

## Electroencephalographic Brain Dynamics Following Manually Responded Visual Targets

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## ***Abstract***

**Background:** Here we model for the first time the perturbing effects of detecting and manually responding to attended visual targets on the dynamics of whole scalp-recorded EEG signals parsed into maximally independent EEG processes by independent component analysis (ICA).

**Methodology/Principal Findings:** Maximally independent EEG processes from fifteen subjects were separated from 31-channel scalp data by infomax independent component analysis (ICA) and then clustered across subjects based on sim

ilarities of their scalp maps and power spectra. Nine classes of maximally independent EEG processes with distinct spatial distributions and target and response event-related reactivities were identified. A cluster of processes with maximal projection to the forehead produced a positive-going potential that peaked immediately before the motor response. Activity resembling a two-cycle circa 5-Hz theta wavelet, dominating the post-motor response-locked event-related potential (ERP) at the frontal midline, was accounted for by phase-linked activity in two clusters of EEG processes projecting to the frontal and central midline. Left and right mu processes, whose scalp projections reversed polarity over hand motor cortex, also exhibited the theta response, which was partially coherent in single trials between frontal and central midline and between frontal midline and contralateral (left) mu processes. The parietal ('P300' or 'P3b') positivity that followed the motor response mainly summed activity in parietal, mu and central occipital process clusters. Midline occipital processes also exhibited stimulus-induced alpha band phase resetting. **Conclusions/Significance:** All these observed patterns of event-related EEG brain dynamics may index local-field based modulation of neural spike-based communication between cortical areas involved in updating of attention, expectancy, memory, and motor preparation during and following target recognition and speeded responding.

## ***Introduction***

The waking brain fulfills intentions through coordinated brain processes that operate within and between multiple brain areas to integrate perception, association and action. Fulfillment of intentions is maximized by features of these processes that support informed anticipation of and selective attention to events and their probable consequences. The dynamics of ongoing encephalographic (EEG) activity recorded from the human scalp differ markedly with state of attention and intention (Makeig and Inlow, 1993; Worden et al., 2000), yet most event-related EEG research has assumed that the effects of events on EEG signals emerge out of a flat baseline, as in the typical averaged event-related potential (ERP). Also, the electrophysiological consequences of stimulus events spread quickly in the brain -- by 100 ms, sensory stimulus information is widely distributed (Hupe et al., 2001), perturbing local field activities in many brain areas (Klopp et al., 2000). There is little chance, therefore, that any but the very earliest features of event-related EEG dynamics are generated within single brain areas.

The adequacy of time-domain response averaging for modeling macroscopic brain dynamics also depends on the assumption that the cortical sources of EEG activity contributing and not contributing to average ERP waveforms are somehow distinct. However, the scalp topographies of unaveraged EEG and averaged ERP data can be quite similar (Makeig et al., 2002a), suggesting that areas contributing to ongoing EEG signals may also contribute to ERP averages. EEG processes not contributing to response averages may also be affected by experimental events, as several types of dynamic EEG response processes are not reflected in ERP averages (Pfurtscheller and Aranibar, 1977; Makeig, 1993; Makeig et al., 2002a). A more comprehensive model of event-related brain dynamics is therefore required to capture features of EEG signals indexing the dynamic interplay between spatially coherent brain processes supporting anticipation of, attention towards, associations to, and behavioral responses following experimental events.

The above considerations suggest that event-related EEG dynamics may be better modeled as coordinated event-related perturbations in multiple, intermittently active local field processes. Since the scalp projections of such processes generally overlap by volume conduction, they cannot be directly identified with the contributing cortical areas. An alternate approach we adopt here is to separate their contributions by temporal differences (Makeig et al., 1996a, 1997).

Following stimuli belonging to an anticipated but infrequently-presented category, the averaged ERP is dominated by a broad vertex-positive peak often called P300 after its earliest appearance in auditory responses (Sutton, et al., 1965; for review, see (Soltani et al., 2001). Results of brain lesion studies (Halgren et al., 1980; Knight et al., 1989) and functional imaging experiments (Ford et al., 1994; Ebmeier et al., 1995; Ardekani et al., 2002) strongly suggest that ‘P300’ actually sums effects of dynamic perturbations of local field activities in several brain regions. A more inclusive model of event-related EEG brain dynamics of such data, therefore, should model how target stimulus presentations and subject motor responses perturb the dynamics of the ongoing EEG signals, both within and across single subjects. Here, we present such a model.

