterality.
- Simple machine learning classifiers can differentiate pathological subjects, and thus validates the new state space reconstruction methods [2].

Next Steps

- Experiment with different approaches for the stroke disconnection detection part.
- Leverage weights of the connections in the inference.
- Add explainability to the pipeline to increase its clinical semantic value.

[1] Adhikari, M. H., et al. Effective connectivity extracts clinically relevant prognostic information from resting state activity in stroke. Brain Communications 3 (4). 2020; https://doi.org/10.1093/braincomms/fcab233

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[4] Narayanan, A., et al graph2vec: Learning Distributed Representations of Graphs. arXiv 2017; https://doi.org/10.48550/arXiv.1707.05005

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Interaction of inter- and intrahemispheric reorganization after stroke

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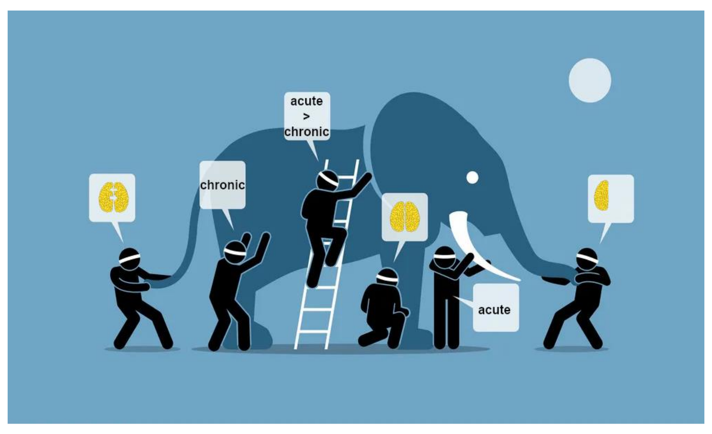
Background

- Current understanding of mechanisms underlying post-stroke motor recovery remains incomplete.
- Different studies examine the importance of intra- vs interhemispheric changes, challenging prevailing theories , e.g. the “interhemispheric imbalance” model[1,2,3]
- However, this is done
  a) in isolation, or
  b) not longitudinal

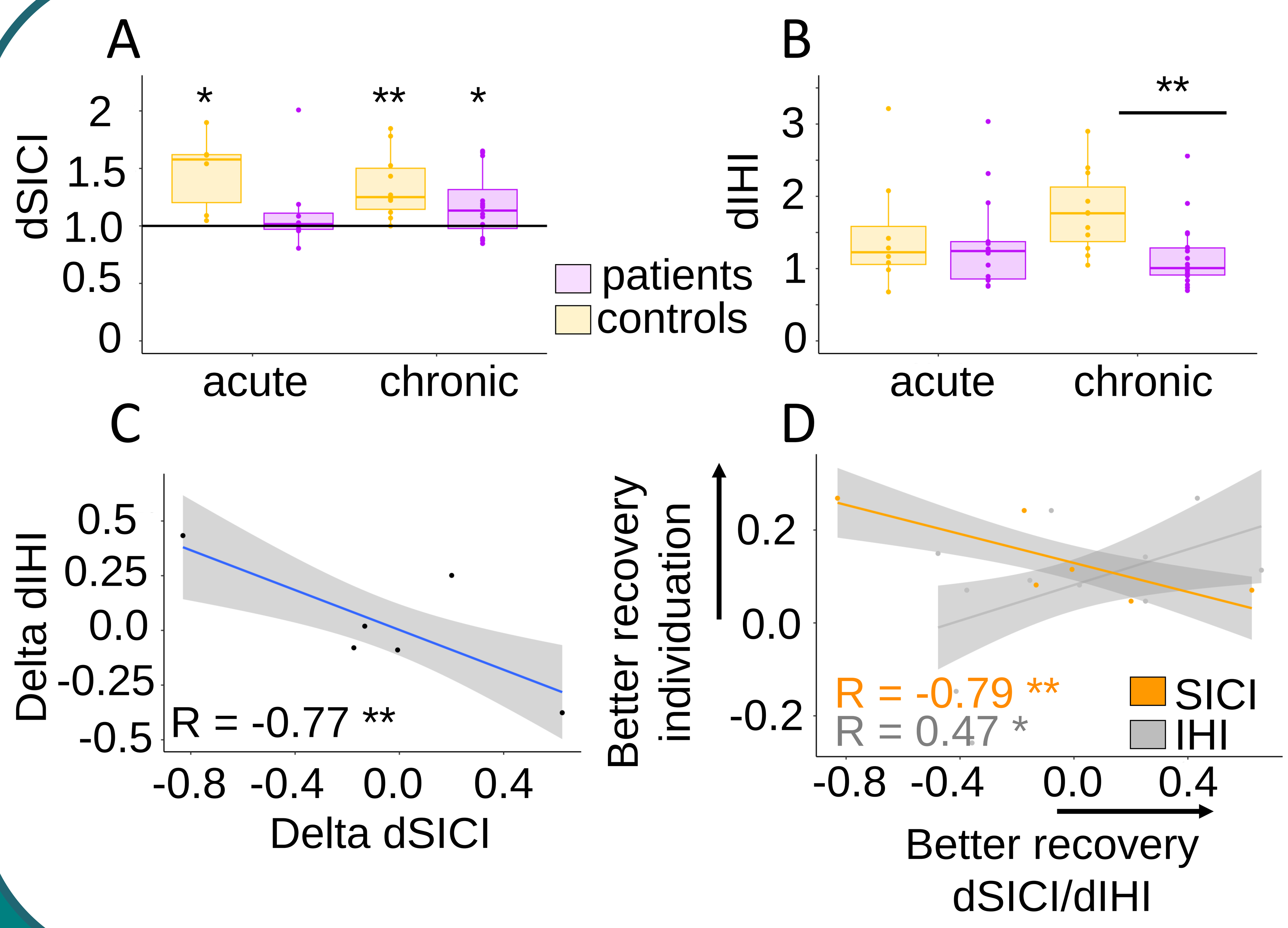
"Blind Men & Elephant Effect"



Objectives

I. **Study inter- & intrahemispheric changes in combination**
II. **Assess changes from acute to chronic**
III. **Understand how neurophysiology correlates with motor recovery**

Main Results



A : **dSICI** was **reduced** in patients only during the **acute** phase.

B : Contrastingly, **dIHI** was **reduced** in patients only during the **chronic** phase of stroke

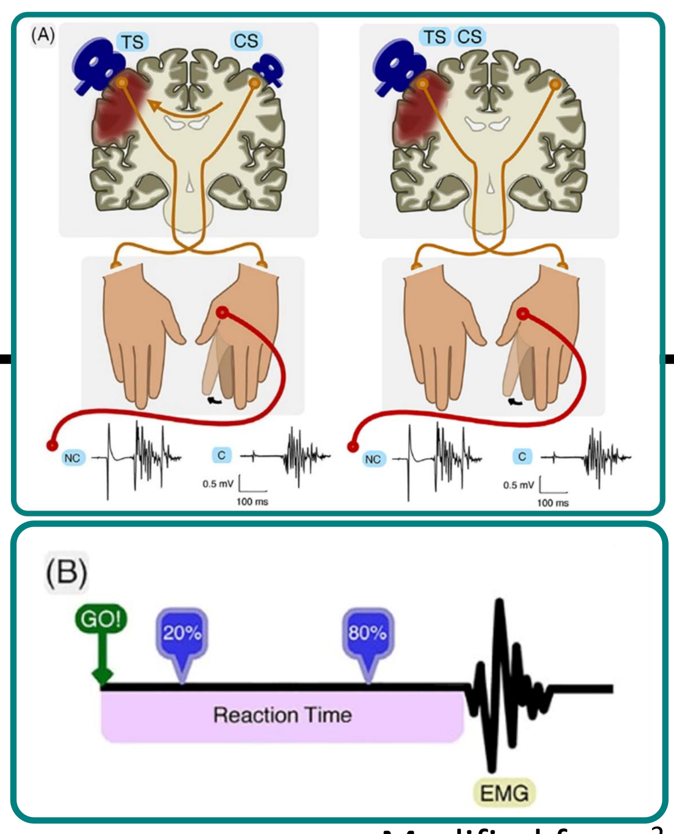
C : Normalization of **dSICI correlated with** the loss of **dIHI**

D : **Recovery of individuation correlated with** the loss of **dIHI** and the normalization of **dSICI**

Methods

- Study duration: 1 year post-stroke
  Acute = week 1 - 4
  Chronic = week 24 - 52
- Participants: 21 patients and 11 age-matched controls
- Interhemispheric inhibition: IHI
- short intracortical inhibition: SICI
- Behavioral outcome: Finger individuation[4]

IHI SICI



$$dIHI = \frac{IHI_{80\%}}{IHI_{20\%}}$$

$$dSICI = \frac{SICI_{80\%}}{SICI_{20\%}}$$

Modified from [2]

- Deltas = chronic - acute

Conclusion

- **There was an inverse relationship between interhemispheric and ipsilesional changes.**
- The normalization of **dSICI and** the loss of **dIHI** over time correlated with poorer recovery of individuation
- Interhemispheric disbalances seem to be driven by ipsilesional reorganization

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4- Ejaz et al., Brain. 2018 Mar 1;141(3):837-847

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Radboud Universiteit

DONDERS INSTITUTE

Exploring the Post-Stroke Frequency-Mediated Dynamic Repertoire of Brain Activity.

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Introduction:

Research on strokes has revealed a restructuring phenomenon around the lesion site[1,2], influencing both local and global brain network structures[3,4,5], along with a noticeable decline in the dominant alpha peaks[3]. This study aims to decipher the evolution of these metrics during stroke recovery and its repercussions on behaviour. Our study centres on investigating longitudinal shifts in peak alpha frequency, exploring information flow, and examining the phase-directed brain network structure within the resting state EEG of adult stroke patients throughout the post-stroke recovery phase. This aims to deepen our understanding of recovery mechanisms, offering insights that can inform and enhance rehabilitation practices. Analyzing EEG data from 30 stroke survivors (mean age = 60, 19 male), recorded post-stroke for Session 1 and three months post-stroke for Session 2. we employ power spectrum density (PSD) to study power fluctuations and amplitude envelope correlation (AEC) and weighted phase lag index (wPLI) to explore frequency-specific functional connectivity, shedding light on large-scale network synchronization and information flow.

Our investigation of post-stroke recovery reveals no significant shifts in peak alpha during EEG recordings but identifies profound reorganisation in functional connectivity. New connections, particularly increased interhemispheric and within-hemispheric connections, are observed through wPLI-based connectivity. AEC analysis further supports reorganisation, showcasing new clusters in interhemispheric connections.

Methodology

N = 30
Mean age: 60
19 Male

128 channel EEG data

Preprocessing

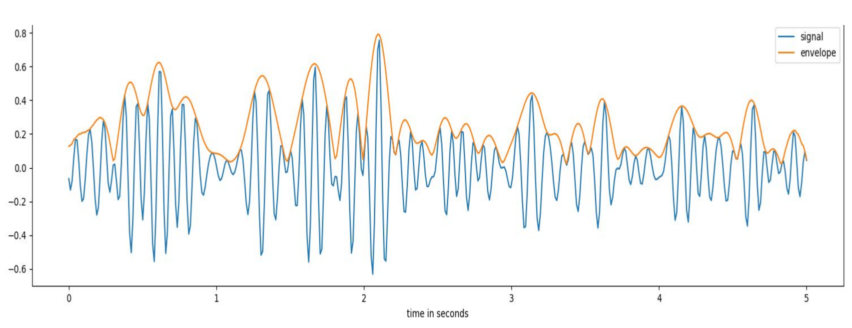
Band Pass Filter
(0, 45)

AutoReject

Functional Connectivity

Power Spectral Density

Amplitude Envelope Correlation



$$r_{xy} = \frac{\sum (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum (x_i - \bar{x})^2 \sum (y_i - \bar{y})^2}}$$

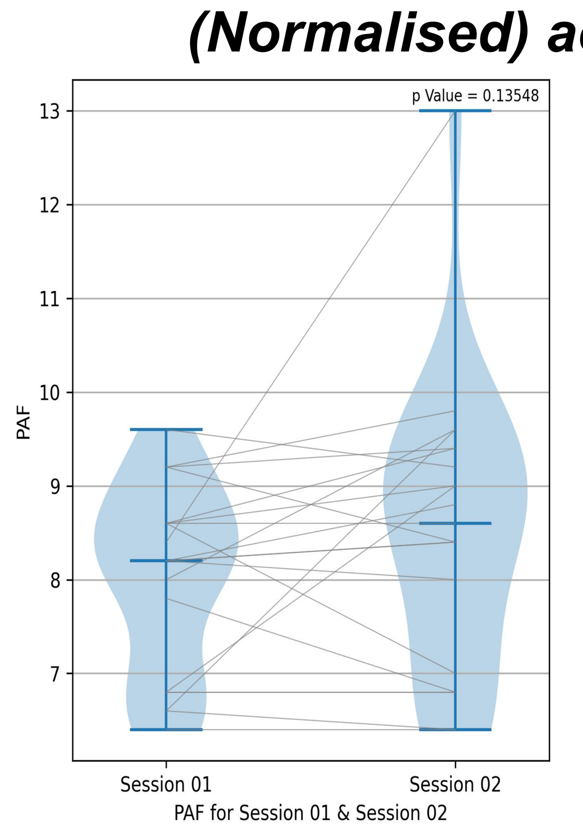
Weighted Phase Lag Index (wPLI)

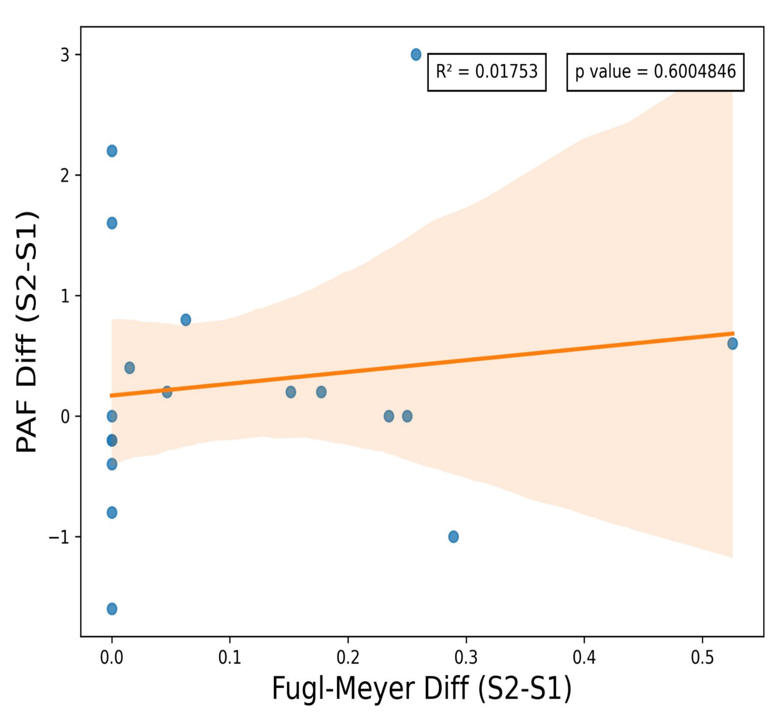
$$\Phi \equiv \frac{|E\{\Im\{X\}\}|}{E\{|\Im\{X\}|\}} = \frac{|E\{|\Im\{X\}| sgn(\Im\{X\})\}|}{E\{|\Im\{X\}|\}}.$$

Weighted Phase Lag Index is a functional connectivity measure that quantifies how consistently 90° (or 270°) phase of one signal lags, compared to another.

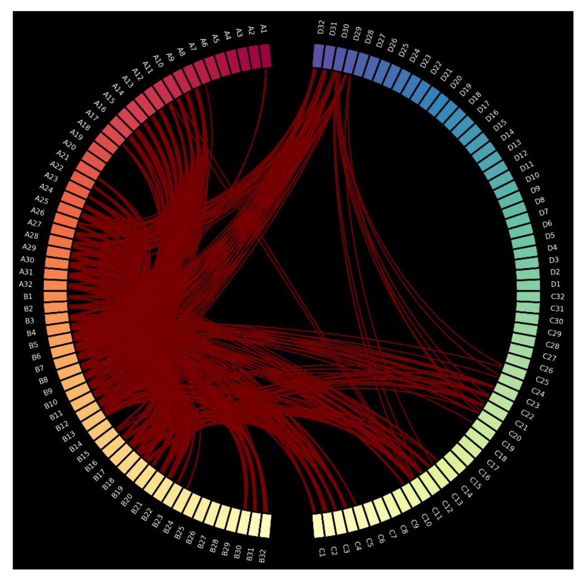
Results

Peak Alpha Frequency & its Correlation with Fugl-Meyer Score (Normalised) across session 1 & 2.

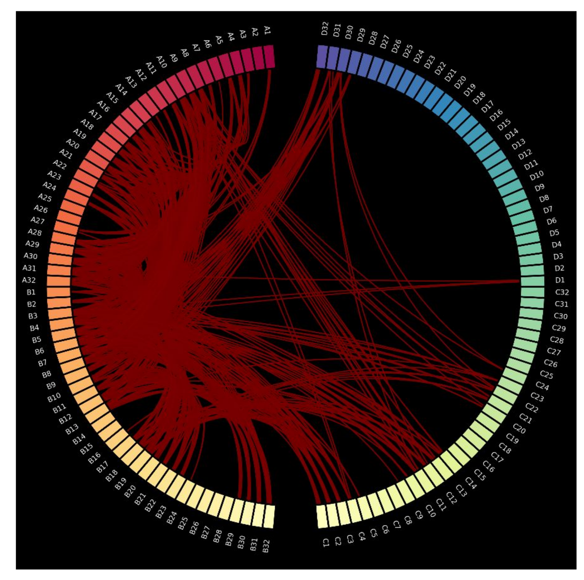




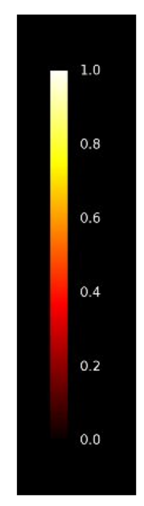
Reorganisation of Functional Connectome Post-Stroke

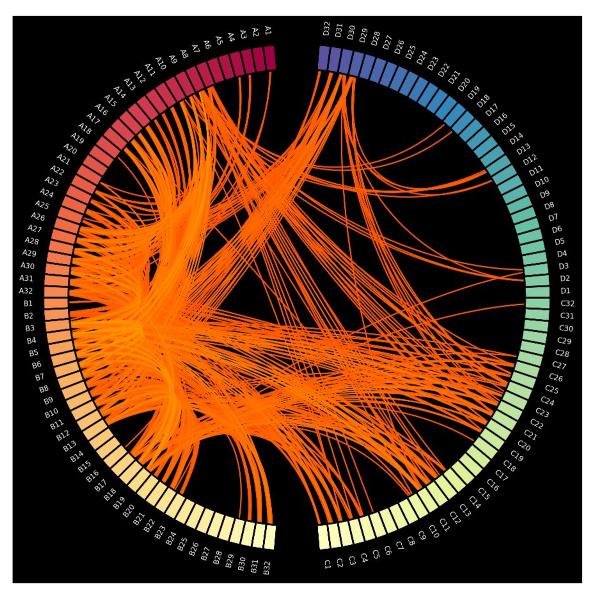


AEC Alpha S1

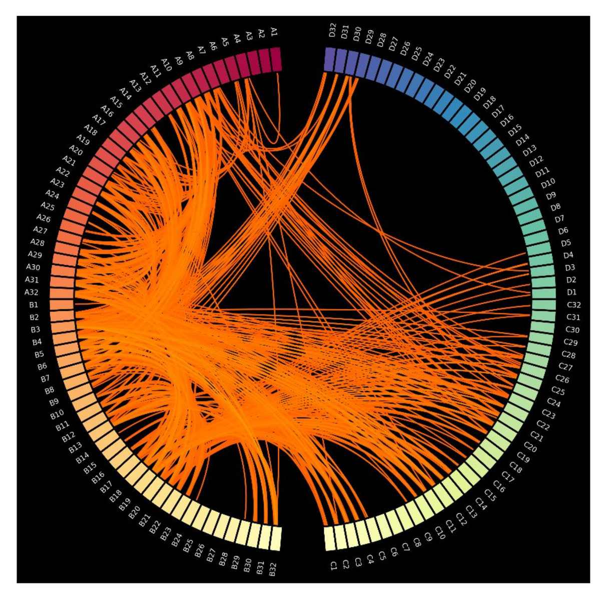


AEC Alpha S2



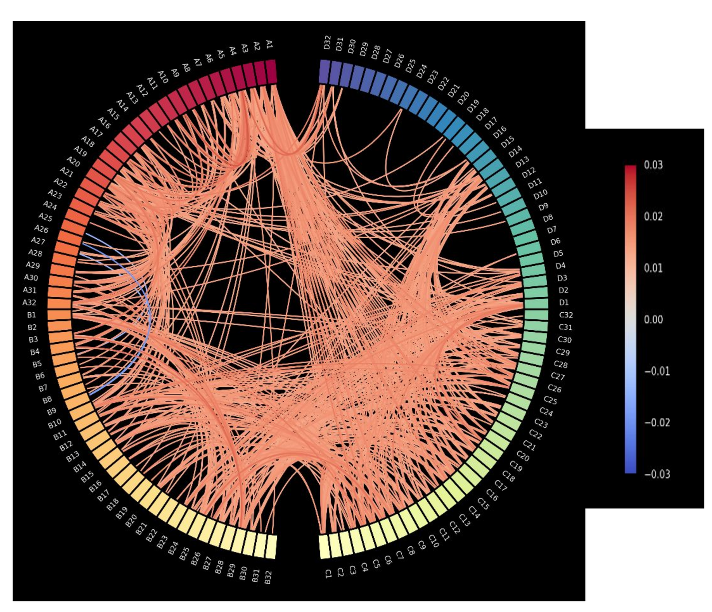


wPLI Alpha S1

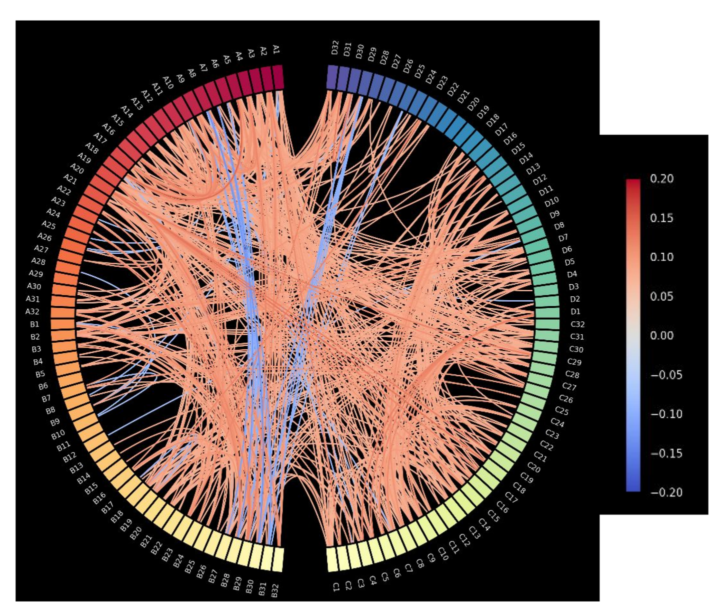


wPLI Alpha S2

Contrasting Connectivity between Session 1 & 2: Residual Connections.



AEC Alpha (S2-S1)



wPLI Alpha (S2-S1)

Conclusion & Future Directions:

In conclusion, our investigation did not reveal significant shifts in peak alpha during EEG recordings in sessions 1 and 2. However, a comprehensive analysis of functional connectivity unveiled notable network reorganization. We identified the emergence of new connections, particularly observing an increase in interhemispheric connections along with within-hemispheric connections facilitated by wPLI-based connectivity. Additionally, the AEC analysis demonstrated reorganization, highlighting the formation of new clusters in interhemispheric connections.

Looking ahead, our future endeavors will focus on delving deeper into connectivity dynamics through the application of graph theoretical measures. This will provide a more nuanced understanding of the intricate network alterations and contribute to the broader comprehension of brain connectivity in our study population.

Acknowledgements

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Enhancing motion discrimination in the blind visual field of stroke patients through Hebbian plasticity depends on the residual structural and functional integrity of the cortical motion pathway

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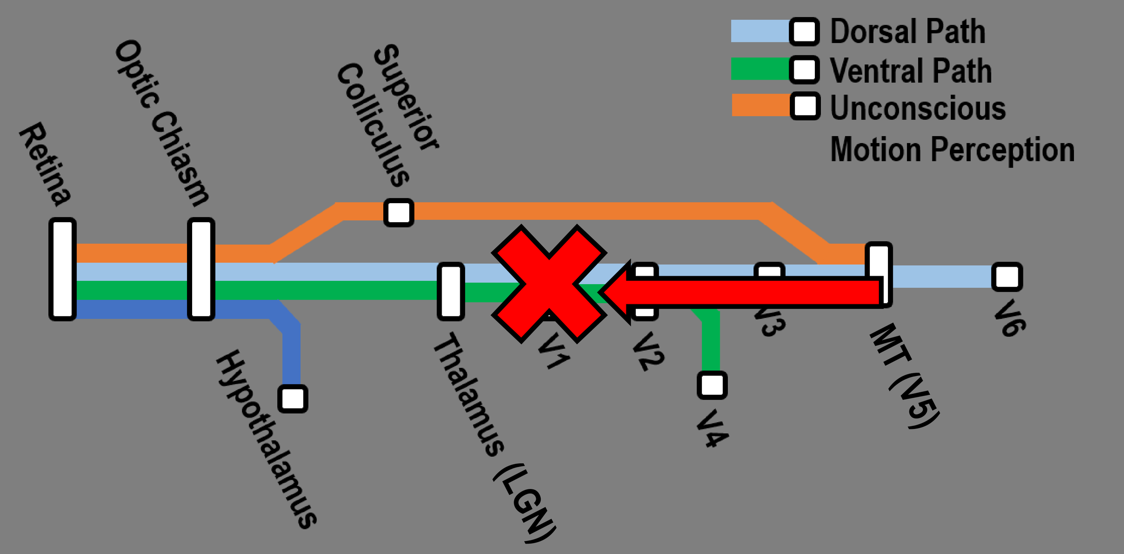
Introduction

- Strengthening the re-entrant visual backprojections from the motion-sensitive medio-temporal area (MT) to the primary visual cortex (V1) through cortico-cortical paired associative stimulation (ccPAS) has been shown to enhance motion discrimination performance in healthy subjects [1].



