

Supplementary Materials

Table S1. Demographic table for the participants

Patient	Gender	Age	Handed-ness	Race	Electrode Type	Coverage Hemisphere	Total No. of Electrode Contacts	No. of CC/PCu Stimulation Channels	Seizure Onset Zone	Epilepsy (years)	Have Whole-Brain CCEP
S11_20	M	33	R	W	SD	R	74	11	R Parietal	6-8	No
S11_26	M	38	R	H	SD	L	114	8	L Insula	21	No
S12_33	F	63	R	H	SD	L	110	3	L Frontal	50	No
S12_37	M	30	L	H	SD	L	130	5	L Frontotemporal	30	No
S12_38	F	36	R	W	SD	L	122	15	L Parietal	9	No
S12_39	M	50	L	W	D	Bi	94	3	Bi Temporal, L Insula	12	No
S12_45	F	48	R	W	SD	L	123	2	L Temporal	16	No
S13_47	M	46	L	B	SD	R	112	12	R Frontal	16	No
S13_57	M	29	R	A	SD	L	128	2	L Temporal	13	No
S14_61	F	30	R	H	SD, D	Bi	92	3	L Temporal, L Frontal	10	No
S14_74	M	20	R	W	SD	L	106	8	Unclear	5	No
S14_75	M	51	R	W	SD	L	88	21	L Frontal	N/A	No
S15_82	M	41	L	W	D	Bi	92	7	Bi Temporal	15	No
S15_83	M	23	R	H	SD	L	125	10	L Temporal	5	No
S15_84	F	25	R	H	D	L	40	22	L Frontal	≈13	No
S15_89	M	27	R	H	D	Bi	100	4	R Insula, R Temporal	3	No
S15_90	M	52	R	H	D	R	48	2	R Temporal	35	No
S16_97	M	27	R	W	D	Bi	68	1	Bi Temporal	7	No
S16_99	M	30	R	H	D	Bi	80	3	R Temporal	7	No
S17_107	F	31	R	H	D	Bi	120	3	L Temporal	15	No
S17_109	M	50	R	W	D	Bi	150	3	Bi Temporal	31	No

S18_124	F	19	R	H	D	Bi	116	6	Unclear	4	No
S18_125	F	19	R	H	D	R	134	6	R Temporal	11-13	No
S18_129	M	23	R	W	D	Bi	117	8	R Temporal, R Insula	4	No
S19_134	M	49	R	W	D	Bi	100	1	Bi Temporal, L Frontal	17	No
S19_137	M	26	R	W	D	L	170	32	R Parietal	16	No
S19_141	F	43	R	W	D	L	140	15	L Parietal	16	No
S20_148	F	52	R	A	SD	R	148	3	R Temporal	≥33	No
S20_152	F	45	R	A	D	Bi	188	33	R Frontal	32	No
S20_156	F	62	R	H	D	Bi	124	11	R Temporal	55	No
S21_161	M	47	R	H	D	Bi	176	13	L Operculum, L Insula, R Frontal	31	No
S21_165	M	51	R	A	D	Bi	100	5	L Temporal	N/A	No
S21_166	F	37	R	W	D	Bi	176	3	Unclear	3	Yes
S21_167	F	23	L	H, W	D	R	168	10	R Insula	4	Yes
S21_169	M	23	R	W	D	Bi	186	19	R Temporal, R Occipital	19	Yes
S21_171	M	52	R	A	D	Bi	252	3	R Frontal, L Temporal	35	Yes
S22_176	F	34	R	W	D	L	156	12	L Temporal	2	Yes
S22_177	M	19	R	W	D	Bi	168	18	Bi Temporal	4	Yes
S22_178	M	28	R	W	D	Bi	252	6	L Temporal	9	Yes
S22_182	F	37	R	W	D	Bi	260	9	Bi Temporal	27	Yes
S22_183	M	33	R	W	D	Bi	174	12	R Temporal	4	Yes
S22_185	F	36	R	W	D	Bi	142	4	L Temporal	36	Yes
S22_188	M	31	R	W	D	Bi	122	13	Bi Temporal	10	Yes
S22_190	F	50	R	W	D	R	116	5	R Parietal	4	Yes
S22_191	F	25	R	H	D	Bi	110	3	R Temporal	19	No
S22_193	M	40	R	H	D	Bi	182	5	R Occipital, R Heterotopia	21	Yes
S23_197	M	20	R	B	D	Bi	214	19	Bi Temporal	15	Yes

