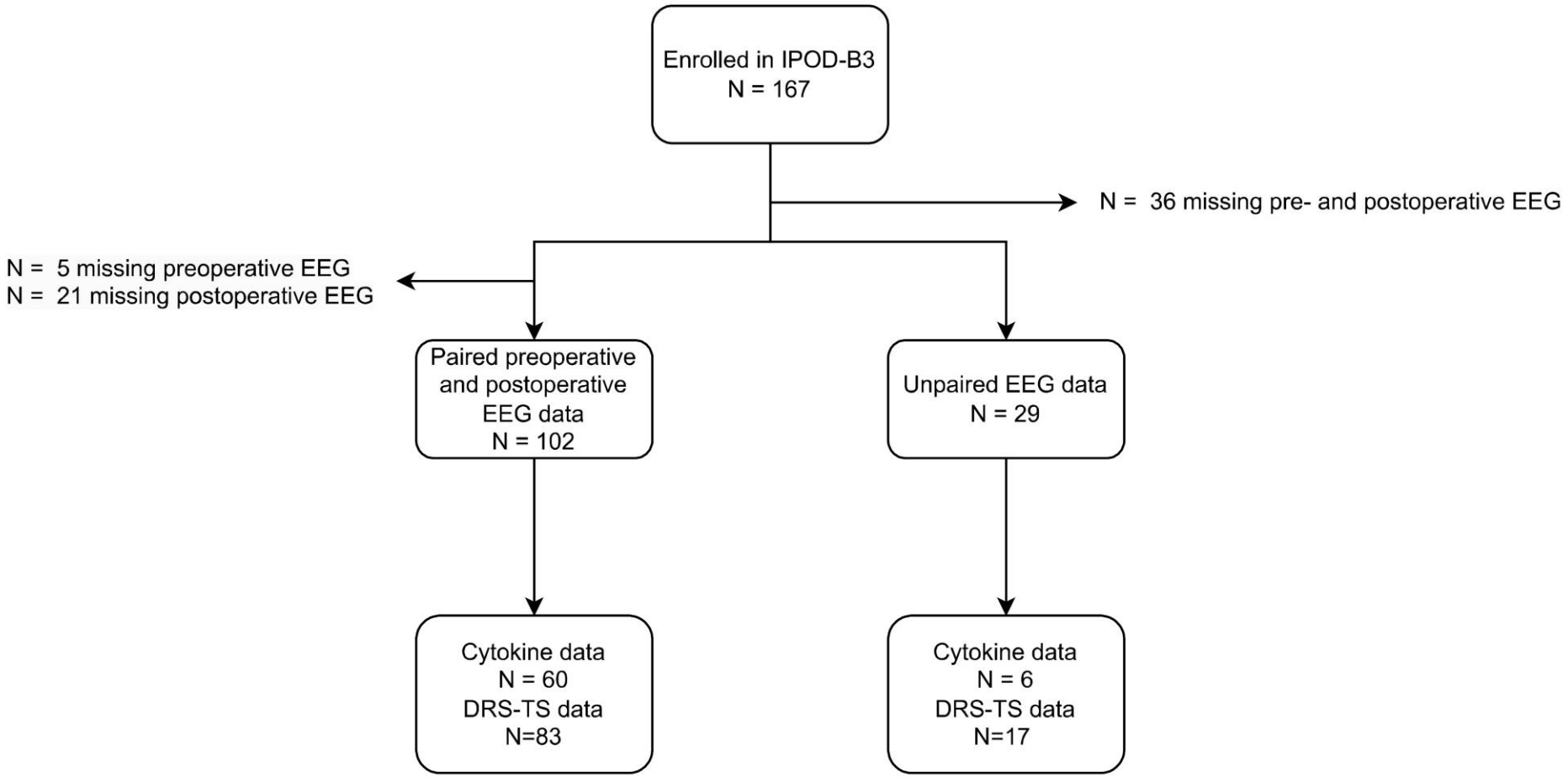
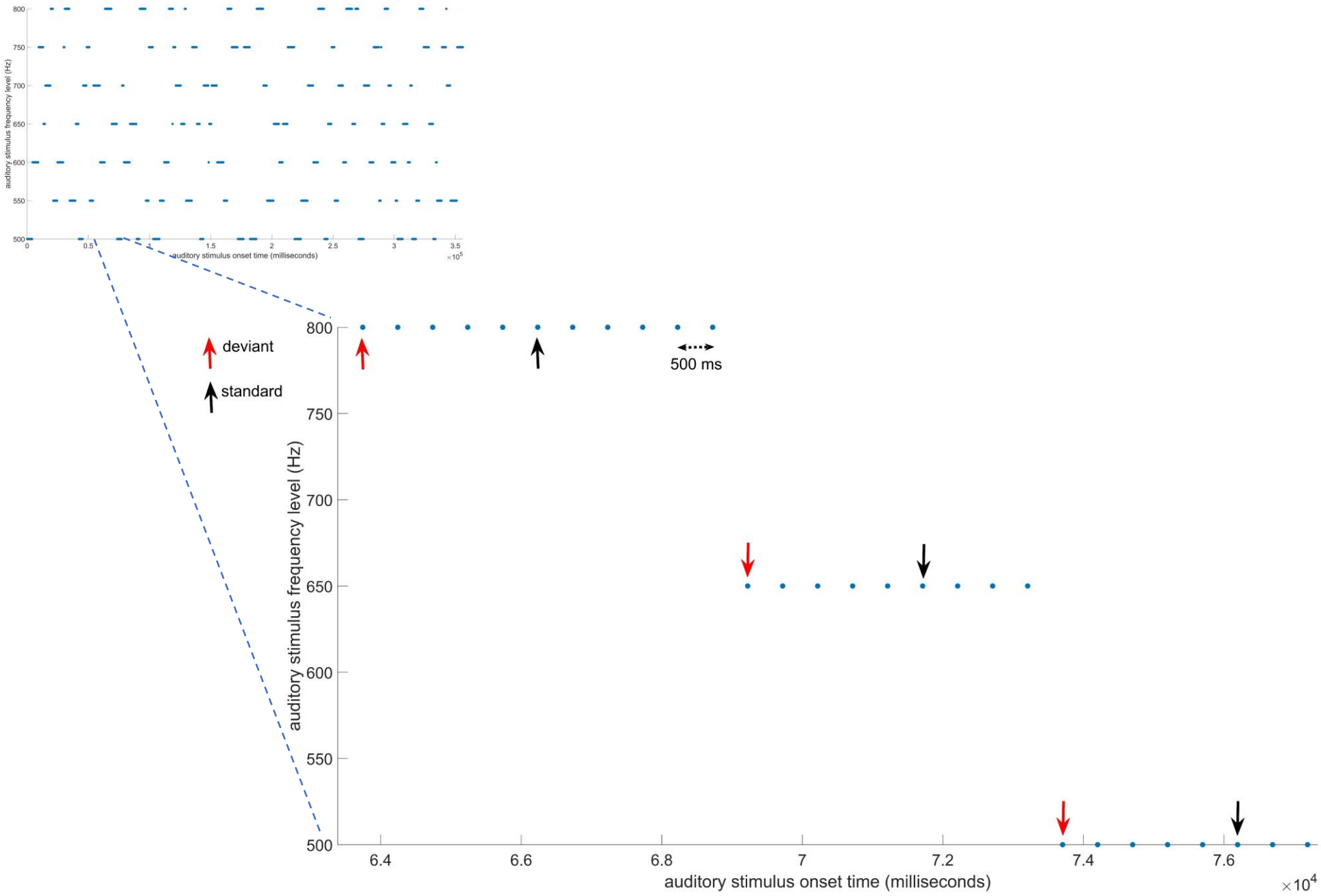
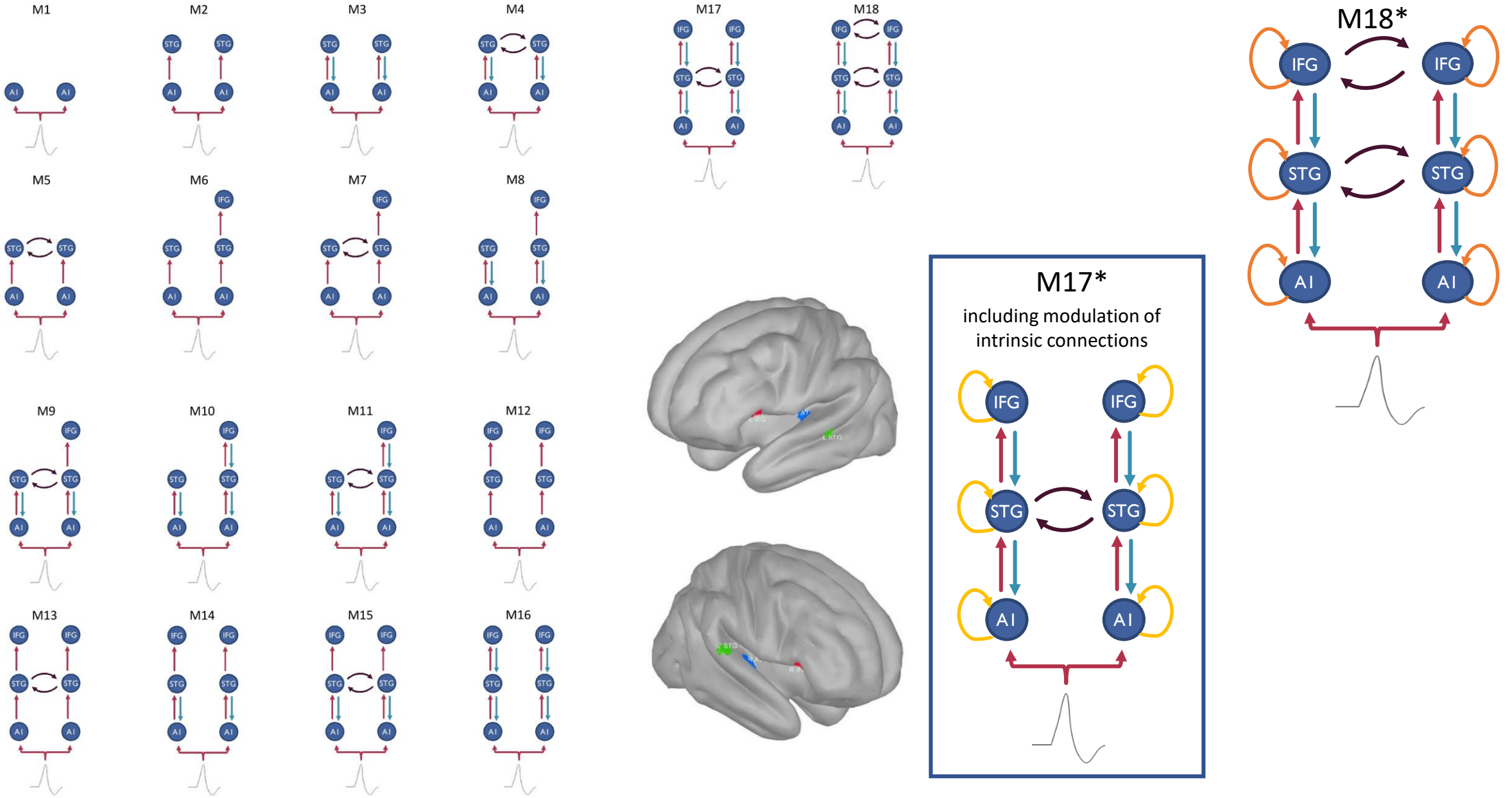


