Supplementary Information

Figure S1. Lesion reconstructions for LPFC Patients. Individual reconstructions of structural scans for all nine patients are shown in neurological convention with cyan indicating lesion site. The last row illustrates the group overlay of lesions, as shown in Figure 1a.

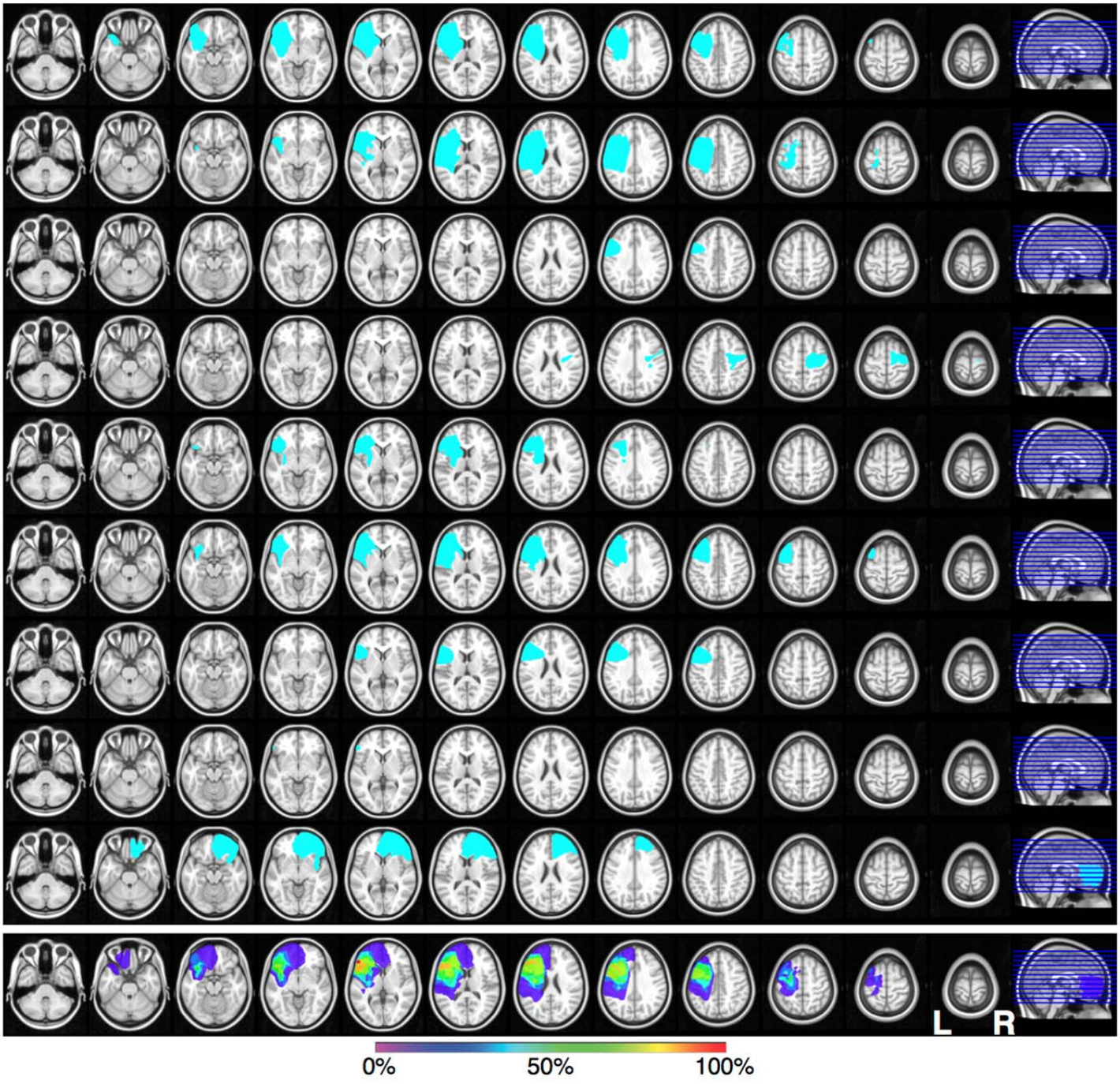

Figure S2. ERP waveforms for LPFC patients (left) and healthy controls (right) at electrode Pz. Time windows of analyses for P3b (0.4 – 0.6 s) are highlighted in yellow. Both groups showed increased P3b amplitude for target tones relative to standard tones in the EDA condition.