## ***Methods***

***Task design.*** Event-related brain potentials (ERPs) were recorded from subjects who attended to randomized sequences of filled disks appearing briefly inside one of five empty squares that were constantly displayed 0.8 cm above a central fixation cross (Fig. 1) following Townsend and Courchesne (1994). The 1.6-cm square outlines were displayed on a black background at horizontal visual angles of  $0^\circ$ ,  $\pm 2.7^\circ$  and  $\pm 5.5^\circ$  from fixation. During each 76-s block of trials, one of the five outlines was colored green and the other four blue. The green square marked the location to be attended. This location was varied in random counterbalanced order across blocks. In each block, 100 stimuli (filled white disks) were displayed for 117 ms within one of the five empty squares in a pseudo-random sequence with inter-stimulus intervals (ISIs) of 250 to 1000 ms (in four equiprobable 250-ms steps).

*[Insert Figure 1 about here]*

Fifteen right-handed volunteers (ages 19 to 53 years, mean 30.4) with normal or corrected to normal vision participated in the experiment. Subjects were instructed to maintain fixation on the central cross while responding only to stimuli presented in the green-colored (attended) square. Subjects were required to press a thumb button held in the right hand as soon as possible following stimuli presented in the attended location (Fig. 1). Thirty blocks of trials were collected from each subject, yielding 120 target and 480 nontarget trials at each location. Subjects were given breaks between blocks. Average-ERP and single-trial analyses of early stimulus-locked activity have been reported previously (Makeig et al., 1999a, 1999b, 2002a).

***EEG recordings.*** EEG data were collected from 29 scalp electrodes mounted in a standard electrode cap (Electrocap, Inc.) at locations based on a modified International 10-20 System, and from two

periocular electrodes placed below the right eye and at the left outer canthus. All channels were referenced to the right mastoid with input impedance less than  $5k\Omega$ . Data were sampled at 512 Hz with an analog pass band of 0.01-50 Hz. To further minimize line noise artifacts, responses were digitally low pass filtered below 40 Hz prior to analysis. After rejecting trials containing electrooculographic (EOG) potentials larger than  $70 \mu\text{V}$  or amplifier blocking, brain responses to stimuli presented at each location in each attention condition were stored separately. Responses to target stimuli were analyzed only when (as in nearly all cases) subjects responded 150-1000 ms after target onset.

***Event-related spectral dynamics.*** To examine stimulus- and response-induced changes in the EEG spectrum, we computed event-related spectral perturbation (ERSP) transforms (Makeig, 1993) for each channel and each clustered independent data component (see below) using the publicly available EEGLAB toolbox (Delorme and Makeig, 2003). ERSPs show changes (in dB) from baseline in spectral power across a broad frequency range (here, 3-50 Hz). The time/frequency analysis used Hanning-windowed sinusoidal wavelets of 3 cycles at 3-Hz, rising linearly to about 15 cycles at 30 Hz. This modified wavelet transform was selected to optimize the trade-off between temporal resolution at lower frequencies and stability at higher frequencies. Constructing surrogate data sets by shuffling the data epoch sub-windows used to construct the time-locked spectral average allowed choosing an initial within-subject significance cutoff (not corrected for multiple comparisons) of  $p < .01$ . To construct between-subject mean ERSPs, we used binomial statistics to select as a significance cutoff a minimum number of subjects required to have significant differences (in the same direction) from baseline at a given time/frequency point ( $p < .0001$ ). ERSP transforms of the data were computed at each channel and then for each clustered data component. To test for partial phase-locking (i.e., non-random phase relationship) between EEG processes and the occurrence of experimental events (stimulus presentations

or motor responses) across trials, we used inter-trial phase coherence (ITC) (Makeig et al., 2002a). To test the presence of non-random phase relationships (possibly including fixed delays) between activities in different (maximally) independent components, we also performed event-related phase coherence (ERC) analysis (Makeig et al., 2002a), again with a single-subject bootstrap significance threshold of  $p < .01$  (uncorrected), between pairs of clustered independent components from the same subject (see below). To exclude the possibility that the observed phase linkage arose only from common phase-locking of the portion of the single-trial data constituting the ERP, we subtracted the concurrent mean ERP from each trial before computing phase coherence.

***Independent component analysis.*** Earlier, we applied Independent Component Analysis (ICA) to sets of 25-75 condition grand-averaged ERPs from two visual spatial selective attention experiments including the one re-analyzed here (Makeig et al., 1999a). ICA separates component processes mixed in scalp data based on their relative temporal independence, which should be maximally expressed in the *unaveraged* data. Here, we present results of performing ICA decomposition on collections of concatenated single-trial EEG epochs recorded during one of these experiments.

Infomax ICA (Bell & Sejnowski, 1995; Makeig et al., 1996a) is one of a family of algorithms that exploit temporal independence to perform blind separation. Lee et al. (1999a) have shown that these algorithms have a common information theoretic basis, differing chiefly in the form of distribution assumed for the sources, which may not be critical (Amari, 1998). Infomax ICA finds a square ‘unmixing’ matrix by gradient ascent that maximizes the joint entropy (Cover & Thomas, 1991) of a nonlinearly transformed ensemble of zero-mean input vectors. Logistic infomax can accurately decompose mixtures of component processes having symmetric or skewed distributions, even without using nonlinearities specifically tailored to them, and can be applied practically to EEG data from 100

or more channels. The number of time points required for training may be as few as several times the number of unmixing weights (the square of the number of channels) though more training data may be preferable. In turn, the number of channels must be at least equal to the number of components to be separated (Jung et al., 2001).