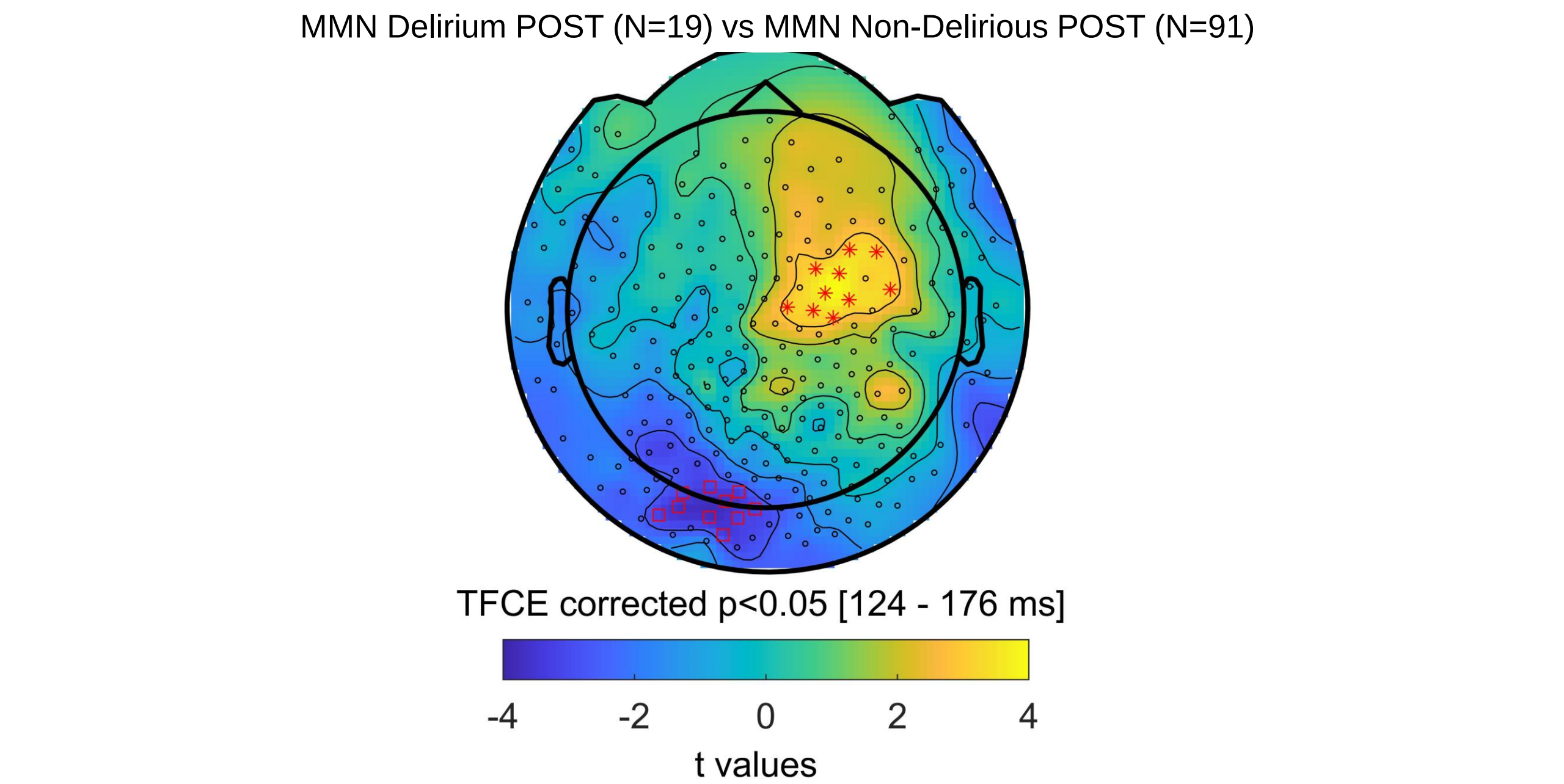
Supplemental Figure 1: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) diagram for the current study data from IPOD-B3 perioperative cohort study. EEG here refers to EEG files with ERP paradigm run.