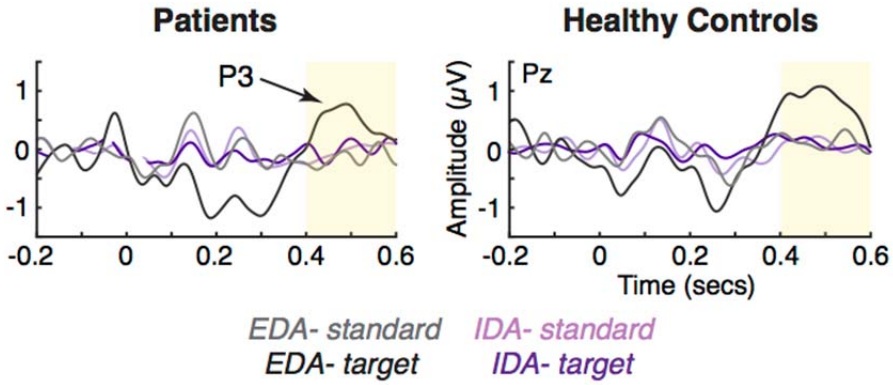

Figure S3. OFC patients show trends of increased theta power during EDA and increased alpha power during IDA. A) Mean theta power (shading indicates SEM) throughout the 500ms post-stimulus period for EDA and IDA are plotted separately for standard (left panel) and target tones (right panel). Time frequency representations of low frequency power aggregated across central electrodes (C3,C1,Cz,C2,C4) in response to standard tones (left panel) and target tones (right panel), averaged separately for EDA (top) and IDA (bottom). B) Mean alpha power (shading indicates SEM) averaged across tones throughout the 500ms post-stimulus period for EDA and IDA. Time frequency representations of low frequency power aggregated across posterior electrodes (PO7,O1,Oz,O2,PO8) averaged across tones, plotted separately for EDA (top) and IDA (bottom).

