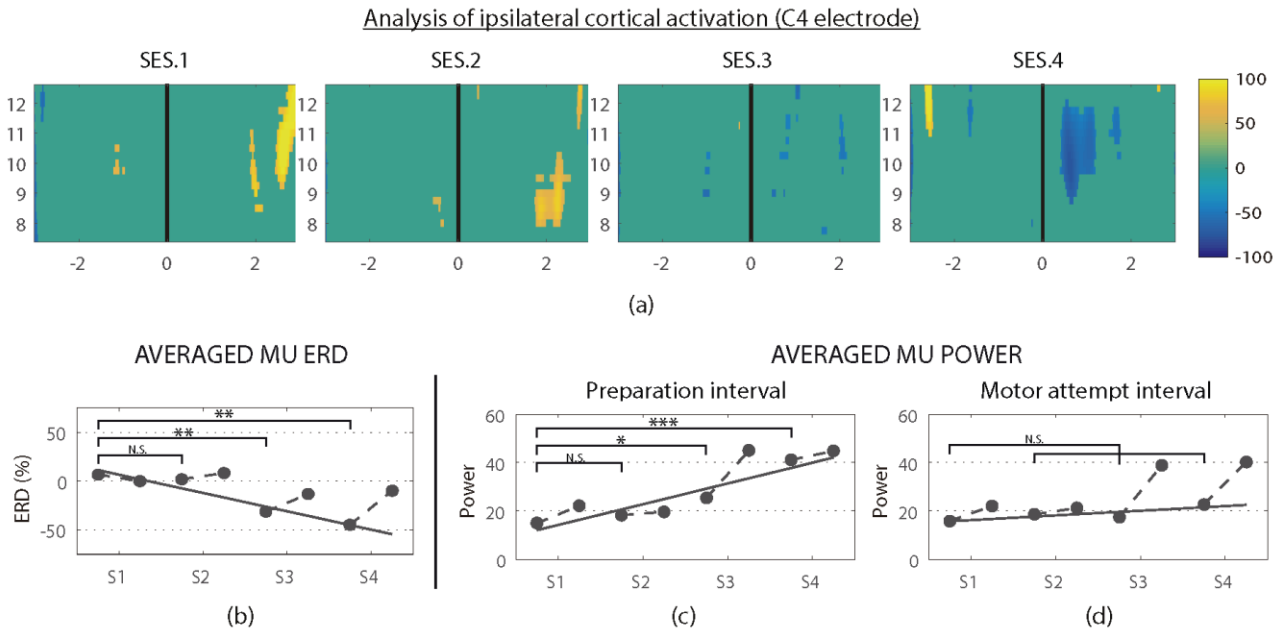
Reactivating the dormant motor cortex after spinal cord injury with EEG-neurofeedback: a case study with a chronic, complete C4 patient

Supplementary Material

Analysis of ipsilateral motor cortical activation

In order to measure the effects of the NF intervention on ipsilateral motor cortical activation, we repeated the analyses described in the "**Effects of the intervention on motor cortical activation**" section but considering the activity of C4 electrode. We performed the same statistical analyses as for C3.

Supplementary Figure 1a depicts the evolution of the ERD maps in C4 electrode. Similarly to what happened in C3, the enhancement of ipsilateral ERD over sessions was also significant ($r_{86} = -0.48$, $p < 0.001$; Supplementary Figure 1b). The post-hoc comparisons between sessions revealed a significant mu ERD enhancement in sessions 3 and 4 with respect to session 1 (Supplementary Figure 1b and Supplementary Tables 5 and 6). Regarding the analysis of absolute mu power (Supplementary Figure 1c), it was significantly enhanced across sessions in the preparation interval ($r_{86} = 0.50$, $p < 0.001$), with significant power increases in sessions 3 and 4 with respect to session 1 (Supplementary Figure 1c and Supplementary Tables 5 and 6). For the motor-attempt interval, there were no significant changes across sessions in absolute mu power (Supplementary Figure 1d).