Goals:

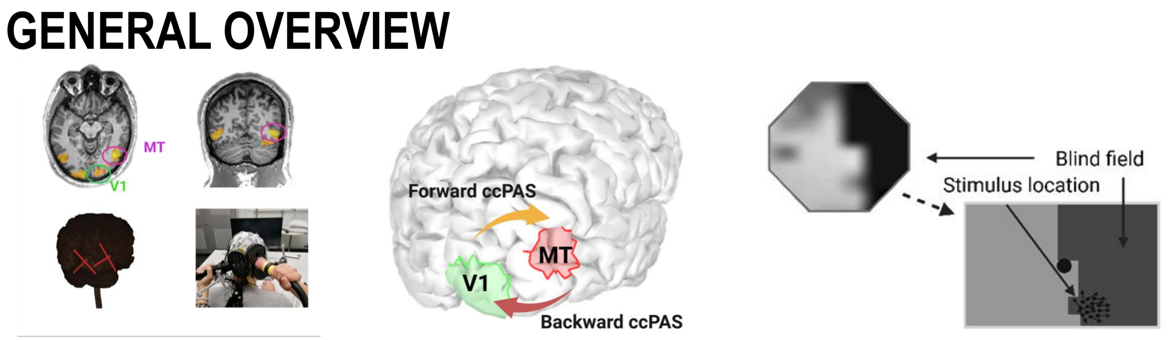
- Investigate whether Backward-ccPAS (BW) and Forward-ccPAS (FW) can modulate performances and plasticity in patients with lesions affecting the primary visual cortex
- Use individual responses to BW PAS to investigate the integrity of the cortical visual system following plastic 're-wiring' of the human connectome

Protocol and Methods

ccPAS

- **16** stroke hemianopic patients.
- ccPAS (**cortico-cortical Paired Associative Stimulation**) intervention: repeated pairing of transcranial magnetic stimulation (TMS) over V1 and medio-temporal area (MT) with specific timings and order.
- Cross-over design: 1 session **Backward ccPAS** (MT-V1); 1 session **Forward ccPAS** (V1-MT).

GENERAL OVERVIEW



BEHAVIOURAL ANALYSIS

- Extracting the normalized direction range (NDR) thresholds using all trials by fitting a Weibull function, which defined the direction range level at which performance reached 75% correct

SINGLE PULSE TMS-EEG ANALYSIS

- Generation of surface head model with subject-specific MRI
- Computation of inverse source models (sLORETA) with dipoles constrained to the cortex
- Definition of subject-specific **MT** and **V1** scouts using functional MRI acquired prior
- Extraction of Local Source Activation (LSA) over the scouts
- Computation of frequency-wise effective connectivity over the extracted scouts using **Spectral Granger Causality**

fMRI ANALYSIS

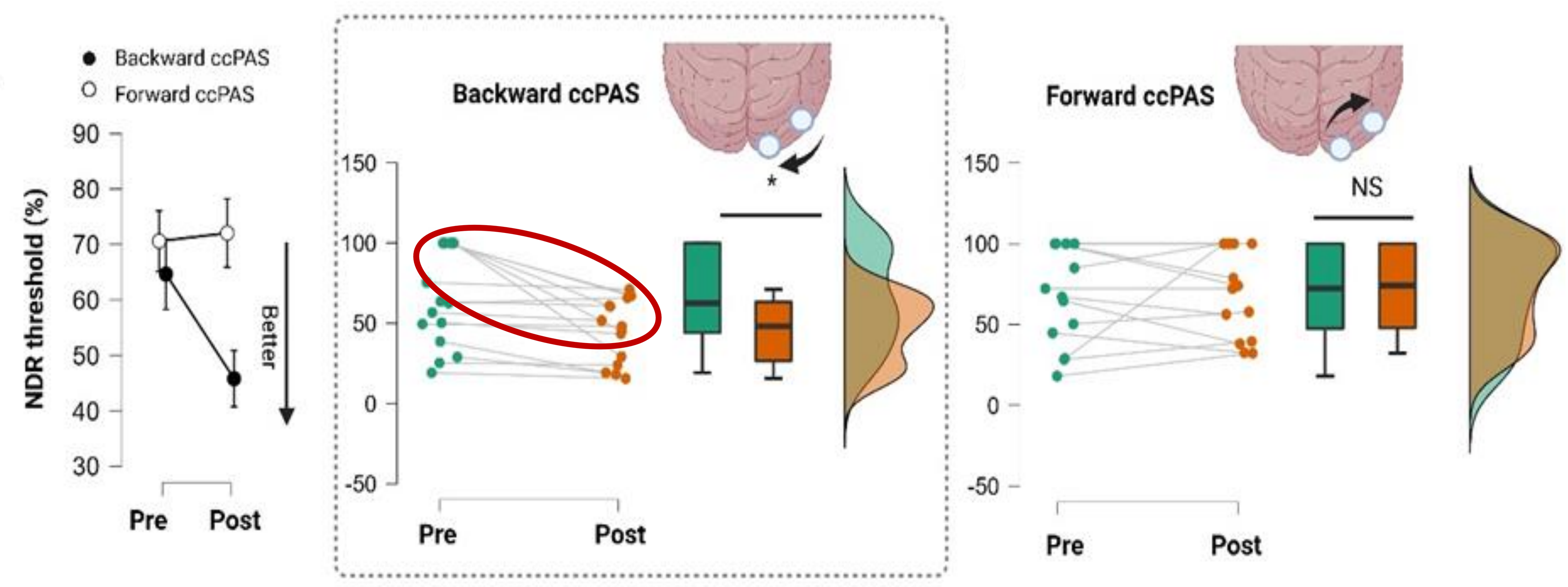
- Physio-physiological interaction (**PhPI**): regions in the whole brain that are correlated with an interaction between two predefined regions (MT and V1)
- Modulation of connectivity between MT and V1 by a third region

MRI ANALYSIS

- Microstructural integrity of V1-MT neural pathways through extraction of **Fractional Anisotropy** (FA)

Results

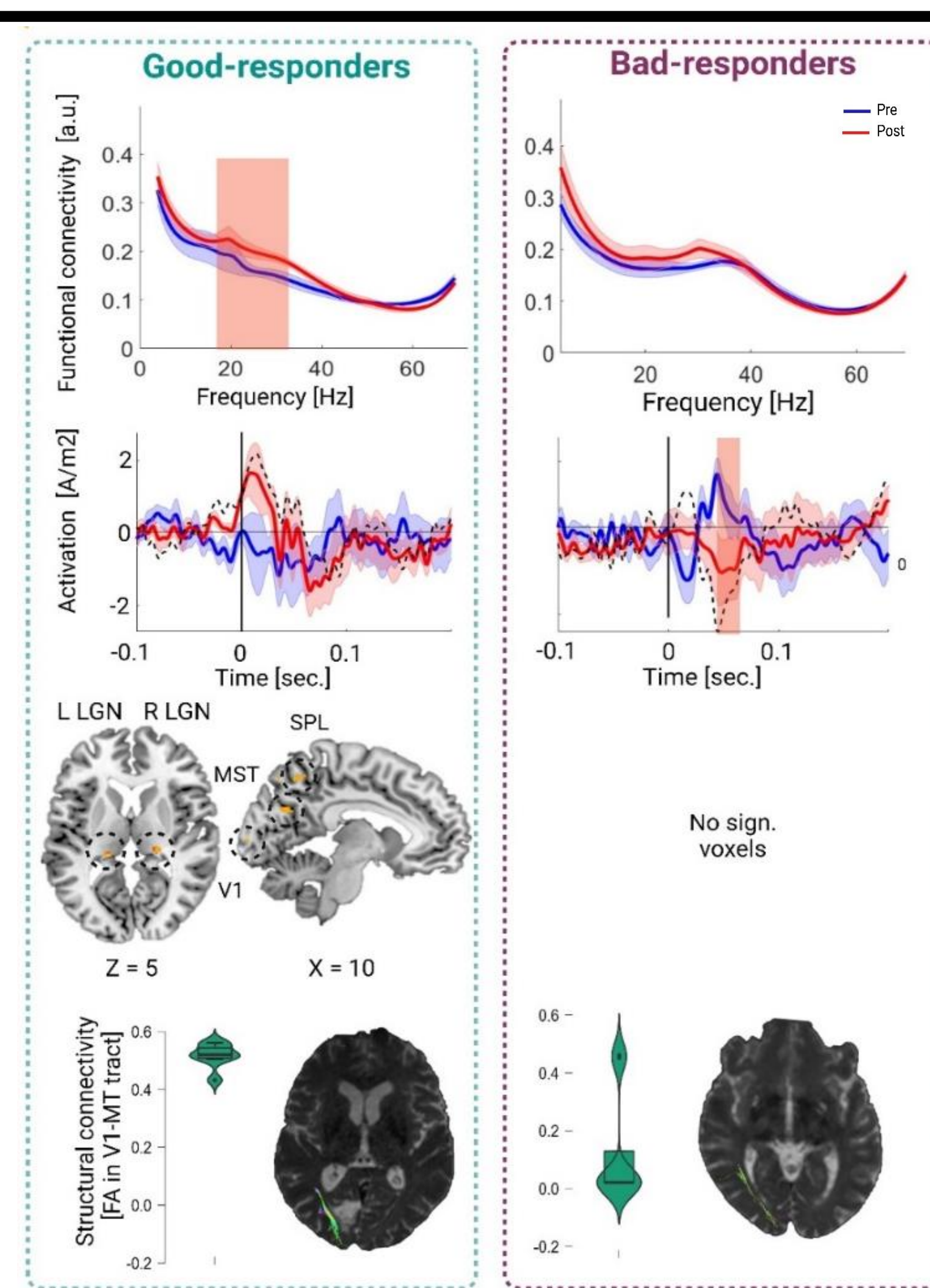
Behaviour



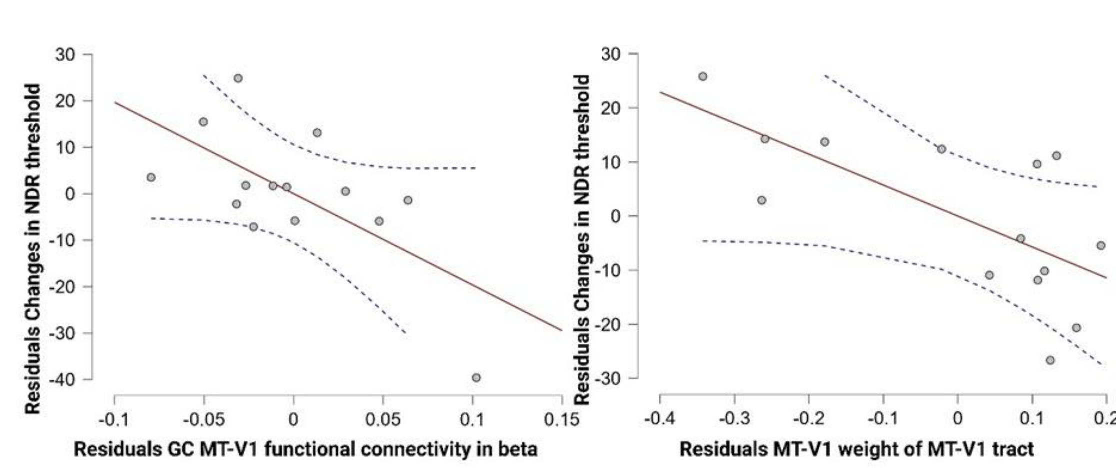
- Behavioural analysis revealed "**Good-responders**" and "**Bad-responders**" to the Backward-ccPAS intervention

Electrophysiology

- **Good-responders**: **Increase in beta MT-V1 re-entrant connectivity**.
- **Bad-responders: Decrease in local source activation** in early components (30-70 ms)
- **Good-responders**: Functional coupling between **MT-V1 and Thalamus/LGN/higher visual areas** before the ccPAS intervention.
- **Good-responders**: **Higher structural connectivity** only **on V1-MT** of lesioned side.



Predictors of Backward-ccPAS effects



- The **stepwise regression model** is significant ($F_{(2,13)} = 11.44$, $p = 0.002$) and explains a good amount of the variance ($R^2=0.62$).
- **MT-to-V1 GC** and the **FA significant predictors** (GC: $t_{(13)} = -2.85$, $p = 0.016$, FA: $t_{(13)} = -3.37$, $p = 0.006$).

Conclusion

- **Backward ccPAS** has also a beneficial effect on motion discrimination in the blind field in visual stroke patients by acting on the effective connectivity of re-entrant MT-V1 fibers. Compared to healthy, the shift from alpha to beta band refects the brain's adaptive response to injury, emphasizing the role of beta oscillations as a potential biomarker in chronic stroke recovery [2].
- **Functional and structural connectivity independently predict ccPAS response in patients**. This functional-structural decoupling could be due to various factors such as the compensatory reorganization of neural networks or differences in the integrity of specific other indirect white matter tracts [3].
- These measures could be used as predictors of the outcomes of functional rehabilitation.

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Structural disconnection in neglect and alertness deficits following acquired brain injury

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INTRODUCTION

- Attention deficits in stroke patients are better explained by alterations in brain connectivity, rather than lesion characteristics [1].
- Specifically, by tract disconnections within and between the dorsal and ventral attention networks (DAN, VAN) (fig. 1).
- DAN and VAN known to be involved in neglect, however the networks involved in alertness deficits remain to be determined.

AIM

- Investigation of relation between the level integrity of parcels and connections in DAN and VAN, and patients' performance in attention tasks, measured through eye-tracking (ET) parameters.
- H1: strong correlations between ET alertness parameters and disruptions in VAN, and between ET neglect parameters and disruptions in both networks.
- H2: higher correlations between ET (neglect and alertness) parameters and tract disconnection, rather than with parcel damage measures.

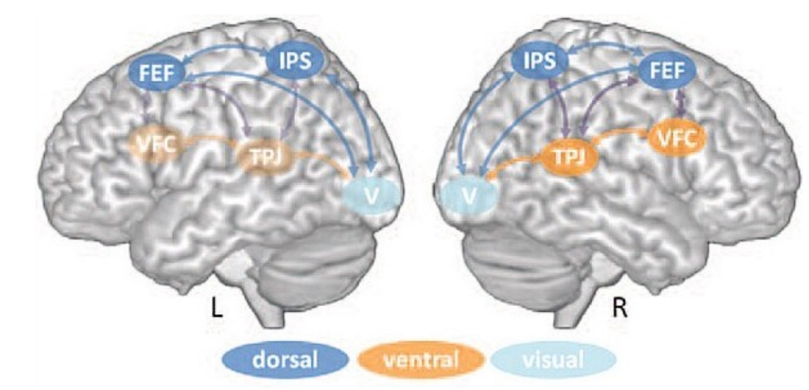


Fig. 1: DAN & VAN

METHODS

Participants:

24 patients with attentional deficits

- Males (n=20)
- Mean age = 57.58, SD age = 13.29
- Right (n=12), left(n=8) or bilateral lesions (n=4)
- Stroke (n=23), tumor (n=1)

Software:

- ITK-SNAP: lesion drawing (fig. 2)


Fig. 2: lesion drawing [2]

- LQT for disconnectome analysis: parcel damage (fig. 3) and tract disconnection (fig. 4) [2]

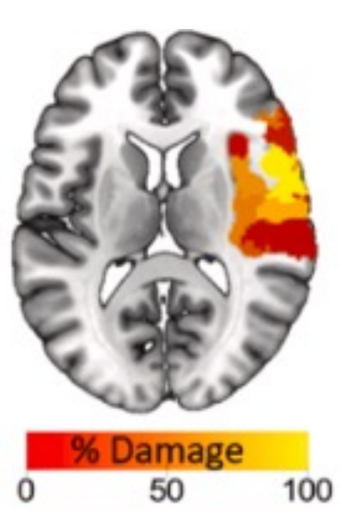


Fig. 3: grey matter parcel lesion loads [2]

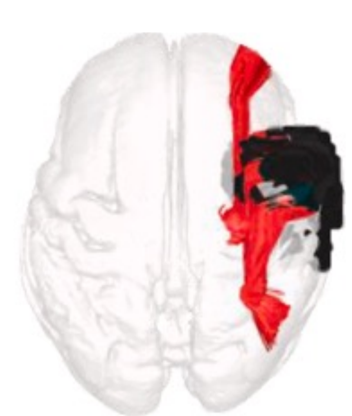
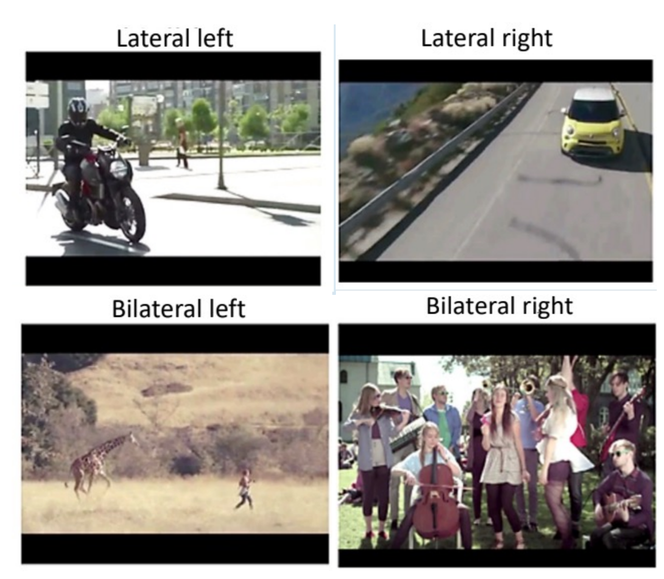


Fig. 4: tract disconnection severity [2]

- ET parameters in VR-based FreeViewing Task (MindFocus, Mindmaze SA) (fig. 5)

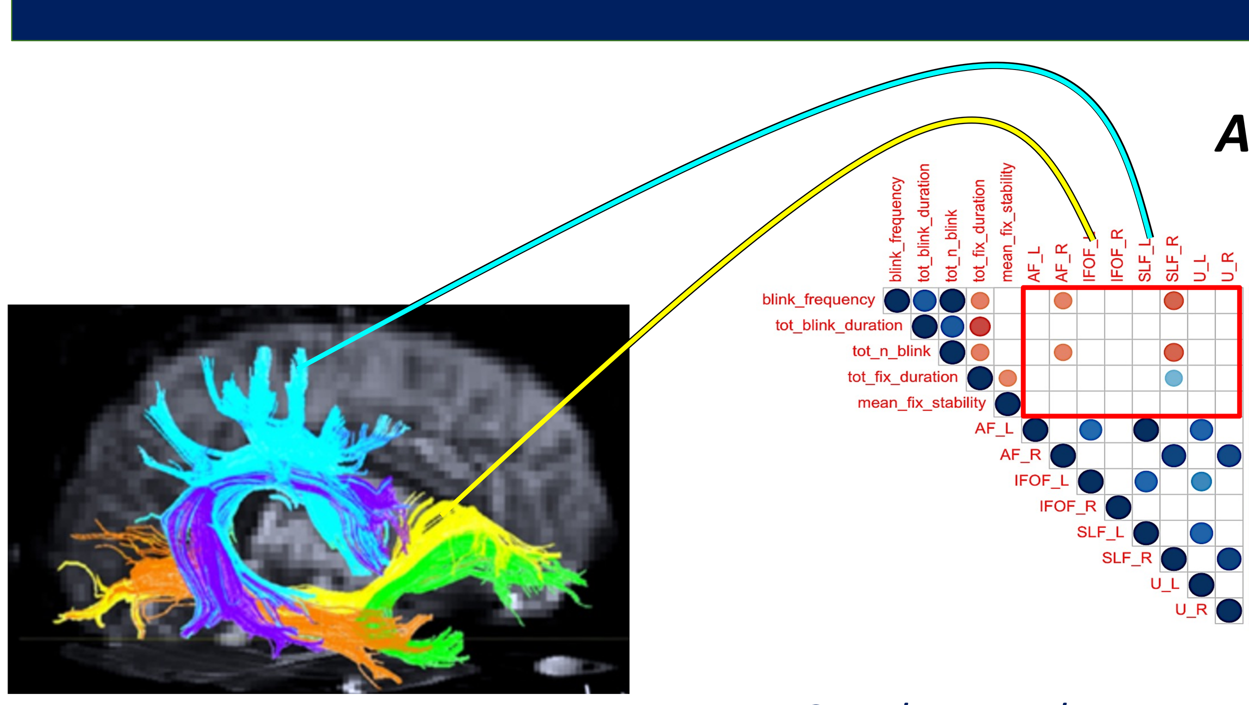


ALERTNESS PARAMETERS
- Blink frequency
- Total blink duration
- Total number of blink
- Total fixation duration

NEGLECT PARAMETERS during videos:
- Gaze laterality
- Fixation laterality
- Total number of left fixation
- Total right fixation duration

Fig. 5: VR-adaptation of Nardo and colleagues' task (2019) [3], 80 videos; examples of ET parameters for alertness and neglect

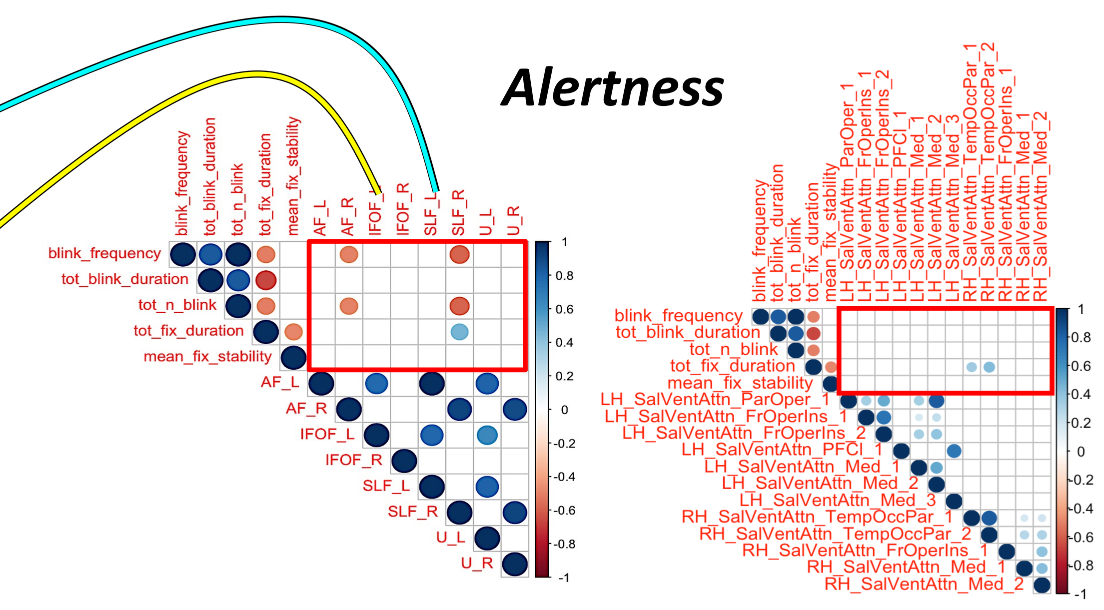
RESULTS


Diffusion tensor tractographies [4]

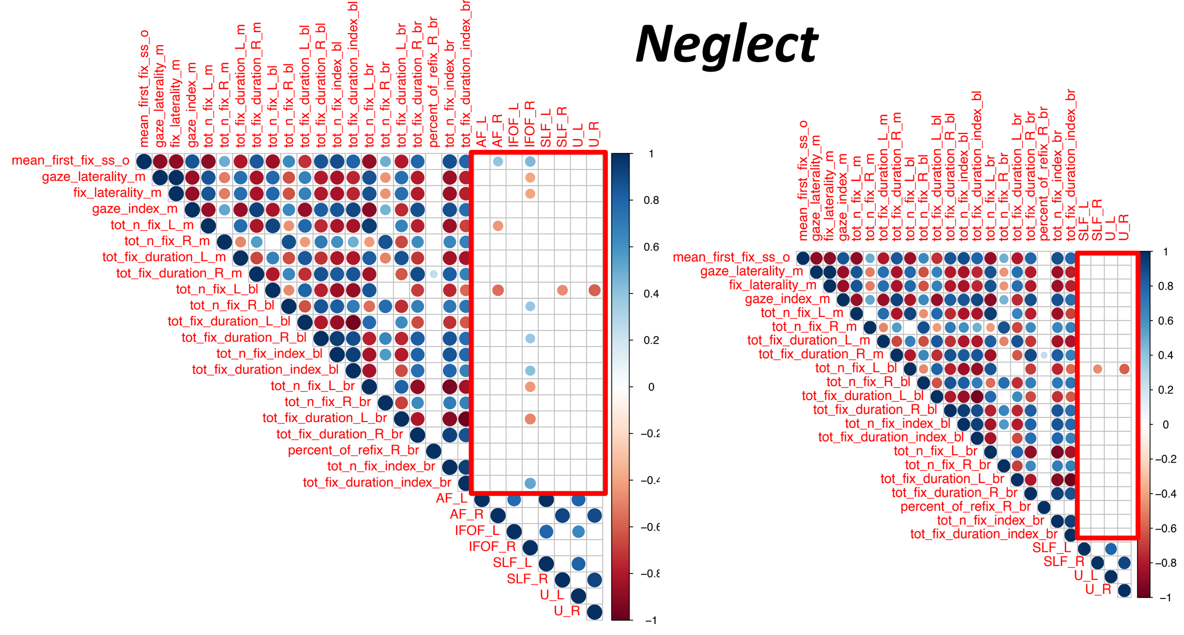
Tracts abbreviations:

- *IFOF = inferior fronto-occipital fasciculus*
- *SLF = superior longitudinal fasciculus*
- *U = U-fibers*
- *AF = arcuate fasciculus*

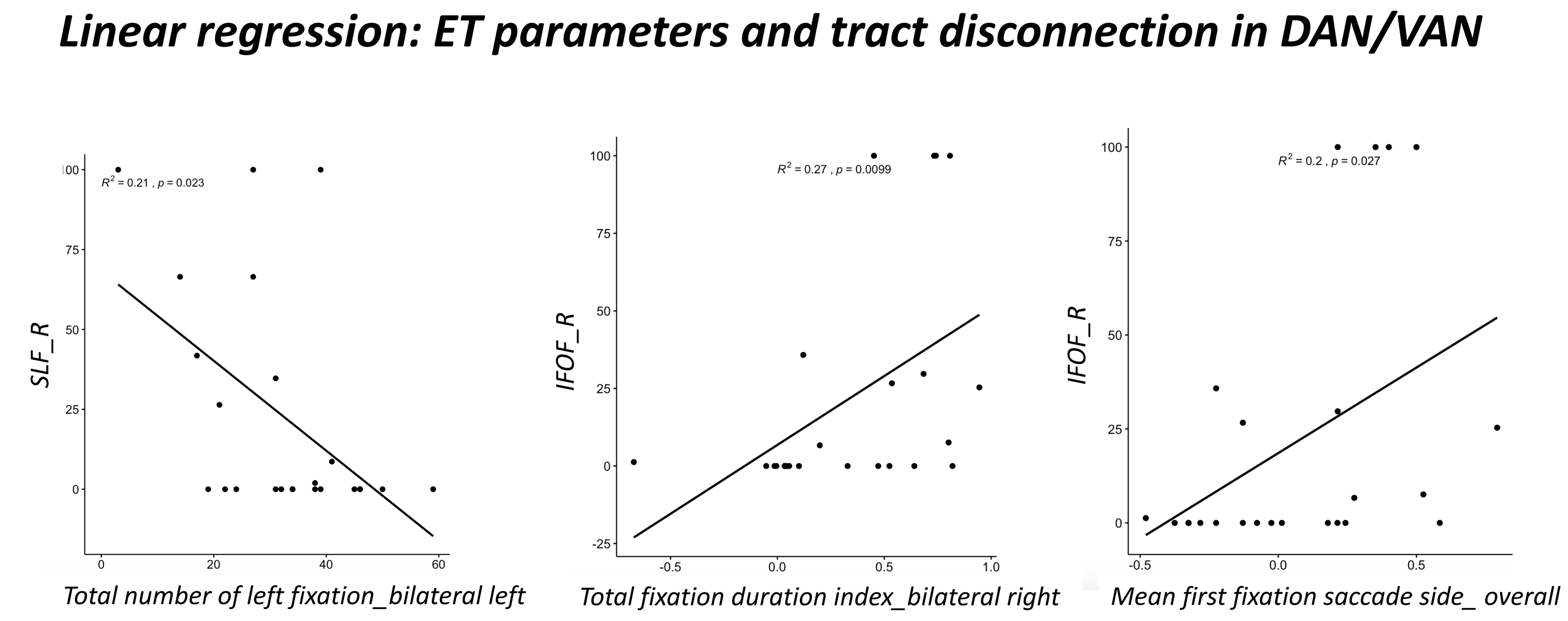
Alertness


Correlograms between alertness ET parameters and tract disconnection (left) and parcel damage (right) in VAN

Neglect

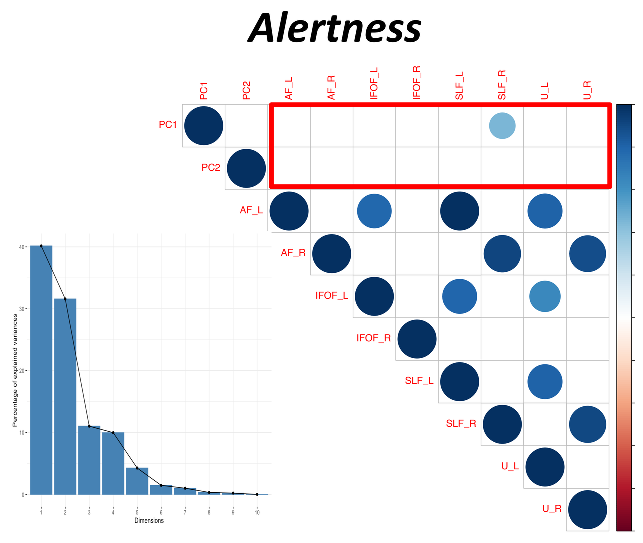

Correlograms between ET neglect parameters and tract disconnection in VAN (left) and DAN (right)

Linear regression: ET parameters and tract disconnection in DAN/VAN

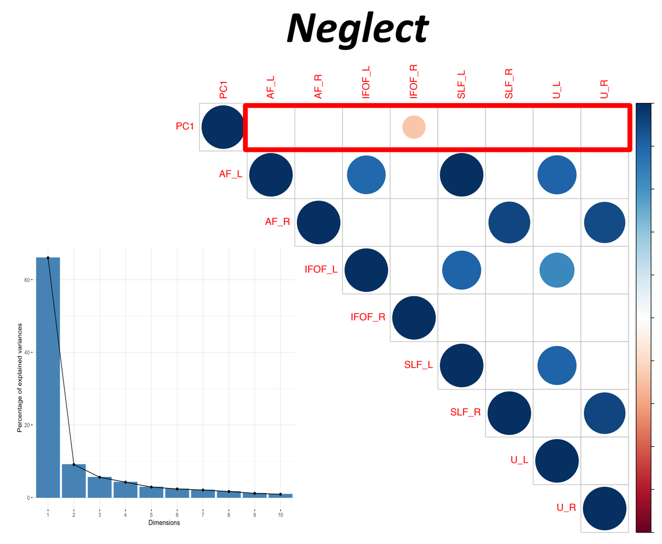


Eye-tracking parameters analysis

Alertness


PCA on alertness ET parameters and correlograms between PC1/PC2 and tract disconnection in VAN

Neglect


PCA on neglect ET parameters and correlograms between PC1 and tract disconnection in VAN

CONCLUSIONS

- Tract disconnection, rather than parcel damage measures, better explain alertness deficits.
- Alertness deficits are strongly explained by disruptions in the VAN, neglect by both (especially in SLF and IFOF).
- Further analyses will consider whether tract disconnection measures could be used as predictive measures of VR-based rehabilitation outcomes.
- Further analyses will compare Lesion Quantification Toolkits analyses with Voxel-based Lesion-Symptom Mapping (VLSM).

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Boosting and mapping rTMS-induced plasticity with novel 100Hz iTBS paradigm

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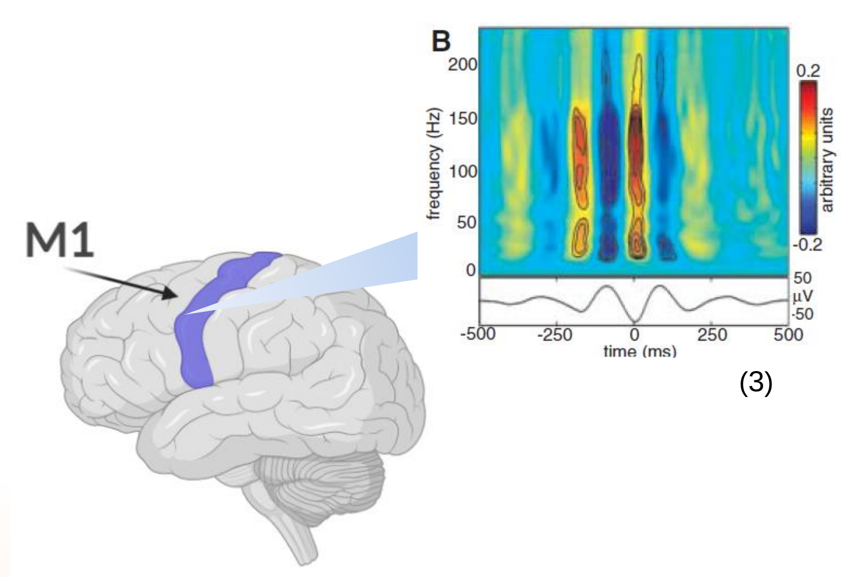
Introduction

Intermittent theta burst stimulation (**iTBS**) is a **plasticity-inducing paradigm** of rTMS, based on endogenous **θ-ɣ coupling** in neocortex. (1)

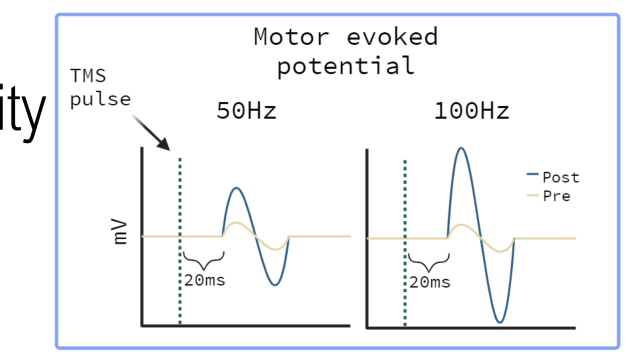
iTBS has **low effect sizes** and **high variability**. (2)



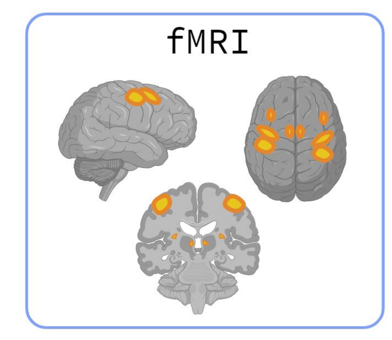
100Hz stimulation more closely **mimics physiological firing patterns** in M1 than the classical 50Hz paradigm. (3)

Aims

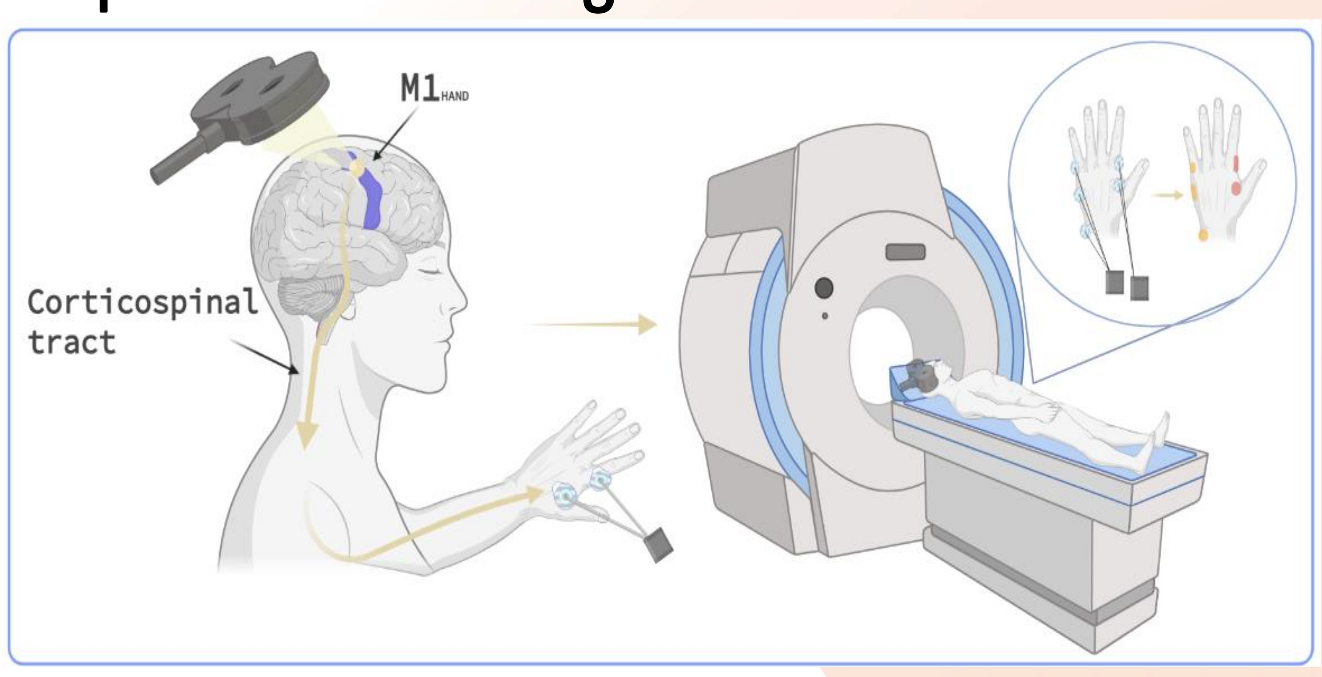
- Increase plasticity induction with 100Hz iTBS



- Understand whole-brain changes to iTBS protocols

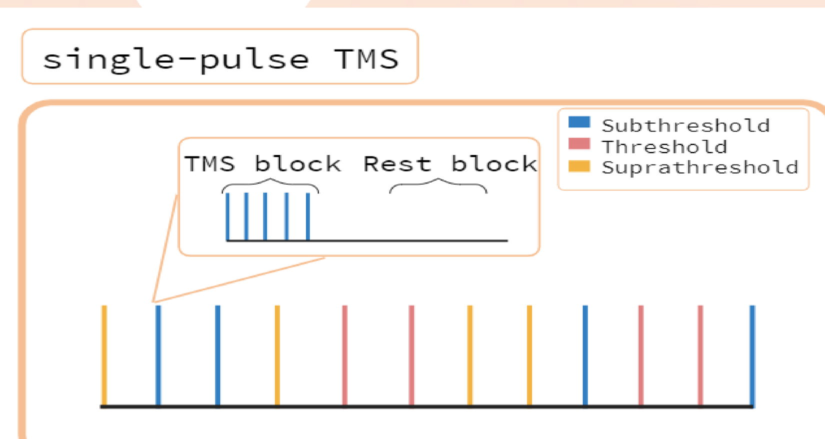


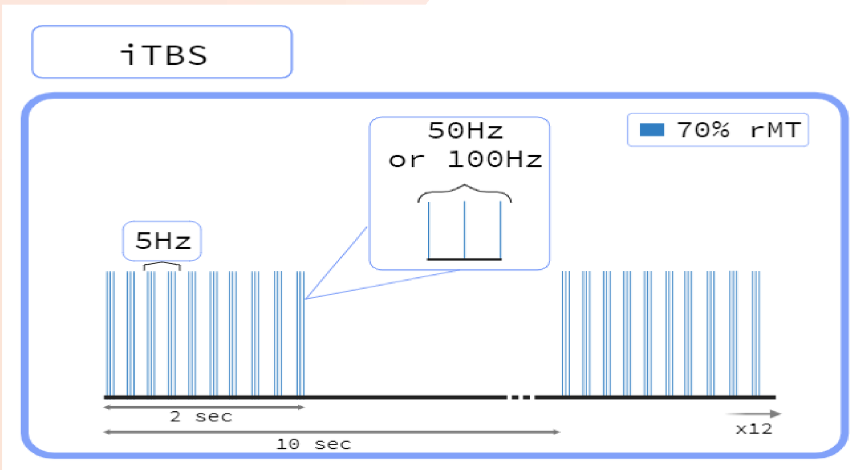
Experimental design



3 sessions of concurrent TMS-fMRI

spTMS + spinal cord fMRI (8 min) → spTMS + brain fMRI (8 min) → 50Hz/100Hz/Sham iTBS + brain fMRI (2 min) → +20 mins → spTMS + brain fMRI (8 min)





Midterm results

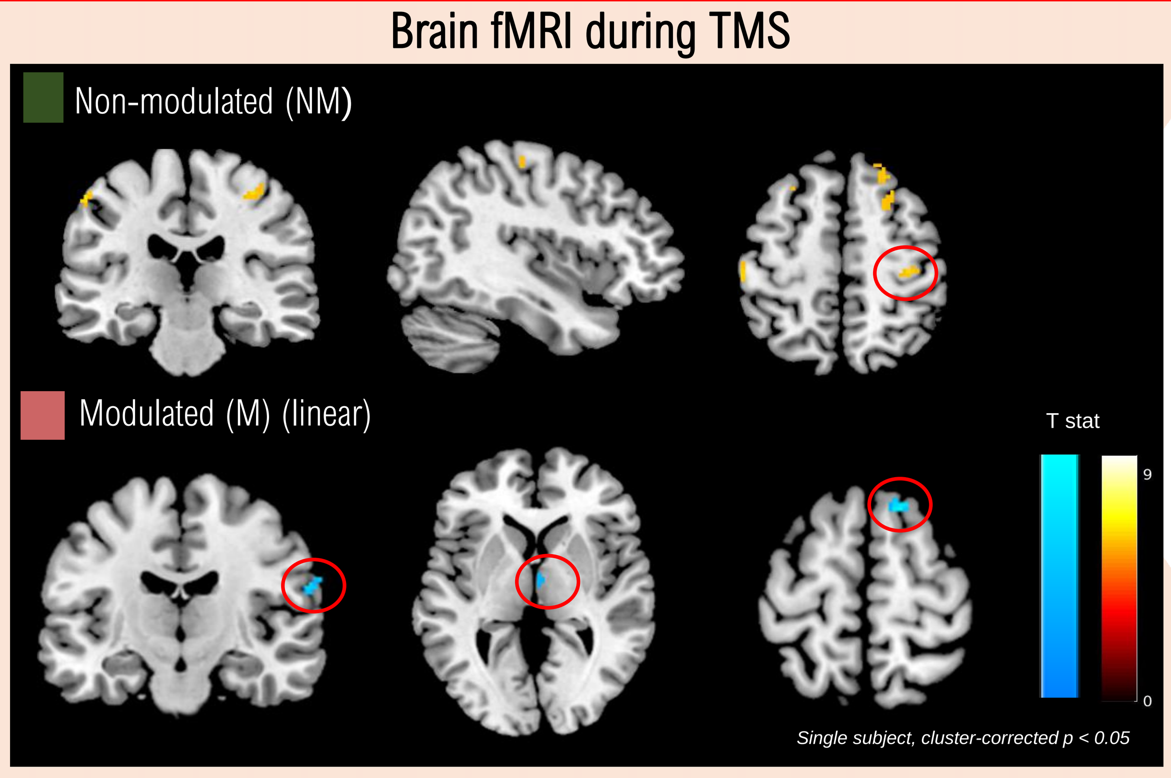
- BOLD signal associated with **TMS onset** (NM) displays robust **M1HAND activation**.

- BOLD signal associated with **corticospinal output variability** (M) in S2, DMN thalamus & frontal pole indicate **sensory processing** and emotional regulation in response to changing MEP amplitude.

Non-modulated (NM) – BOLD correlates with TMS onset

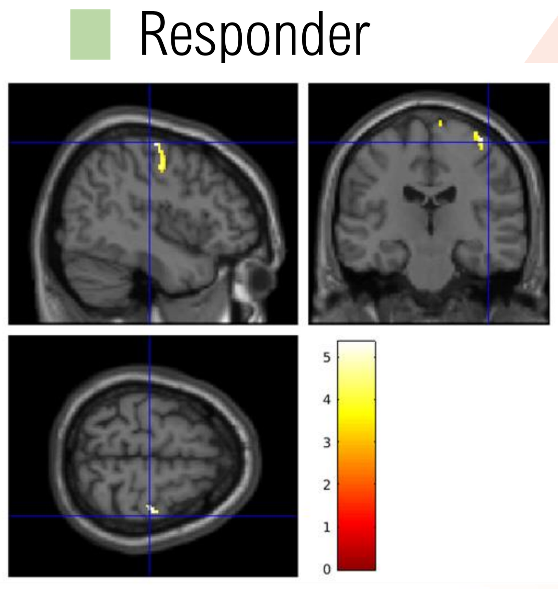
Modulated (M) (linear) – BOLD correlates with MEP variability

Brain fMRI during TMS

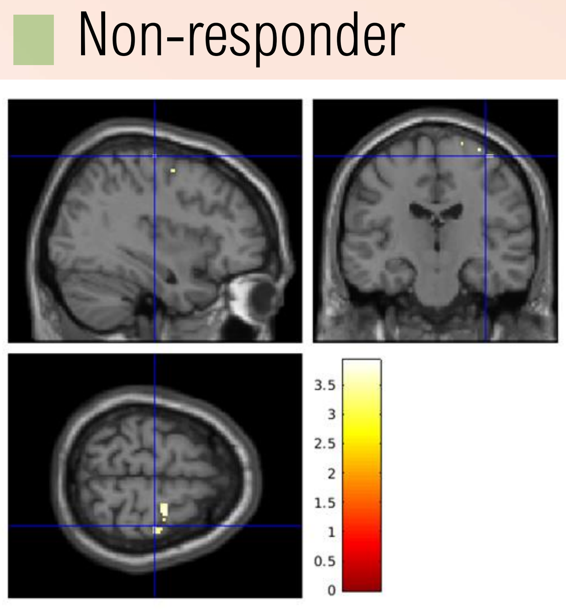


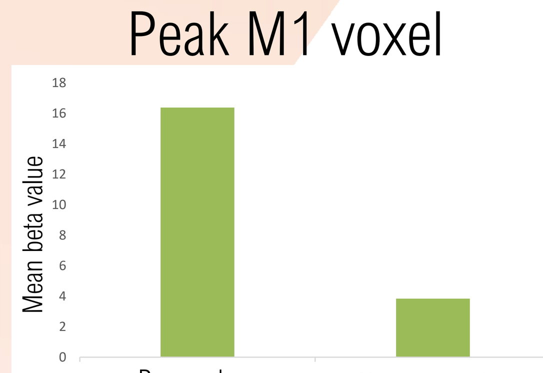
Responders show additional M1 recruitment correlated with TMS onset at baseline.

Responder



Non-responder





Single subjects, P<0.001, Unc.