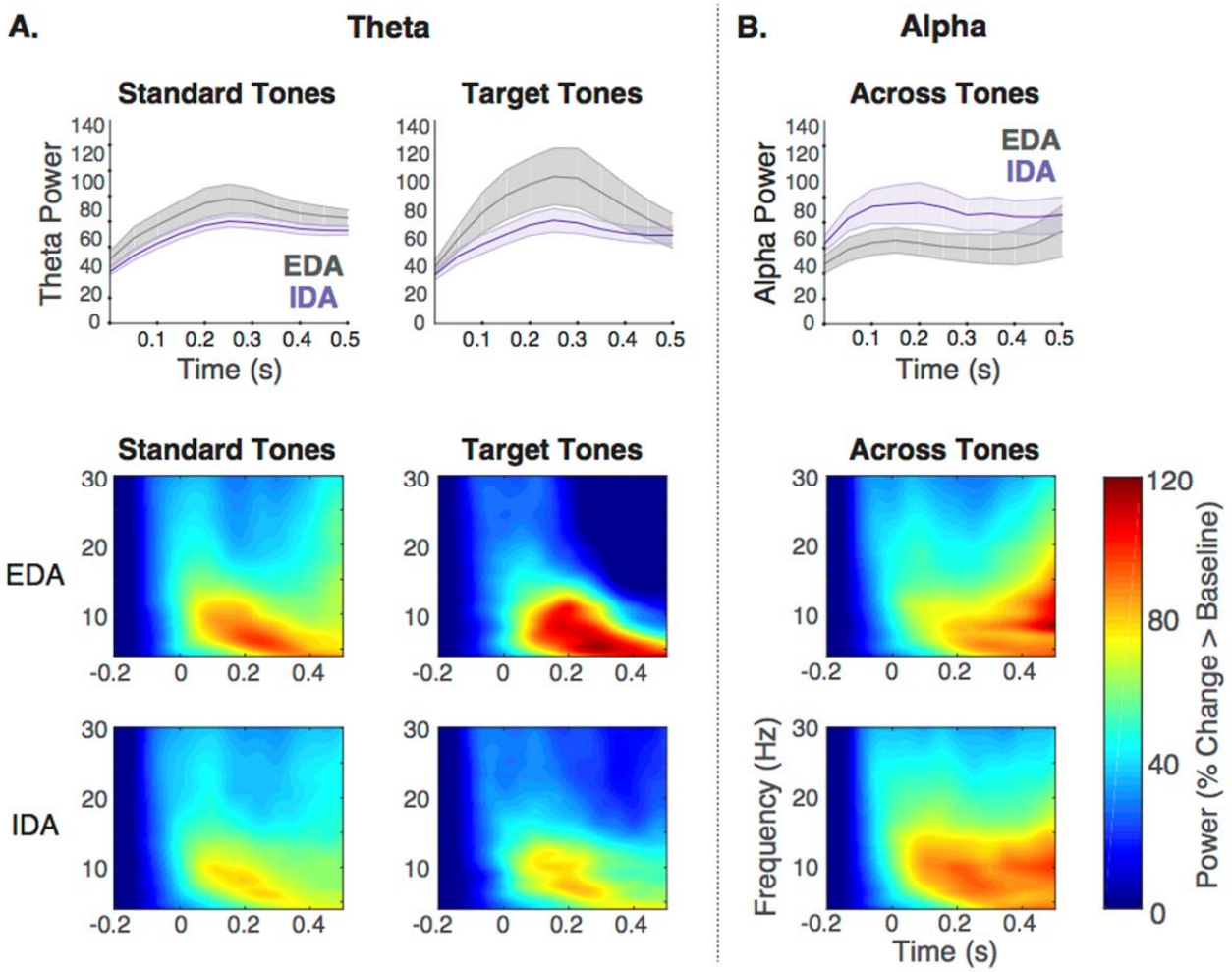

Figure S4. Correlation between theta power and accuracy. There is a positive correlation between mean accuracy (as measured by d prime) and frontocentral midline theta power (percent change from baseline) averaged across the 500ms post-stimulus time window during the EDA condition.

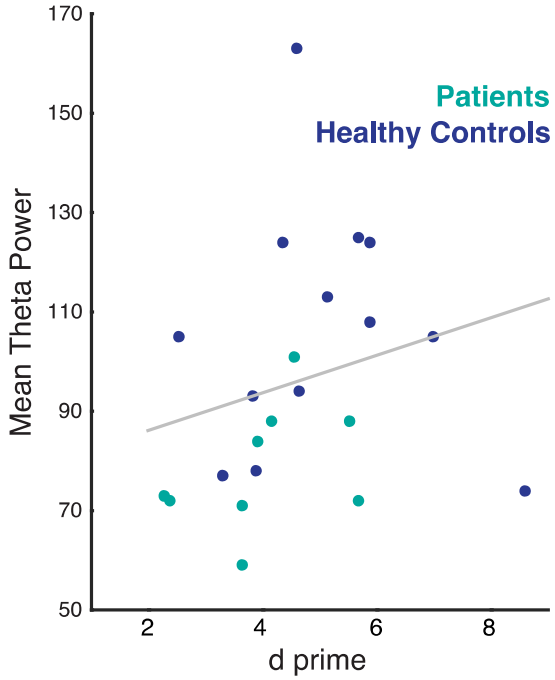

Table S1. Demographic information, cognitive functions, and clinical characteristics of LPFC patients and healthy controls.

	Patients	Healthy Controls
Demographic Information		
Gender	5 F ; 4 M	7 F ; 6 M
Age (mean/SD)	57.4 ± 12.2	57.4 ± 11.9
Years of Education (mean/SD)	18 ± 4.5	17.7 ± 2.4
Handedness	1 L ; 8 R	2 L ; 11 R
Cognitive Function		
IQ (mean/SD)	112 ± 9	--
Clinical Characteristics		
Years elapsed (mean/SD)	10 ± 7	--
Lesion Volume in cm^3 (mean/SD)	103 ± 79	--

Methods and Results

P3b Event-Related Potential (ERP)

Processing and Analysis. EEG data were high-pass filtered at 1Hz, and notch filtered at 60 Hz for data collected at Berkeley and 50 Hz for data collected at Oslo. Ocular and muscle artifacts were corrected for using independent component analysis (ICA). Electrodes with excessively noisy signals were interpolated from the neighboring electrodes using spherical spline interpolation (Perrin et al. 1989). Continuous EEG data were then segmented into 3000ms epochs, beginning at 1000ms prior to stimulus onset. Each trial was visually inspected for remaining artifacts, which were further removed. Data were re-referenced offline to an average reference before data analysis. EEG data pre-processing and analysis were performed using EEGLAB (Delorme & Makeig, 2004), FieldTrip (Oostenveld, Fries, Maris & Schoffelen, 2010), and custom Matlab scripts (Mathworks, Natick, MA, USA). Given that trial numbers for each tone type were matched between EDA and IDA conditions, the mean number of correct trials was identical for both conditions: standard tones: mean = 224, S.D. = 56; and target tones: mean = 54, S.D. = 12."

EEG signals were bandpass filtered at 1-15Hz for ERP analysis. ERPs were quantified by the mean amplitude measure relative to a -200 to 0 pre-stimulus baseline. The P3b mean amplitude was measured over parietal sites across a 400-600ms post stimulus time window. The P3b mean amplitude was measured over parietal sites (P1, Pz, P2) across a 400-600ms post stimulus time window. EEG measures were examined using a repeated-measures ANVOA with attention (externally-directed attention, or EDA, vs. internally-directed attention, or IDA) and tone (standard vs. target) as within-subject

factors. Significant two-way interactions were further examined with paired-samples t-tests between tones within each condition. All statistical analyses were performed using SPSS (IBM, Armonk, NY, USA).