As first demonstrated by simulations (Makeig et al., 1996b), when training data consist of a mixture of fewer *large* source components than channels, plus many more *small* source components, as might be expected in actual EEG data, large source components are accurately separated into separate output components, with the remaining output components consisting of mixtures of smaller source components. In this sense, performance of the infomax ICA algorithm degrades gracefully as the amount of ‘noise’ in the data increases. For more details about applying ICA to ERP and EEG data, see Makeig et al. (1999a, 2002a) and Jung et al. (2000a, 2000b).

Infomax ICA was applied to sets of 400 to 600 single 1-s trials (31 channels, 256 time points) time locked from -200 ms before to 800 ms after onsets of target stimuli presented at any of the five stimulus locations (Fig. 1) using the automated Runica algorithm of Makeig et al. (1997) (available for download in the EEGLAB toolbox of Delorme & Makeig, 2002). Trials in which the subject did not respond with a button press (fewer than 5%) were removed from the data. Learning batch size was 50. Initial learning rate began near 0.0004, and was gradually reduced to  $10^{-6}$  during 50-150 training iterations that required about 30 min of computer time. Results of the analysis were relatively insensitive to the exact choice of learning rate or batch size. Reducing the stopping weight change from  $10^{-6}$  to  $10^{-7}$  did not appear to change the resulting decompositions qualitatively, although when decomposing data from many more channels we have since noted an advantage in using a stopping weight change of  $10^{-7}$ .



**Component clustering.** Commonly in evoked response research, neural activity expressed in periocular data channels is ignored for fear of mislabeling eye-activity artifacts as brain activity. Some ICA components of EEG records can be identified as accounting primarily for eye movements, line or muscle noise, or other artifacts (Makeig et al., 1996a; Jung et al., 2000a, 2000b). Subtracting the projections of artifactual components from averaged or single trial data can eliminate or strongly reduce these artifacts while preserving the remaining non-artifactual EEG phenomena in all of the data channels. ICA thus makes it possible, for the first time, to examine periocular EEG activity apart from eye movements. Here, the total of  $31 \times 15 = 465$  component maps and mean activity log spectra for the 15 subjects were clustered using a modified Mahalanobis distance measure (Enghoff, 1998) on vectors coding differences in the component 31-channel (x,y) map gradients and activity log spectra which were first reduced to 12 and 5 dimensions respectively by principal component analysis (PCA). Cluster membership was in some cases then adjusted by eye for uniformity. Four distinct component clusters accounted for eye blinks, horizontal eye movements and left and right temporal muscle noises respectively. After localization of the equivalent current dipole best-accounting for the mean scalp map for each component cluster, cluster-mean event-related time/frequency (ERSP, ITC and ERC) perturbation results were visualized in three dimensions using animation (Delorme et al., 2003).

## **Results**

*[Insert Figure 2 about here]*

### **Target- and manual-response locked activities**

As previously reported, performance level (percent manual responses following targets by 150-1000 ms) was high (>95%). The mean subject-median reaction time (RT) was 352 ms. The ERP time locked to onsets of target stimulus followed by a subject button press contained the expected late positive complex (LPC) or ‘P300’ positivity following early stimulus-locked peaks (P1, N1, P2 and N2, see Fig. 2A). The scalp topography of the positive complex varied continuously through its extent (Fig. 2A, *scalp maps*). In the grand average of the same epochs each time locked to the subject response (Fig. 2B), the early response-locked peaks become smeared out and the LPC and succeeding negative dip more concentrated. In two-dimensional ‘ERP-image’ plots of the total of 8,413 single trials from all 15 subjects (Fig. 2C-F), potential fluctuations in single trials are shown as color-coded horizontal lines, here sorted (across subjects) by reaction time (RT) and smoothed vertically with a 300-trial moving average. The ERP images clearly show that the early visual response peaks at central posterior site Pz (Fig. 2E) are time-locked to stimulus onset, while the late positivity at Pz immediately follows the button press (compare Fig. 2E and 2F) except in trials with quickest RTs. These were contributed largely by two fast-responding subjects whose responses preceded LPC onset.

At frontocentral channel Fz, however, the late positivity in the stimulus-locked grand average (Fig. 2C, bottom) was largely composed of two response-locked positive peaks, separated by 200 ms, that together with intervening and flanking negativities could be modeled by a two-cycle, 5-Hz wavelet (Fig. 2D). The single LPC peak at Fz in the stimulus-locked ERP (Fig. 2A) smears out the two-cycle pattern that is captured clearly in the response-locked average (Fig. 2B), while highlighting a slower stimulus-locked positivity in faster-RT trials (Fig. 2C).