S23_201	M	27	R	H	D	Bi	188	12	L Temporal	8	Yes
S23_202	F	48	R	A	D	Bi	194	19	L Occipital	≥16	Yes
S23_205	F	48	R	W	D	Bi	184	10	R Temporal	8	Yes
S23_206	M	57	R	W	D	Bi	122	5	L Temporal	29	Yes
S23_208	M	57	R	H	D	Bi	250	16	L Temporal, Bi Parietal	28	Yes
S23_209	M	47	R	H	D	Bi	248	30	L Temporal	39	Yes
S23_210	M	52	R	W	D	Bi	204	31	Bi Temporal	7	Yes
S23_211	F	32	R	NHPI	D	Bi	198	6	R Temporal, R Operculum	13	Yes
S23_212	M	35	R	H	D	Bi	218	2	Bi Temporal	10	Yes
S24_218	F	56	R	H	D	Bi	206	17	R Insula, L Temporal	41	Yes
S24_220	M	32	R	W	D	Bi	216	26	Bi Temporal	13	Yes
S24_221	F	44	R	H	D	Bi	234	10	L Insula	3	Yes
S24_222	F	49	R	W	D	Bi	174	15	L Temporal	≥15	Yes
S24_229	M	31	R	W	D	Bi	152	23	Bi Temporal	12	No
S24_233	F	44	R	H	D	Bi	214	3	Bi Temporal	31	No
S24_236	M	26	R	W, B	D	Bi	218	7	R Temporal	22	Yes

F: female, M: male, L: left, R: right, Bi: bilateral, W: white, H: hispanic, B: black, A: asian, NHPI: native hawaiian and other pacific islander, SD: subdural, D: depth CC/PCu.: Cingulate/Precuneus

Table S2. Significance inference table for comparisons between outflow and inflow connectivity, separately for SM+ and CLX+ sites in the cingulate

comparison	condition	estimate	tvalue	nObs	nSbj	CI	p	p_adj
outflow vs. inflow	Seed: SM+, Connection: ipsilateral	0.043	6.21	3074	108	[0.03, 0.06]	8.60E-10	0.00
outflow vs. inflow	Seed: CLX+, Connection: ipsilateral	-0.027	-2.97	1864	181	[-0.04, -0.01]	1.14E-02	0.02

Table S3. Table of descriptive statistics for the three-way factorial design of laterality of bodily responses × CCEP laterality × stimulation hemisphere for the Sensory-Motor sites (corresponding to the main Figure 4h left)

bodily response	CCEP cross-hemi. type	stim. hemisphere	med	average	sd	n	se	upper	lower
contr-RESP	contralateral	left	0.190	0.202	0.196	189	0.014	0.231	0.174
contr-RESP	contralateral	right	0.192	0.228	0.196	278	0.012	0.251	0.204
contr-RESP	ipsilateral	left	0.369	0.353	0.191	261	0.012	0.377	0.329
contr-RESP	ipsilateral	right	0.344	0.346	0.200	617	0.008	0.362	0.330
nolat-RESP	contralateral	left	0.163	0.179	0.214	186	0.016	0.210	0.147
nolat-RESP	contralateral	right	0.202	0.226	0.222	193	0.016	0.258	0.194
nolat-RESP	ipsilateral	left	0.319	0.306	0.206	451	0.010	0.326	0.287
nolat-RESP	ipsilateral	right	0.321	0.313	0.211	567	0.009	0.330	0.295

med: median, sd: standard deviation, se: standard error, upper/lower: +/-2 standard errors

Table S4. Table of descriptive statistics for the three-way factorial design of laterality of bodily responses × CCEP laterality × stimulation hemisphere for the Complex sites (corresponding to the main Figure 4h right)

bodily response	CCEP cross-hemi. type	stim. hemisphere	med	average	sd	n	se	upper	lower
contr-RESP	contralateral	left	0.083	0.095	0.127	90	0.013	0.122	0.068
contr-RESP	contralateral	right	0.116	0.132	0.198	333	0.011	0.154	0.110
contr-RESP	ipsilateral	left	0.202	0.190	0.189	43	0.029	0.247	0.132
contr-RESP	ipsilateral	right	0.175	0.211	0.242	212	0.017	0.244	0.178
nolat-RESP	contralateral	left	0.136	0.144	0.194	385	0.010	0.163	0.124
nolat-RESP	contralateral	right	0.126	0.143	0.185	311	0.011	0.164	0.121
nolat-RESP	ipsilateral	left	0.225	0.244	0.212	439	0.010	0.264	0.224
nolat-RESP	ipsilateral	right	0.162	0.176	0.215	477	0.010	0.196	0.157

med: median, sd: standard deviation, se: standard error, upper/lower: +/-2 standard errors