Conclusion

Preliminary analyses reveal:

-BOLD signal associated with corticospinal output variability can **disentangle discrete sensorimotor circuits.**

→ A potential **diagnostic tool** to assess **extent of impairment** in motor disorders

- Robust **motor network** associated with **MEP facilitation** represents a potential **screening marker** for patients **likely to benefit from iTBS treatment for motor stroke recovery.**

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Unravelling the underlying networks of post-stroke fatigue: from connectivity analyses to non-invasive deep brain stimulation intervention

SSRC2023

Fabienne Windel[1,2], Elena Beanato[1,2], Philipp Koch[3], Gabriel Girard[4,5], Pierre Vassiliadis[1,2], Takuya Morishita[1,2] & Friedhelm Christoph Hummel[1,2,6]

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INTRODUCTION

- **Fatigue** is a common symptom in stroke survivors with reported **prevalence ranging from 32-92 %** [1]
- Overlap with other symptoms, considered a **multidimensional phenomenon with limited treatment success** [2]
- It differs from acute fatigue resulting from effort, is **not restored by rest** [3,4] and has been shown to **negatively impact rehabilitation, functioning, and quality of life** [5,6]
- Inconclusive evidence: No association of lesion location with PSF [7], disconnectome unpredictive for fatigue [8], it however has been linked to acute caudate infarcts [9] & thalamic lesions [10], indicating a potential **involvement of deeper brain structures in PSF**

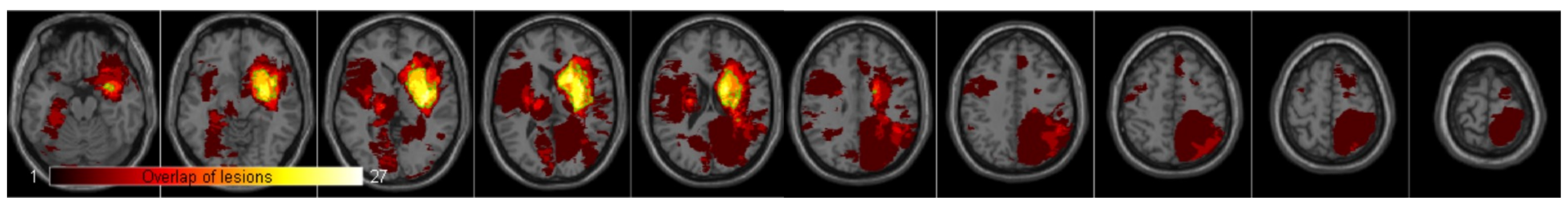
➢ **To inform novel treatment strategies it is therefore of importance to uncover the underlying networks of PSF**

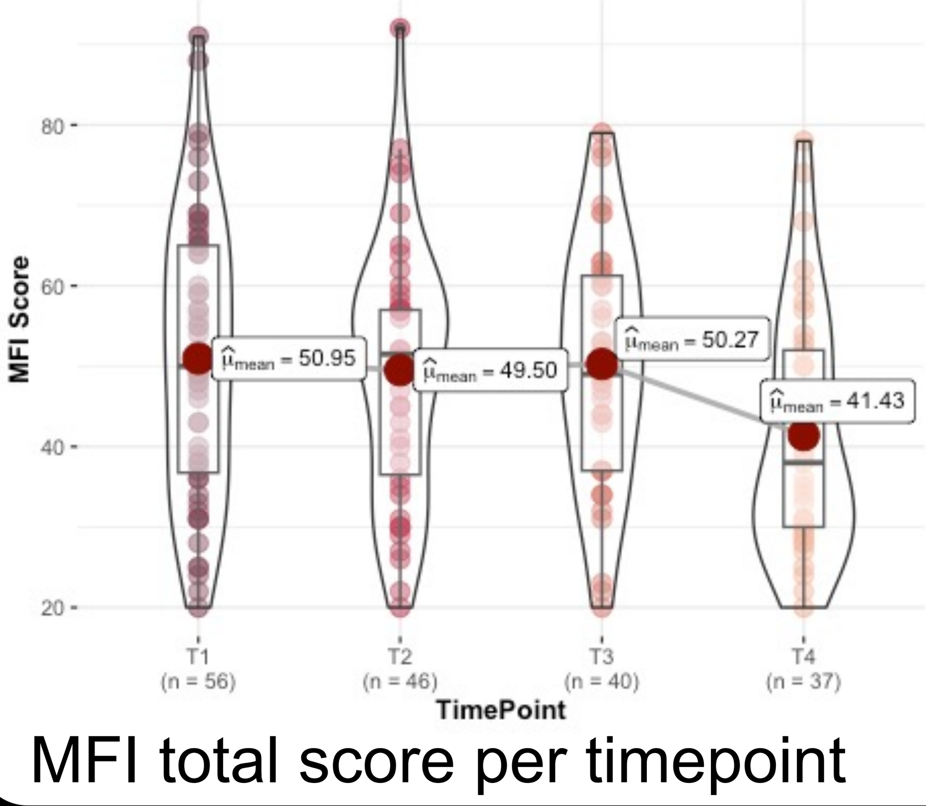
LESION SYMPTOM MAPPING

TiMeS

Multivariate Lesion Symptom Mapping (MLSM)

- Adapted from Zhang et al. 2014 [11]: relation of fatigue score to the entire lesion map (≠ each isolated voxel) is modelled using a nonlinear function → intervoxel correlations are intrinsically considered
- Lesion correction method from DeMarco & Turkeltaub 2018 [12]: lesion volume regressed out of each voxel in the lesion maps





MFI total score per timepoint

N = 27 included

Rest excluded due to missing behavioural / lesion data or for having no voxels inside the minimum lesion cut-off mask

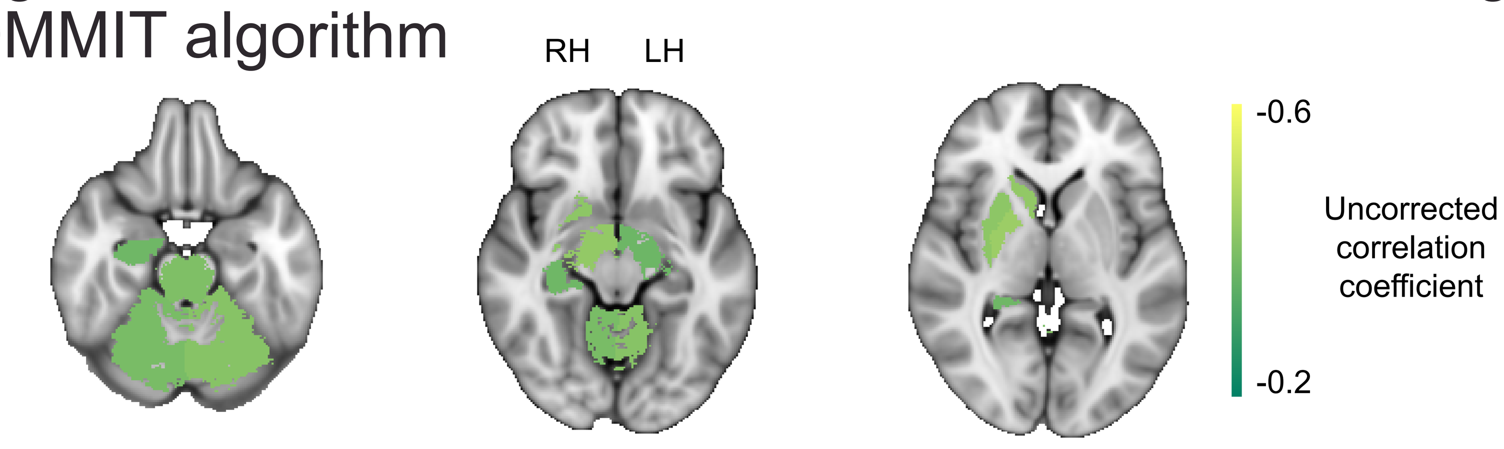
No significant clusters
Lesion location alone might not account for difference in fatigue

CONNECTOMICS

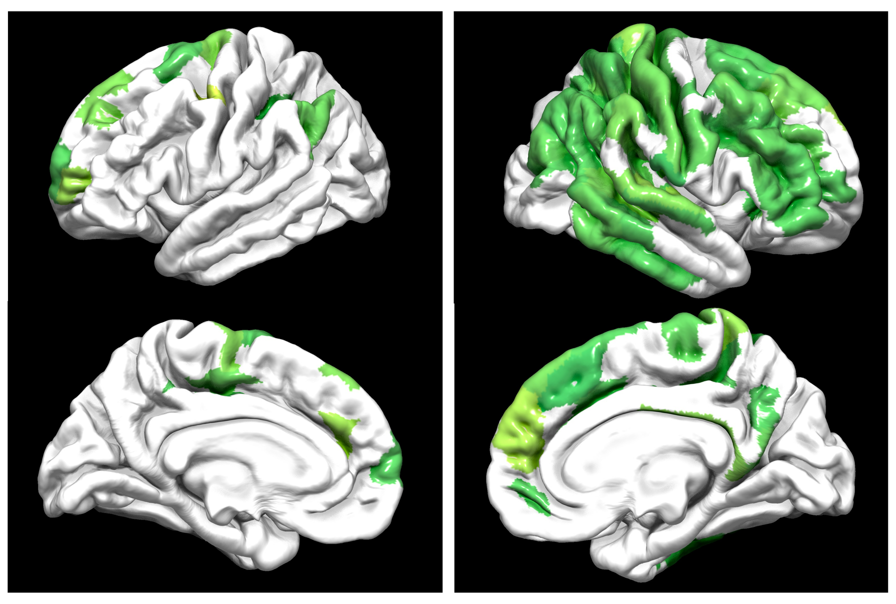
TiMeS

Diffusion-weighted imaging (DWI) analysis

- Adapted from Koch et al. 2021 [13]: Whole brain probabilistic tractography using 10 million streamlines, weighted based on the Stick and Ball model using COMMIT algorithm



Subcortical positive clusters



LH & RH cortical positive clusters

N = 45 included

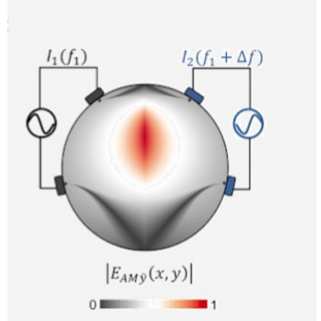
Correlation disconnectome & MFI summed score

Mean correlation coefficient for each area of the Glasser atlas + subcortical areas

Future perspective:
Longitudinal analysis & predictive modelling
Comparison to attention, sleep, depression & anxiety questionnaires

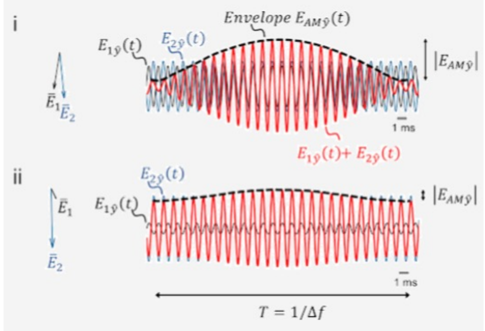
tTIS STUDY

Targeting deep brain structures non-invasively: Transcranial electric temporal interference stimulation (tTIS)



Succesfully applied in	Target structure
Motor skill learning [14] & reinforcement learning [15]	**Striatum**
Associative memory & spatial navigation (Both in preparation)	**Hippocampus**

Grossman et al. 2017 [16]



30 healthy participants

30 stroke patients

30 traumatic brain injury patients

VISIT 1
Explanation of the study
Signing the consent form
Medical history
Inclusion
Questionnaires

VISIT 2
Task + fMRI
Striatal tTIS

VISIT 3
Task + fMRI
Striatal tTIS

Multidimensional Fatigue Inventory (MFI)
Fatigue Scale for Motor & Cognitive Function (FSMC)

Active tTIS vs. control stimulation

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[7] Lerdal et al. (2009). *Journal of pain and symptom management*, *38*(6), 928-949.
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[13] Koch et al. (2021). *Brain*, *144*(7), 2107-2119.
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[15] Vassiliadis et al. (2023). *Nature Human Behaviour* (accepted)
[16] Grossman et al. (2017). *cell*, *169*(6), 1029-1041.

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אוניברסיטת בן-גוריון בנגב
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جامعة بن-غوريون في النقب

Neurotechnology-based intensive upper-extremity supplementary training for inpatients with sub-acute stroke: A feasibility study

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Background:

- Intensive and high-dose high-quality upper extremity training may enhance motor recovery compared to standard care.
- Such programs do not exist due to limited resources, patient compliance, and administrative challenges.
- Our aim was to examine the feasibility, potential efficacy, and the required resources for an intensive technology-based upper extremity training delivered during inpatient stroke rehabilitation.

Methods:

Twelve sub-acute stroke subjects with hemiparesis underwent fourty 60-minute sessions over a 4-week period, in addition to standard care (additional 40 hours).
The training included two game-based virtual reality platforms to practice proximal (tech 1) and distal (tech 2) movements with daily assessments.

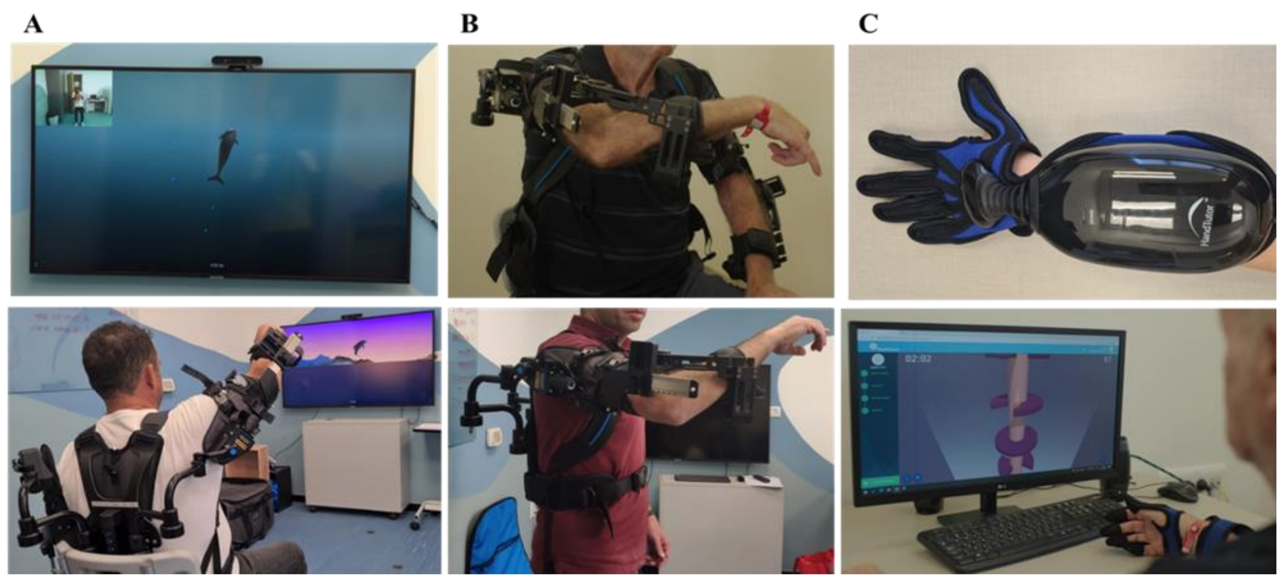

Figure 1:
A. Tech 1, MindPod by Mindmaze.
B. Ekso UE Vest for arm weight support.
C. Tech 2, Hand Tutor - ergonomic wearable glove.

Feasibility Results:

A. Training adherence. Eight out of our 12 subjects finished 40 sessions.

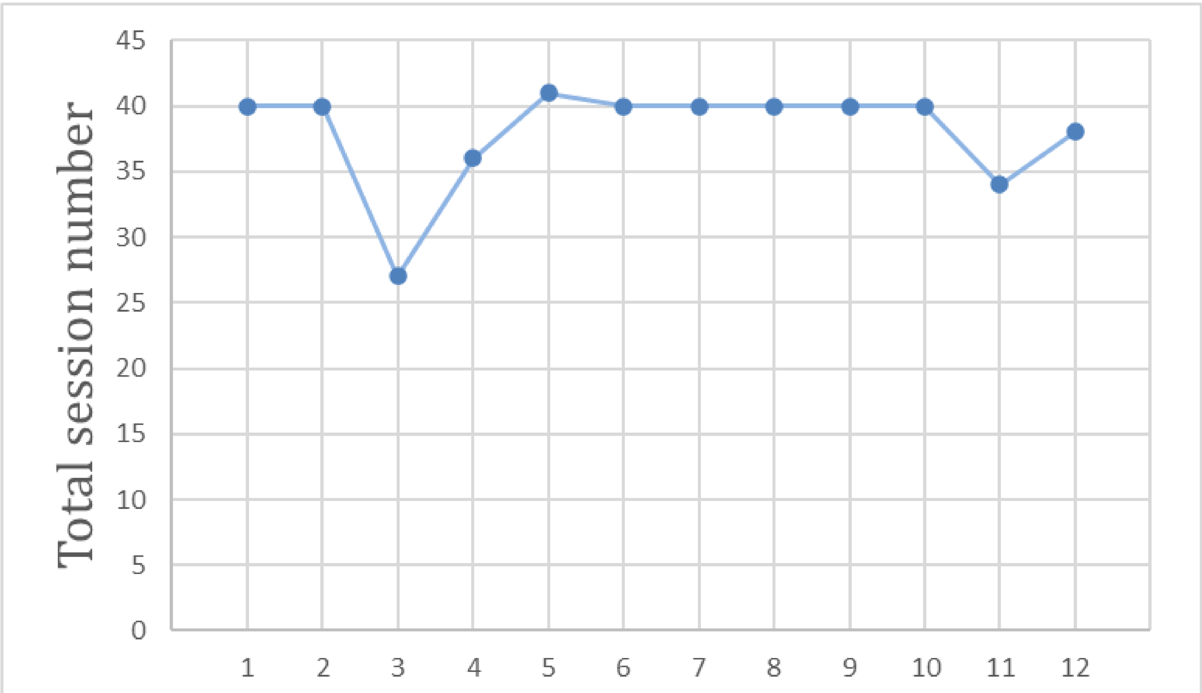

Figure 2: Number of the total intervention sessions each participant completed. Each point is a subject

B. Mean time on task was 35 minutes (out of 60) for tech 1 (A) and 37 for tech 2 (B). Mean total arm distance (tech 1), was 246 meters (C).

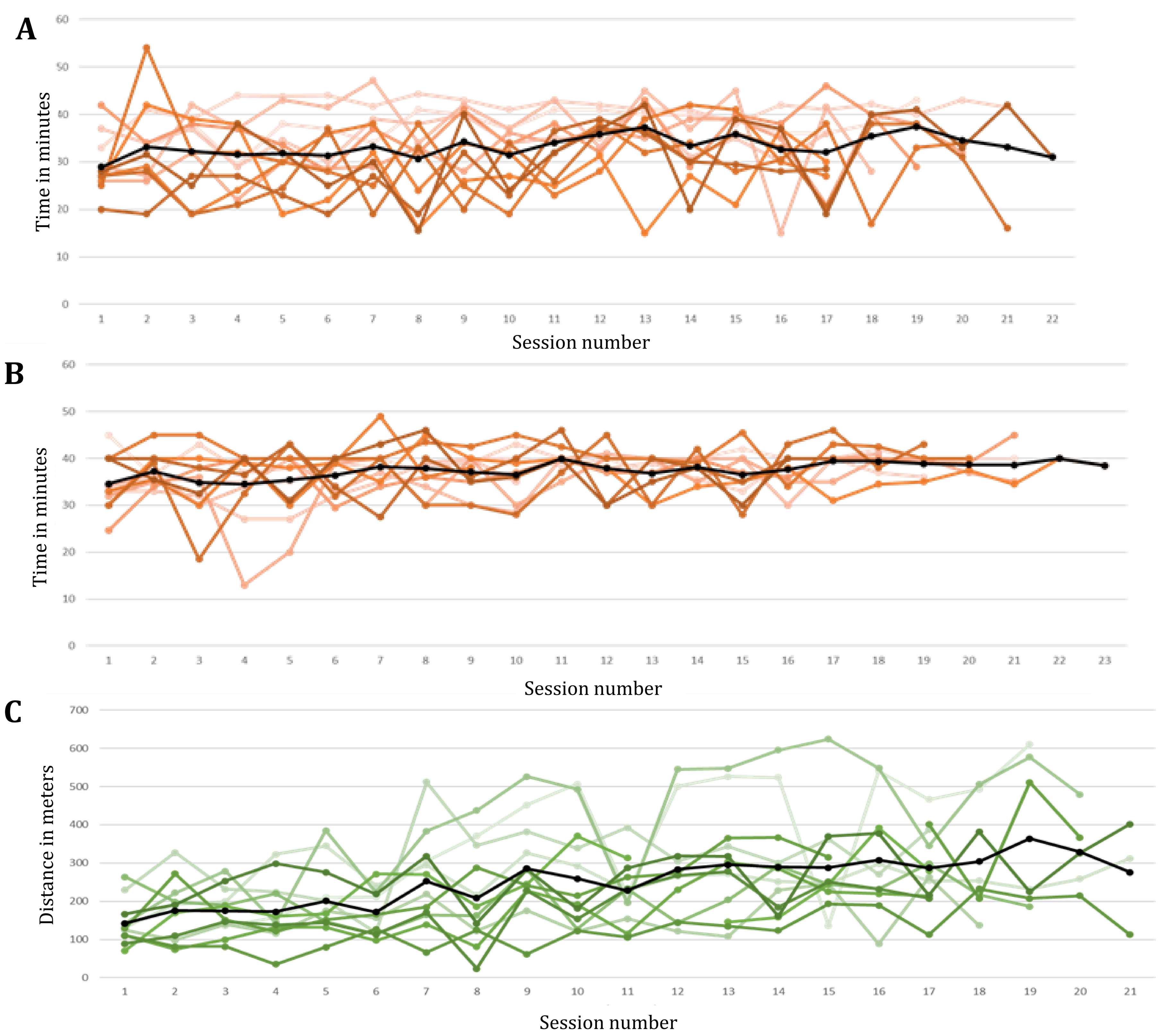

Figure 2:. A. Total time on task Tech 1 (shoulder and elbow movement practice) B. Total time on task Tech 2 (wrist and fingers movement practice). C. Total arm distance for tech 1. The data is represented for each of the sessions. Each subject is represented by a different curve. The average of all subjects represented by a black line.

C. Participation – Tech 1 – subjects were highly engaged

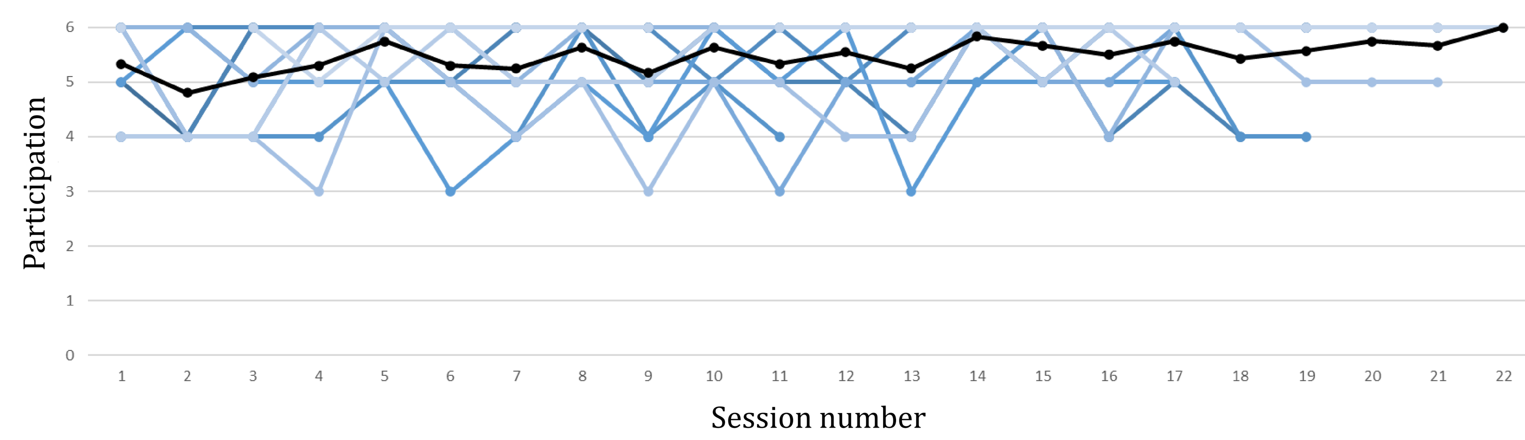

Figure 3: Pittsburg rehabilitation participation scale scores. Reported by the clinicians after each session (max score is 6). All 12 subjects are represented. Each subject is represented by a different line. The average of all subjects represented by a black line. The mean participation of subjects was 5.42 (SD 0.49).

D. Motivation – Intervention was highly motivating

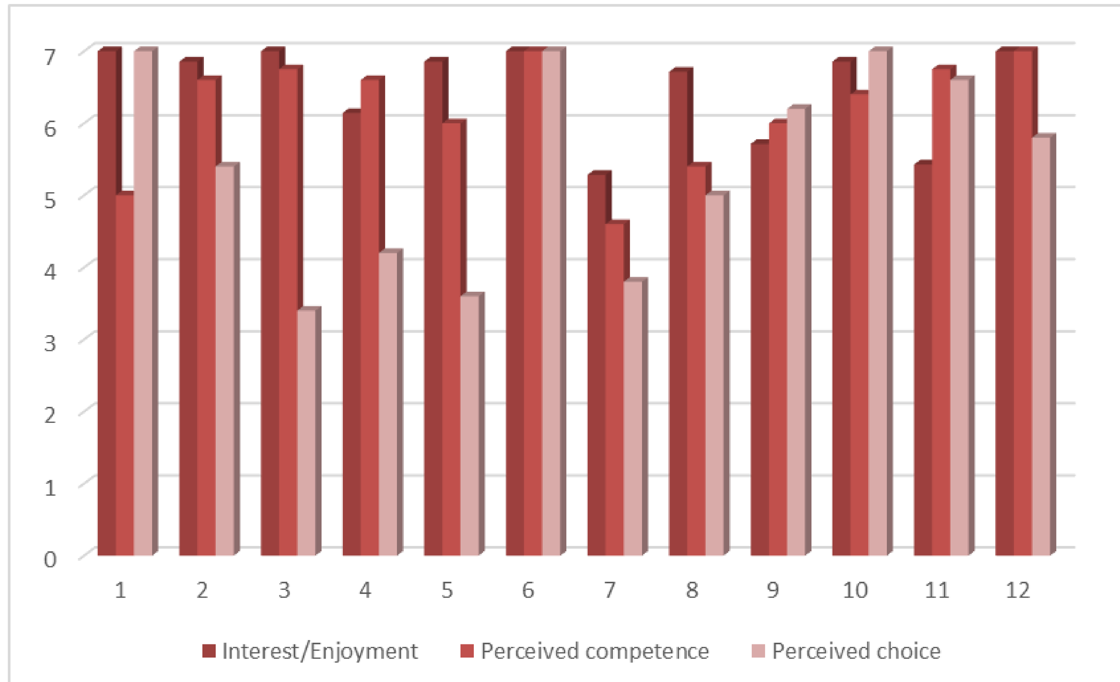

Figure 4: Intrinsic Motivation Inventory scores. Was filled at the end of the intervention. All subjects are represented. Each category is max score 7.