*[Figure 3 about here]*

### ***Event-related spectral perturbations***

Figure 3 summarizes the grand mean time course of changes in log spectral scalp EEG power time locked to button presses (solid vertical line) across the EEG frequency range. During and just prior to the button press, a circa 3-dB increase in theta band power peaks near 4 Hz in bilateral central and posterior cortex. This remained significant ( $p < .01$ ) for 14 of the 15 subjects even after the subject-mean ERP was subtracted from each trial (not shown).

A concurrent (but weaker) theta activity increase is maximal at frontocentral and parietal scalp sites near 6 Hz. The theta increase at these sites is accompanied by blocking of circa 10-Hz and 22-Hz mu activity, maximal at the left and right central scalp but also widespread over posterior scalp. Following the button press, a late central bilateral increase in beta activity (maximal at 16-18 Hz) appears. Finally, a diffuse increase in 3-10 Hz activity beginning 500 ms after the button press reflected increased subject eye activity following the target response prior to artifact component removal.

*[Insert Figure 4 about here]*

### ***ICA decomposition***

Characterizing the sources of event-related potential (Fig. 2) or power spectral perturbation (Fig. 3) processes is difficult because the scalp sensors are relatively far from the actual brain sources and therefore each sum the volume-conducted activities of several source areas. Infomax ICA, applied to the concatenated single trials for each subject after removing trials containing out-of-bounds or uncharacteristic artifacts, decomposed the whole set of concatenated EEG signals into 31 spatially-fixed, temporally maximally independent component processes. Figure 4 shows two single trials (black traces) from one subject at site Pz after removal of six artifact components, together with the

projections of the activities of the three independent components (colored traces and maps) most strongly contributing to each trial. Since infomax ICA provides a complete linear decomposition, the observed data (black traces) are in each case the sum of the remaining  $31-6=25$  component projections (3 colored traces plus 22 smaller component projections). In the upper trial and typically, the single-trial LPC is accounted by ICA as summing contributions of several independent EEG processes. Component IC1 (ranked 1<sup>st</sup> by total variance for this subject and included in the P3b cluster) accounts for the largest part of the upper trial, while in the lower trial the same component process shows a pattern of mixed low alpha and beta activity. Note that the post-response positivity of this is actually larger than in the positive deflection in the whole data (black trace) which sums contributions of the (plotted) three plus those of the remaining (not plotted) 22 components.

### ***Independent component clusters***

Cluster analysis applied to the normalized scalp topographies and power spectra of all 465 components from the 15 subjects (see Methods) identified at least 13 clusters of components with similar power spectra and scalp projections. These clusters showed functionally distinct activity patterns. Four clusters accounted for artifacts associated with eye blinks, lateral eye movements, left and right temporal muscle activity, respectively (not shown). Mean properties of nine non-artifact component clusters are shown in Figs. 5-8 which present the mean scalp map, response-locked ERP, normalized ERP image, and event-related spectral perturbation (ERSP) image of each cluster.

*[Insert Figure 5 about here]*

***Inferior frontal (P3f) cluster.*** After subtraction of components accounting for blinks and eye movements, the response-locked ERP at both periocular channels contained a broad, circa 2- $\mu$ V positive-going scalp potential peaking 39 ms before the recorded button press. Figure 5A-D show the

mean scalp map and dynamic properties of a cluster of 10 independent components from 10 subjects largely accounting for this evoked response feature, dubbed P3f in our previous report based on decomposing the matrix of 25 condition ERPs from these experiments (Makeig et al., 1999a). Although the components in this P3f cluster projected most strongly to the two periocular channels, artifact activity produced by eye blinks and eye movements were accounted, for each subject, by other (and much larger) artifact components. Note, in the ERP image (Fig. 5C), the absence of sharp excursions, not regularly time-locked to experimental events, which would be associated with blinks and eye movements. Instead, this component class accounts for nearly all the (P3f) positivity before the button press (Fig. 5B), particularly in quicker-response trials (Fig. 5C).

The P3f cluster-mean response-locked positivity begins near 150 ms, consistent with recent neurophysiological evidence (Klopp et al., 2000; Hupe et al., 2001). The P3f positivity peaks 39 ms before the button press. Subtracting the button travel time (~25 ms, roughly estimated from EMG recording during one experimental session) and the neuromuscular conduction time (~15 ms) suggests the P3f peaks near or at the moment of the brain motor command. It is thus tempting to speculate that the P3f process might originate in frontal structures involved in motivated decision making and response selection, such as orbitofrontal cortex (Ikeda et al., 1996), though the present data do not allow more specific conclusions.