Results. Repeated-measures ANOVA were performed to examine the P3b amplitude as a function of attention and tones. As with the power analyses, we first tested for attention and tone effects in healthy controls in order to validate the task. In the healthy controls, there was a main effect of attention ($F(1,12) = 21.51$, $p = .001$) with larger P3b amplitude during EDA relative to IDA, as well as a main effect of tone ($F(1,12) = 18.43$ $p = .001$), driven by larger P3b amplitude for target tones than standard tones. These main effects were modified by an attention x tone interaction ($F(1,12) > 27.47$, $p < .001$). Pair-samples t-tests were used to follow up this interaction, indicating larger P3b mean amplitude for target tones during EDA relative to IDA ($t(12) = 5.28$, $p < .001$), but no difference was observed for standard tones ($t(12) = 0.08$, $p = .937$). The LPFC patients showed a similar pattern of results. Repeated measures ANOVA for P3b revealed a main effect of attention ($F(1,8) = 10.02$, $p = .013$), as well as an attention x tone interaction ($F(1,8) = 7.09$, $p = .029$). The interaction was driven by larger P3b mean amplitude during EDA compared to IDA for target tones ($t(8) = 2.97$, $p = .018$), but not standard tones ($t(8) = -0.61$, $p = .556$).

These findings indicate that the P3b ERP component was unlikely to be the primary driving force of the power findings. Since the P3b was measured at posterior sites, our main comparison focused on alpha power as that was also measured at posterior sites. Our results revealed the healthy controls showed significantly greater alpha power during

IDA relative to EDA, whereas the LPFC patients did not show any differences between attention states. Both findings contrast with the findings of a larger P3b amplitude during EDA relative to IDA in both groups. For completeness, we also considered theta power even though theta power was measured at central cites. Although the healthy controls showed similar patterns for both P3b and theta power, the patients showed a different pattern of results for the two measures. Specifically, both the attention effect and attention x tone interaction for the P3b were significant in LPFC patients, yet neither effects were significant for theta power. Importantly, as theta power was measured at central sites and a laplacian reference was used in all power analyses, volume conduction from the posterior P3b to the centrally measured theta power is unlikely.

Effects of Fatigue

We examined the possibility that the observed group differences in the power measures may be attributable to effects of fatigue by examining global changes in theta and alpha power throughout the duration of the task. To do so, we averaged theta/alpha power separately across the post-stimulus time window (0-500ms) for each trial included in the main analysis, and then fitted a regression line of the power values in chronological order over the course of the task irrespective of tone types and attentional conditions. This yields a slope value of theta/alpha power for each subject that captures its overall change over the course of the task.

We first determined whether the slope for theta and alpha power in patients changed over time. One-sample t-tests indicate that the slope was not different from zero

for both theta power ($t(8) = 0.23$, $p = .82$) and alpha power ($t(8) = 0.92$, $p = .39$). For completeness, we ran the same analysis for healthy controls and found that the slope also was not different from zero for both theta power ($t(11) = -0.21$, $p = .84$) and alpha power ($t(11) = 0.71$, $p = .49$). Next, we compared the slopes between groups. Independent-samples t-tests indicate that the slopes of patients and healthy controls did not differ from each other for both theta power ($t(20) = 0.31$, $p = .76$) and alpha power ($t(20) = 0.47$, $p = .64$). These findings suggest that fatigue or time-on-task did not contribute to the differences we observed in EEG measures.

Selectivity of Lesion Location

We tested a clinical control group consisting of nine patients with lesions in the orbitofrontal cortex (OFC) in order to ascertain the selectivity of LPFC lesions in externally and internally directed attention. These patients performed the same task as the other groups and we implemented identical time frequency and statistical analyses. As illustrated in Figure S3, OFC patients showed patterns in these measures similar to those observed in healthy controls: greater fronto-central theta power during EDA relative to IDA, and greater posterior power during IDA relative to EDA. While this observation is consistent with the numerical values of theta and alpha power observed for the two attentional conditions, statistical analyses only revealed trends for attentional modulations in both theta power ($F(1,8) = 2.67 – 4.35$, $p = .070 – .141$) and alpha power ($F(1,8) = 3.59 – 9.53$, $p = .015 – .095$) across the post-stimulus time windows, corrected for multiple comparisons.

LPFC Damage Disrupts Attentional Regulation

Notably, while the rostrolateral prefrontal cortex (RLPFC) is considered to be part of the frontoparietal control network (Christoff et al., 2017; Dixon et al., in press) and there is some overlap in Brodmann areas between RLPFC and OFC, the majority of our OFC patients (6 out of 9) have focal lesions restricted to the medial wall of the OFC. However, as the location of most of the lesions in our OFC patient cohort is not part of the frontoparietal control network, these results enable us to partially disentangle the unique contribution of the LPFC in attentional modulations of EDA and IDA.