Action-related dynamic changes in inferior frontal cortex effective connectivity: a TMS/EEG coregistration study

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Table S1

		Rest		Move	
		Active	Sham	Active	Sham
APB	IFC	0.05 ± 0.05	-0.14 ± 0.05	64.13 ± 11.60	63.96 ± 12.42
	STS	0.28 ± 0.26	0.36 ± 0.33	75.79 ± 8.49	77.18 ± 9.65
FDI	IFC	-0.03 ± 0.09	-0.14 ± 0.09	122.42 ± 24.48	125.10 ± 27.16
	STS	0.85 ± 0.80	0.90 ± 0.87	110.05 ± 12.26	115.56 ± 14.48
ADM	IFC	-0.08 ± 0.07	-0.23 ± 0.07	79.15 ± 13.93	84.07 ± 15.87
	STS	0.35 ± 0.25	0.64 ± 0.64	131.59 ± 18.15	127.76 ± 20.36

Table S1. *Baseline-corrected RMS of EMG activity (± SE; in µV) recorded from the three muscles across the different stimulation (active and sham TMS) and task (Rest, Move) conditions.*

Table S2

		Thumb		Index		Little finger	
		Active	Sham	Active	Sham	Active	Sham
APB	IFC	64.13 ± 11.60	63.96 ± 12.42	32.95 ± 5.55	35.11 ± 6.29	6.49 ± 1.75	7.39 ± 1.42
	STS	75.79 ± 8.49	77.17 ± 9.65	56.99 ± 8.06	58.16 ± 8.29	12.65 ± 3.32	10.10 ± 2.55
FDI	IFC	7.11 ± 2.63	11.79 ± 3.17	122.42 ± 24.48	125.10 ± 27.16	7.09 ± 1.25	8.14 ± 1.34
	STS	19.31 ± 3.05	18.13 ± 3.33	110.05 ± 12.26	115.56 ± 14.48	17.20 ± 4.49	14.44 ± 2.78
ADM	IFC	4.44 ± 0.98	5.06 ± 1.73	15.43 ± 3.42	16.05 ± 3.89	79.15 ± 13.39	84.07 ± 15.87
	STS	9.83 ± 1.55	8.29 ± 1.26	23.04 ± 3.92	21.91 ± 3.85	131.59 ± 18.15	127.76 ± 20.36

Table S2. *Baseline-corrected RMS of EMG activity (± SE; in µV) recorded from the three muscles across the different stimulation conditions (active and sham TMS) and finger movements (abduction/adduction of the thumb, index and little finger).*

Table S3

ROI_{int1}	k	Hem	Structure	BA	x	y	z	*t*-value
1	26	R	Anterior Cingulate	24	5	25	17	3.69
			Anterior Cingulate	32	10	25	22	2.62
2	18	L	Middle Frontal Gyrus	6	-20	17	54	4.55
			Superior Frontal Gyrus	6	-20	18	59	4.35
			Cingulate Gyrus	6	-20	7	46	2.39
			Medial Frontal Gyrus	6	-15	12	45	2.30
			Superior Frontal Gyrus	8	-20	17	45	2.24
3	19	R	Middle Frontal Gyrus	6	30	-8	42	2.59
			Precentral Gyrus	6	35	-12	47	2.37
			Precentral Gyrus	4	40	-12	47	2.27
4	14	R	Insula	13	35	10	13	3.62
5	11	L	Inferior Occipital Gyrus	18	-35	-83	-4	-2.56
			Middle Occipital Gyrus	18	-35	-83	0	-2.51
			Inferior Occipital Gyrus	19	-35	-78	-5	-2.48
			Middle Occipital Gyrus	19	-40	-77	8	-2.25
6	21	R	Middle Frontal Gyrus	11	30	38	-19	-2.67
			Inferior Frontal Gyrus	47	25	33	-10	-2.54
			Inferior Frontal Gyrus	11	25	33	-18	-2.51
			Orbital Gyrus	11	20	38	-23	-2.33
			Superior Frontal Gyrus	11	25	43	-15	-2.21
7	41	L	Middle Temporal Gyrus	21	-40	8	-34	-2.80
			Middle Temporal Gyrus	38	-35	3	-38	-2.76
			Superior Temporal Gyrus	38	-35	8	-34	-2.76
			Uncus	38	-25	3	-38	-2.60
			Inferior Temporal Gyrus	20	-35	-2	-38	-2.50
			Uncus	20	-25	-2	-38	-2.48
			Uncus	28	-20	3	-30	-2.38
			Uncus	36	-20	-2	-34	-2.33
8	33	R	Cuneus	19	20	-86	37	2.96
			Precuneus	19	20	-81	41	2.95
			Precuneus	7	25	-76	41	2.36
			Superior Parietal Lobule	7	30	-75	45	2.35
			Inferior Parietal Lobule	39	40	-66	40	2.23
9	42	R	Superior Parietal Lobule	7	20	-55	58	2.83
			Precuneus	7	20	-56	53	2.76
			Inferior Parietal Lobule	40	40	-41	48	2.46
			Postcentral Gyrus	5	40	-46	58	2.43
			Postcentral Gyrus	2	40	-36	57	2.29
			Postcentral Gyrus	3	40	-31	61	2.25
			Postcentral Gyrus	40	40	-31	57	2.25