Subjects showed big motor recovery following intervention :

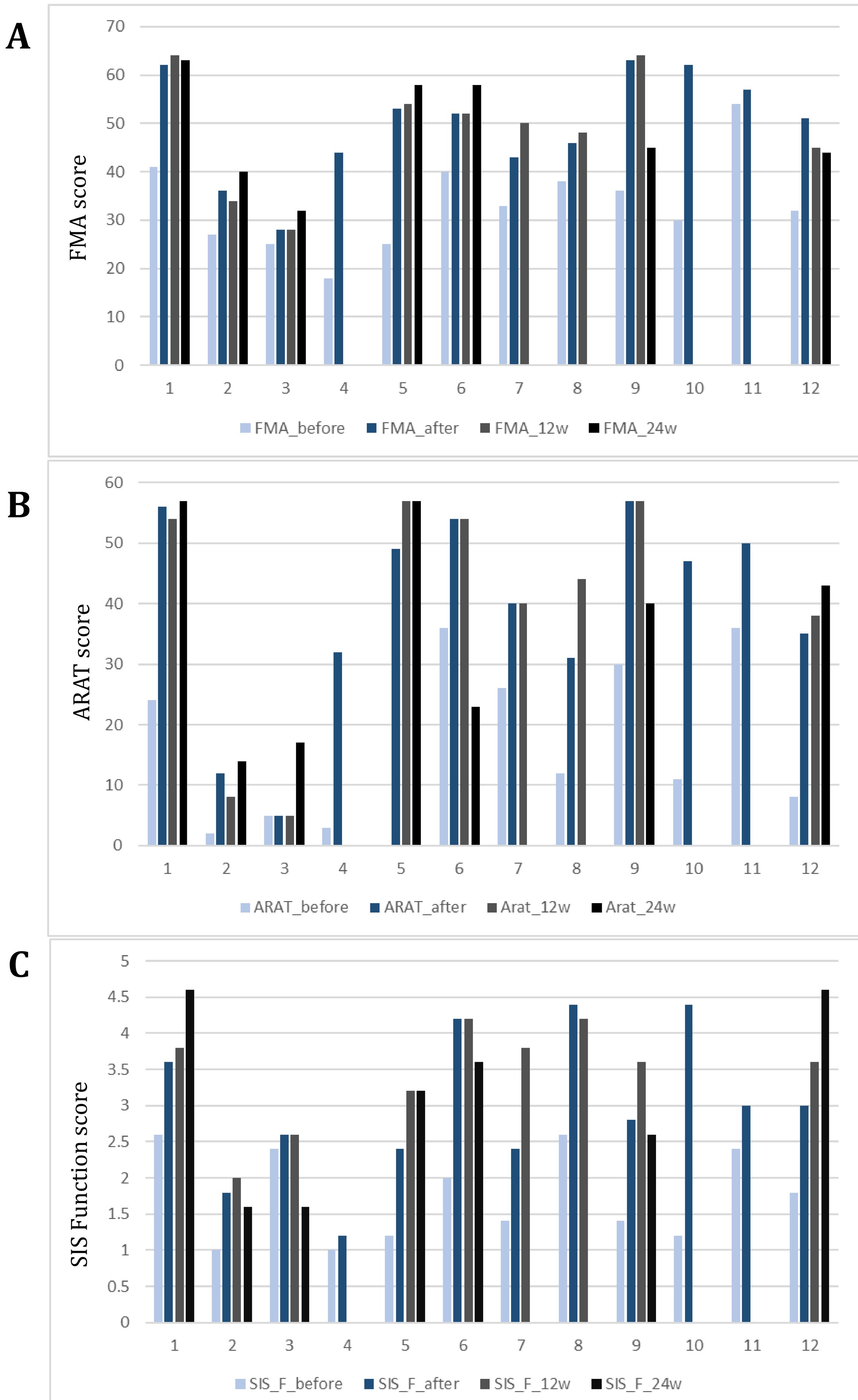

Figure 5: Motor scores from 4 time points – before and after the intervention, 12 and 24 weeks after the stroke. A. Fugl-Meyer motor scores (Max score is 66). B. Action Research Arm Test motor scores (max score is 57). C. Stroke Impact Scale hand function scores (Max score is 5). The higher the scores – the better the motor function is.

Conclusion:

- Intensive upper extremity training is feasible and well received by subjects with sub-acute stroke.
- Successful implementation depends on the clinical setting, technologies, and resources.
- We call for studying the implementation of this protocol on multiple subjects at a time and during clinical days, and for randomized control trials to study the efficacy of the intervention.
- Our preliminary results suggest that sub-acute intensive rehabilitation may improve motor recovery after a stroke.

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Feasibility study of a post-stroke rehabilitation program combining aerobic exercise and tDCS to improve walking performance in sub-acute hemiplegic patients. The ESTIMAH study

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2. Lyon Neuroscience Research Center, Trajectoires team (Inserm UMR-S 1028, CNRS UMR 5292, Lyon1 & Saint-Etienne Universities), France
3. Inter-university Laboratory of Human Movement Biology, "Physical Ability and Fatigue in health and disease" team (F-42023), Saint-Etienne "Jean Monnet" & Lyon 1 & "Savoie Mont-Blanc" universities, Saint- Etienne, France

Illustrations of the aerobic training on cycloergometer plus tDCS and on walking training with treadmill and body weight support.

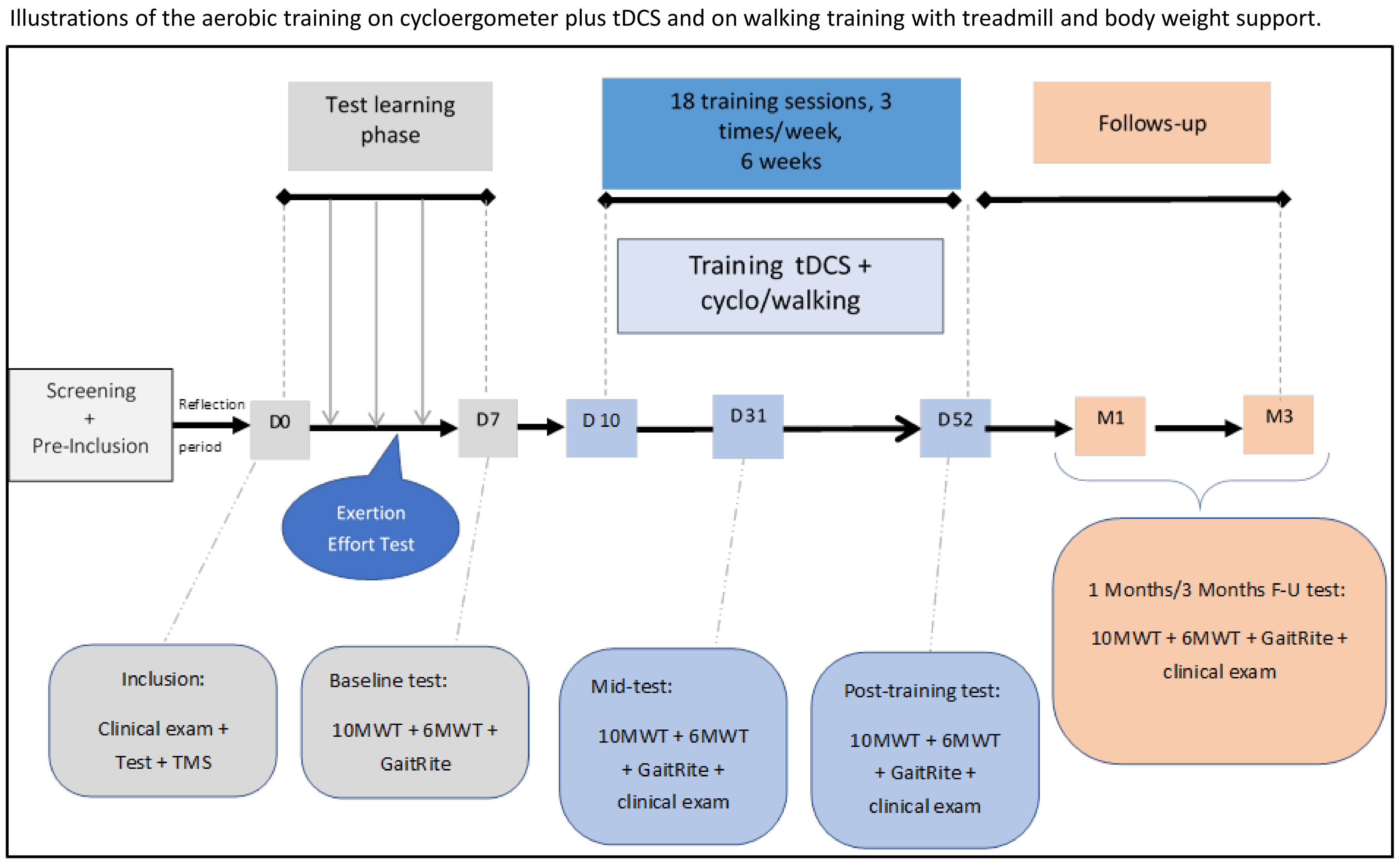

Figure 1: study schedule

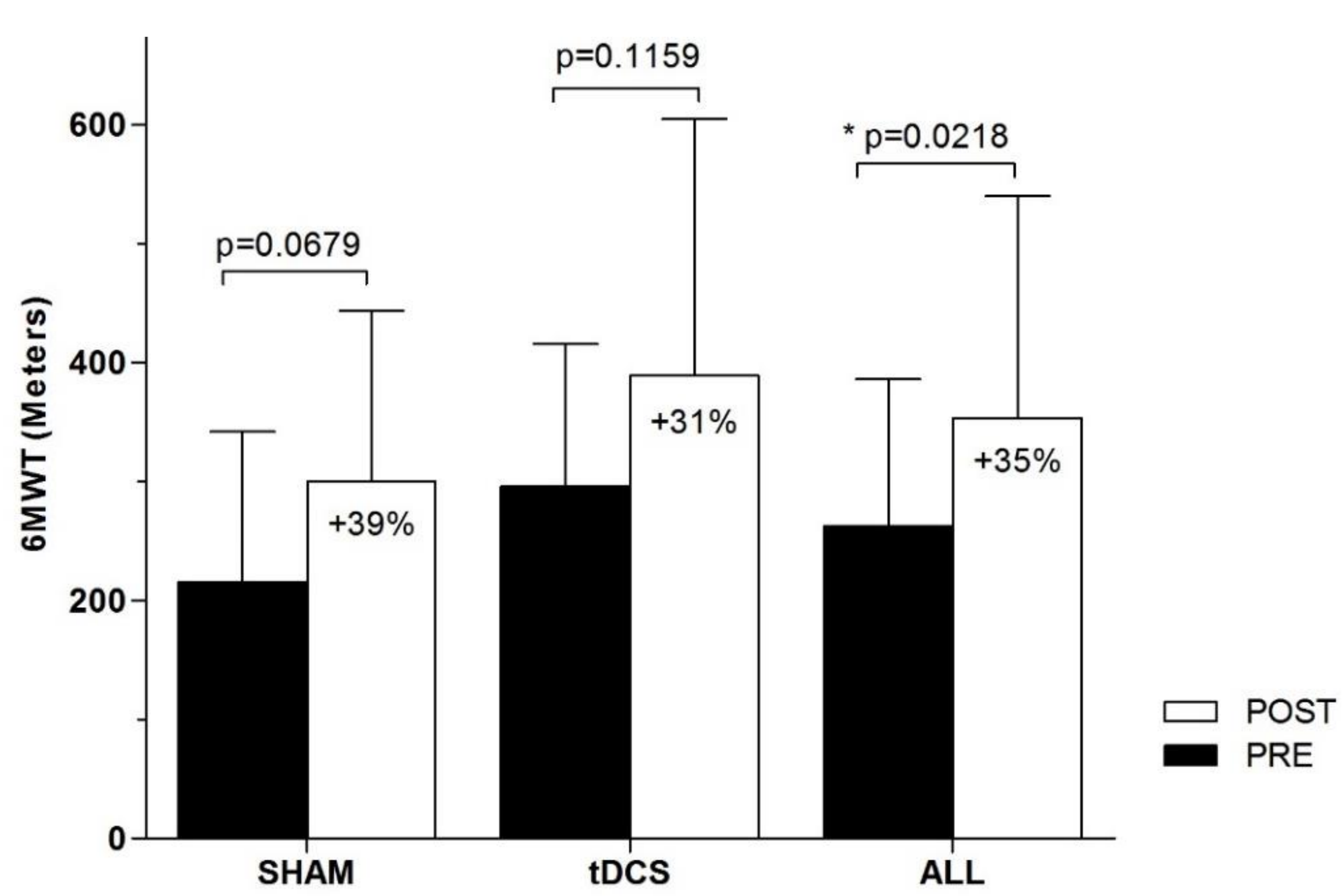

Figure 2: Comparison of 6MWT performances before and after retraining between the STIM group and the SHAM group.

AE	At least 1	At least 2
TDCS	56%	17%
SHAM	47%	3%

A

AE	Headaches	Itching	Tingling	Redness
TDCS	9%	9%	35%	48%
SHAM	0%	0%	92%	8%

B

Figure 3: Frequency of adverse effects (A) and their occurrence rate (B) between the STIM and SHAM groups. AE : adverse event

Introduction

- Limited improvement of post-stroke gait capacity have been shown with exercise training programs.
- Neuromodulation techniques such as transcranial Direct Current Stimulation (tDCS) may enhance the efficacy of exercise training programs.
- In this aim, we have designed an aerobic training program coupled with cortical stimulation by tDCS for hemiplegics stroke patients. The first objective was to evaluate the feasibility and tolerance of this program and secondly its effects on the walking performance.

METHODS

- This study was performed on 13 patients suffering an initially complete hemiplegia due to a first-ever stroke (age: 58.5 ± 12 years, 5 women, 7 men, post stroke delay: 3 ± 1.5 months).
- All patients followed 18 sessions, 3 times a week over 6 weeks, combining cycloergometer and walking training. Walking training was achieved with treadmill and body weight support (Figure 1).
- Anodal tDCS stimulation (2 mA) was applied over the lower limb ipsilesional motor area during the first 20 minutes of each session.
- The tolerance and adverse events (AE) were collected through a survey filled in after each session.

RESULTS

- Intention-to-treat feasibility stood at 76%, while per-protocol analysis yielded a more favorable rate of 83%. No major AE was reported, but 27% of the sessions was associated with minor AE.
- 56% reported at least one adverse reaction, and 17% reported two.
- Adverse events were minors (Table A & B)
- Performances demonstrated notable improvements across all patients, comparing the pre and post program assessments.
  - 6MWT: +35% (p=0.022) (Figure 2)
  - 10MWT: +12% increase (p=0.17)
  - VO2max: +21% p=0,008; Pmax= +35% p>0,05
- There were no significant difference between group.

CONCLUSIONS

The combined intervention of a-tDCS on the M1 lower limb and aerobic exercise is safe and feasible for subacute poststroke patients with moderate motor impairment. An efficacy study should rule on the benefit of the combination of these two complementary techniques.

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Neural mechanisms underlying improved new-word learning with high-density transcranial direct current stimulation

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INTRODUCTION

Aphasia is frequent in patients with brain lesions and recovery often limited. New treatments allowing patients to regain language functions are therefore necessary. Transcranial direct current stimulation (tDCS) is promising but effects remain inconsistent because it is not known which neural processes need to be targeted. Here, we investigated the neural and behavioral effects of high-definition (HD)-tDCS combined with new-word learning in healthy participants.

METHODS

- → **36** healthy young participants (mean age 25.11 years, range 18-43,18 males and 18 females)
- → Learning of **RARE** words

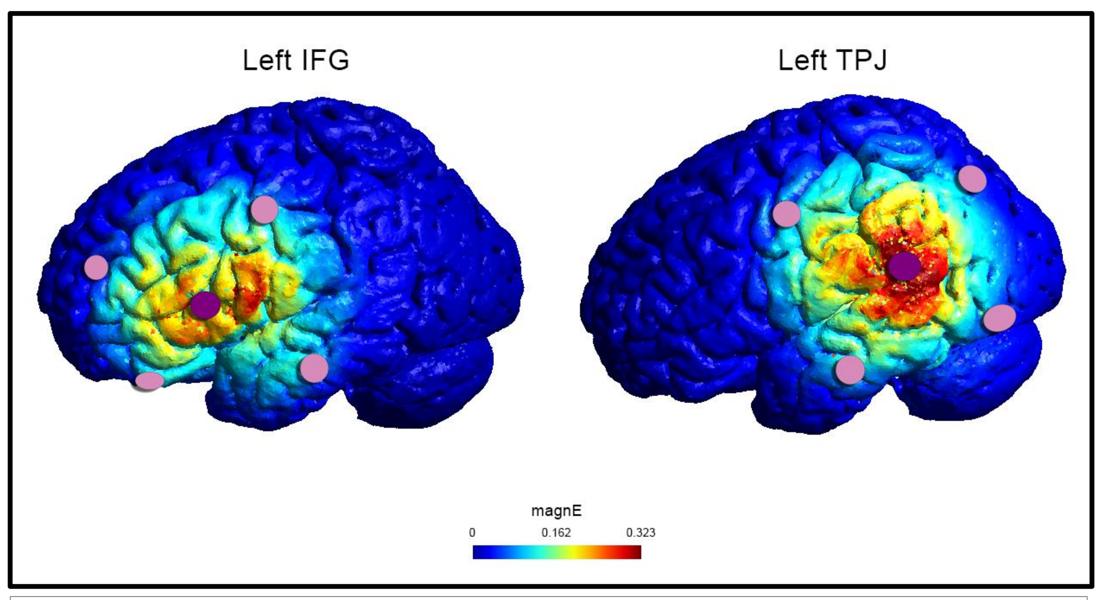

Figure 1. Stimulation of left IFG and left TPJ simulation of stimulation with HD-tDCS.

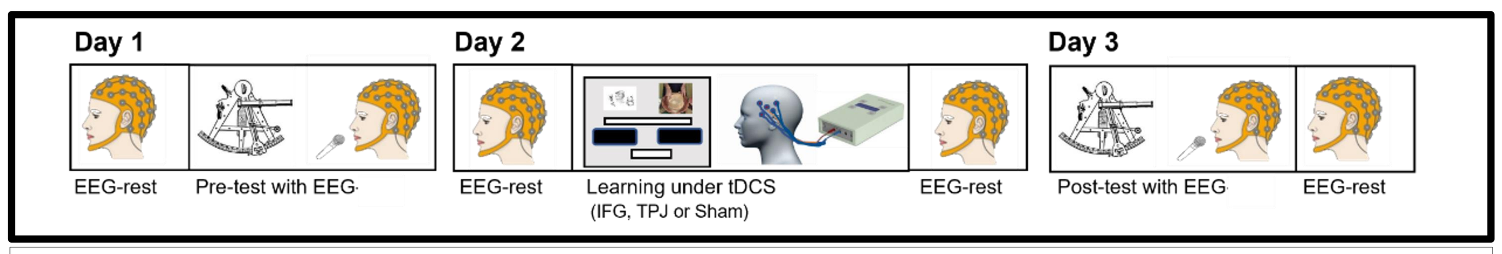

Figure 2. Experimental Design.

Power and FC Analysis at left IGF, left TPJ and lentiform nucleus.

Short Term Changes (day 2) → training and stimulation effects after - before stimulation.

Long-Term Changes (day 1 to day 3) → difference between day 1 and day 3.

RESULTS

<u>Behavioral Effects (Fig. 3):</u>
Significant verb learning improvement with left IFG stimulation.

<u>Local Activation (Fig 4):</u>
Stimulation of left TPJ → increased local activation during naming.
But no correlation with learning.

<u>Network Interactions (Fig. 5):</u>
Stimulation of left IFG
→ Short-term: Increased theta-band FC between left IFG and left striatum
→ Long-term: Increased theta-band FC between left IFG and left TPJ.
Correlate with improved verb learning.

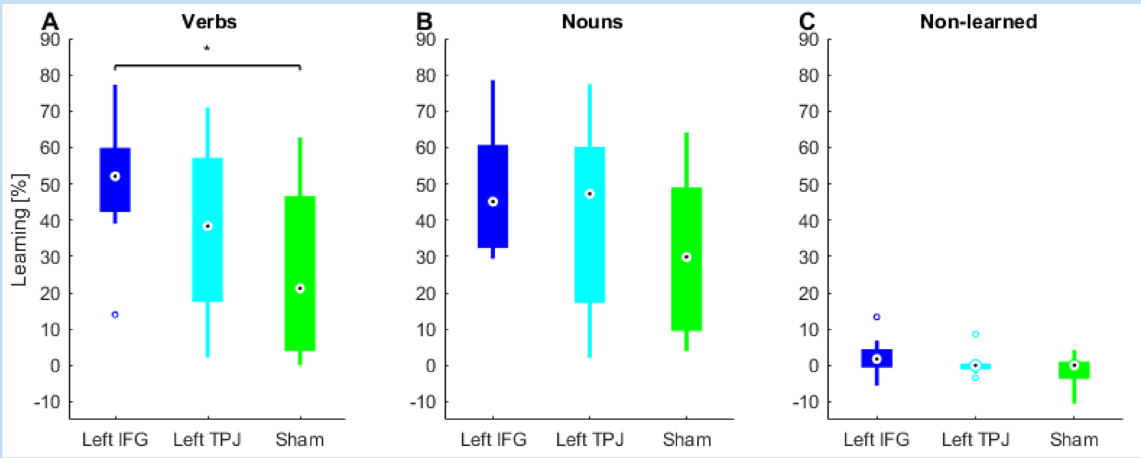

Figure 3. Behavioral effects of tDCS on rare word learning. *Learning of verbs (A), nouns (B) and non-learned control words (C) for each stimulation condition.*

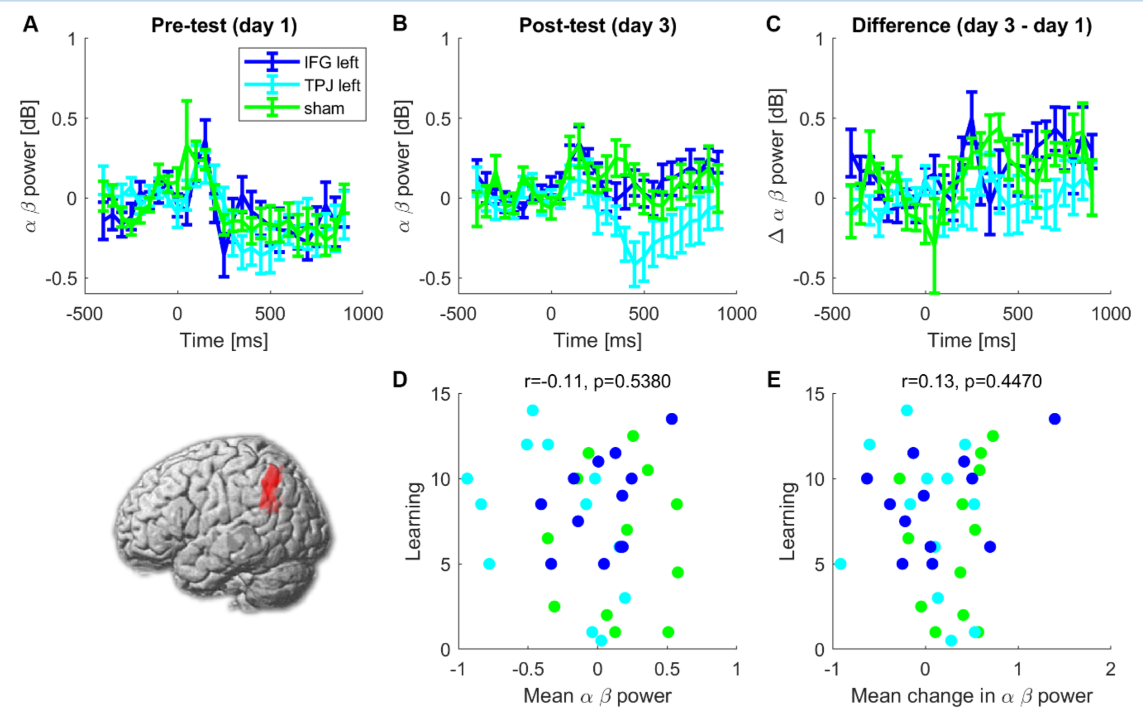

Figure 4. Alpha and beta power decrease, indicating activation at TPJ, and impact on learning. *(A) Pre-test activation in all conditions. (B) Post-test activation only after TPJ stimulation. (C) Change from pre- to post-test. Time course is shown as mean ± standard error. (D) No correlation between post-test activation and learning. (E) No correlation between activation change and noun learning.*

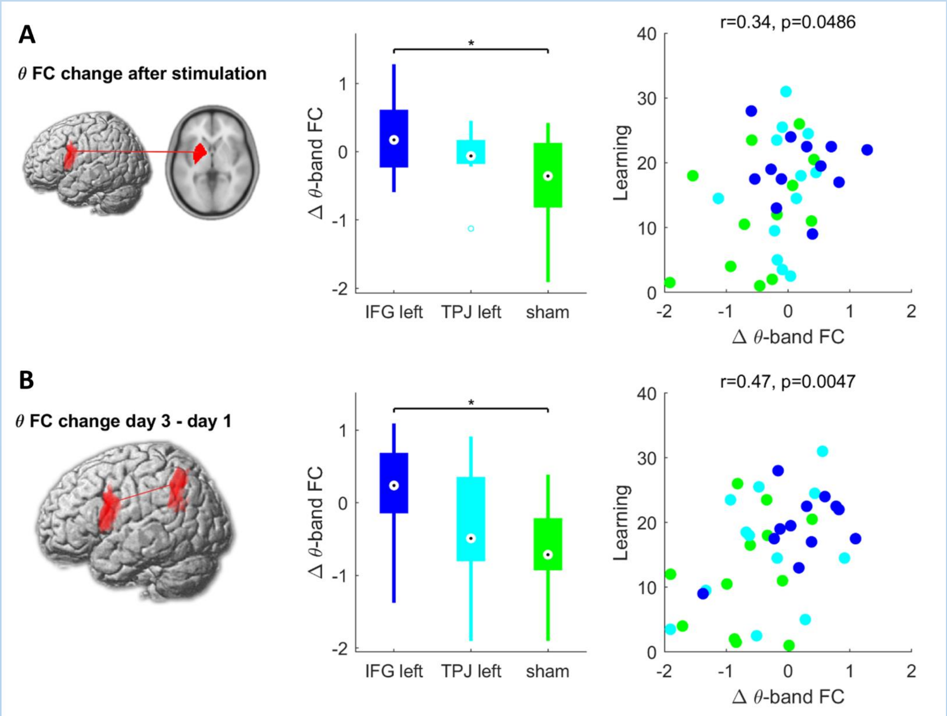

Figure 5. Network effects of tDCS and their impact on learning. *(A). tDCS over left IFG led to an short-term increase in theta-band FC between left IFG and lentiform nucleus. This correlated with better verb learning. (B) tDCS over left IFG led to a long-term increase in theta-band FC between left IFG and TPJ. This correlated with better verb learning.*

DISCUSSION

- Need of neuromodulation **targeting network interactions** rather than localized activation.
- Activating one area with a behavioral task and another area with HD-tDCS can lead to enhanced interactions between them.
- Nuanced impacts on nouns and verbs, highlighting the complex interplay between HD- tDCS, local activation, and network-level processing in language tasks.

