Cortical reorganization and clinical outcomes after stroke: a longitudinal TMS/EEG evaluation

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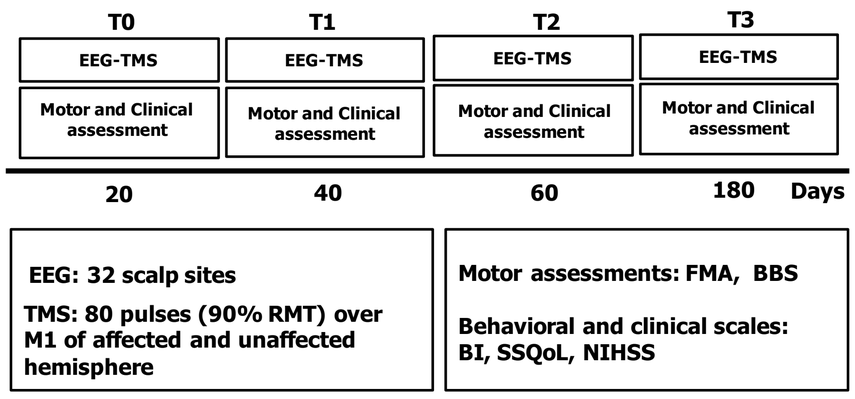
Introduction

Since early days after stroke, the brain undergoes a complex reorganization to allow compensatory mechanisms that promote functional recovery. Characterizing specific neurophysiological markers of motor recovery after stroke could improve clinical decision making. In this study we have tracked the time-course of motor cortical reorganization in a stroke patients group.

Experimental timeline



Methods

10 patients in the sub-acute phase of ischemic subcortical stroke were evaluated within 20 days (t0) and after 40 (t1), 60 (t2) and 180 (t3) days after stroke. 10 healthy age-matched volunteers were used as control group. For each time-point, cortical reactivity (in terms of local mean field power) and cortical oscillatory activity (in term of event related spectral perturbations) measures, evoked by 80 single TMS pulses over the motor cortex, were assessed for the affected (AH) and unaffected (UH) hemisphere, combining TMS-EEG. These measurements were paralleled with motor and clinical evaluations. Repeated measures ANOVA and Friedman test were used to evaluate changes over time of all measures.

Patient No.	Age (years)	Gender	Affected Hemisphere	Infarct site	AH RMT	UH RMT	NIHSS	Symptoms
1	71	M	L	Internal capsule	N	90	0	mild hemiparesis
2	71	M	R	Internal capsule	44	50	2	mild hemiparesis, facial palsy
3	69	M	L	Internal capsule	83	75	5	mild hemiparesis, aphasia
4	52	M	R	Corona radiata	N	66	6	hemiparesis, facial palsy
5	78	F	R	Lenticular nucleus	52	50	2	mild hemiparesis
6	68	M	R	Superior capsule	N	68	9	hemiplegia, facial palsy
7	46	M	L	Internal capsule	N	52	4	severe hemiparesis, dysarthria
8	42	M	L	Internal capsule	N	57	8	hemiplegia, facial palsy
9	56	M	L	Internal capsule	82	89	7	mild hemiparesis,
10	50	F	R	Internal capsule	N	67	10	hemiplegia, facial palsy

Data analysis

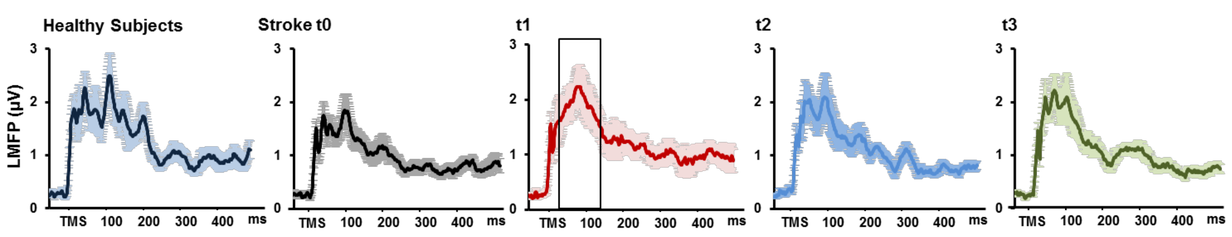
Cortical reactivity: Local mean field power (LMFP) of a ROI close to stimulated M1 of AH and UH was calculated. For each Time, LMFP of mean TMS-evoked potentials was obtained for three temporal windows: 0-50, 50-100, and 100-150 msec. Repeated measure ANOVA with factors Hemisphere (AH vs UH), Time (t0, t1, t2, t3) and temporal window (0-50, 50-100 and 100-150 ms) was performed.