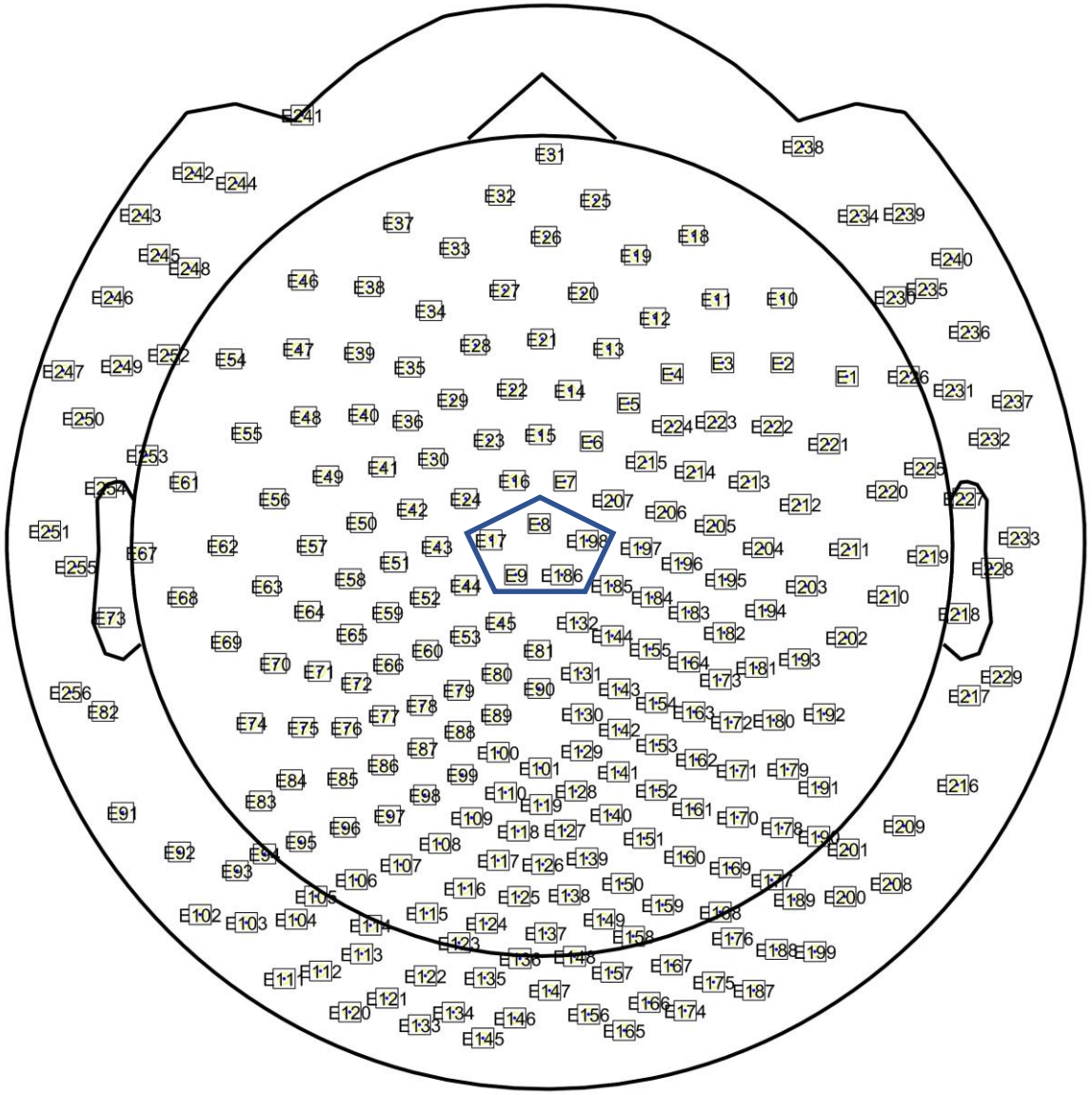
Supplemental Figure 2: The auditory oddball roving paradigm.

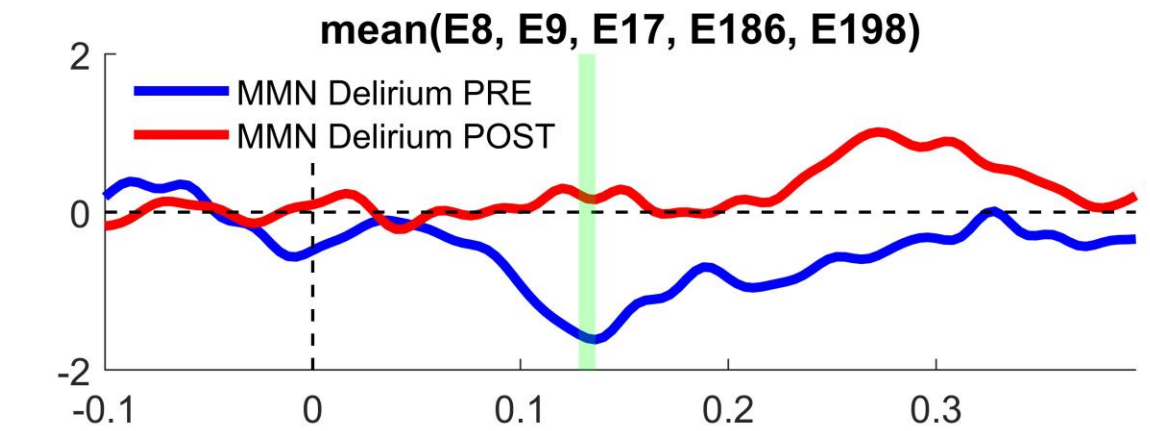


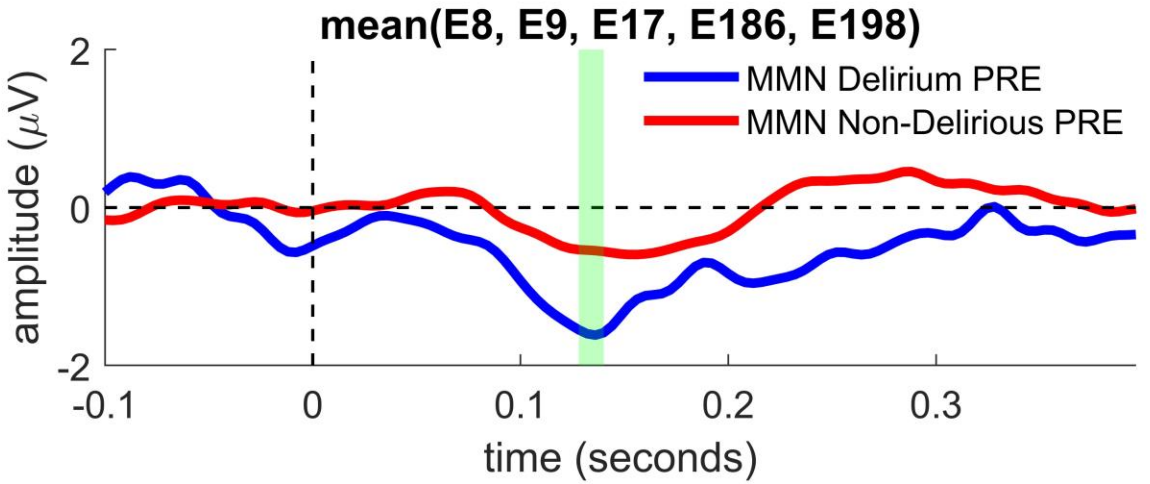
Supplemental Figure 3: Schematic display of 20 different models used in dynamic causal modeling of deviant stimulus effects (MMN responses) in SPM12. Each model receives subcortical input at the A1 sources eliciting further transient perturbations in the remaining sources. The models incorporate a different number of sources/nodes (2, 4, 5, 6) as well as a different type and arrangement of connections (forward, feedback, lateral). Sources: In the left view of the brain **(1)** left A1 – in blue; **(2)** left IFG – in red; **(3)** left STG – in green; in the right view of the brain **(4)** right A1 – in blue; **(5)** right IFG – in red; **(6)** right STG – in green. The 'winning' **model M17*** schematic is highlighted inside a rectangle.



