## Supplementary Information

**Figure S1.** Lesion reconstructions for OFC Patients. Individual reconstructions of structural scans for all nine patients with cyan indicating lesion site. Group overlay of lesions is shown in Figure 1a.

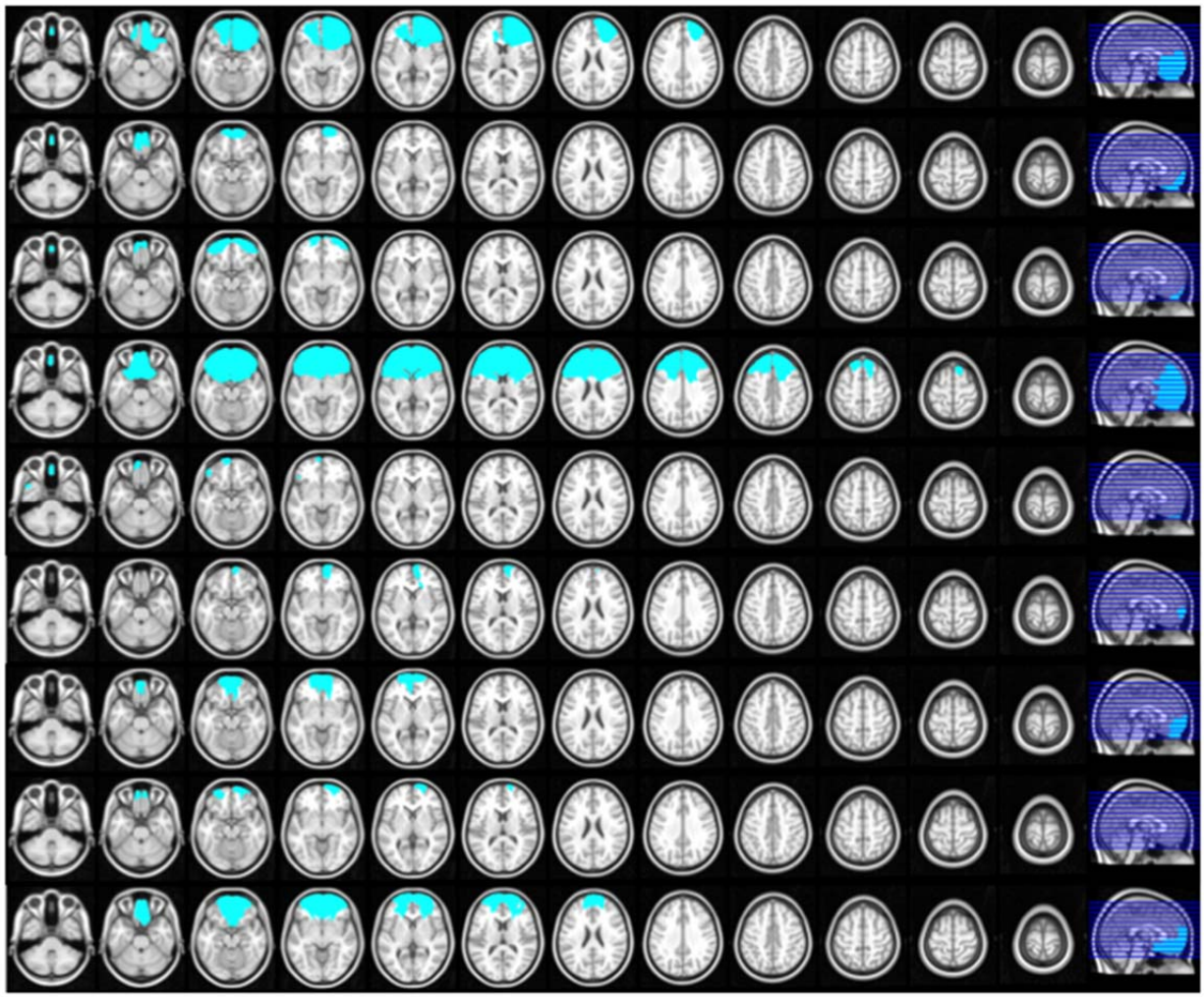

**Figure S2.** Correlation between N1 peak amplitude and d prime. There is a negative correlation between the N1 peak amplitude for target tones during the attend condition and d prime across both OFC patients (OFC; shown in teal) and healthy controls (HC; shown in blue).