Impact of comorbid sleep-disordered breathing and atrial fibrillation on the long-term outcome after ischemic stroke

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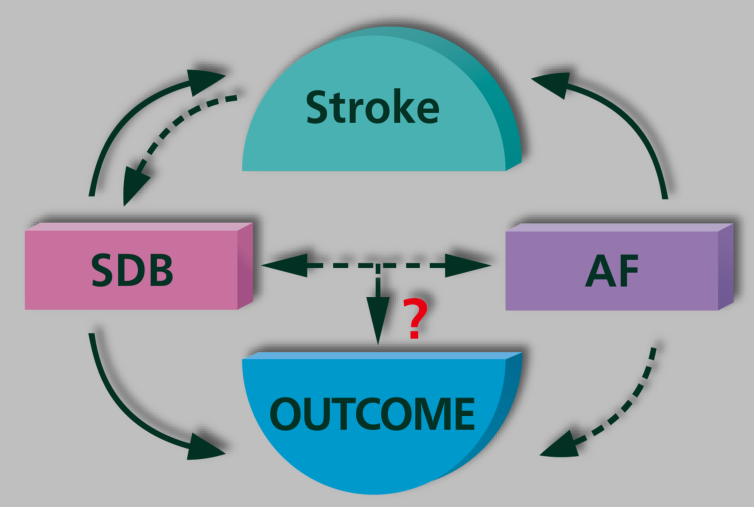
accepted 1st December 2023 STROKE/2023/042856R2 Stroke

BACKGROUND



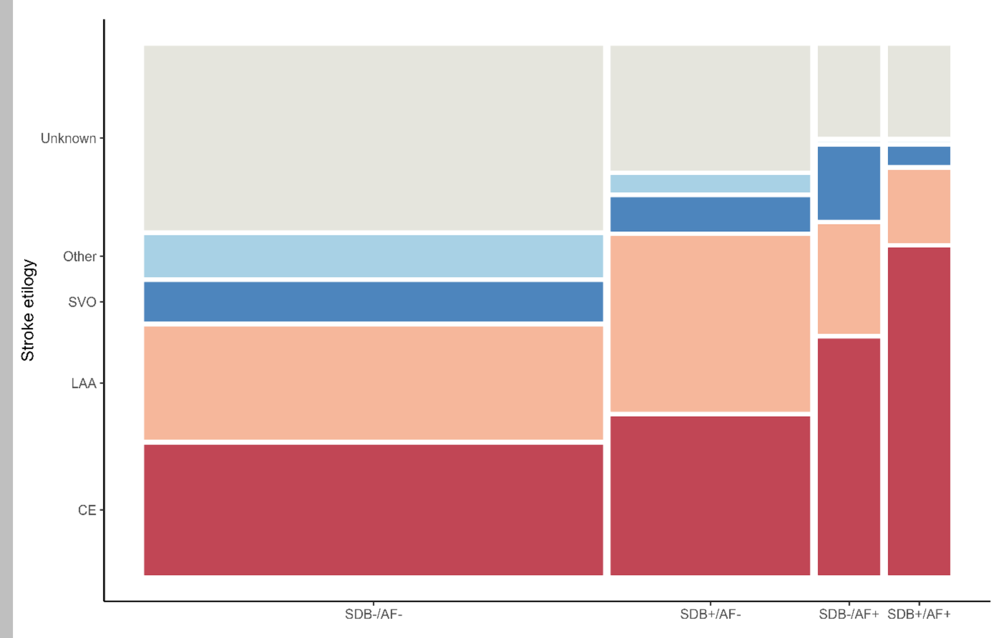
Sleep-disordered breathing (SDB) and atrial fibrillation (AF) are highly prevalent in stroke patients and recognized as independent risk factors for stroke. As potentially modifiable entities, little is known about the impact of comorbid SDB and AF on the long-term outcomes after stroke.

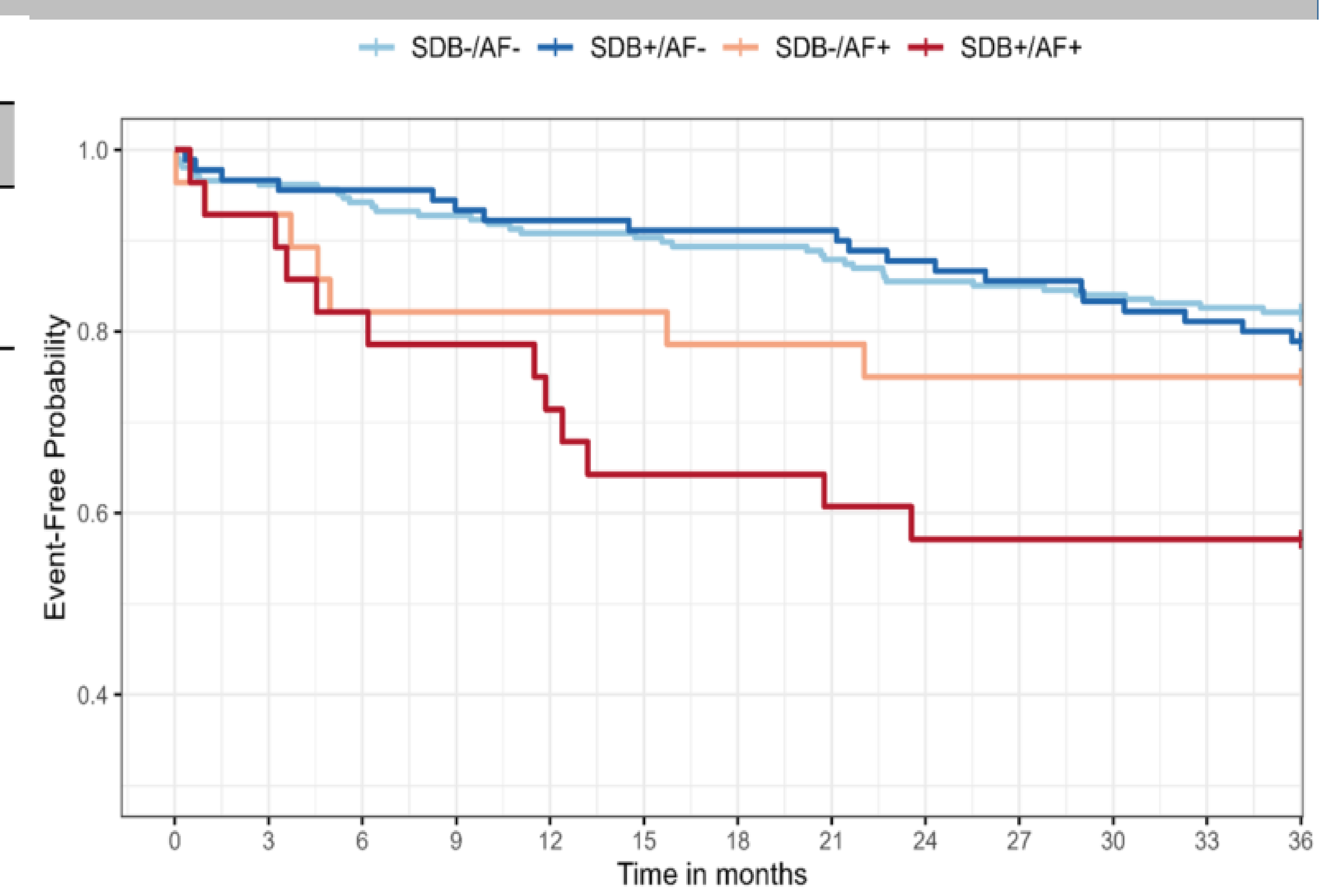
RESULTS

Table 1. Frequency of AF in AHI ≥15/h vs. AHI<15/h.

	No AF	AF	Odds Ratio (95% CI)
AHI < 15/h (Reference)	207	28 (11.9%)	**1.97**
AHI ≥ 15/h	90	28 (23.7%)	(95%CI: 1.05-3.68)

*Covariates: age, sex, BMI, hypertension, diabetes mellitus, dyslipidemia, and heart failure.





SDB-/AF-: AHI<15/h without AF (n=207); SDB+/AF-: AHI≥15/h without AF (n=90); SDB-/AF+: AHI<15/h with AF (n=28); SDB+/AF+: AHI≥15/h with AF (n=28).

METHODS

In this prospective cohort study, 437 patients with acute ischemic stroke or transient ischemic attacks (TIA) were analyzed. Patients were screened for SDB by respiratory polygraphy during acute hospitalization. Screening for AF was performed using a 7-day electrocardiogram (7d-ECG) up to three times in the first 6 months. Follow-up visits were scheduled at 3, 12, 24, and 36 months post-stroke. Cox regression models adjusted for various factors (age, sex, body mass index (BMI), hypertension, diabetes, dyslipidemia, and heart failure) were used to assess the impact of comorbid SDB and AF on subsequent death or cerebro-cardiovascular events (CCVE).

Sleep Deficiency & Stroke outcome study (n=437)

CONCLUSIONS

Stroke patients with comorbid moderate-to-severe SDB and AF have a higher risk of long-term cerebro-cardiovascular morbidity and mortality compared to patients with only moderate-to-severe SDB and to patients with neither moderate-to-severe SDB nor AF. AF appears to be the dominant independent risk factor. Thus, it is important to consider both conditions as cumulative and potential modifiable cerebro-cardiovascular risk factors, because of the availability of specific treatment options. Further studies are needed to confirm our observations and to assess the utility of other measures of SDB severity (e.g. nocturnal hypoxemic burden and night-to-night variability) to better understand the interrelationship between SDB, AF and cerebro-cardiovascular diseases.

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Characterise disturbances in the perception of the affected upper limb following stroke with the new Affected Limb Perception Questionnaire (ALPQ)

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Background

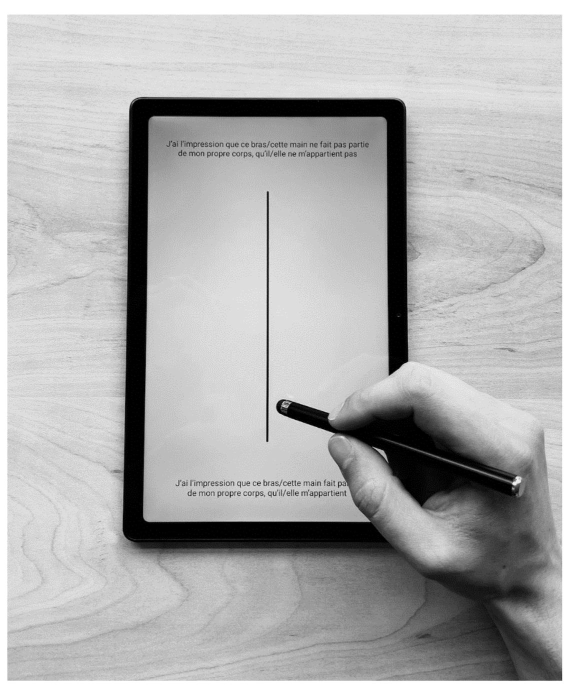
- Body Perceptions (BPs) can be altered after stroke[1,2]
- BPs alterations are not systematically assessed in clinical routine
- BPs alterations might affect patient's quality of life[3] and recovery

Objective

Characterise disturbances in the perception of the affected upper limb (UL) following stroke, by:

- estimating the prevalence of BPs alterations,
- evaluating their evolution as well as the correlation with sensorimotor deficits, lesions and recovery.

Methods



The ALPQ items[4] are listed in Figure B, and include as well anosognosia and anosodiaphoria for hemiplegia. Each item is answered on a VAS scale from 0 to 14. VAS > 0 are followed by additional questions on intensity and frequency of the sensation.

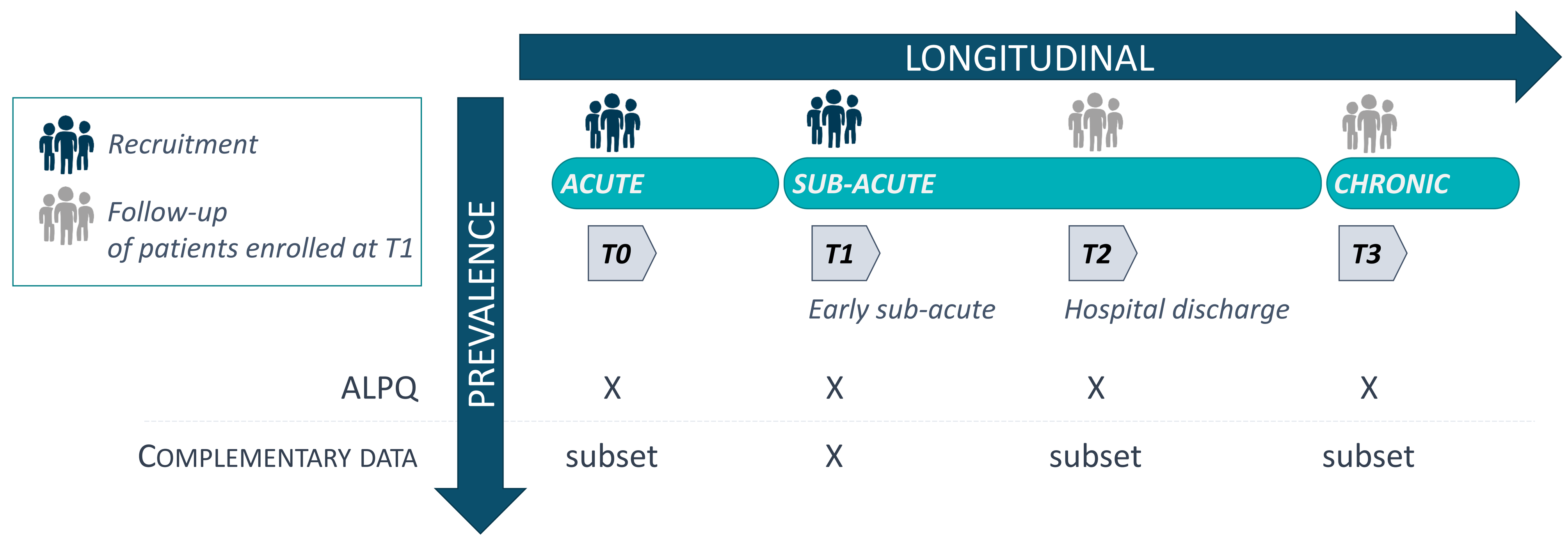


Figure A. Study design – Stroke patients are recruited in the acute (T0, < 15 days after stroke) and sub-acute (T1, 15 days to 3 months after stroke) phase. Patients seen at T1 are followed-up at hospital discharge (T2) and at the chronic phase (T3). Sensorimotor and cognitive functions, as well as UL usage are also evaluated.

Preliminary Results – *Analyses of the first 53 sub-acute stroke patients followed up to hospital discharge (T2) (N=53)*

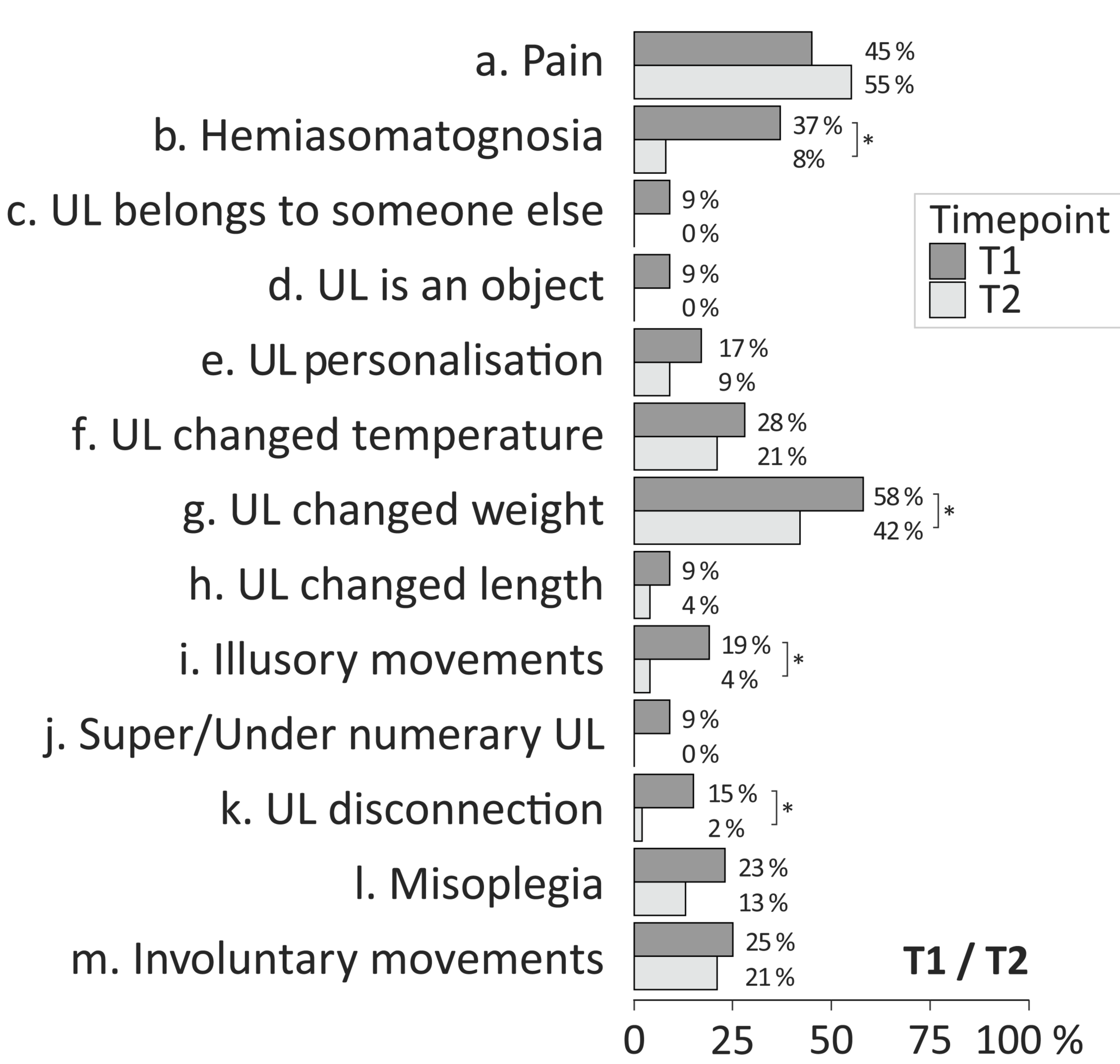


Figure B. Overall Prevalence
Percentages of patients reporting an altered UL perception (VAS > 0) for each item of the ALPQ.
** p-value <0.05 (McNemar's test with Yates correction)*

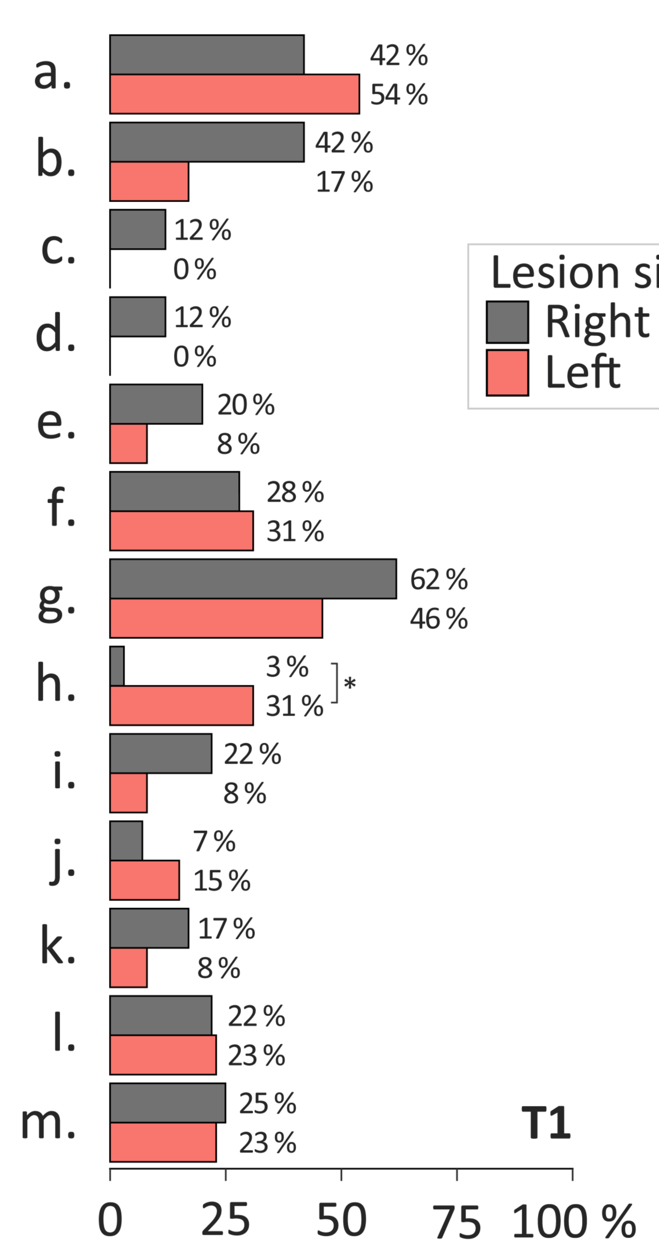


Figure C. Effect of lesion lateralisation
Prevalence of altered UL BPs split per lesion side at T1.
** p-value <0.05 (two-prop. z-test with Yates correction)*

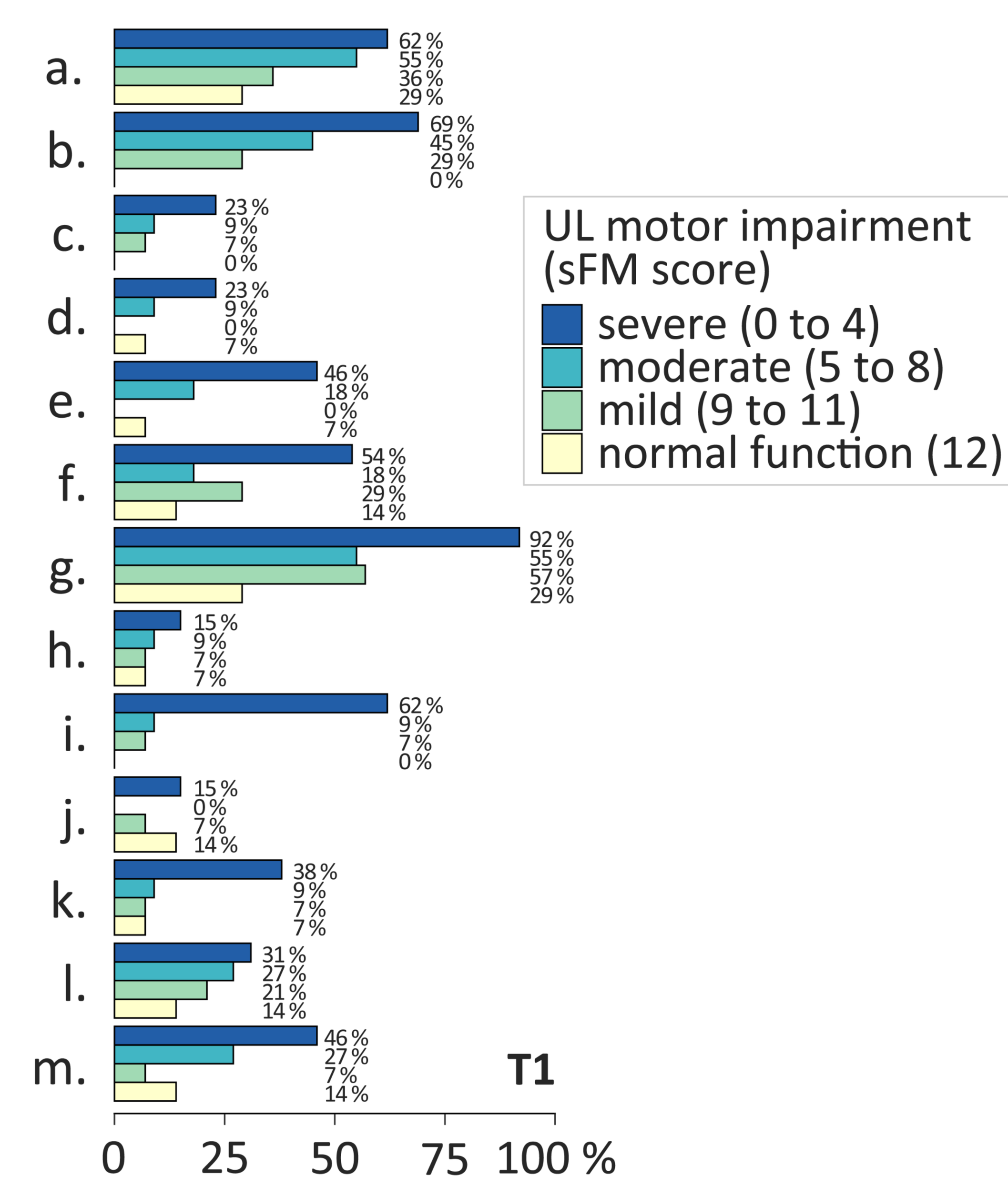


Figure D. Effect of motor impairment (MI)
Prevalence of altered UL BPs split per severity of the affected UL MI, as per the UL score in the short Fugl-Meyer (sFM)[5].