Supplemental Figure 4: Topographical plot of t-values for differences in MMN amplitudes between Delirium POST and Non-Delirious POST subjects' data for the average in the evaluated time interval [124-176 ms]. Significant differences ($p<0.05$, TFCE-corrected for multiple comparisons) of MMN amplitudes being smaller in Delirium POST compared to Non-Delirious POST subjects are highlighted with red asterisks.

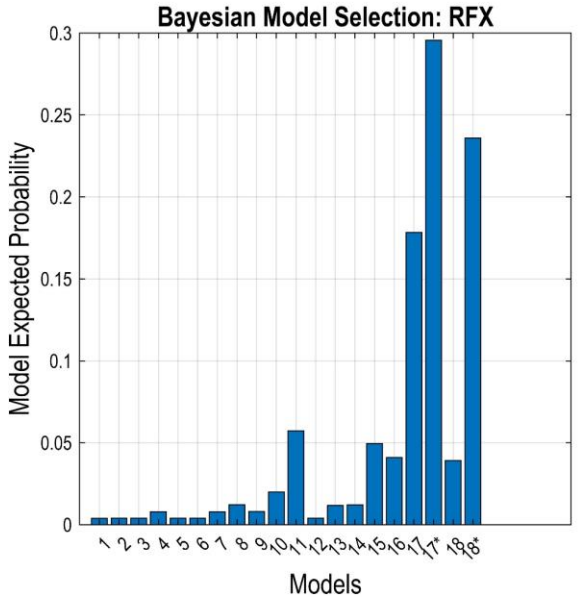


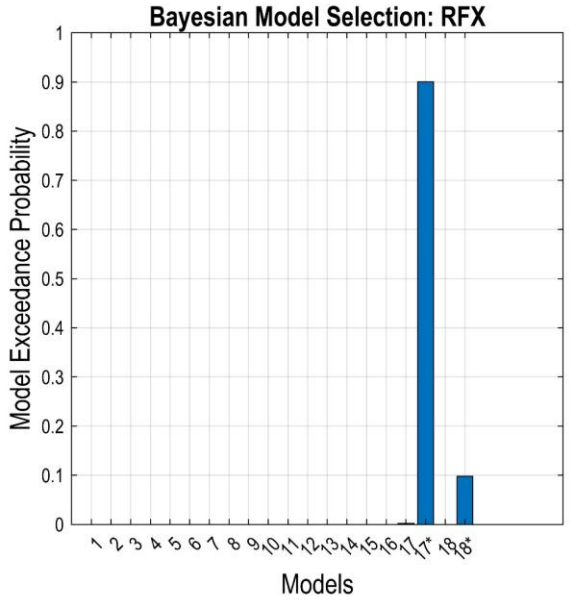




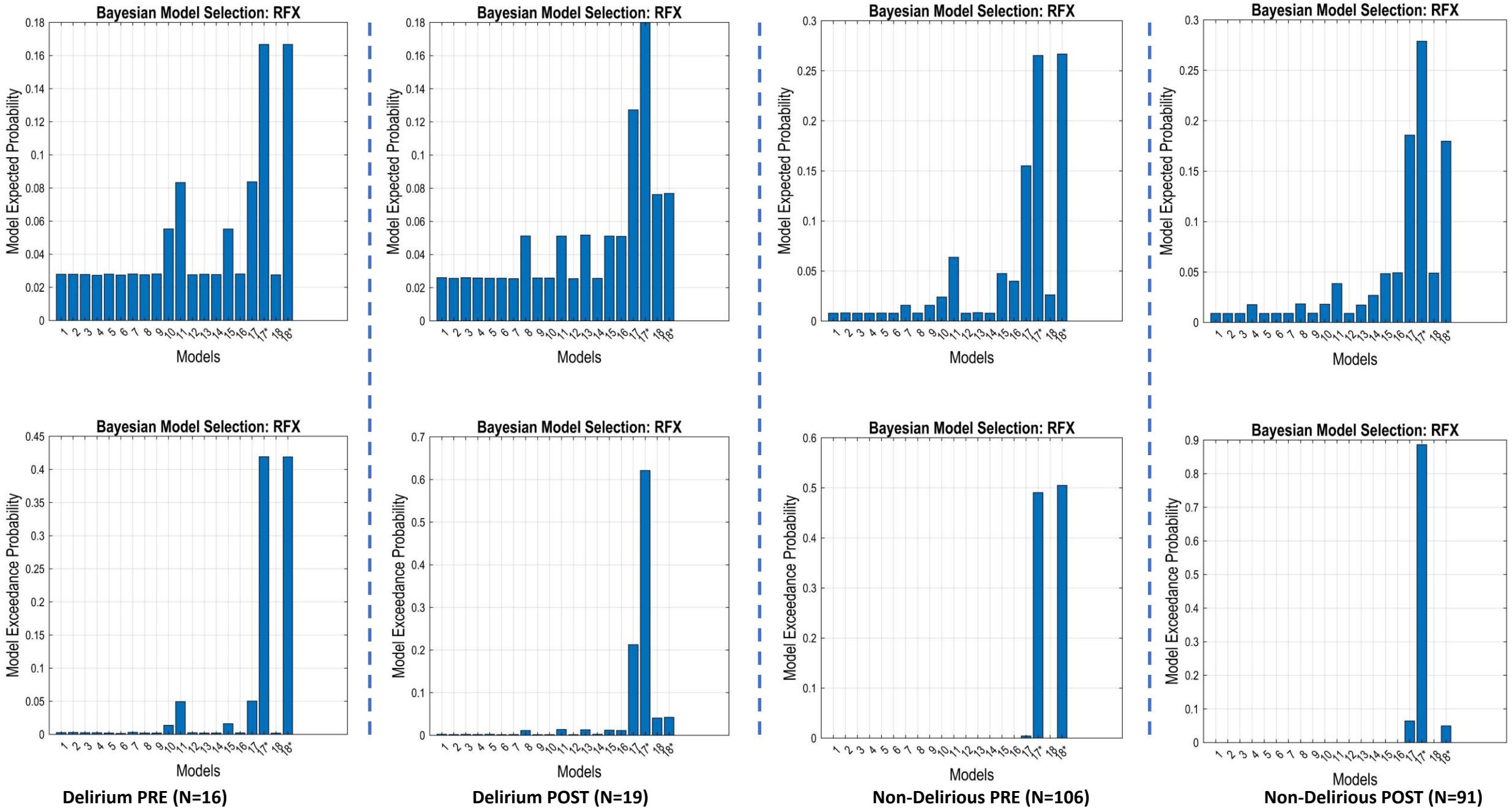
Supplemental Figure 5: Plot of significant differences in MMN amplitudes between Delirium POST and Delirium PRE, as well as between Delirium PRE and Non-Delirious PRE during the evaluated time interval [124-176 ms], highlighted in vertical green bars. The latter highlights time periods of significant differences between the compared MMN amplitudes, corrected for multiple comparisons over all time points in the evaluated time interval [124-176 ms]. For this a null distribution of extreme t-values across all time points in the time interval of interest was used, obtained from 5000 data label permutations. The mean of MMN amplitudes (difference waves) from 5 frontocentral sensors is shown in respective line plots.