Supplementary Figure 1. Analysis of ipsilesional cortical activation (C4 electrode). (a) Significant time-frequency ERD maps of C4 electrode, reflecting the motor cortical activation during the motor-attempt screenings performed at the beginning of each session. These maps represent the average ipsilateral cortical activation of the patient when he attempted to move his paralyzed right hand. Maps cover the entire alpha ([7.5-12.5] Hz) frequency range in the [-3, 3] s time interval (i.e., preparation + motor attempt). Time-frequency pairs that did not reach statistical significance in the bootstrap resampling procedure were assigned a value of 0. Bottom part of the figure: (b) evolution of the mu ERD; (c) evolution of the mu absolute power during the preparation interval (i.e., resting baseline); (d) evolution of the mu absolute power during the motor attempt interval. The solid black lines represent the inter-session trend of the pre- screenings of each variable (computed as the trend followed by the data of the pre- screenings). The results of the post-hoc pairwise comparisons for each variable between the pre- screenings of session 1 and sessions 2, 3 and 4 are also depicted. N.S.: $p > 0.05$; *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$.

Detailed quantification of the effects on tonic EEG

Supplementary Table 1 shows the power values of the pre- screenings for eyes-closed resting-state activity and for the eyes-open sustained-attention task. Supplementary Table 2 provides the detailed results of the statistical analysis, comparing the data of session 1 with sessions 2, 3 and 4. This analysis is performed in terms of the percentage of change in upper-alpha power, the effect size (measured as a variation of Cohen's d statistic[1] as calculated by Busk and Serlin[2]), and the paired statistical comparisons between the power values.

	Session 1	**Session 2**	**Session 3**	**Session 4**
Resting state (eyes-closed)	8.10	19.70	21.37	21.03
Task-related activity	4.79	6.20	8.37	12.39

Supplementary Table 1. Upper-alpha power values in the motor-unrelated EEG pre-screenings (averaged over the feedback electrodes: C3, Cz, C4, CP3, CPz, CP4). Power values are given in μV/Hz.

	% Increase	**Effect Size**	**t-stat**	**p-value***
Resting state				
Session 1 vs 2	143.3%	1.607	t(175)=-6.98	< 0.001
Session 1 vs 3	163.9%	1.838	t(282)=-9.93	< 0.001
Session 1 vs 4	159.7%	1.791	t(194)=-7.14	< 0.001
Task-related activity				
Session 1 vs 2	29.4%	0.195	t(92)=-0.526	1
Session 1 vs 3	74.8%	0.496	t(126)=-2.27	0.025
Session 1 vs 4	158.8%	1.053	t(122)=-4.71	< 0.001

Supplementary Table 2. Statistical analyses measuring the effects of the intervention on tonic EEG (upper-alpha power averaged over the feedback electrodes: C3, Cz, C4, CP3, CPz, CP4) measured in resting state and task-related activity. **% Increase** and **Effect Size** represent the change in sessions 2, 3 or 4 with respect to session 1. The **t-statistic** and the **p-value** of the t-test are also reported. *Notice that the reported p-values were corrected with a Bonferroni-equivalent procedure (i.e., the reported p-values are the result of multiplying the original p-value times the number of comparisons: 6). Therefore, statistical significance is considered when the reported p-values are lower than 0.05.

Detailed quantification of the effects on motor cortical activation

Contralateral motor cortical activation (C3 electrode)

Supplementary Table 3 shows the values of ERD and absolute mu power over the contralateral hemisphere (C3 electrode) during the preparation interval and the movement attempt interval. Supplementary Table 4 provides the detailed results of the statistical analysis, comparing the data of session 1 with sessions 2, 3 and 4. This analysis is performed in terms of the percentage of change in ERD/mu power, the effect size (measured as a variation of Cohen's d statistic[1] as calculated by Busk and Serlin[2]), and the paired statistical comparisons.

	Session 1	**Session 2**	**Session 3**	**Session 4**
Mu ERD	4.60	0.42	-30.17	-50.69
Mu power: preparation interval	8.93	11.84	16.98	23.04
Mu power: motor attempt interval	9.34	11.89	11.85	11.36

Supplementary Table 3. ERD and mu power values of C3 electrode (i.e., contralateral activity) in the pre- motor task. ERD values are given in percentage (ERD/ERS formula according to Pfurtscheller and Lopes da Silva[3]), and power values are given in µV/Hz.