Table S3. *Anatomical locations of local maxima for the ROIs underpinning task-related IFC-TEP differences in the first interval (Int1: 56-67 ms). Representative voxels are labeled according to the Automated Anatomical Labeling (AAL) template (Tzourio-Mazoyer et al., 2002).Talairach coordinates are reported, with proper correction from MNI space (Brett et al., 2002).*

Table S4

ROI$_{int2}$	k	Hem	Structure	BA	x	y	z	*t*-value
1	96		Rectal Gyrus	11	-5	13	-22	2.71
			Medial Frontal Gyrus	25	-5	9	-17	2.64
			Anterior Cingulate	25	5	9	-9	2.55
			Medial Frontal Gyrus	11	10	24	-14	2.53
			Anterior Cingulate	32	5	19	-9	2.48
			Inferior Frontal Gyrus	47	15	28	-18	2.46
			Inferior Frontal Gyrus	11	15	28	-22	2.37
			Orbital Gyrus	47	15	23	-22	2.35
			Subcallosal Gyrus	11	-10	24	-14	2.35
			Uncus	34	-15	4	-21	2.32
2	45		Cuneus	19	-20	-91	28	2.79
			Cuneus	18	-15	-81	27	2.29
			Cuneus	19	20	-86	37	3.41
			Cuneus	18	15	-81	27	3.18
			Cuneus	7	20	-76	31	2.40
			Cuneus	17	5	-77	13	2.28
			Precuneus	19	20	-81	36	2.88
			Precuneus	7	15	-76	36	2.66
			Precuneus	31	10	-72	27	2.32
3	15	R	Superior Temporal Gyrus	22	64	-43	21	3.75
			Inferior Parietal Lobule	40	59	-43	21	3.69
			Supramarginal Gyrus	40	59	-48	21	3.39
			Superior Temporal Gyrus	13	54	-43	21	2.91
			Superior Temporal Gyrus	39	54	-53	12	2.57

Table S4. *Anatomical locations of local maxima for the ROIs underpinning task-related TEP differences in the second interval (Int2: 77 - 86 ms). See Table S3 caption for notes.*

Supplementary results

Group differences in task-related changes in the first interval (56-67)

The main text reports that we observed similar modulations in a time window around 60 ms in both experiments (see Figures 3 and 4 for the main experiment, interval 1, and Figure 8 for the control experiment). In order to check whether task-related IFC-TEP changes observed in the first significant interval (56-67 ms; Figure 4) were specific to IFC stimulation, we provided a further analysis in which we directly compared the IFC-TEPs with the data from the control experiment. Specifically, we considered the three regions of electrodes showing significant modulations in the main experiment and extracted the mean EEG signal from the same electrodes using data from the control experiment. Then, we performed a Group (IFC and STS) x Stimulation (active and sham) x Region (frontal, left and right temporo-parietal) x Condition (Move and Rest) ANOVA on the mean EEG signal.