Table S5. Significance inference table for comparisons between sensory-motor (SM) and complex (Complex) sites, separately for inflow and outflow connectivity with the insula

direction	comparison	estimate	tvalue	nObs	nSbj	CI	p	p_adj
cing->ins	SM+ vs. CLX+	0.11298592	4.46361273	483	18	[0.06, 0.16]	1.04434E-05	0.000
ins->cing	SM+ vs. CLX+	0.03715031	1.44345922	472	20	[-0.01, 0.09]	0.146144983	0.146

Table S6. Table of descriptive statistics for the three-way factorial design of laterality of CCEP direction $\times$ insular subregions $\times$ responsiveness for the "Sensory-Motor" cingulate/precuneus area (corresponding to the main Figure 6b left)

direction	seed	target	med	average	sd	n	se	upper	lower
outflow	SM+	aINS	0.273	0.248	0.277	186	0.020	0.288	0.207
outflow	SM+	pINS	0.222	0.212	0.287	125	0.026	0.264	0.161
outflow	SM-	aINS	0.275	0.258	0.273	101	0.027	0.312	0.204
outflow	SM-	pINS	0.002	0.040	0.225	143	0.019	0.077	0.002
inflow	SM+	aINS	0.206	0.201	0.249	193	0.018	0.237	0.165
inflow	SM+	pINS	0.261	0.242	0.243	110	0.023	0.289	0.196
inflow	SM-	aINS	0.289	0.263	0.282	113	0.027	0.316	0.210
inflow	SM-	pINS	0.068	0.080	0.233	126	0.021	0.121	0.038

med: median, sd: standard deviation, se: standard error, upper/lower: ± 2 standard errors

Table S7. Table of descriptive statistics for the three-way factorial design of laterality of CCEP direction $\times$ insular subregions $\times$ responsiveness for the "Complex" cingulate/precuneus area (corresponding to the main Figure 6b right)

direction	seed	target	med	average	sd	n	se	upper	lower
outflow	CLX+	aINS	0.083	0.125	0.274	94	0.028	0.182	0.069
outflow	CLX+	pINS	0.044	0.093	0.239	89	0.025	0.144	0.043
outflow	CLX-	aINS	0.177	0.160	0.242	49	0.035	0.229	0.091
outflow	CLX-	pINS	0.062	0.049	0.201	56	0.027	0.103	-0.004
inflow	CLX+	aINS	0.036	0.103	0.268	83	0.029	0.162	0.044
inflow	CLX+	pINS	0.126	0.111	0.244	74	0.028	0.168	0.054
inflow	CLX-	aINS	0.011	0.019	0.219	45	0.033	0.084	-0.046
inflow	CLX-	pINS	-0.004	0.010	0.187	47	0.027	0.065	-0.044

med: median, sd: standard deviation, se: standard error, upper/lower: ± 2 standard errors

Table S8. Significance inference table for comparisons between Sensory-Motor (SM+) and nearby silent sites (SM-), separately for inflow and outflow connectivity with the insular subregions; and for comparisons between the outflow and inflow connectivity. It corresponds to the main Figure 6c.