Oscillatory evoked activity: Time-frequency responses evoked by TMS, for each hemisphere, were computed by means of a complex Morlet wavelet transform (2-40 Hz, 38 frequency steps, *c* 3.5). The power in the frequency ranges between 2-4 Hz (delta), 4-7 Hz (theta), 8-12 Hz (alpha) and 13-30 Hz (beta) was extracted. Evoked activity in each time point and hemisphere was compared by means of separated ANOVAs with factors Time (t0, t1, t2, t3) and Hemisphere (AH vs UH), separately for each frequency band.

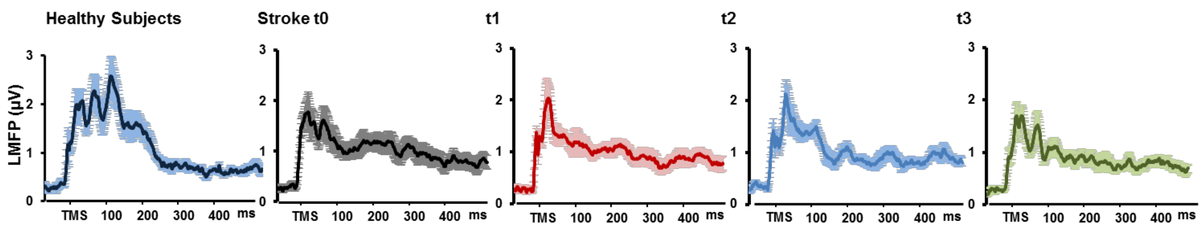
Behavioural and clinical evaluation: For each session, sensory-motor and balance functions were evaluated by assessing performance in: Fugl-Meyer Assessment scale (FMA) and Berg Balance Scale (BBS). To evaluate the ability in daily living, quality of life and more global aspects of clinical recovery, Barthel Index (BI), Specific Stroke Quality of Life scale (SSQoL) and National Institutes of Health Stroke Scale (NIHSS) were used.