The analysis showed a series of main effects and interactions, including a significant 4-way interaction ($F_{2,44} = 5.60$, $p = 0.007$), indicating different task-dependent TMS effects across regions in the two groups (Figure S1). To further test this interaction, post-hoc pairwise comparisons were computed to compare Move and Rest conditions across groups, stimulations and regions. TEPs induced by active stimulation of the IFC were larger (more negative) in the Move condition relative to the Rest condition over the frontal region ($p < 0.001$). Larger (more positive) TEPs were also detected in the Move condition relative to the Rest condition over right temporo-parietal electrodes ($p = 0.012$), whereas TEPs were smaller in the Move condition relative to the Rest condition over the left temporo-parietal region ($p = 0.004$). In contrast to IFC-TEPs, TEPs induced by active stimulation of STS did not show differences between conditions over the frontal ($p = 0.28$) and left temporo-parietal ($p = 0.99$) regions, and showed a non-significant trend for larger amplitudes in the Move condition relative to the Rest condition ($p = 0.078$) in the right temporo-parietal region. No differences between conditions were found for TEPs induced by sham stimulation (IFC-TEPs: all $p > 0.60$; STS-TEPs: all $p > 0.39$). These findings suggest that action-related modulations of frontal and left temporo-parietal TEPs were specific to the stimulation of the IFC site and were not consistently observed following stimulation of the STS site.

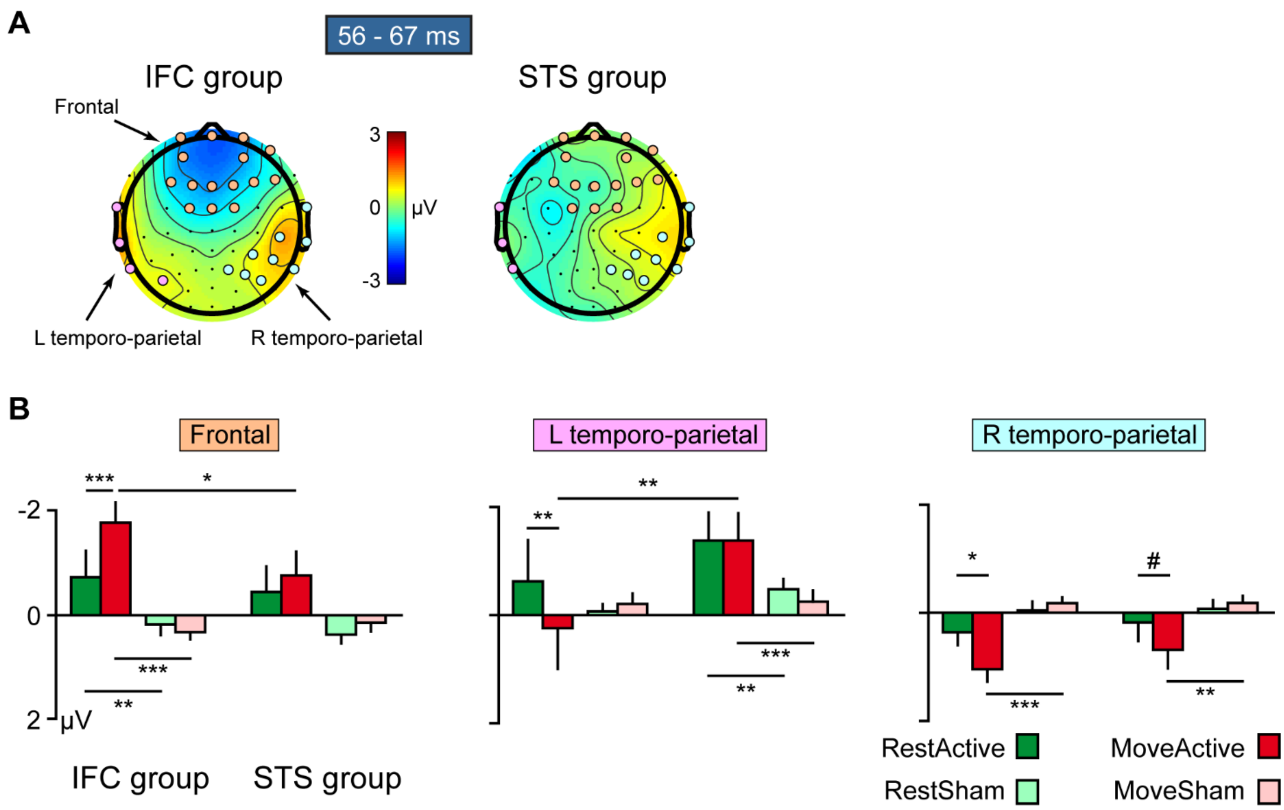

***Figure S1. Task-dependent changes in IFC-TEPs and STS-TEPs in the 56-67 ms interval**. A) Scalp maps for the Stimulation x Condition interaction (contrast: [MoveActive - MoveSham] - [RestActive - RestSham]) are depicted for the two groups (IFC and STS) separately. The three electrode sets considered for the analyses are highlighted in different colors. B) Bar plots represent mean values by region, stimulation, and condition. Hash marks and asterisks indicate marginally significant and significant comparisons, respectively: # = $p < 0.08$; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$. In addition to the Move vs. Rest comparisons reported in the text, further post-hoc comparisons are shown. Error bars represent SE.*