The far-frontal (P3f) component cluster response might account for the 280-ms 'P2a' peak noted in responses to (foveal) visual 'oddball' stimuli by Potts et al. (1998). Potts and Tucker (2001) report that P2a is maximal near the eyes but can be recorded over most of the face and may also be found in attention conditions involving no subject button press. The scalp map of the previously reported ERP-derived 'P3f' component (Makeig et al., 1999a) also included bilateral parietal features not found in the equivalent single-trial data component cluster. The temporal and far-frontal projections joined in the

ERP-derived P3f component did not cohere in the single-trial data and so were not associated by ICA in the single-trial P3f cluster components. This points to the advantage of decomposing by ICA a sufficient number of unaveraged EEG data trials over decomposition of even a fairly large set of averaged responses.

*[Insert Figure 6 about here]*

**Theta response clusters.** Figure 6 shows mean properties of four classes of components exhibiting the two-cycle post-response evoked-response pattern seen clearly in the response-locked data at site Fz (Fig. 2D). These consist of two clusters of EEG components projecting maximally to the frontal and central midline scalp (Fig. 6A-H) plus two clusters of components accounting for mu activity (near 10 and 22 Hz) whose scalp maps (Fig. 6I,P) reverse polarity above left and right hand motor cortex, respectively. Note that while the scalp projections of these component clusters all overlap, the response-locked ERP averages and normalized ERP images of the single-trial activations (Fig. 6C,G,K,O) show that the phase/latency of the theta-burst pattern appears consistent across quicker and slower responses.

**Frontal midline cluster.** In the RT-sorted frontal midline (FM) cluster ERP-image plot (Fig. 6C), the two negative wave fronts follow the curving trace marking stimulus onsets, the second of these merging with the fastest RT-locked responses. Activity in the frontal midline component cluster (FM in Fig. 6A) appears to resemble other reported frontal midline EEG activity: theta bursts or trains ( $fm\theta$ ) appearing during mental concentration (Mizuki et al., 1980;Gevins et al., 1997) and brief bursts of theta activity linked to and following the error-related negativity (ERN) (Luu and Tucker, 2001; Makeig et al., 2002b), an ERP peak whose latency (~60 ms post-response) matches the first negativity in the FM-

cluster post-response ERP. Inverse source modeling places the generating cortical domain of all these potentials in and/or near the dorsal anterior cingulate. ICA decomposition showed, however, that the two-cycle post-response theta burst pattern appeared not only in the frontal midline cluster, but also in the response-locked ERPs from the central midline, mu and parietal clusters with non-zero relative phase (cf. Fig. 5C,G,K,O).

Phase coherence analysis of consistent phase relationships between the FM and CM clusters, and between the FM and L $\mu$  clusters, time locked to and following the motor response showed that significant theta phase coherence appeared in the data even after the respective component ERPs were subtracted from each trial, indicating a transient post-response phase linkage between these otherwise maximally independent processes (cf. Fig. 11). The transient theta phase coupling between FM and CM components resembles extensive theta-band ‘brain synchronization events’ that follow other significant events, possibly in support of rapid, attention-related cortical resetting motivated by ‘top-down’ evaluation of their significance and possible consequences (Makeig et al., 2002b).

*Central midline cluster.* Though the vertex-centered component cluster (CM, Fig. 6E-H) shares the theta ERP feature (*red arrows*, Fig. 6G) with the mid frontal and other clusters, it does not contribute to the slower (P3b) positivity associated with the central parietal (Fig. 5E) and central occipital (Fig. 9E) component clusters even though these have strongly overlapping scalp projections. The scalp map associated with this component cluster (Fig. 6E) resembles that of P3 responses to ‘novel’ stimuli (P3a or P3-novel) (Courchesne et al., 1975), though the response-locked ERP contribution of this component cluster is quite different from the P3a response (see, for example, Polich and Comerchero, 2003).

*Mu clusters.* The left and right mu component clusters (L $\mu$  and R $\mu$  in Fig. 6I,M) show expected features -- spectral peaks near 10 Hz and 22 Hz that are blocked after the movement, and equivalent

dipoles located near hand motor cortex (and/or adjacent post-central somatosensory areas) and oriented roughly orthogonal to the central sulcus. Both the ERP and ERSP peaks are larger in the left mu cluster (contralateral to the response hand) than in the right. In common with the midline clusters, the mu component clusters show the theta power increase (Fig. 6L,P) and the theta-burst ERP pattern immediately following the button press. They also make appreciable contributions to the parietal (P3b) cluster ERP, particularly to the late co-called ‘Slow Wave’ phase of the stimulus-locked LPC that, unlike the central LPC (or P3b), exhibits a polarity reversal over the central scalp. This late phase of the stimulus-locked LPC was confined to a single component by ICA analysis of the 5x5 matrix of ERPs in these experiments (Makeig et al., 1999a), but was here separated into at least separate left and right mu rhythm processes by unaveraged data analysis.