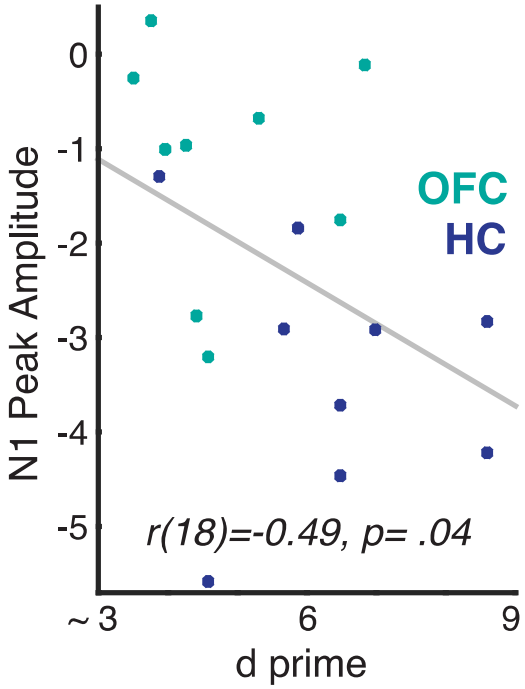

**Table S1.** Demographic information and clinical characteristics of OFC patients and healthy controls.

| | OFC Patients | Healthy Controls |
|---|---|---|
| **Demographic Information** | | |
| Gender | 6 F ; 3 M | 6 F ; 3 M |
| Age (mean/SD) | 51.6 ± 9.7 | 52.1 ± 12.8 |
| Years of Education (mean/SD) | 15.2 ± 2.2 | 17.2 ± 1.3 |
| **Clinical Characteristics** | | |
| Years elapsed since injury (mean/SD) | 15 ± 13 | -- |
| Lesion Volume in $cm^3$ (mean/SD) | 72 ± 70 | -- |

## Methods

### Patient Characteristics

Nine patients with lesions in the orbitofrontal cortex (OFC), and nine matched healthy controls participated in the experiment. Demographic and clinical information are presented in Table S1. The two groups did not differ in gender nor age ($p > .90$). Healthy controls had more years of education than patients ($p = .03$); however, this variable did not correlate with any behavioral or ERP measures ($p > .15$). Exclusion criteria included a history of psychiatric disease, substance abuse requiring treatment, premorbid head injury, comorbid neurological disease, IQ < 85, or sensory impairment. The OFC group consisted of nine patients, seven of which had bilateral damage and two with unilateral damage (1 right, 1 left). Their lesions resulted from low-grade meningioma resection (n=3 at Oslo) or traumatic brain injury (n=1 at Oslo; n=5 at Berkeley). Maximal lesion overlap occurred in Brodmann Areas 10 and 11. Individual lesion reconstructions are shown in Figure S1.

### Lesion Reconstruction

Lesion reconstructions were based on structural MRIs obtained after study inclusion. Lesions were outlined by manually drawing on Fluid Attenuated Inversion Recovery (FLAIR), T1 and T2 weighted images of each participant's brain using MRIcron (www.mccauslandcenter.sc.edu/mricro/mricron/) and Adobe Photoshop CC 2015 (http://www.adobe.com/). T1, T2 and FLAIR images were first co-registered to a T1 MNI Template (normalized from 152 T1 scans), using Statistical Parametric Mapping software's (SPM8:www.fil.ion.ucl.ac.uk/spm/) New Unified Segmentation routine. The

manual delineation of the lesions was performed on axial mosaics of the normalized T1 scans. When available, high-resolution FLAIR and T2-weighted images were used as aids to determine the borders of the lesions. The resulting lesion masks were converted to three-dimensional MNI space using the Statistical Parametric Mapping software's (SPM8:www.fil.ion.ucl.ac.uk/spm/) Mosaic to Volume routine. Lesions were reconstructed under the supervision of a neurologist (RTK). We calculated lesion sizes using the MRIcron descriptive statistics function after a lesion had been manually delineated.

**Task Paradigm and Stimuli**

Subjects were presented with a series of standard tones (800Hz) and target tones (1000Hz) in a random order with probabilities of 0.8 and 0.2, respectively. All auditory stimuli were pure tones presented through stereo speakers at 75dB. The duration of each tone was 200ms, and the inter-trial interval was randomly jittered between 800-1200ms. Subjects were asked to keep their eyes fixated at the cross in the center of the screen throughout the task.

In the attend condition, subjects were instructed to focus on the tones and press a button as quickly and accurately as possible when a target tone is heard. Mean reaction time and d prime were computed for each subject. In the ignore condition, they were instructed to refrain from paying explicit attention to the tones. Each block began with 25 tones in the attend condition followed by 25 tones in the ignore condition, or vice versa. The order of these two conditions was counterbalanced within subjects. Subjects completed a maximum of 14 blocks of attend and ignore conditions, consisting of 280

standard and 70 target tones in each condition. Stimuli presentation was operated by Eprime.

**EEG Data Acquisition and Analysis**

EEG was recorded continuously from 64 active electrodes mounted on a cap according to the 10-20 system using the Biosemi ActiveTwo system (www.Biosemi.com). Data were amplified and digitized at 1024 Hz, with a bandpass filter of 0.16 – 100 Hz. Vertical and horizontal eye movements were recorded from an electrode placed below the right eye, and two electrodes placed at the right and left outer canthus.