comparison	condition	estimate	tvalue	p	nObs	nSbj	CI	p.adj
SM- vs. SM +	Flow: CIN->pINS	-0.152	-3.754	1.94E-04	263	15	[-0.23, -0.07]	0.001
SM- vs. SM +	Flow: CIN->aINS	0.091	2.186	0.054	287	16	[-0.00, 0.18]	0.086
SM- vs. SM +	Flow: pINS->CIN	-0.134	-3.768	3.42E-04	233	15	[-0.21, -0.06]	0.001
SM- vs. SM +	Flow: aINS->CIN	0.093	2.516	0.015	289	18	[0.02, 0.17]	0.031
aINS vs. pINS	Seed: SM+, Flow: outflow (CIN->INS)	-0.075	-2.431	0.015	240	10	[-0.13, -0.01]	0.031
aINS vs. pINS	Seed: SM+, Flow: inflow (INS->CIN)	0.017	0.547	0.633	236	10	[-0.05, 0.08]	0.633
outflow (CIN->INS) vs. inflow (INS->CIN)	Terminal: aINS, Seed: SM+	0.034	1.460	0.144	299	8	[-0.01, 0.08]	0.192
outflow (CIN->INS) vs. inflow (INS->CIN)	Terminal: pINS, Seed: SM+	-0.020	-0.630	0.530	177	9	[-0.04, 0.08]	0.606

Table S9. Significance inference table for comparisons between Complex (CLX+) and nearby silent sites (CLX-), separately for inflow and outflow connectivity with the insular subregions; and for comparisons between the outflow and inflow connectivity. It corresponds to the main Figure 6d.

comparison	condition	estimate	tvalue	p	nObs	nSbj	CI	p.adj
CLX- vs. CLX +	Flow: CIN->pINS	-0.026	-0.558	0.567	102	16	[-0.12, 0.06]	0.928
CLX- vs. CLX +	Flow: CIN->aINS	0.114	2.170	0.036	105	16	[0.01, 0.22]	0.289
CLX- vs. CLX +	Flow: pINS->CIN	-0.041	-0.871	0.367	87	16	[-0.13, 0.05]	0.928
CLX- vs. CLX +	Flow: aINS->CIN	-0.005	-0.105	0.891	79	16	[-0.11, 0.09]	0.928
aINS vs. pINS	Seed: CLX+, Flow: outflow (CIN->INS)	0.014	0.360	0.717	137	13	[-0.06, 0.09]	0.928
aINS vs. pINS	Seed: CLX+, Flow: inflow (INS->CIN)	0.003	0.089	0.928	108	13	[-0.07, 0.08]	0.928
outflow (CIN->INS) vs. inflow (INS->CIN)	Terminal: aINS, Seed: CLX+	-0.015	-0.438	0.653	129	13	[-0.08, 0.05]	0.928
outflow (CIN->INS) vs. inflow (INS->CIN)	Terminal: pINS, Seed: CLX +	-0.012	-0.312	0.746	116	13	[-0.09, 0.06]	0.928

Category	Lateralization	S11_20	S11_26	S12_33	S12_38	S12_39	S14_75	S15_82	S15_84	S16_99	S17_107	S18_124	S18_129	S19_134	S19_137	S19_141	S20_152	S21_161	S21_165	S21_166	S21_167	S22_176	S22_177	S22_178	S22_182	S22_183	S22_188	S22_190	S23_197	S23_202	S23_205	S23_209	S23_210	S24_218	S24_220	S24_221	S24_222	S24_229	S24_236
Complex	contr-RESP	0	0	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	1	0	2	1	0	0	0	0	0	0	0	2	0	1	0	3	0	0	5	0
	ipsi-RESP	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	0	4	0	0	0	0	0	0	0	0	1	0	0	2	0	0	
	nolat-RESP	0	6	0	0	3	0	0	1	0	0	6	2	3	12	4	17	3	19	7	0	3	6	5	10	12	0	0	4	2	4	0	16	1	7	3	3	13	5
Sensory-Motor	contr-RESP	9	1	0	3	0	0	0	16	4	1	0	0	0	6	7	4	0	0	0	0	2	0	0	2	0	5	9	2	0	0	12	0	0	0	4	2	0	0
	ipsi-RESP	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	3	0	0	2	0	1	0	0	0	0	1	0	0	0	0	0	0	0	
	nolat-RESP	3	2	1	0	0	8	6	2	0	0	1	1	0	13	3	1	0	0	0	3	2	0	0	21	2	10	10	4	0	4	9	0	2	0	3	7	0	0

Examples of subjective responses:

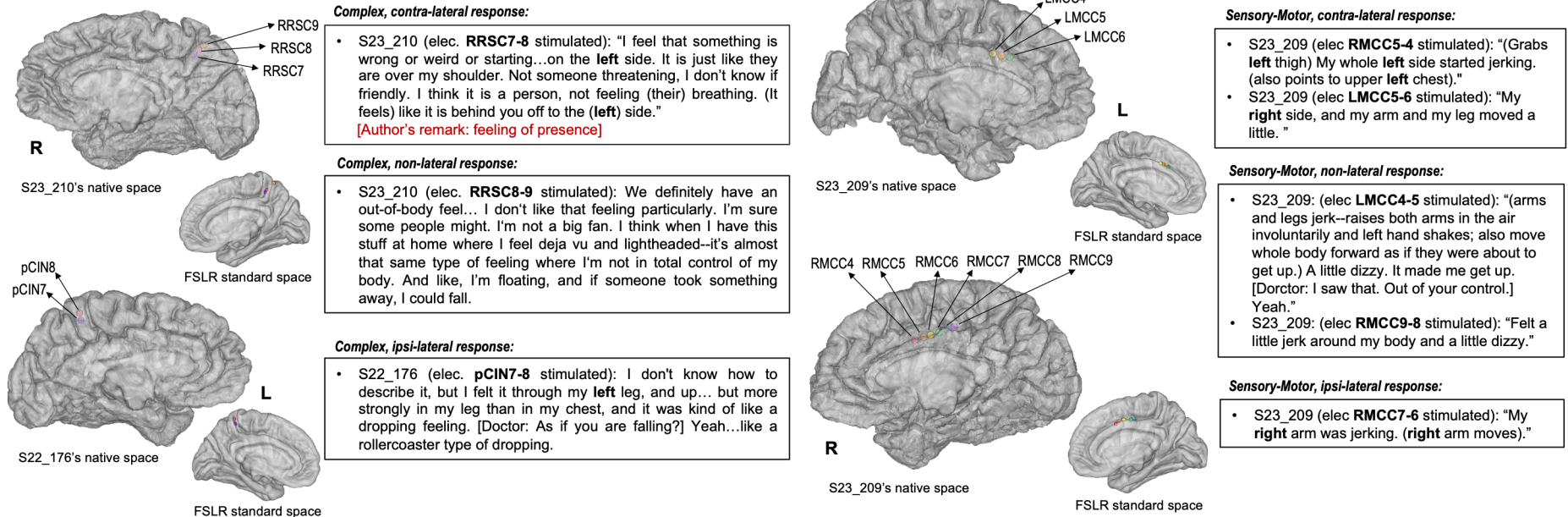


Figure S2. Examples of lateralized bodily effects (contralateral, non-lateral, and ipsilateral) for complex and sensory-motor responses are presented. Six types of responses collected from three randomly chosen patients are shown. The electrode localizations are visualized in the native subject space and in a standard surface space (FS_LR).