*[Insert Figure 7 about here]*

**Central parietal (P3b) cluster.** Fig. 7A-D show the mean scalp map and activity patterns, respectively, for a bilaterally distributed cluster of components that project most strongly to posterior and central scalp sites, making a substantial contribution to the slow post-response ‘P300’ (or ‘P3b’) positivity (Fig. 7B). The mean cluster scalp map (Fig. 7A) resembles that of the response-locked LPC peak (Fig. 2B). The ERP image of the normalized activity of this component in single trials (Fig. 7C) shows a series of small positive and negative post-stimulus and stimulus-locked wave fronts, followed by a large response-locked positivity accounting for 62% of 300-ms post-response LPC variance at Pz. The size of the P3b contribution is clearly lower in slowest-response trials (Fig. 7C, top). The ERSP (Fig. 7D) contains a strong (3-dB) low-theta increase. This cluster comprised 15 components from nine of the 15 subjects. This does not imply that the other six subjects had no central parietal LPC. Rather, the



cluster analysis did not assign such components from the other six subjects to this cluster, possibly because of differences in their scalp maps, equivalent dipole orientations, and/or activity spectra. Examination of the raw ERP waveforms of the six subjects not contributing to the cluster confirmed the absence of a typical central parietal positivity in their target responses.

The significance of main bulk of the stimulus-locked P300 (often called P3b) peaking over central parietal cortex has long been debated. Through volume conduction, the central parietal component cluster, identified here on the basis of scalp map and power spectral similarities, makes the largest cluster contribution to the P3 positivity at both Fz and Pz, though contributing only about a third of peak amplitude at both sites. Our results (Fig. 2E) clearly show that in these experiments this peak is largely time locked to and predominantly follows the motor response beginning at about the moment of the motor command coincident with the P3f peak (Fig. 10B). It cannot, therefore, index activity involved in making the motor decision, which may occur as early as the onset of the P3f process. The equivalent dipole distribution of the cluster was the broadest of the nine clusters, the strongest commonality between the individual dipoles being their orientation toward the central parietal scalp. It is possible, therefore, that more advanced three-dimensional component clustering methods applied to decompositions of more subjects and data channels might allow further distinctions among processes in this cluster. Between-subject variability in locations of P3b generators have also been reported by researchers using other source analyses (e.g., Moores et al., 2003).

***Posterior alpha clusters.*** Figure 8 shows properties of three clusters of posterior components having a circa 10-Hz peak in their activity spectrum, most pronounced in the central cluster (10 components, 7 subjects) (Fig. 8F inset). As better shown in Figure 9 (*lower left*), the stimulus-locked ERP contribution of the two lateral posterior alpha clusters (Fig. 8C,K) includes an early stimulus-locked peak

accounting for most of the P1 peak (near 145 ms) in the stimulus-locked ERP, while of the succeeding N1 peak is accounted for by dips in several cluster response waveforms (Fig. 8C,E,G). The initial stimulus-locked response feature of the central posterior cluster is followed by a train of circa 10-Hz stimulus-locked waves produced by partial phase resetting, following stimulus onset, of intermittent alpha activity in these components with no mean increase in mean alpha power (cf. Makeig et al., 2002a). The central cluster also makes an appreciable low-frequency contribution to the grand response-locked LPC peak (Fig. 8F) that in the cluster average (Figs. 8F, 10B) begins 150 ms before the response, while the small contributions of the lateral clusters to the response-locked ERP are brief and begin just before the button press.

*[Insert Figure 8 about here]*

*Cluster ERSPs.* The mean response-related spectral perturbations of these clusters (Fig. 8D,H,L) are weak. Post-response alpha blocking for all three clusters is brief. The lateral clusters exhibit little 20-Hz post-response blocking, but beta augmentation near 14 Hz in the lateral clusters begins even before the response.

*[Insert Figure 9 about here]*

***Component localization.*** Figure 9 shows the results of submitting the grand mean scalp maps for each of the nine independent component clusters to equivalent-dipole analysis using BESA3.0 (Megis Software, Munich). Residual scalp map variances unaccounted for by the projection of the single cluster equivalent dipoles were small (range, 0.87% - 9.55%; mean, 4.93%) reflecting a close match

between the mean component maps and the projection of a single equivalent-dipole across all 31 EEG channels. In general, equivalent dipole locations are expected to be medial to the active cortical domains whose synchronous activities they represent. As the equivalent dipoles for components in the P3b cluster were scattered across parietal and central cortex, the equivalent dipole for the mean map of this cluster is unnaturally deep.

Though equivalent dipole locations of components in the two frontal midline clusters were overlapping (Fig. 9), their mean equivalent dipole locations are generally consistent with origins in or near the dorsal anterior cingulate and cingulate motor area, respectively, implicated by fMRI and neurophysiologic experiments in motor response selection and anticipation of the consequences of events, particularly those involving errors (Shima and Tanji, 1998; Luu and Tucker, 2001; Manthey et al., 2003; Ullsperger and von Cramon, 2003). The target responses considered here were all correct responses. However, the response-locked dynamics we report here are generally consistent with single-trial EEG dynamics that follow speeded motor responses the subject immediately realizes to be in error (Makeig et al., 2002b).