EEG data were down-sampled to 512 Hz, then high-pass filtered at 1 Hz, 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). Across subjects, the average number of electrodes that required interpolation was 2.22 (i.e. 3.5% of all electrodes). One subject required interpolation on electrode Pz and another subject required interpolation on electrode P2. None of the other interpolated electrodes were relevant to the ERP analyses. 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).

To ensure that conditional effects in EEG measures were not simply due to differences in signal-to-noise ratio resulting from a mismatched number of trials across conditions, the number of trials consisting of standard and target tones between attend and ignore conditions were matched (by random sampling) within subjects. Standard and target tones in the attend and ignore conditions were averaged separately across subjects within each group for statistical comparisons.

EEG signals were bandpass filtered at 1-15Hz for ERP analysis. All ERPs were quantified by the peak or mean amplitude measure relative to a -200 to 0 pre-stimulus baseline. The N1 and N2 peak amplitudes were measured over fronto-central midline sites (FC1, FCz, FC2) as the most negative point within a post stimulus time window of 80-120ms and 200-300ms, respectively. The P3b mean amplitude was measured over parietal sites (P1, Pz, P2**)** and averaged across a 400-600ms post stimulus time window.

**Statistical Analyses**

To examine group differences in behavioral measures, an independent samples t-test was conducted separately for mean reaction time and d prime. Group differences in EEG measures were examined using a repeated-measures ANVOA with condition (attend vs. ignore) and tone (standard vs. target) as within-subject factors, and group (OFC vs. controls) as between-subject factor. 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

### Behavioral Measures

To follow up on the finding of reduced d prime in OFC patients, we also examined group differences in hit rate and false alarm rate. We found that OFC patients also showed a near significant decrease in hit rate ($t(16)=-1.98$, $p=.069$), but no difference in false alarm rate ($t(16)=1.27$, $p=.224$) compared to the controls.

### Event-Related Potentials

Repeated-measures ANOVA were performed to examine group differences in the N1, N2, and P3b amplitudes as a function of condition and tones.

For N1, there was a main effect of group ($F(1,16) = 17.90$, $p = .001$), driven by smaller N1 peak amplitude in the OFC patients relative to the controls. Neither the main effect of attention ($F(1,16) = 0.02$, $p = .887$) nor the attention by group interaction ($F(1,16) = 0.43$, $p = .524$) were significant.

For N2, there was a condition by tone interaction ($F(1,16) = 10.04$, $p = .006$), driven by larger N2 peak amplitudes for target relative to standard tones during the attend condition ($t(17) = 3.68$, $p = .002$), but not the ignore condition ($t(17) = -1.30$, $p = .21$). Neither the main effect of group ($F(1,16) = 0.79$, $p = .387$) nor the attention by group interaction ($F(1,16) = 1.40$, $p = .254$) were significant.

Repeated-measures ANOVA for P3b revealed a main effect of condition ($F(1,16) = 15.76$, $p = .001$), a main effect of tone ($F(1,16) = 21.85$, $p < .001$), and a condition by tone interaction ($F(1,16) = 11.52$, $p = .004$). The pattern of results is similar to N2, with the P3b mean amplitude being larger for target tones than standard tones during the attend condition ($t(17) = -4.30$, $p < .001$), but not the ignore condition ($t(17) = -1.35$, $p = .20$). Neither the main effect of group ($F(1,16) = 2.03$, $p = .174$) nor the attention by group interaction ($F(1,16) = 0.01$ $p = .926$) were significant.

*Post-Hoc Analysis.* As we observed a pattern of results for the P1 that is similar to the N1, we performed the same repeated-measures ANOVA post-hoc for this ERP component. The P1 peak amplitude was measured over fronto-central midline sites (FC1, FCz, FC2) as the most positive point within a post stimulus time window of 20-50ms. The main effect of group was marginally significant ($F(1,16) = 3.86$, $p = .067$), driven by smaller P1 peak amplitudes in the OFC patients relative to the controls. Neither the main effect of attention ($F(1,16) = 0.21$, $p = .653$) nor the attention by group interaction ($F(1,16) = 0.003$, $p = .955$) were significant. This finding raises the possibility that the OFC can potentially modulate auditory sensory responses as early as 20ms post-stimulus; however, this particular result remains to be confirmed by future studies.

**Impact of Brain Lesion Volume**

For OFC patients, we also examined the impact of lesion volume on behavioral and electrophysiological measures. In terms of behavioral measures, there were no significant correlations between lesion volume and RT to attended targets ($r(9) = .27$, $p = .48$) as well as d prime ($r(9) = -.47$, $p = .20$). For EEG measures, lesion volume was

included as a covariate in repeated measures ANOVA separately conducted for each ERP component. Lesion volume did not significantly interact with either condition ($p > .15$) or tone ($p > .65$) for any of the ERP components.