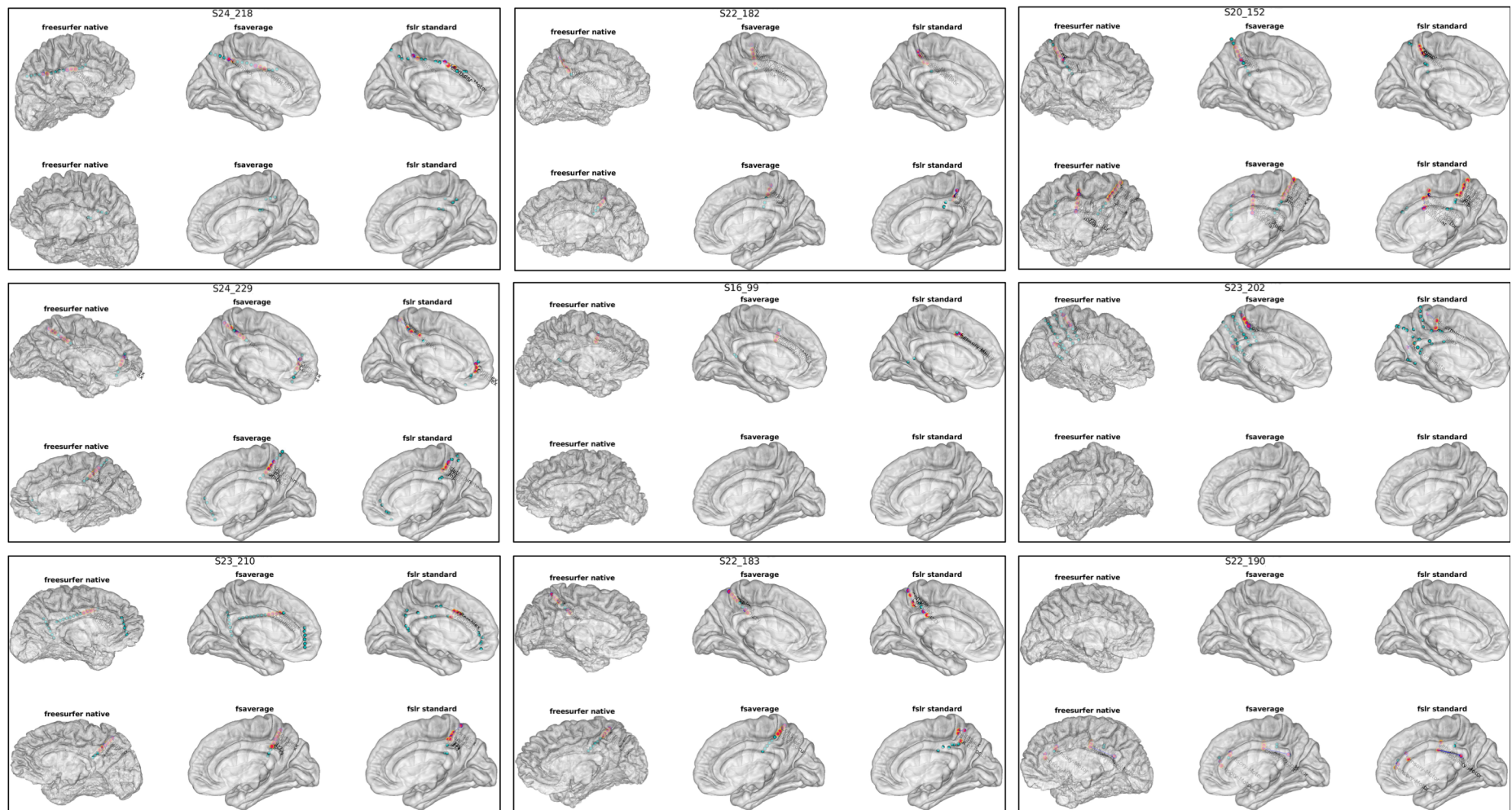
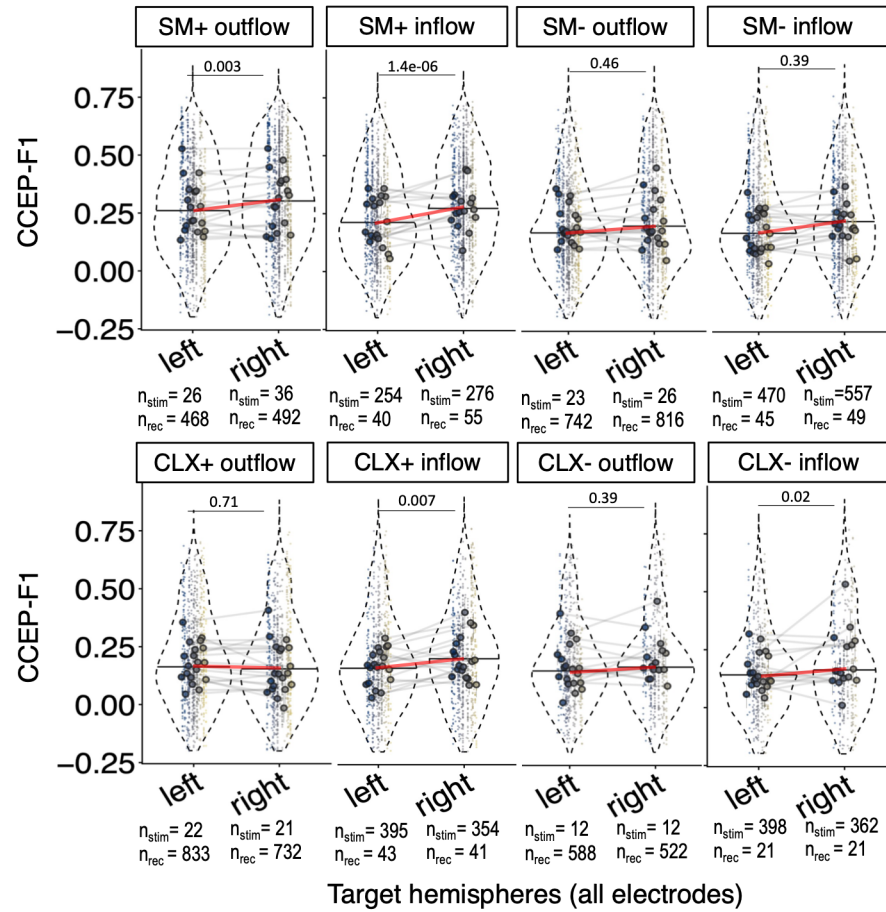