The equivalent dipole for the P3f cluster is located below the orbitofrontal surface of the brain, most probably because there were only two (periocular) electrodes on the forehead and the spherical model used in dipole fitting is insufficient for describing the frontal skull. Though the mean cluster scalp map of the central occipital alpha cluster ( $C\alpha$ ) is fit by a single equivalent dipole located in the central occiput (Fig. 9), for many components in this cluster a better model of the component scalp map could be obtained from a symmetric two-dipole model that placed dipoles in left and right pericalcarine cortex (not shown). Synchronization of bilateral generator regions via callosal connectivity might be compatible with the sharper (circa 10-dB) alpha peak in activity spectra for these components.

*[Insert Figure 10 about here]*

**Cluster ERP time courses and contributions.** Together, the nine component clusters accounted for 91.1% of the variance of the 1-s response-locked grand mean ERP at all channels, as well as for 90.8% of the variance of the stimulus-locked grand mean ERP. Fig. 10A-B show the envelopes (most positive and negative channel values, across all channels, at each time point) of the stimulus-locked and response-locked grand mean ERPs (black) and the envelope of the summed back-projections to the scalp of the components comprising the nine clusters.

The normalized grand average activity time courses for the nine clusters are shown in Fig. 10C-H for comparison with the time courses of the grand mean ERP (Fig. 10A,B). Note that stimulus-locked component-cluster ERP activity first appears in the lateral posterior alpha clusters (at 100 ms). Onset of the stimulus-locked ERP of the P3b cluster at about the same time is soon followed by the far-frontal P3f cluster onset (near 120 ms, Fig. 10C). The stimulus-locked ERP deflection begins at the same time in the four theta-pattern clusters (Fig. 10E). Six of the nine clusters have a trough in their stimulus-locked ERP near 200 ms, confirming the spatial complexity of the N1 peak as indicated by invasive measures (Klopp et al., 2000), and comparable to previous analysis of non-target epochs from this data set (Makeig et al., 2002a).

In the response-locked cluster ERPs, note that the P3f cluster activity appears to begin early, while response-related activity in the P3b-cluster ERP begins 10-20 ms before the P3f peak, concurrent with a posterior-negative peak in the left-mu cluster ERP. The posterior-positive peaks in the response-locked ERPs of both mu clusters, the early shoulder of the P3b-cluster ERP peak, the central-cluster ERP slow wave and the negative-going peak of the FM cluster ERP occur together about 100 ms after the P3f peak.

*[Insert Figure 11 about here]*

Figure 11 shows the individual and summed independent component cluster contributions to the grand mean ERP at Fz and Pz. At Pz, no component cluster contributes more than a third of the stimulus-locked response peak amplitude (Fig. 11C), nor to the response-locked average (Fig. 11D). The largest contributor to the Fz response, the P3b cluster, contributes about half of the positive response peak amplitude (Fig. 11A-B), the P3f cluster about a third, casting doubt on claims that peak amplitude of the ERP at Fz predominantly indexes frontal activity.

*[Insert Figure 12 about here]*

**Theta synchronization.** A single frame from an animation showing the joint response-related theta-band dynamics of the nine component clusters in an analysis window centered after the button press is shown in Figure 12. [Clicking on Fig. 12 should start the repeating animation]. Note that the transient theta phase coherence between the mu, parietal and midline components is not uniform: phase linkages between FM and CM, FM and L $\mu$ , and R $\mu$  and P3b clusters (indicated by cylindrical connections) are significant, whereas no significant phase linkage occurs in this time period between the FM and P3b clusters, nor between the CM and L $\mu$  clusters. This selectivity diminishes the possibility that the observed transient phase linkages were produced by appearance of post-response EEG activity not separated out by ICA into one or more independent components and therefore attributed by the ICA model to spatially stable independent components with nearby sources. However, we cannot discount

this possibility and can only claim, based on the results presented, that the independence of the identified component structure in the theta band transiently collapses following the speeded response.

*[Insert Figure 13 about here]*

Figure 13 demonstrates the theta phase linkages between the four theta-producing clusters in the time domain using phase-sorted ERP-image plots of single-trial activities. In Fig. 13A, the single trial activity of the FM cluster components are shown, sorted by phase at 5 Hz in the same time window as in Fig. 11, then smoothed with a 300-trial moving window. Fig. 13B shows the single-trial activities of CM cluster components from the nine subjects contributing to both clusters, using the same trial sorting order as in Fig. 13A. Sorting CM activities by FM theta phase induces a noticeable though partial phase sorting of the CM activity as well, demonstrating their partial phase coherence. Similarly sorting the same CM components by theta phase (Fig. 13C), then exporting the trial sorting order to the FM components, confirms the partial phase alignment of CM and FM. The sorted and smoothed stimulus onset times (left vertical traces) are bowed, suggesting a relation between theta phase and subject reaction time.