All 232 = (16+19+106+91)

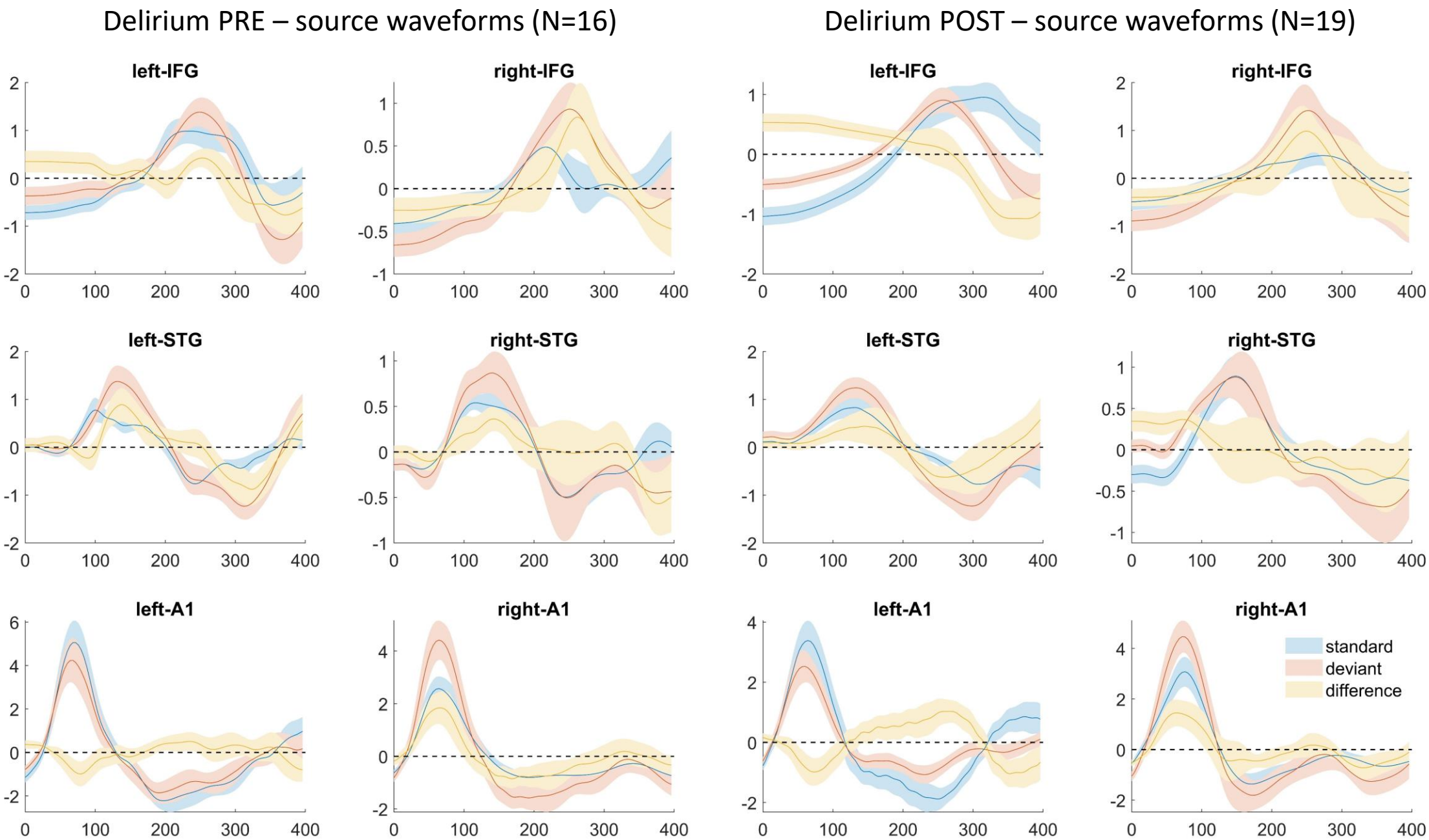




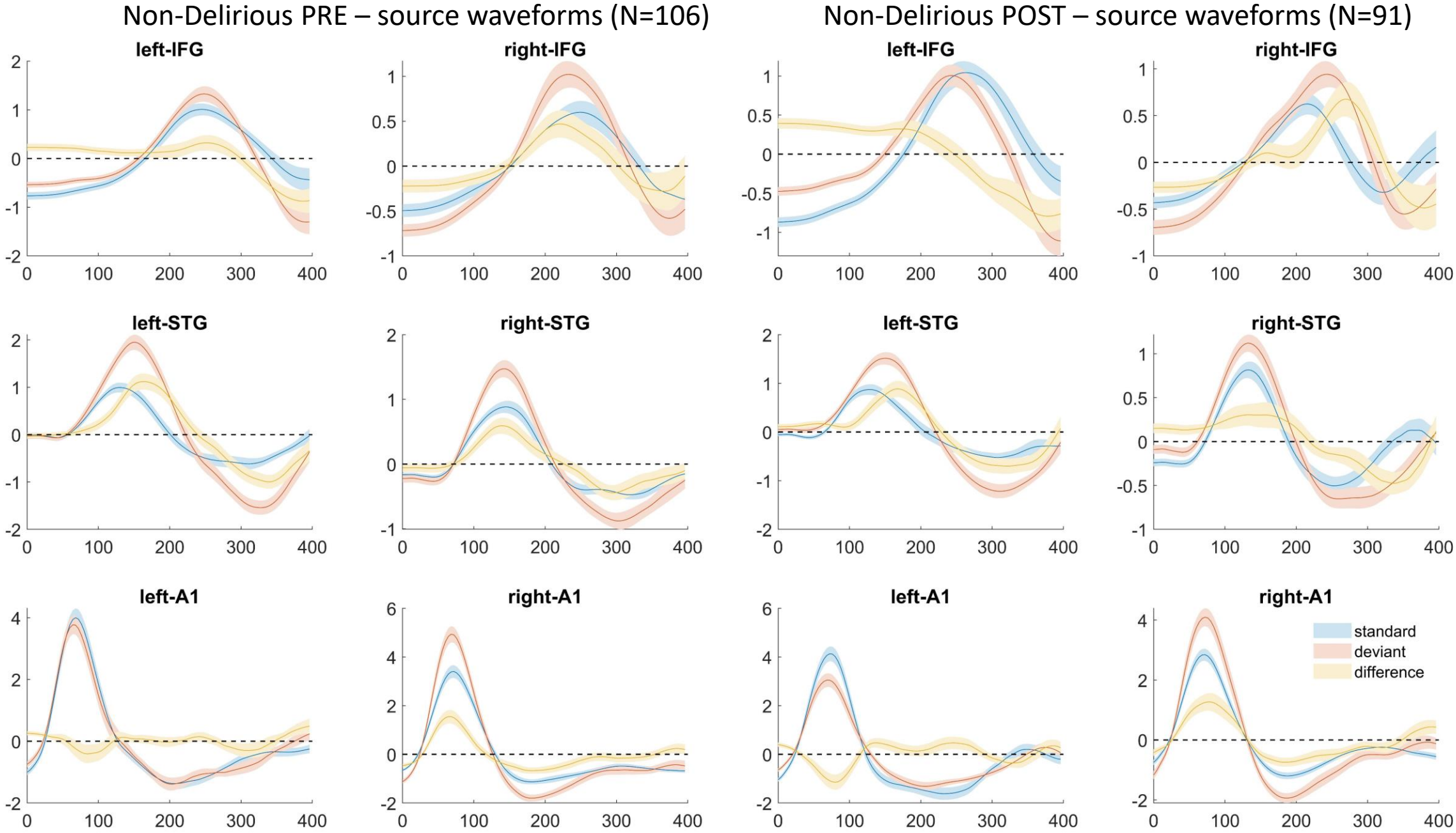
Supplemental Figure 6A: Population level best model resulting from a Bayesian model comparison : Random effects Bayesian model selection showed that **Model #17*** had the greatest evidence.



Supplemental Figure 6B: Population level best model resulting from a Bayesian model comparison : Random effects Bayesian model selection showed that **Model #17*** had the greatest evidence.



Supplemental Figure 7A: Grand average source waveforms for standard, deviant and difference waves from data belonging to Delirium PRE and Delirium POST conditions. The shaded areas display the standard error of the means.