References:

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[2] Bassolino et al., *Brain Commun* (2022)
[3] Serrada et al., *Front Neurol* (2021)
[4] Konik et al., *Under review* (https://osf.io/p6v7f)
[5] Rinne et al., *PLoS ONE* (2016)

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Take home message – While the recruitment is ongoing, preliminary analyses indicate a noteworthy percentage of patients reporting altered feelings towards their UL at hospital entrance (T1).

- This occurs whether they suffered from a right or left brain lesion.
- The more severe the MI, the higher the prevalence of reported BPs, although MI is not a necessary condition.
- A substantial portion of patients still suffer from altered perception of their UL at hospital discharge (T2).

A quantitative, digital method for Human Figure Drawings analysis to reveal distortions in body perception after stroke

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[b] Villa Beretta Rehabilitation Center, Valduce Hospital Como, Costa Masnaga, Italy
[c] School of Health Sciences, HES-SO Valais-Wallis, Sion, Switzerland
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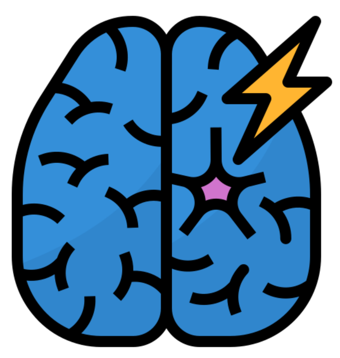
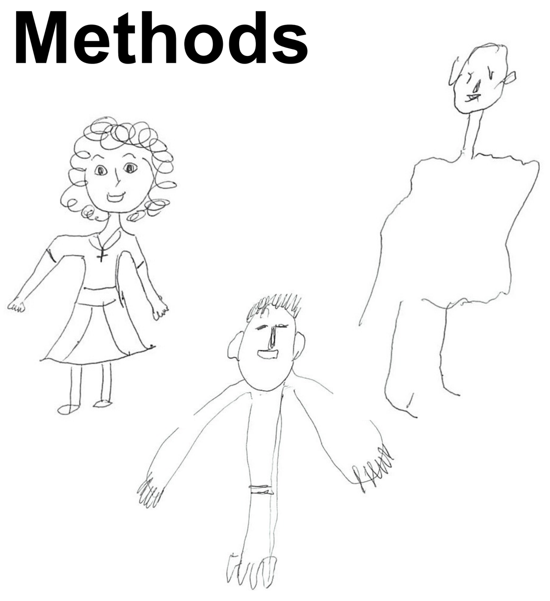
Introduction



Stroke may cause sensorimotor deficits of the upper (UL) and lower limb (LL) associated with alterations in body perception (BP). A qualitative indication of BP can be obtained by asking patients to draw a human figure (HFD). To overcome the lack of quantitative methods for HFD analysis, we developed a digital application named QDraw allowing the extraction of qualitative and quantitative features. The objectives of this study were:

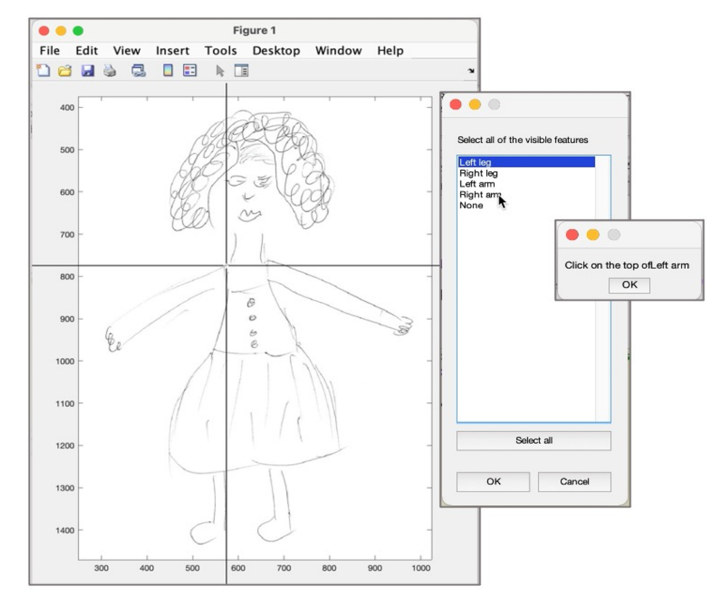
- To investigate whether QDraw app analysis could reveal distortions of BP in stroke patients;
- If any, to investigate the brain lesions associated with these distortions.

Methods



HFD were collected from 56 chronic stroke patients presenting moderate to severe UL sensorimotor deficits and no to mild LL sensorimotor deficit and 46 healthy controls. We computed an Asymmetry Index (AI) for the arm and leg lengths extracted by the QDraw app: AI = $\left|\frac{(Left - Right)}{(Left + Right)}\right| \times 2 \times 100$

- We run a voxel lesion symptom mapping on the AI for the UL and LL to evaluate possible associations with brain lesions.



Behavioral Results

HFD features	Prevalence (%) HC	Prevalence (%) P	Statistical comparison p-value
Face features			
Nose	93%	61%	**<0.001***
Mouth	100%	64%	**<0.001***
Both eyes	100%	71%	**<0.001***
Both ears	46%	14%	**0.002***
Upper and lower body features			
Both UL	100%	95%	0.280
Both UL connected	98%	79%	**0.005***
Both hands	89%	63%	**0.004***
Both LL	100%	98%	0.649
Both LL connected	98%	75%	**0.002***
Both feet	98%	66%	**<0.001***

Table 1. Prevalence and statistical comparison of the presence of main body features extracted from HFD of healthy controls (HC) and chronic stroke patients (P). *One-tailed Fisher's exact test (HC; N = 46; P; N=56).*

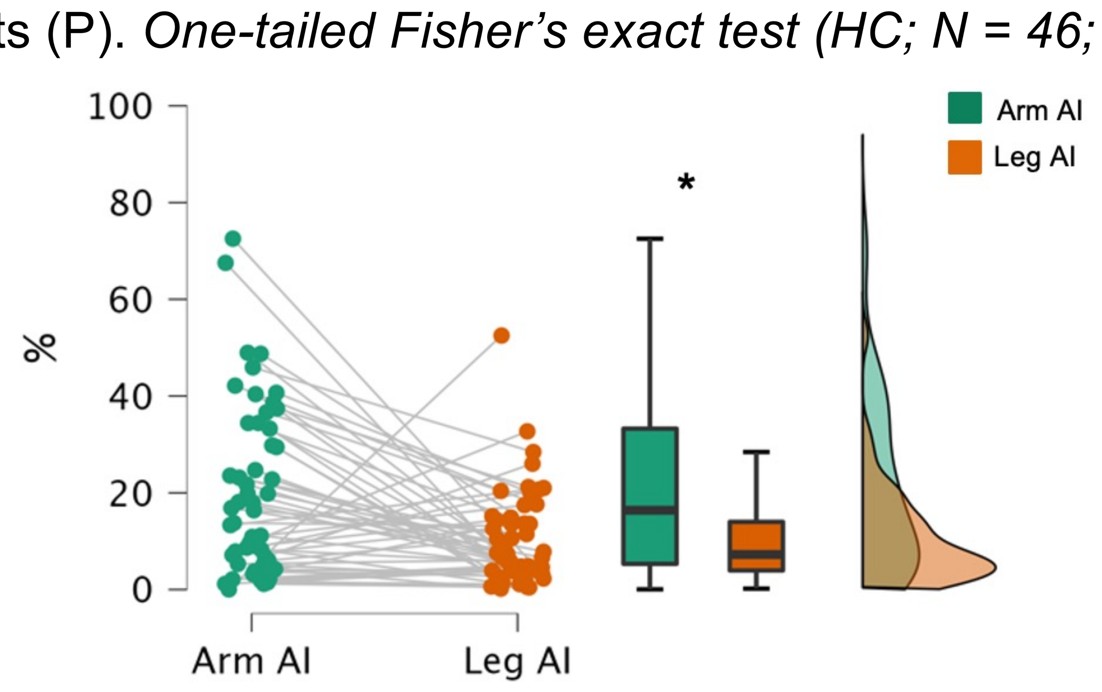


Fig. 1. A significant difference between arm and leg AI was found in patients' HFD, with arm-AI significantly higher than leg-AI, indicating greater distortions of arms compared to legs. *Wilcoxon signed-rank test; N=52; z=3.206; p=0.001.* No significant difference between arm and leg AI was found in healthy controls' drawings. *Wilcoxon signed-rank test; N=46; z=1.185; p=0.241.*
*Significant differences that resist after Bonferroni correction.

Brain Lesion Results

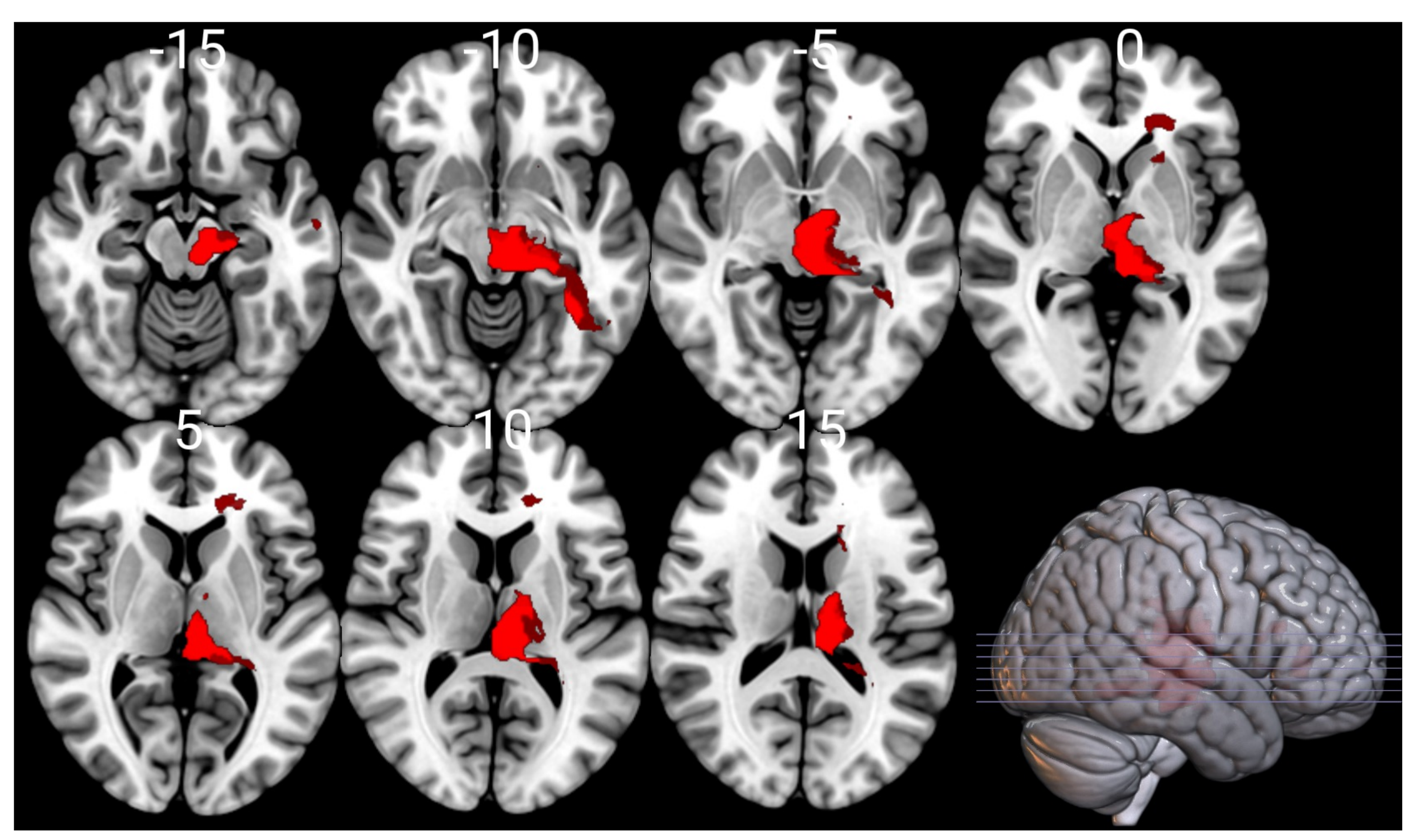


Fig. 2. Voxel lesion symptom mapping was run for arm AI and leg AI (N = 36; LBD = 19; RBD = 17). Lesion volume was regressed out. Significant clusters of voxels ($p < 0.05$, FDR-corrected) associated with greater UL distortions were found in the thalamus, hippocampus, para-hippocampal cortex and fusiform gyrus and smaller clusters were found in the caudate nucleus, the middle temporal gyrus and in the frontal white matter.
Importantly, no significant association was found for LL-AI.

Conclusion

The new quantitative, digital app QDraw resulted to be effective in analysing HFD and in revealing an altered perception of the UL in chronic stroke patients. This UL distortion seems associated with lesions to brain areas dedicated to the processing of multisensory information (thalamus), bodily (fusiform gyrus and middle temporal gyrus) and motor (caudate nucleus) signals as well as to mnestic processes (hippocampus and para-hippocampal cortex).

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Efficacy of a new VR-based serious game for the rehabilitation of unilateral neglect in brain injury patients

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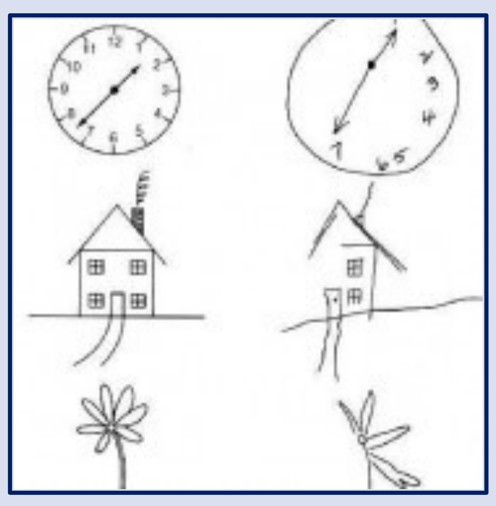
Introduction

In Switzerland, **40,000** new cases of **acquired brain injury** (ABI) occur annually resulting in **motor** and/or **cognitive** deficits.[1] A notable manifestation is **unilateral neglect**, where patients fail to attend, respond or orient to stimuli on the contralateral side of a hemispheric lesion. [2]

Fig 1: Copying task in left neglect

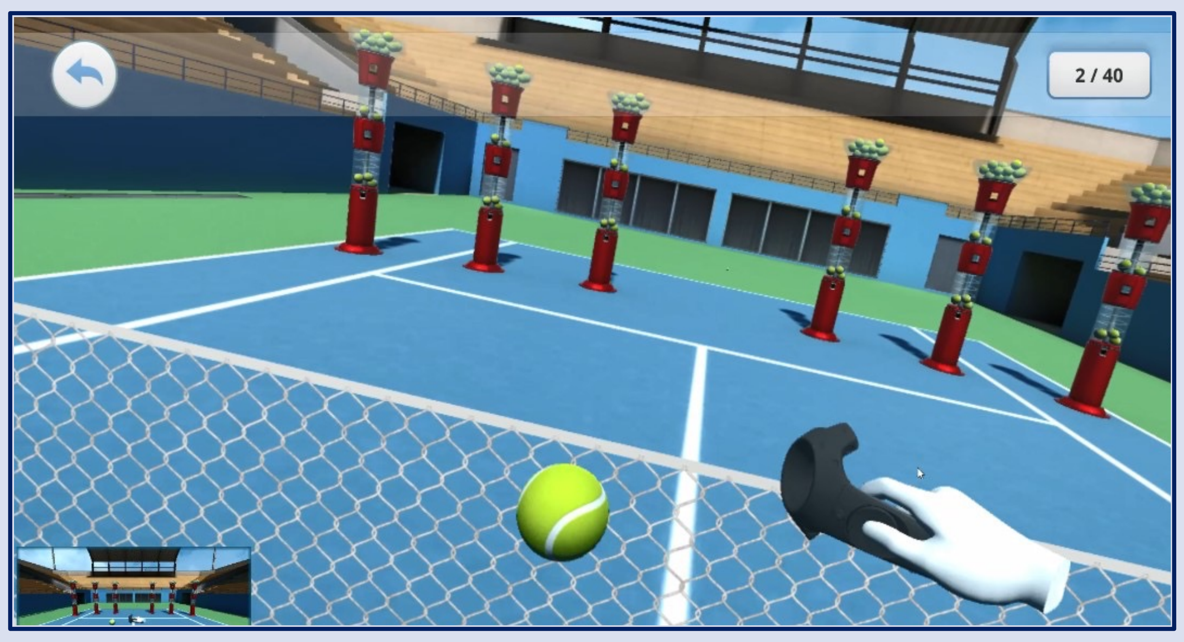


Virtual Reality (VR) rehabilitation games complement traditional methods, such as **prism adaptation**, offering an **immersive** and **innovative** tool.

Aim of the study

- Identify **predictors for success** in VR-based rehabilitation games to **tailor training programs** based on individual attentional deficits in ABI patients.
- Understand how patients with neglect deficits **respond to prism adaptation in VR** (Fig 2).

Fig 2: Virtual environnement of the tennis VR game



Methods

- **18 ABI** patients with left, right, or no neglect who played a **VR Tennis game with prism adaptation.**
- **Game Metrics:** Hand position, Accuracy (= Scores), Ball trajectory, completion percentage (= Sessions).
- **Patients Data**: Age, Sex, Neglect type, time between injury and start of training, cognitive combordities.
- Statistical analysis **with Linear Mixed Models (R)**

Fig 3: Data neglect distribution

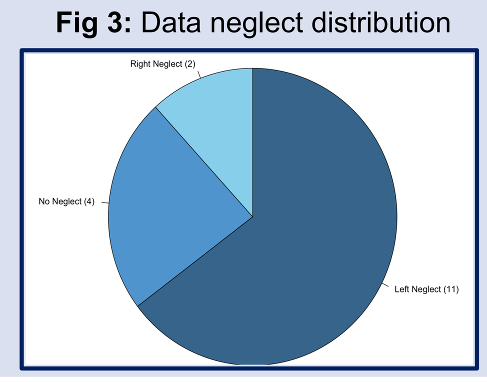
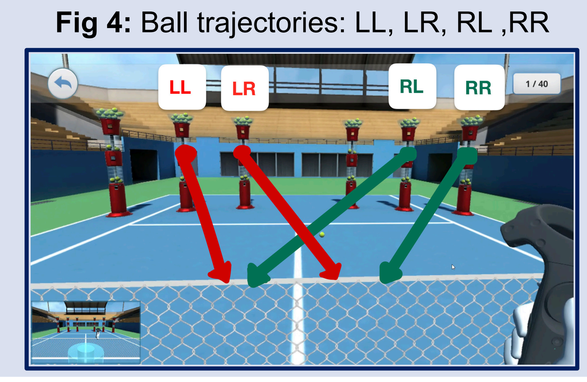


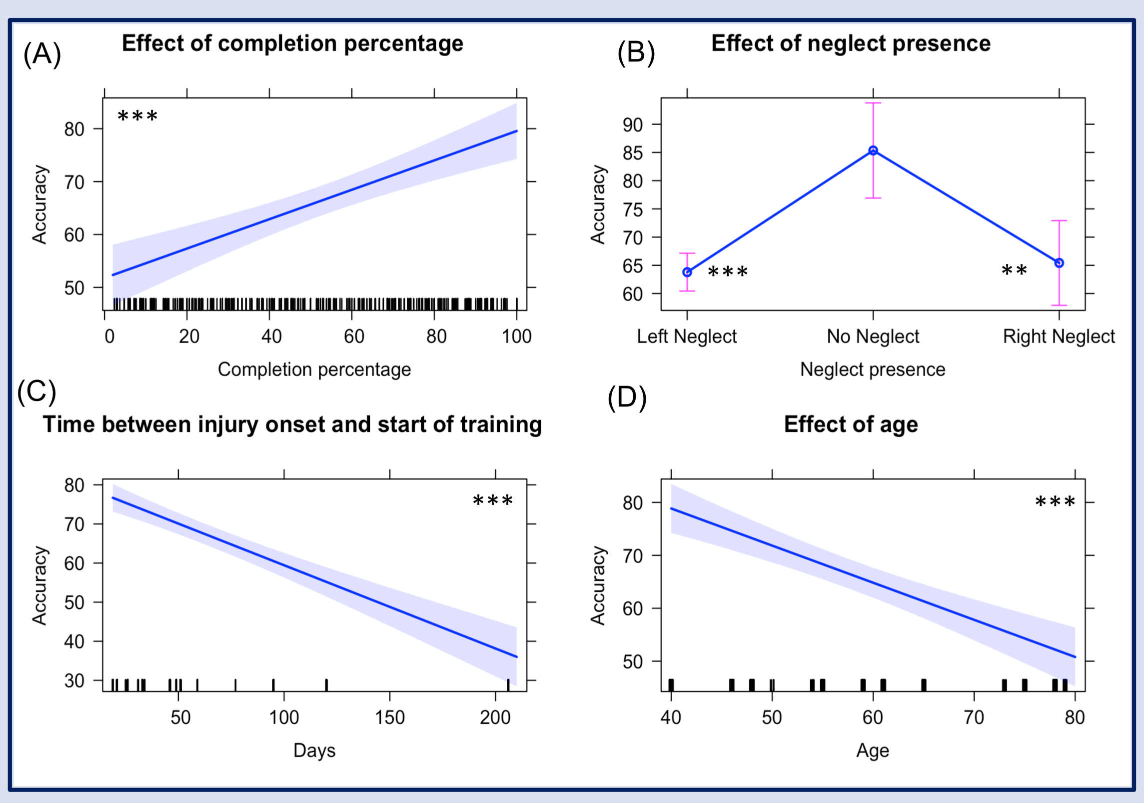
Fig 4: Ball trajectories: LL, LR, RL ,RR