Cortical reactivity

Affected Hemisphere



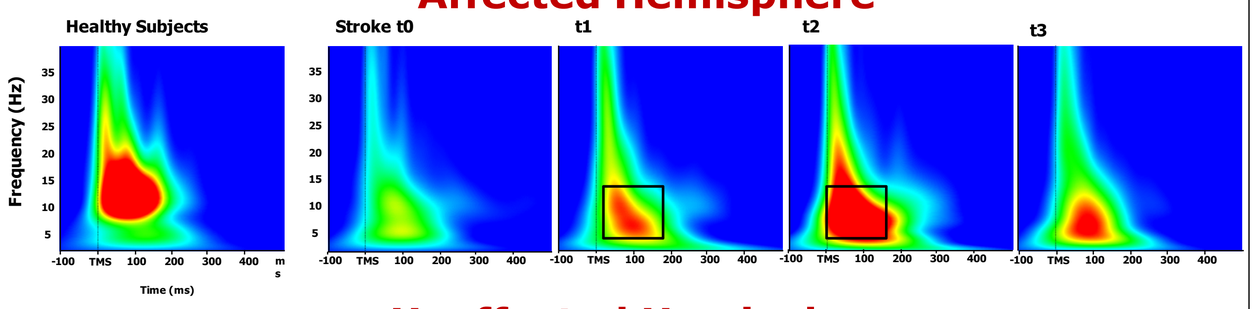
Unaffected Hemisphere



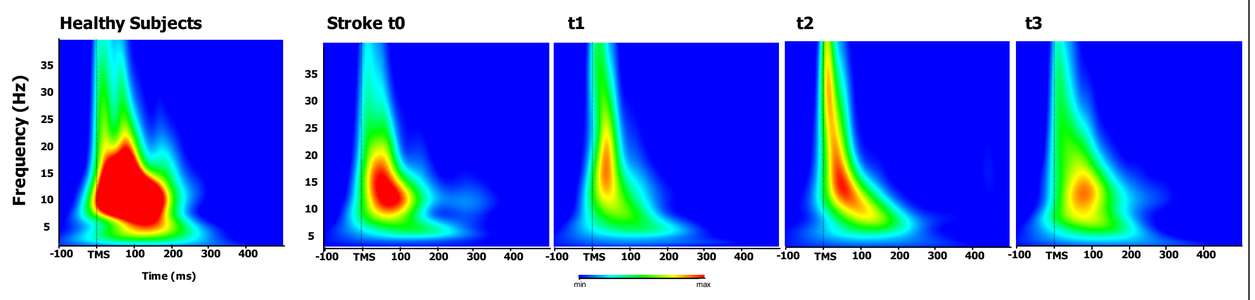
Significant interaction of Time x Hemisphere x Temporal window ($p<0.05$), due to a cortical reactivity increase in the temporal window 50-100 ms, 40 days after the stroke onset, in AH respect to other Times and respect to all Times of UH (all $p<0.05$).

Oscillatory evoked activity

Affected Hemisphere



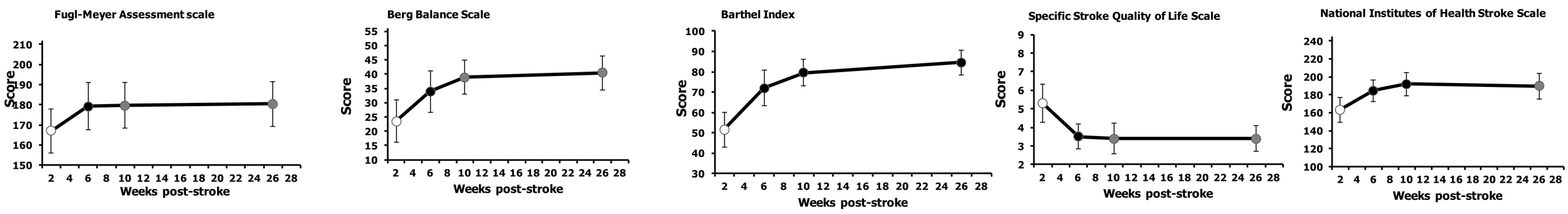
Unaffected Hemisphere



Significant interaction of Time x Hemisphere, when testing for alpha band modulation ($p<0.01$). Higher values of alpha-evoked activity (all $p<0.05$) both in t1 on AH respect to UH and in t2 respect to all times of evaluation of AH and UH. The control group was characterized by a significant increase of alpha activity in AH and UH compared to stroke group at baseline evaluation.

Motor Assessment

Clinical Scales



Significant effect of Time both in the motor and clinical scales (all $p<0.05$). Significant improvements of all Times respect to t0. The vast bulk of recovery was observed in the first 40 days with some additional improvements in the following months. Grey circle indicates a significant difference compared to t0; black circle indicate significant differences respect to t0 and previous times.

Conclusions

This study tracks longitudinally the motor cortical changes following stroke, highlighting a significant increase in evoked alpha oscillations and specific timing-related modulations of cortical reactivity that occurred between 40-60 days after stroke, over the affected hemisphere. These changes are accompanied by the amelioration of clinical and behavioural outcomes. Alpha-evoked oscillations could be considered a good biomarker of motor functional recovery. Our findings provide new insights into how and when neuromodulatory interventions could drive neuroplasticity in a functional direction.

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