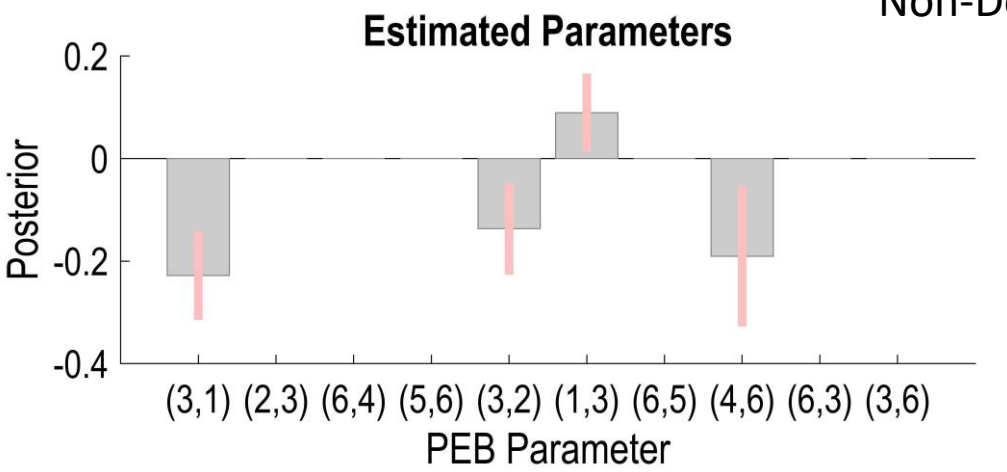


Supplemental Figure 7B: Grand average source waveforms for standard, deviant and difference waves from data belonging to Non-Delirious PRE and Non-Delirious POST conditions. The shaded areas display the standard error of the means.

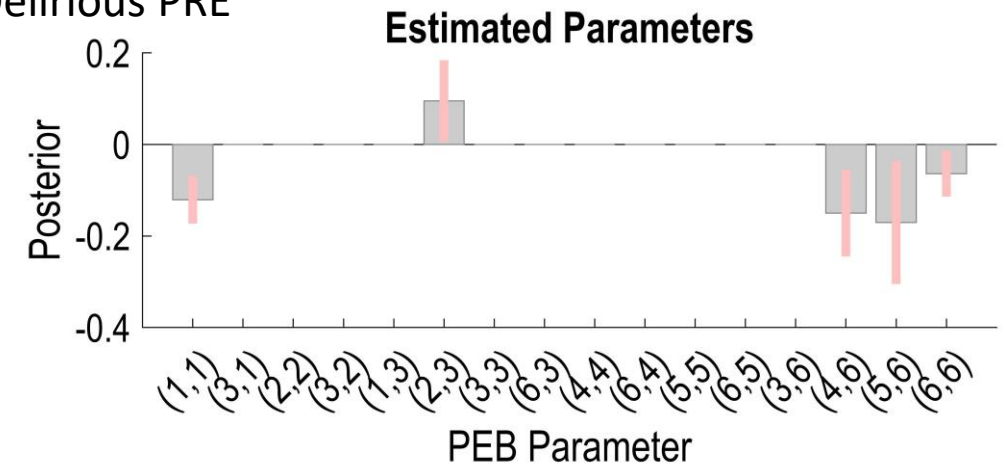
Parametric Empirical Bayes (PEB)

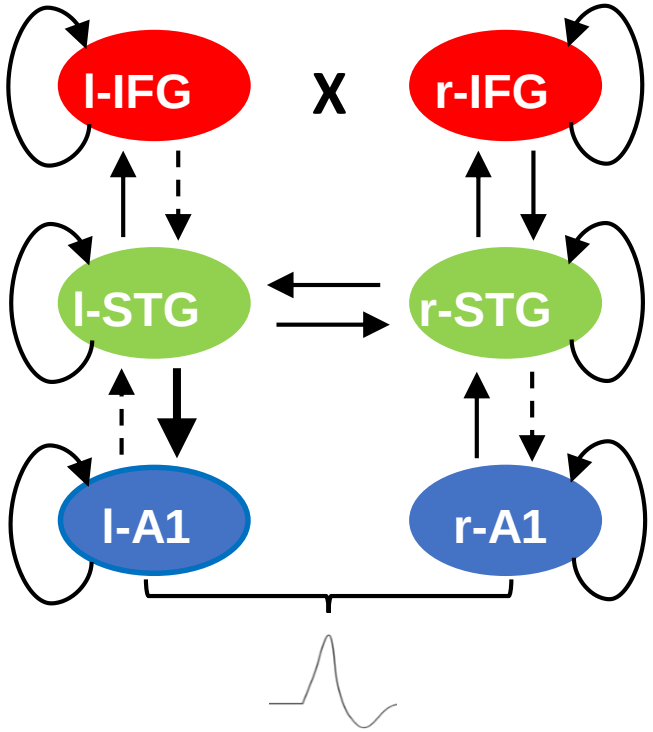
Non-Delirious POST vs Non-Delirious PRE

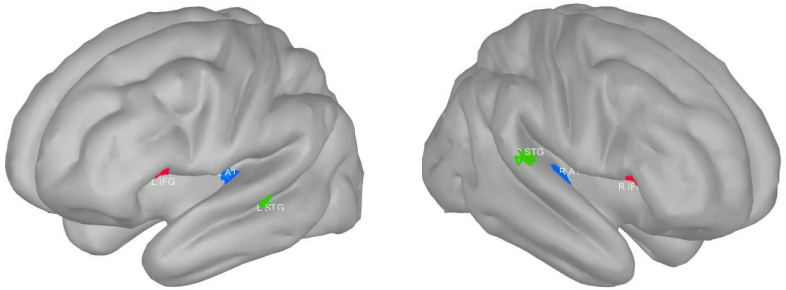
Standard Connectivity – "matrix A"