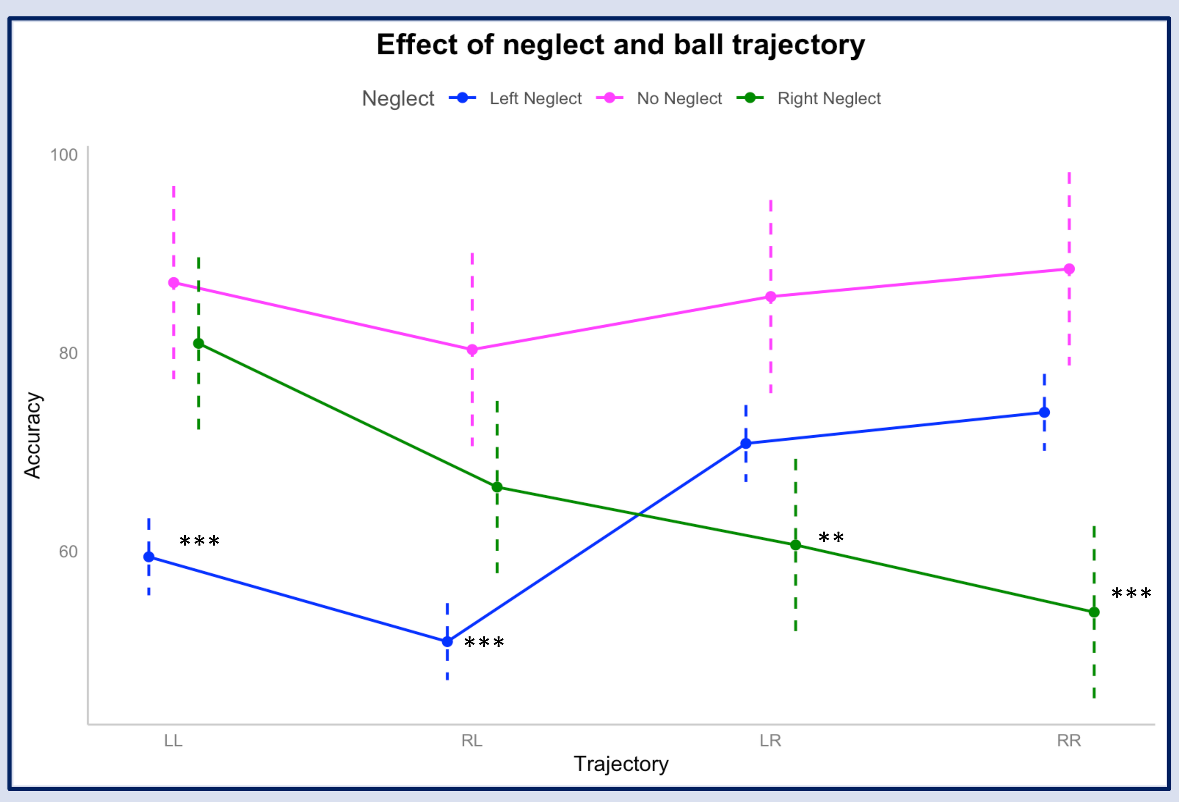


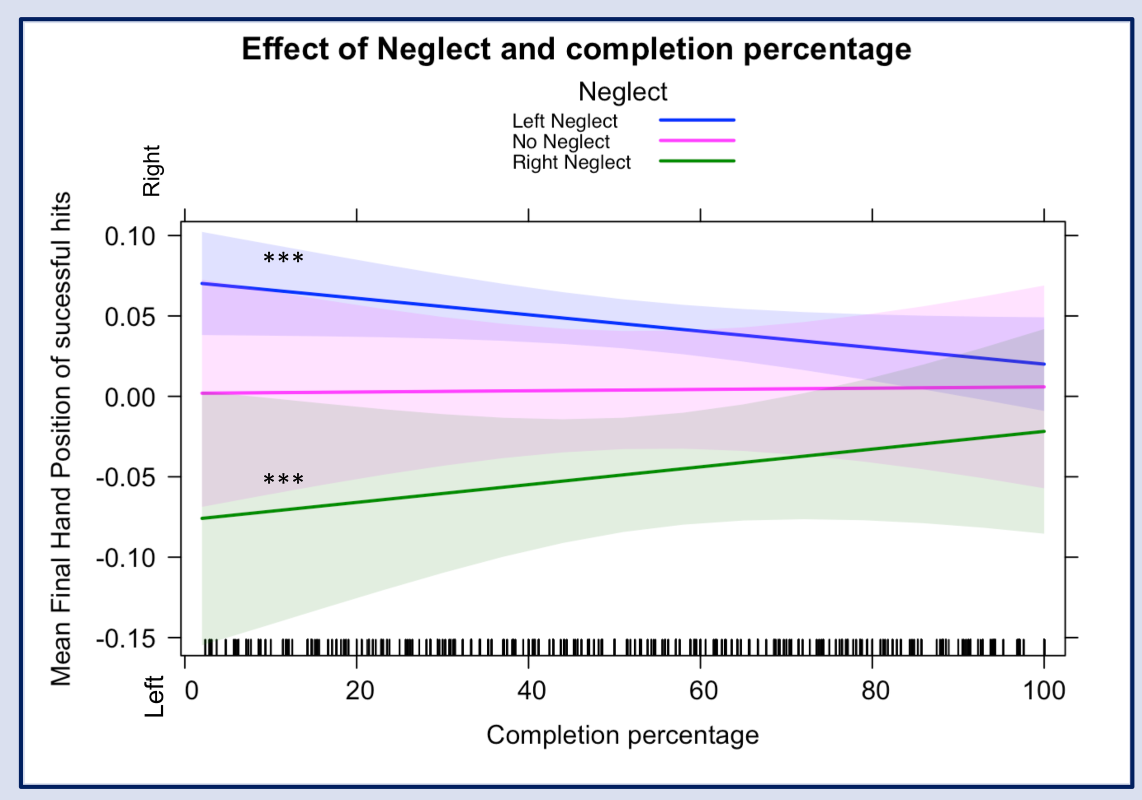
Results

1. *Statistical analysis : Linear mixed models*

P-values
*** < 0.001
** < 0.01







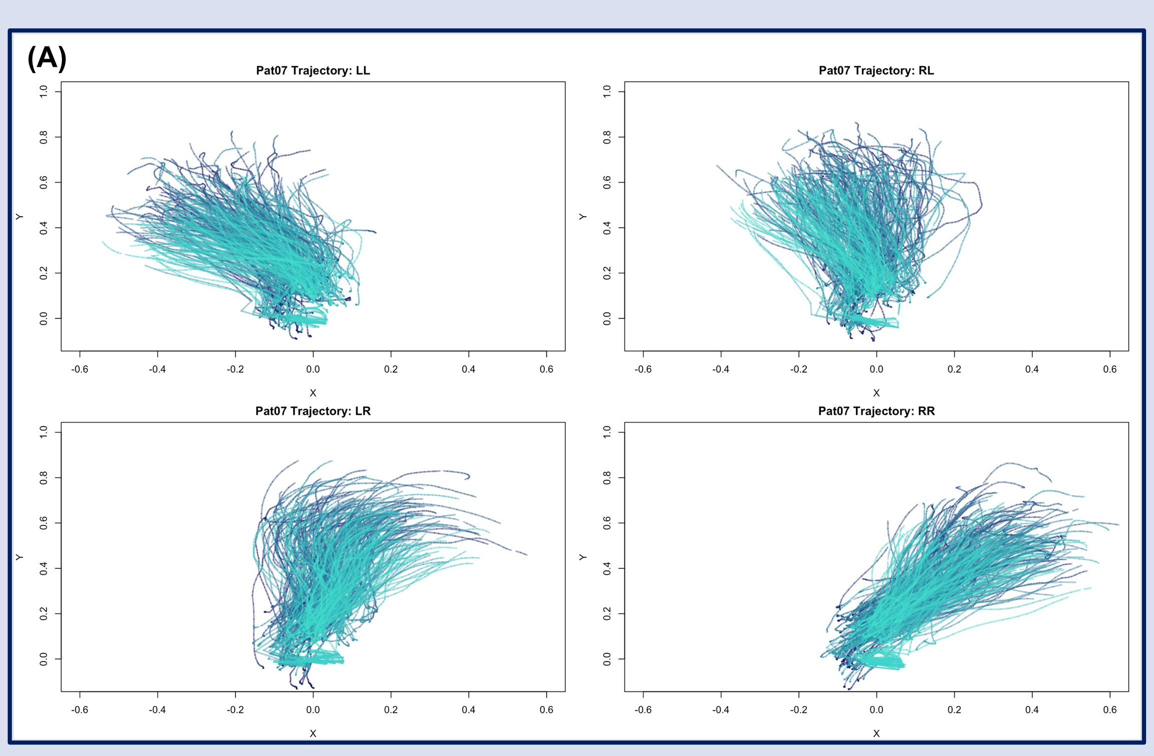
Accuracy significantly improves with **sessions** (A), is higher in **females** and patients **without** neglect (B), decreases with the **delay** between injury onset and training start (C), declines with **age** (D) and **tonic alertness deficits.**

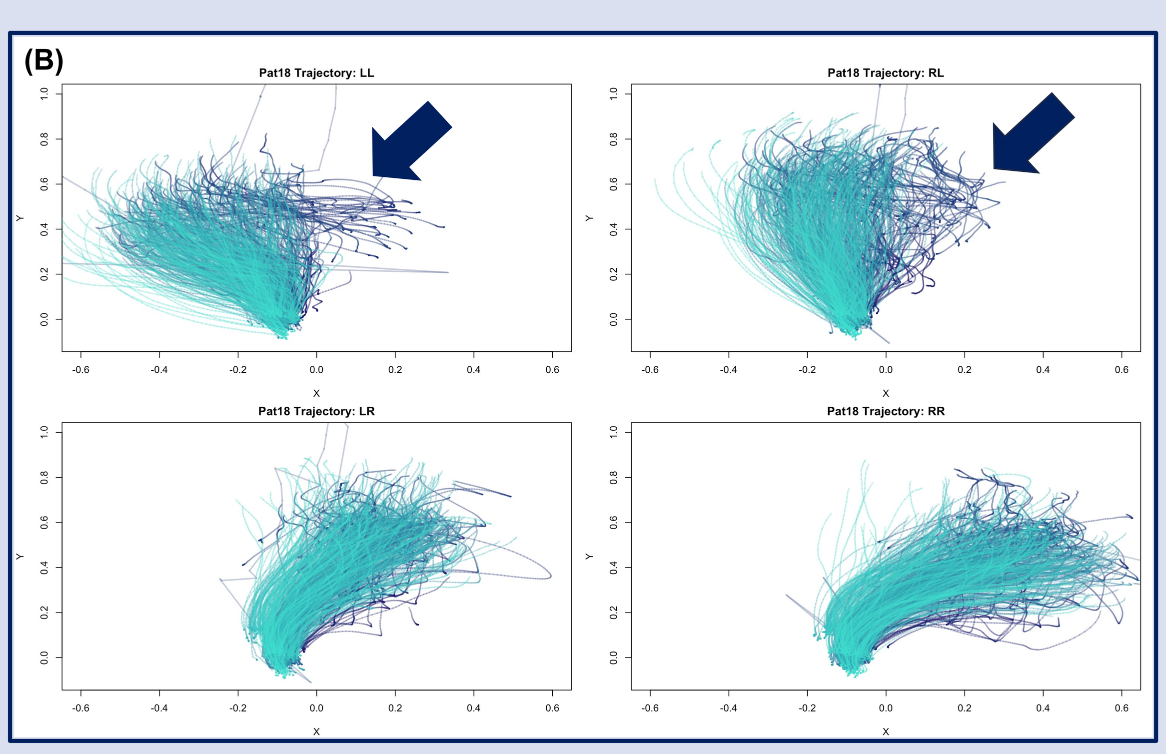
For the accuracy, there is a significant (***) **interaction** between **trajectories and neglect**. In post-hoc anova tests, compared to no neglect patients, patients with **left neglect** show significantly **lower accuracy** when trajectories end on the left (**LL, RL**), while those with **right** neglect demonstrate the **opposite pattern**.

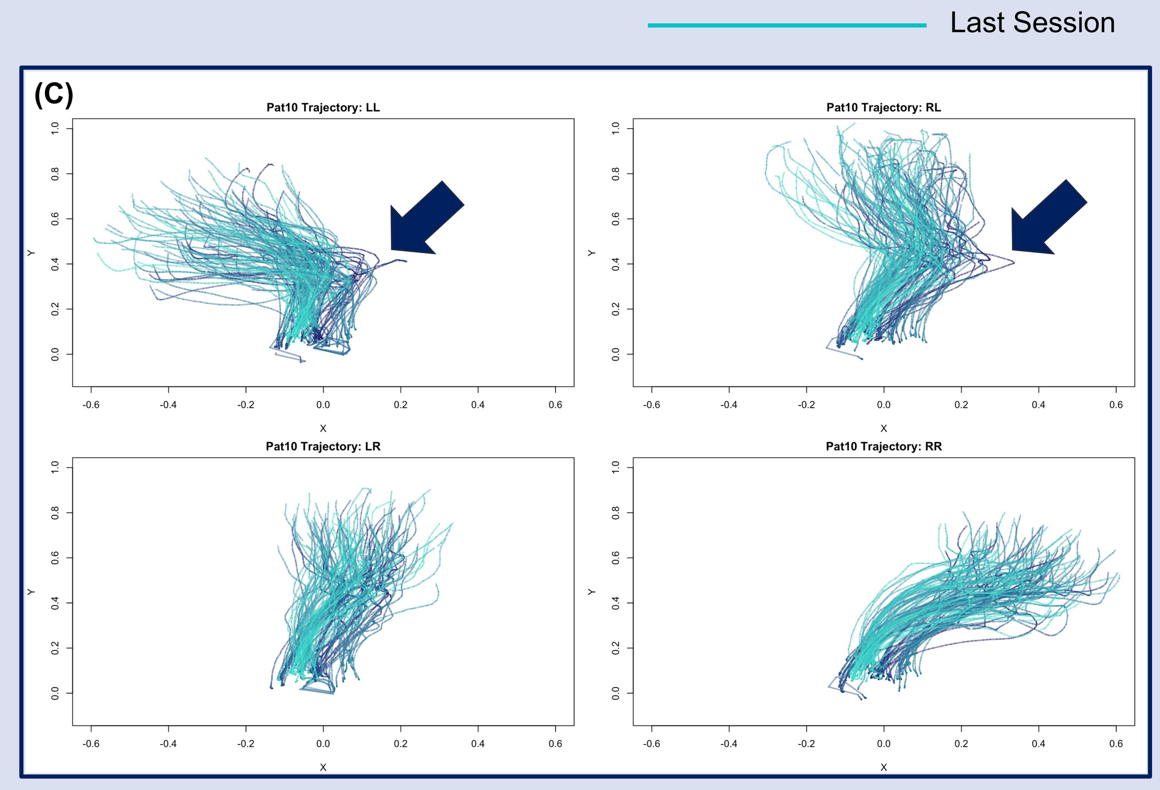
Compared to patients **without neglect**, those with left neglect significantly hit the ball more when their hand is on the right and vice-versa for right neglects. Across sessions, patients show a significant **improvement** in their **hand position.** (***)

2. *Visualization of the hand trajectories*

First Session
Last Session







Example of the hand trajectories of a patient without neglect for the 4 ball trajectories (A)

Examples of hand trajectories of two **left neglec**t patients (B and C): hand trajectories predominantly **lean to the right** when ball trajectories finish on the left side (**LL, RL**). Left movements are more challenging than right ones, especially during the **first sessions**. Those patients **improve** their movements **across sessions**, as their hands go further to the left for the last ones.

Conclusion

The new VR version of prism adaptation effectively trains unilateral deficits, leading to an improvement in terms of accuracy and hand trajectories across sessions. Among the tested predictors, younger age, female sex, no neglect, an early start of training after injury onset and less cognitive comorbidities appeared to be the key determinants for a successful outcome during this VR training.

References:
1. Maladies cardiovasculaires - OFSP. https://www.bfs.admin.ch/bfs/fr/home/statistiques/sante/etat-sante/maladies/cardiovasculaires.html, Statistiques sur les lésions cérébrales. https://www.fragile.ch/fr/informations-sur-les-lesions-cerebrales/faits-et-chiffres/
2. Terruzzi, S., Albini, F., Massetti, G., Etzi, R., Gallace, A., & Vallar, G. (2023, March 13). The Neuropsychological Assessment of Unilateral Spatial Neglect Through Computerized and Virtual Reality Tools: A Scoping Review.
Fig 1: https://www.sporkability.org/spork-exclusive/2016/10/4/half-of-your-world-is-invisible-hemispatial-neglect

Exploring attention recovery and cerebral modulation following a new Virtual-Reality training in patients with stroke

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INTRODUCTION

Frequent deficits observed after a stroke;

→ Neglect symptoms; unawareness of the neglect hemifield (Fig.1)

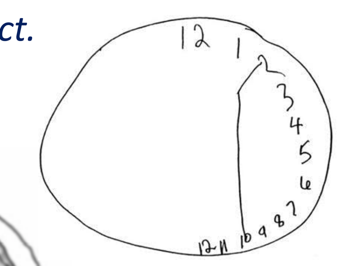
→ Other attentional deficits such as alertness, selective, or divided attention deficits

Virtual-Reality-based training through cognitive tasks in a virtual environment is a promising new therapy

→ To reduce attention deficits, including hemineglect symptoms

Recovery through cortical plasticity and reorganization; recruitment of additional neuronal networks (Fig.2)

Figure 1. Spatial neglect.



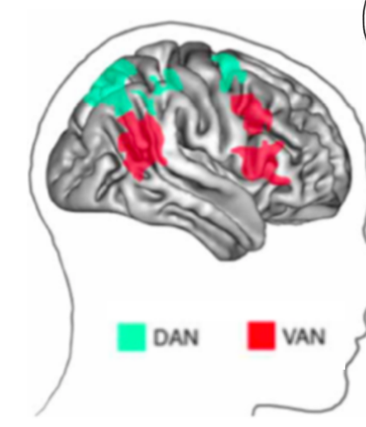


Figure 2. Attentional networks in the right hemisphere. Adapted from Bartolomeo et al. 2012.

AIMS

To investigate whether Virtual-Reality training on patients induces:

(1) Changes in the cerebral functioning and in the modulation of the attentional networks **(2)** Behavioral changes on attentional components

METHODS

Table 1. Demographic data of patients.

Inclusion criteria	ID	Age [years]	Sex	Side of lesion	Neglect[1]	ΔTAP neglect[2] [ms] Left Stimuli	Right Stimuli
• Attention or executive functions deficit • Age < 80 years • No major psychiatric disorders or contraindications for MRI • Standard multidisciplinary rehabilitation during their hospitalization	1	74	M	Right	Left	-37	499
	2	79	M	Bilat	Left	397	55
	3	46	M	Right	Left	280	14
	4	46	M	Right	Left	119	40
	5	48	F	Right	Left	364	221
	6	56	M	Right	Left	370	519

[1]According to clinical diagnosis [2]Difference Pre-Post for the median reaction times in the TAP neglect (Test of Attentional Performances)

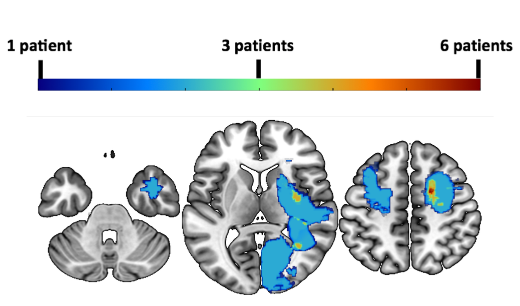


Figure 3. The overlap of patients' lesions. The overlap is maximal in the right subcortical and cortical portions of the temporal and parietal regions.

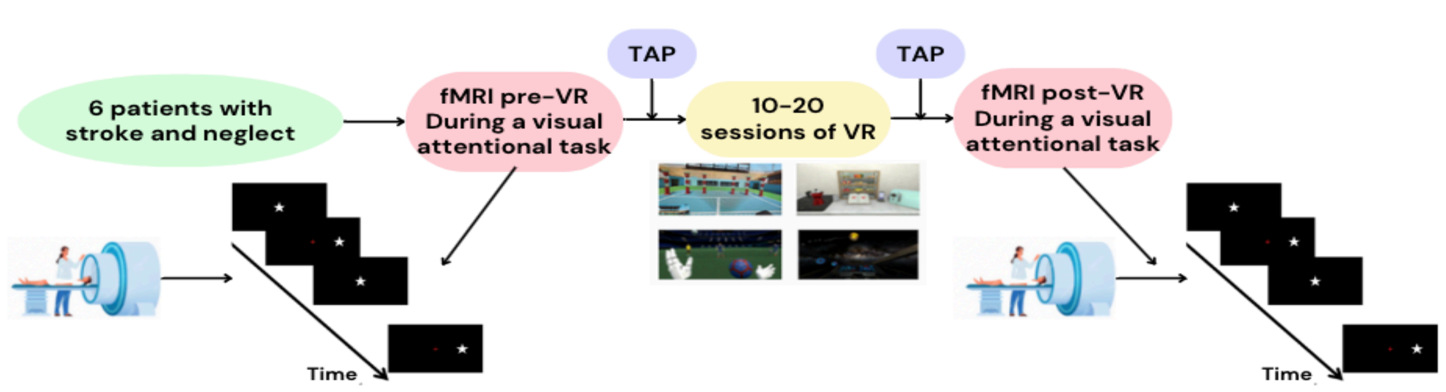


Figure 4. Experimental design of the study. VR = Virtual-Reality.

RESULTS

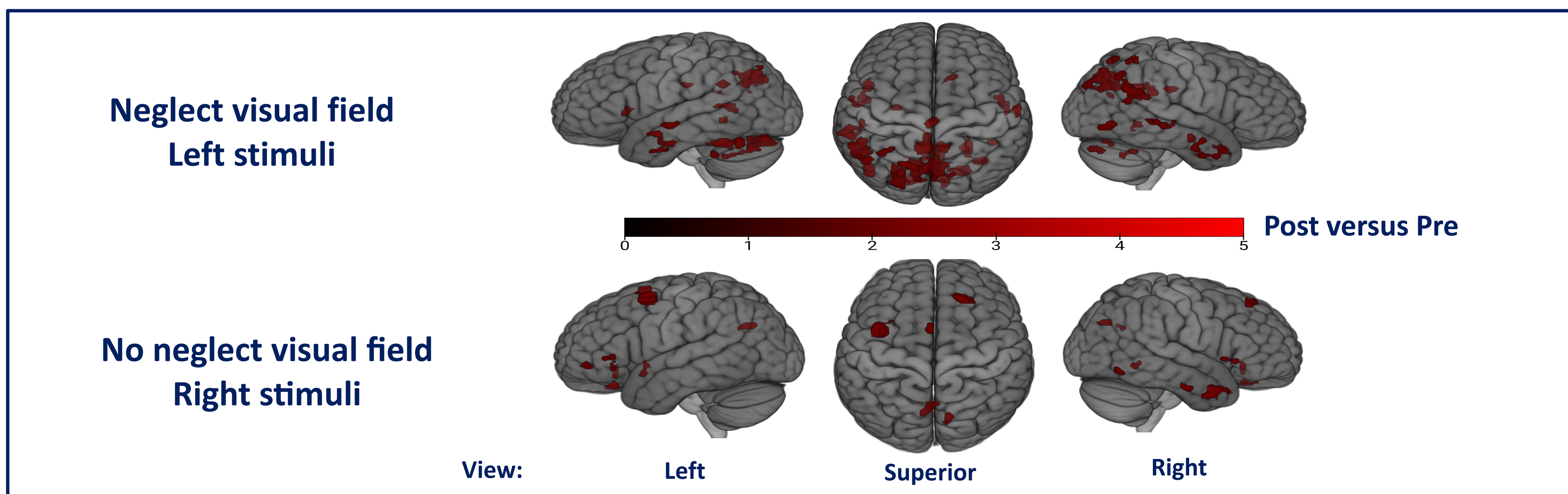


Figure 5. Differences of activation between Pre- and Post-VR training. Threshold at p < 0.01, cluster extent k > 23. Pre-Post comparison didn't lead to any significant activation. Post-Pre comparison did lead to significant activation.

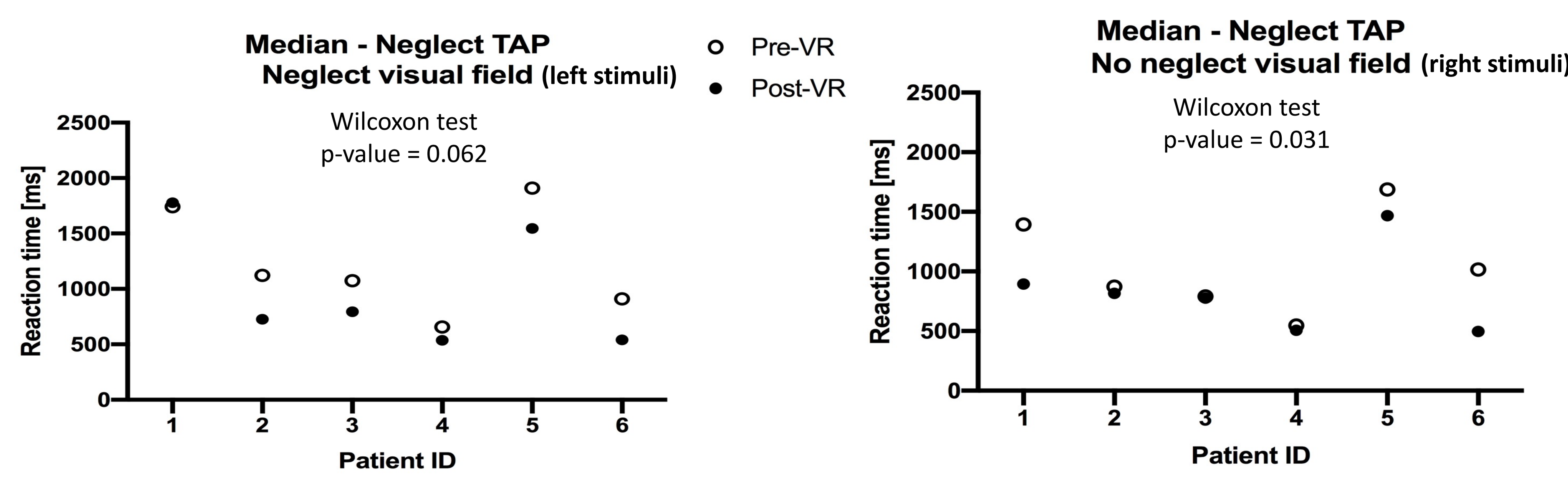


Figure 6. Differences between Pre- and Post-VR training for the median reaction times in the TAP neglect.

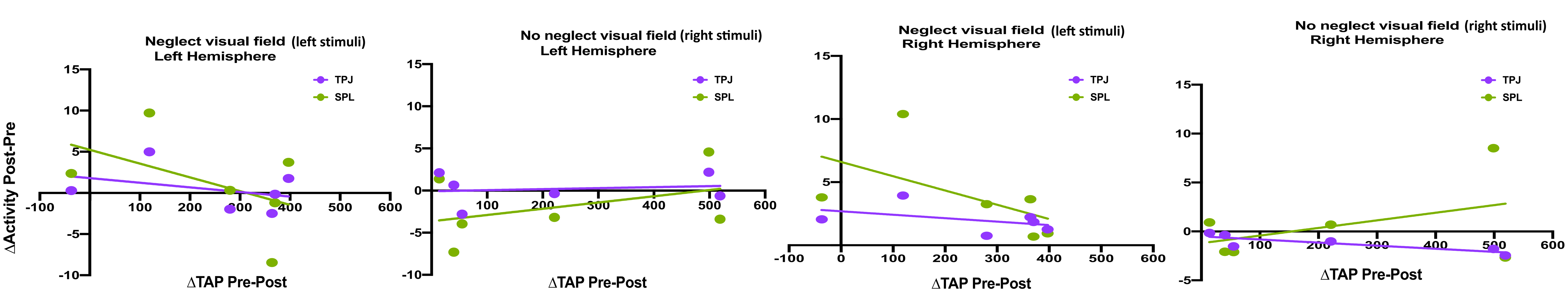


Figure 7. Correlations between the differences of activation Post-Pre and the differences of median reaction times Pre-Post in the TAP neglect. TPJ = temporoparietal junction (VAN) ; SPL = superior parietal lobule (DAN). For the left stimuli (neglected space), greater improvement in attention processing <-> lower recruitment of the left- and right-sided VAN (TPJ) and DAN (SPL). For the right stimuli (not neglected space), greater improvement in attention processing <-> greater recruitment of the left- and right-sided VAN and DAN (except for the right-sided VAN, for which greater improvement involves lower recruitment).

CONCLUSION

Brain modulations (1): increased cerebral activity after VR training (Fig.5) , especially for left (neglected) visual stimuli.

→ Modulations and rebalancing of activation between the attentional networks in both hemispheres.

Behavioral changes (2): in the standardized test (Fig. 6), nearly significant improvements of attention for the left visual space (neglected space) and significant improvements for the right visual space.

→ Limitation: too few patients?

Correlation (1) and (2): the improvement in attention processing (neglect) observed after VR training is linked to reduced VAN and DAN recruitment (Fig.7).

→ Optimization and increased efficacy of the attentional networks after our VR program.