Despite a long history, the investigation of clinical depression using task-related, cognitive- event-related potentials (ERPs) and quantitative EEG measures at rest have produced two distinct lines of research with little, if any, overlap in theory or findings. Whereas both literatures are typically limited by uncertainties attributable to volume conduction, a surface Laplacian (or CSD) transformation provides reference-free ERP/EEG measures that are closer to the underlying neuronal generators (10). Using a CSD-PCA approach, we recently exported a sharply localized novel vertex source (CSD) component that is unique to novel stimuli and substantially reduced in depressed patients (11). In another study, condition-dependent (eyes open vs. closed) CSD-based EEG predicted antidepressant treatment response (12). Moreover, the novel EEG response is self-associated with alpha phase locking to a slower rhythm (delta) (13). This convergence of temporal and spatial findings in clinical depression suggest that CSD-based TF measures may be identifiable with the NVS.

## Methods

Participants. Depressed patients (n = 49; 22 male; age 39 ± 10.7 yrs) and healthy adults (n = 49; 35 male; 31 ± 10.7 yrs) with no history of any psychopathology or neurological disease.

Novelty Oddball Task. An auditory novelty oddball task was implemented on a Neuronic Stimsyst (fig. 1). Eight trial blocks consisted of 300 ms (60 ms rise and fall time) and novel sound (100-400 ms duration) that were presented in pseudorandom order (1000 SSAs). Unique novel sounds (i.e., animal sounds, musical instruments, environmental sounds, p = 12) were intermixed with a frequent target (300 ms; p = 76) and an infrequent target (100 ms; p = 12). All stimuli were presented binocularly stereotactically at 5.8° BFO. Subjects were instructed to focus their eyes on a fixation cross displayed on a computer monitor, and respond with a button press preference, usually, and when they had the infrequent target onset (response hard counterbalanced across blocks).

ERP Recordings. ERP methods and results were detailed in ref. 9. ERPs were recorded from 67 scalp sites (ActiViee) using an active recording reference composed of sites p03 (common reference) and p10 (right ear). Neural data were filtered offline to alpha, beta, and gamma bands. Continuous data were exported to Neuronic format using Polygraph. All power bands were divided into epochs for each of the 98 participants (200 ms prestimulus + 1000 ms poststimulus). Continuous EEG data were blink corrected using a spatial, singular value decomposition (NeuroScan). Stimulus-locked data (200-1200 ms) were extracted for each subject and band combination.

CSD-ERP Recordings. CSD waveforms (temporal CSD or vertex) were computed from CSD waveforms at each scalp site, and rereferenced to a common reference composed of sites PO1, PO2, and TP9. Back-referenced waveforms were calculated from the grand mean vertex CSD. ERP waveforms were decomposed into “early” (50-200 ms) and “late” (300-600 ms) components.

CSD-Results. ERP results are depicted in ref. 10. CSD ERPs were statistically compared between groups (Mann-Whitney U = 72; z = -1.987; p = 0.05). The enhanced early vertex alpha synchronization in depressed participants following salient, but task-irrelevant, distracters is associated with a primary ERSP maximum (red). The precise time-lock eroked vertex desynchronization (ERD; blue) at and above alpha frequencies. Differences between patients (right) and controls (left) are prominent below 15 Hz and take the form of both an initial event-related desynchronization (ERD; blue) and a later contralateral event-related desynchronization (ERD; blue) at and above alpha frequencies. Between patients (right) and controls (left) are prominent below 15 Hz and take the form of both an initial event-related desynchronization (ERD; blue) and a later contralateral event-related desynchronization (ERD; blue).

## Results

### Novelty Vertex Source

The enhanced early vertex alpha synchronization in depressed participants following salient, but task-irrelevant, distracters is associated with subsequent reductions in both the novelty vertex source and the subsequent reduction in condition-dependent, posterior alpha desynchronization following novel sounds.

The findings thereby provide a common framework for interpreting tonic and event-related alpha abnormalities in major depression.

CSD-4TfPCA shows promise as a useful integrative tool for identifying and characterizing better predictors of antidepressant treatment outcomes.

CSD-HPCA is a comprehensive approach for dealing with the temporal and spatial processes underlying the trial-by-trial event-related EEG.

Being based on CSDs, these results directly reflect neuronal current generator patterns, and are not confounded by errors and artifacts related to the recording reference or volume conduction that plague all voltage measures of the EEG.

## References