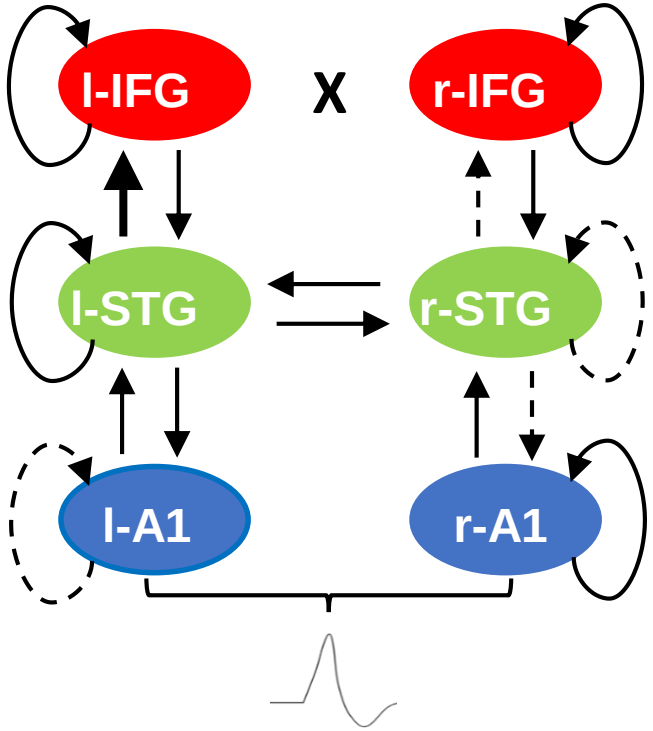


"B matrix" modulation effect

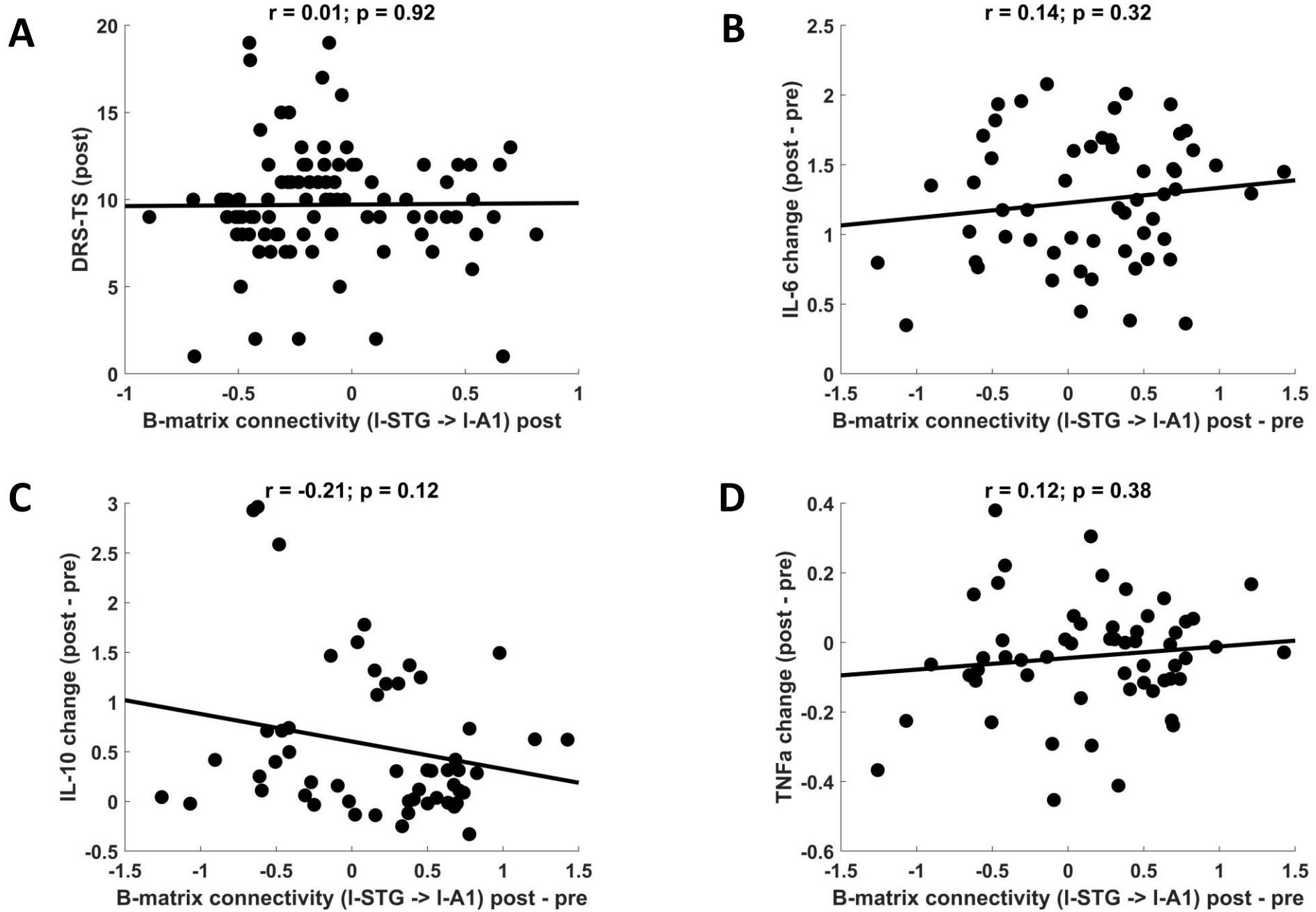




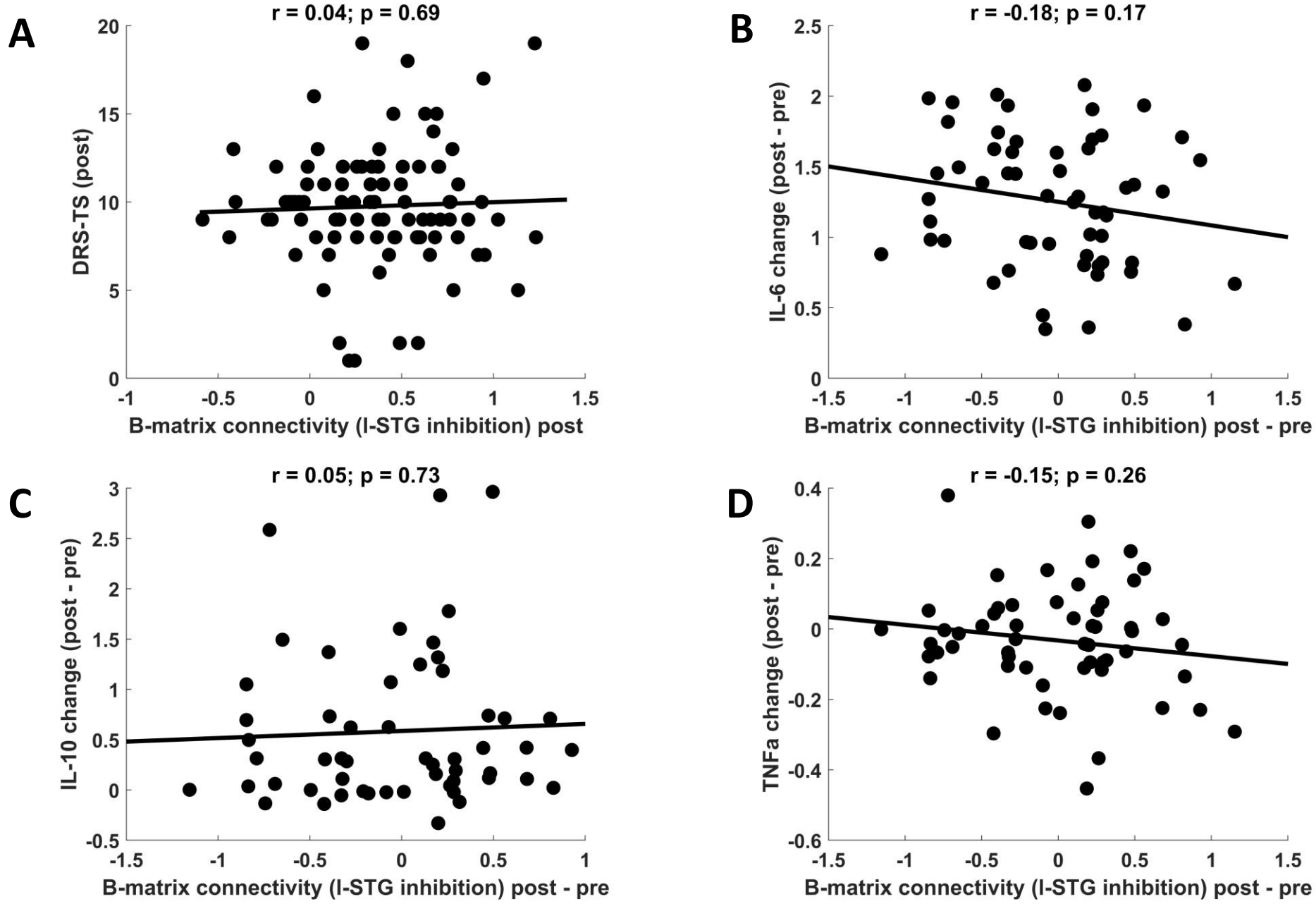




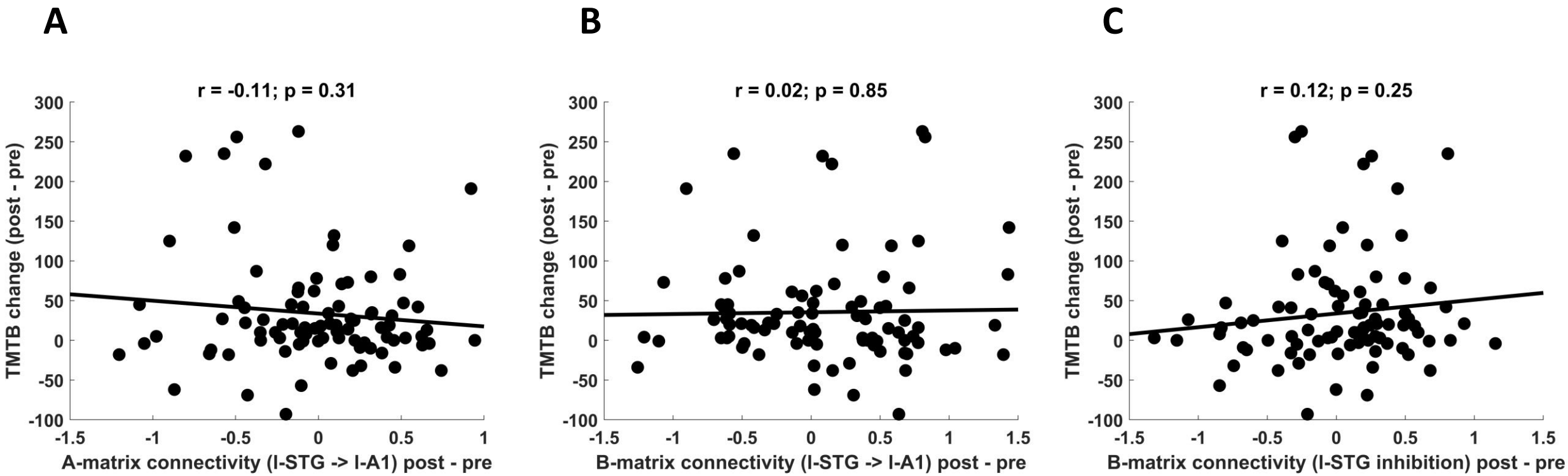
Supplemental Figure 8. Sources: **(1)** left A1; **(2)** left IFG; **(3)** left STG; **(4)** right A1; **(5)** right IFG; **(6)** right STG. (x,y) as y -> x. For the two-group difference, positive estimated parameters indicate stronger connectivity in 1st group than 2nd group and negative parameters indicate the opposite. Posterior probabilities larger than 95% (corresponding to a strong evidence level) are shown.



Supplemental Figure 9: Correlations between "B matrix" connectivity changes (feedback connectivity from l-STG to l-A1 due to relative deviant stimulus effects) with DRS-TS and cytokine levels. Cytokine levels were log10-transformed.



Supplemental Figure 10: Correlations of the change in intrinsic excitability/inhibition in l-STG (due to relative deviant stimulus effects) with DRS-TS scores post-surgery, as well as with change in inflammatory biomarkers represented by measured cytokine levels (IL-6, IL-8, IL10, and TNFa). Cytokine levels were log10-transformed.



Supplemental Figure 11: Correlations of the change in (A) extrinsic feedback connectivity from l-STG to l-A1 (due to standard stimulus effects),
(B) extrinsic feedback connectivity from l-STG to l-A1 (due to relative deviant stimulus effects), as well as
(C) In intrinsic excitability/inhibition in l-STG (due to relative deviant stimulus effects) with the change in Trail Making Test-B (TMT-B) measure scores.

Supplemental Table 1:
Baseline characteristics of study participants.

Suppl. Table 1: Baseline Characteristics of Study Participants by Postoperative Delirium Status during the EEG[a]

	Non-Delirious (N = 112)	Delirious (N = 19)	All (N = 131)
Patient characteristics			
Age, mean (SD), y	72.2 (4.6)	72.2 (3.4)	72.2 (4.4)
Sex, No. (%)			
Male	71 (63.4)	11 (58)	82 (63)
Female	41 (36.6)	8 (42)	49 (37)
Education, No. (%)[b]			
<12 Years	0 (0)	0 (0)	0 (0)
12 Years	25 (22)	2 (12)	27 (21)
>12 Years	87 (78)	15 (88)	102 (79)
TMTB, mean (SD), sec	80.3 (32.3)	83.2 (31.9)	80.7 (32.0)
MoCA, mean (SD)[c]	23.2 (3.1)	23.1 (2.5)	23.2 (3.0)
GDS-15, mean (SD)[d]	2.1 (2.4)	3.1 (2.0)	2.2 (2.3)
ASA score, mean (SD)[e]	3.0 (0.6)	3.2 (0.7)	3.0 (0.6)
NSQIP-SC, mean (SD)[f]	15.32 (9.18)	21.79 (11.89)	16.30 (9.82)
NSQIP-D, mean (SD)[f]	2.30 (2.62)	4.56 (4.19)	2.64 (2.99)
Diabetes, No. (%)[g]			
No	82 (73)	16 (84)	98 (75)
Oral	15 (13)	1 (5)	16 (12)
Insulin	15 (13)	2 (11)	17 (13)
CHF (30 days prior), No. (%)[h]	3 (3)	1 (5)	4 (3)
Smoker Status, No. (%)[i]	17 (15)	2 (11)	19 (15)