Using the same logic, we extracted sLORETA estimates from the nine ROIs identified in the main experiment for the first interval (56-67 ms; Figure 5) using data from the control experiment. Figure S2 depicts mean sham-corrected sLORETA estimates for the two groups, computed in the nine ROIs. Except for the right ventral prefrontal ROI (ROI6), no significant differences between Move and Rest conditions were observed in the control group.

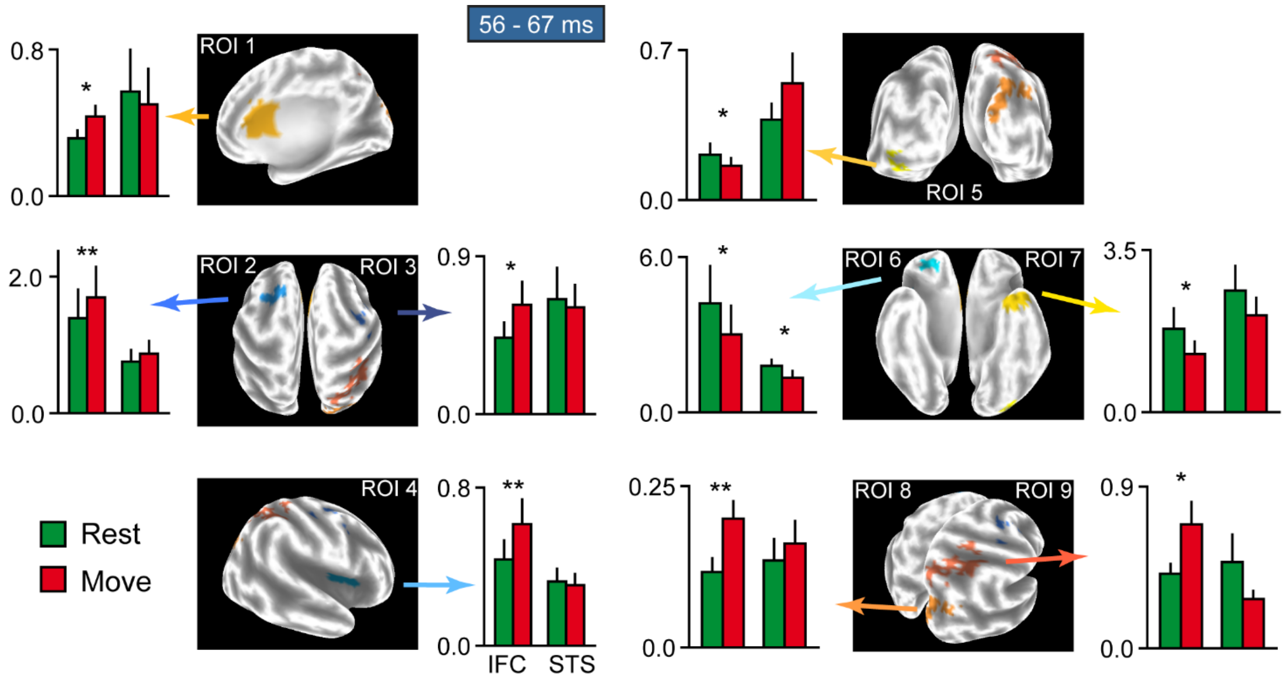

Figure S2. Task-related changes in current source estimates in the 56-67 ms interval*. Mean activities for Rest and Move conditions were extracted from selected ROIs, at 56-67 ms. The ROIs are shown in different colors and overlaid on a three-dimensional model of a standard brain. Bar plots depicts mean values for each ROI for the two experimental conditions and groups. Significant differences between conditions are reported as follows: * = p < 0.05; ** = p < 0.01. Error bars represent SE.*

Supplementary references

S1. Brett, M., Johnsrude, I.S., Owen, A.M., 2002. The problem of functional localization in the human brain. Nat Rev Neurosci 3, 243-249.

S2. Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage 15, 273-289.