	% Increase	**Effect Size**	**t-stat**	**p-value**
ERD				

Session 1 vs 2	-90.8%	-0.081	t(43)=0.23	1
Session 1 vs 3	-755.4%	-0.678	t(40)=3.03	0.039
Session 1 vs 4	-1201.2%	-1.078	t(37)=3.92	0.0033
Power in rest interval				
Session 1 vs 2	32.6%	0.64	t(43)=-1.69	0.87
Session 1 vs 3	90.1%	1.77	t(40)=-3.46	0.012
Session 1 vs 4	157.9%	3.11	t(37)=-3.03	0.039
Power in motor-attempt interval				
Session 1 vs 2	27.3%	0.56	t(43)=-1.31	1
Session 1 vs 3	26.9%	0.55	t(40)=-1.38	1
Session 1 vs 4	21.6%	0.44	t(37)=-0.97	1

Supplementary Table 4. Statistical analyses measuring the effects of the intervention on contralateral (C3 electrode) mu ERD and mu power during the preparation and motor attempt intervals. **% Increase** and **Effect Size** represent the change in sessions 2, 3 or 4 with respect to session 1. The **t-statistic** and the **p-value** of the t-test are also reported. *Notice that the reported p-values were corrected with a Bonferroni-equivalent procedure (i.e., the reported p-values are the result of multiplying the original p-value times the number of comparisons: 9). Therefore, statistical significance is considered when the reported p-values are lower than 0.05.

Ipsilateral motor cortical activation (C4 electrode)

Supplementary Table 5 shows the values of ERD and absolute mu power over the ipsilateral hemisphere (C4 electrode) during the preparation interval and the movement attempt interval. Supplementary Table 6 provides the detailed results of the statistical analysis, comparing the data of session 1 with sessions 2, 3 and 4. This analysis is performed in terms of the percentage of change in ERD/mu power, the effect size (measured as a variation of Cohen's d statistic[1] as calculated by Busk and Serlin[2]), and the paired statistical comparisons.

	Session 1	**Session 2**	**Session 3**	**Session 4**
Mu ERD	6.55	1.89	-31.53	-44.87
Mu power: preparation interval	14.86	18.18	25.37	41.10
Mu power: motor attempt interval	15.83	18.53	17.37	22.66

Supplementary Table 5. ERD and mu power values of C4 electrode (i.e., ipsilateral activity) in the pre-motor task. ERD values are given in percentage (ERD/ERS formula according to Pfurtscheller and Lopes da Silva[3]), and power values are given in μV/Hz.

	% Increase	**Effect Size**	**t-stat**	**p-value**

ERD				
Session 1 vs 2	71.1%	0.093	t(43)=0.35	1
Session 1 vs 3	581.7 %	-0.763	t(40)=3.60	0.0077
Session 1 vs 4	-785.6%	-1.031	t(37)=3.81	0.0045
Power in rest interval				
Session 1 vs 2	22.3 %	0.548	t(43)=-1.64	0.97
Session 1 vs 3	70.7 %	1.736	t(40)=-3.17	0.026
Session 1 vs 4	176.6 %	4.336	t(37)=-4.64	< 0.001
Power in motor-attempt interval				
Session 1 vs 2	16.9%	0.36	t(43)=-1.22	1
Session 1 vs 3	9.7%	0.21	t(40)=-0.25	1
Session 1 vs 4	43.1%	0.92	t(37)=-2.02	0.46

Supplementary Table 6. Statistical analyses measuring the effects of the intervention on ipsilateral (C4 electrode) mu ERD and mu power during the preparation and motor attempt intervals. **% Increase** and **Effect Size** represent the change in sessions 2, 3 or 4 with respect to session 1. The **t-statistic** and the **p-value** of the t-test are also reported. *Notice that the reported p-values were corrected with a Bonferroni-equivalent procedure (i.e., the reported p-values are the result of multiplying the original p-value times the number of comparisons: 9). Therefore, statistical significance is considered when the reported p-values are lower than 0.05.

References

1. Cohen J. Statistical power analysis for the behavioral sciences. *Statistical Power Analysis for the Behavioral Sciences* 1988; 2nd: 567.
2. Busk PL, Serlin R. Meta-analysis for single case research. In: *Single-case research design and analysis*. 1992, pp. 197–198.
3. Pfurtscheller G, Lopes da Silva FH. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin Neurophysiol* 1999; 110: 1842–1857.