COPD History, No. (%)	21 (19)	4 (21)	25 (19)
OSA, No. (%)	36 (32)	9 (47)	45 (34)
BMI, mean (SD)	28.75 (5.58)	30.05 (6.09)	28.94 (5.63)
Blood Pressure, mean (SD)[j]	132.1 (20.4)	125.1 (19.1)	131.0 (20.2)
Hypertension, No. (%)[k]	80 (71)	16 (84)	96 (73)
Katz IADL, mean (SD)[l]	5.9 (0.5)	5.8 (0.4)	5.9 (0.5)
Stroke/TIA, No. (%)	11 (10)	1 (5)	12 (9)
Hearing Impairment, No. (%)[m]	24 (22)	7 (39)	31 (24)
Procedure characteristics			
Surgery Type, No. (%)[n]			
Vascular	25 (23)	5 (26)	30 (24)
Cardiac	22 (21)	10 (53)	32 (25)
Thoracic	11 (10)	1 (5)	12 (10)
General	12 (11)	0 (0)	12 (10)
Spinal or Orthopedic	27 (25)	3 (16)	30 (24)
Urological or Gynecological	10 (9)	0 (0)	10 (8)
Blood Loss, mean (SD), mL[o]	730.6 (2126.9)	3535.7 (7992.0)	1134.7 (3669.4)
Operation Time, mean (SD), min[n]	287.2 (141.1)	418.5 (215.6)	307.0 (160.0)

Abbreviations: TMTB, Trail Making Test B; MoCA, Montreal Cognitive Assessment; GDS, Geriatric Depression Scale; ASA, American Society of Anesthesiologists; NSQIP, National Surgical Quality Improvement Project risk of serious complications (SC) or death (D) from surgery; CHF, Congestive Heart Failure; COPD, Chronic Obstructive Pulmonary Disease; OSA, Obstructive Sleep Apnea; BMI, Body Mass Index; IADL, Index of Activities of Daily Living; TIA, Transient Ischemic Attack.

[a]Percentages have been rounded and may not total 100.
[b]N = 129. Years of education was not collected for 2 participants.
[c]N = 128. MoCA was not collected prior to surgery for 3 participants.
[d]N = 127. GDS was not collected for 4 participants.
[e]N = 129. 2 participants are missing an ASA score because the surgery was cancelled.
[f]N = 125. 1 participant withdrew before surgery. The surgery was cancelled for 3 participants. The surgery type was not supported by the calculator for 2 participants.
[g]Diabetes treated with an oral antidiabetic drug or insulin prior to surgery.
[h]Congestive heart failure in the 30 days prior to surgery.
[i]Current smoker within 1 year prior to surgery.
[j]Preoperative systolic blood pressure collected at a clinic visit. N = 125. 1 participant withdrew before surgery. The surgery was cancelled for 4 participants. 1 participant did not have preoperative blood pressure from a clinic visit recorded in the medical record.
[k]Hypertension treated with medication.
[l]N = 128. Katz IADL was not collected for 3 participants.
[m]N = 128. Hearing impairment unknown for 3 participants.
[n]N = 126. 1 participant withdrew before surgery. The surgery was cancelled for 4 participants.
[o]N = 118. 1 participant withdrew before surgery. The surgery was cancelled for 4 participants. Blood loss was not recorded in the medical record for 8 participants.