Figure S3. Randomly selected examples illustrating the mosaic distribution of responsive and silent sites in the cingulate cortex and precuneus. For each participant, electrode locations are shown in three surface coordinate systems: FreeSurfer native space, FSaverage, and FS_LR. Misalignments between native-space electrode locations and their projections to standard surface spaces can be observed in some cases (e.g., S22_182 in FSaverage and S23_202 in FS_LR). Responsive sites are shown in red, and silent sites are shown in blue.



direction	roi	estimate	T-value	p	nObs	nSubID	CI	p_adj
L < R	Flow: outflow, Seed: sm+	0.03	3.54	0.000	2353	106	[0.01, 0.05]	0.003
L < R	Flow: inflow, Seed: sm+	0.05	5.24	0.000	2032	103	[0.03, 0.07]	0.000
L < R	Flow: outflow, Seed: sm-	0.01	1.19	0.232	2202	177	[-0.01, 0.03]	0.464
L < R	Flow: inflow, Seed: sm-	0.01	1.60	0.109	2069	217	[0.00, 0.03]	0.393
L < R	Flow: outflow, Seed: clx+	0.00	0.37	0.716	1865	176	[-0.02, 0.02]	0.716
L < R	Flow: inflow, Seed: clx+	0.04	3.27	0.001	1495	168	[0.01, 0.06]	0.007
L < R	Flow: outflow, Seed: clx-	-0.02	-1.68	0.098	1014	122	[-0.04, 0.00]	0.393
L < R	Flow: inflow, Seed: clx-	0.04	2.84	0.005	773	143	[0.01, 0.07]	0.023

Figure S4. Comparisons of left versus right hemispheric causal electrophysiological connectivity (indexed with F1) with the cingulate sites for the cingulate's inflow and outflow pathways, across SM+ (responsive sites for sensory-motor responses), SM- (silent sites near SM+), CLX+ (responsive sites for complex responses), and CLX- (silent sites near CLX+). A statistical inference table is shown on the right.

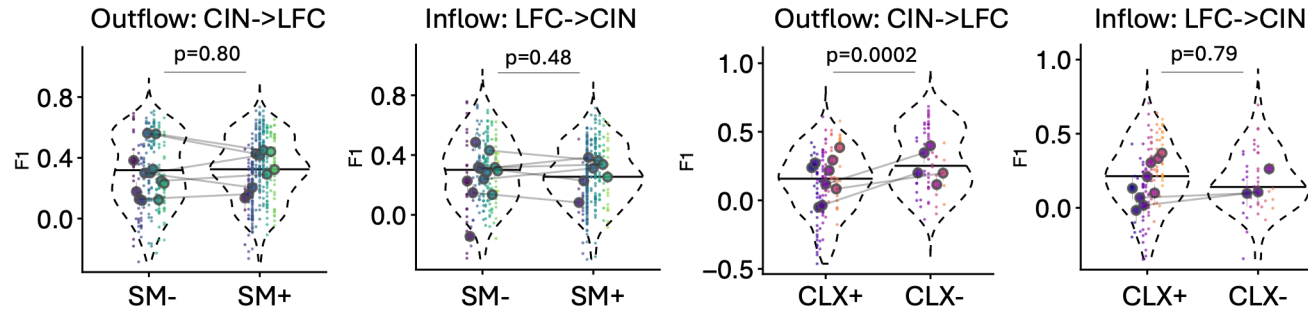


Figure S5. CCEP between the lateral frontal cortex (LFC) and the cingulate sites, including the responsive sites (SM+ and CLX+) and the nearby silent sites (SM- and CLX-). The CCEPs with the LFC did not discriminate the responsive sites from the silent sites, except for the outflow connectivity of the Complex sites which showed the opposite pattern as hypothesized.