## ***Discussion***

The nine independent component clusters, identified here across subjects on the basis of similarity of their scalp projections and activity spectra, resemble classes of EEG phenomena long described by neurologists from observing paper or electronic data displays – central and lateral alpha, left and right mu, and frontal-midline theta rhythms. By separating the time courses and EEG contributions of these processes, ICA allowed exploration of their individual and joint event-related dynamics. Our modeling of theta synchronization in midline, motor and parietal cortex (e.g., Fig. 12) would not have been possible without using the temporal information contained in the higher-order statistics of the single-trial EEG time courses to identify and separate maximally independent processes with overlapping scalp maps. The clear separation of ‘alpha-ringing’ in the stimulus-locked response from the other LPC activities (Fig. 10A) exemplifies the power of ICA to identify and separate temporally and most probably functionally distinct activities generated in different brain areas.

The obtained clusters largely reproduce the component clusters obtained from ICA decomposition of brief (100-ms) post-stimulus time windows following non-target and target stimuli in these experiments (Makeig et al., 2002a), the major difference being the inclusion of the ‘P3b’ component cluster in the target-response data. After removal of clear ocular and muscle artifact components, the nine identified EEG component clusters together accounted for over 90% of the grand-mean ERP (at all channels) and nearly 60% of the whole single-trial EEG data after artifact removal. By contrast, the ERP data themselves accounted for only 6% of post-stimulus EEG variance.

***Event-related spectral perturbations.*** Traditionally, event-locked averaging scalp channel EEG data to form an ERP is assumed to reject, by random phase cancellation, ‘background’ EEG rhythms whose statistics are assumed to be unperturbed by experimental events. It is debatable, however, whether

partial synchronies of local field activity across the relatively large (cm<sup>2</sup> or more) domains of neuropile required for the production of scalp EEG (Nunez, 1981) may not be statistically altered during top-down cognitive and behavioral processes such as, here, speeded selective responding to actively anticipated but relatively infrequent visual stimuli. The observed spectral perturbations may reflect, in part, common modulatory influences of central neurotransmitter-labeled brainstem systems involved in orienting and arousal, which project widely to cortex and are known to change the spectral properties of cortical field activity (Frei et al., 2001; Hasselmo et al., 2002; Aston-Jones et al., 2001).

Note that many of the ERSPs for the different clusters (Figs. 5-8) share features. This is possible for two reasons: First, the infomax independence metric is weighted toward separation by phase differences rather than by power spectral differences. Common patterns of spectral modulation might arise, for example, through actions of the central neurotransmitter-labeled modulatory systems. Second, ‘independent’ components returned by infomax decomposition of EEG data may never be *strictly* independent, given finite data, but are instead determined to be *maximally* independent. This is not a mere play on words but a possibly advantageous feature of infomax decomposition allowing it to separate activity from different cortical areas even when the independence of synchronous activities within those areas is neither continuous nor absolute.

Alpha blocking following visual stimuli cueing visual attention, and mu-blocking accompanying cued finger movements are well known (Hari et al., 1997; Pfurtscheller et al., 2000). A late beta increase following target responses was also seen in an auditory experiment (Makeig, 1993). The response-locked theta increase appeared in every subject, was not eliminated by removing the subject-mean ERP from each trial, was partially phase-coherent among at least four component clusters, and deserves further study.



To test the effect of the average ERP on the observed spectral perturbations, we computed the cluster ERSPs again after removing the component mean ERP from each trial (not shown). All the significant effects shown in Figs. 5-8 remained significant.

***Evoked responses.*** Our results show that in this speeded response paradigm, at least, the ERP ‘P300’ positivity is near-strictly time locked to, and predominantly follows the motor response. Further, this positivity is indeed a late positive complex of potentials generated in several brain areas, confirming results of invasive recording (Smith et al., 1990) and clinical group-difference studies (Potts et al., 1998). ICA decomposed the unaveraged EEG signals summing to the target-response ERP into event-related activity into several classes of brain EEG processes originating predominantly in frontal, central, parietal and occipital cortex. This result adds to longstanding doubts as to the specificity of ERP peak measures. In particular, it shows that parietal sources may account for less than half of the peak amplitude of the stimulus-locked LPC at Pz (Fig. 11), the most commonly used index of ‘P300’ magnitude. Altogether, we found four component clusters contributing to the LPC maximum at Pz -- in descending order, central parietal, left and right mu, and central occipital alpha EEG processes. As well, the (threefold) largest EEG contributor to the stimulus-locked LPC peak at Fz response potential is volume-conducted from the same parietal (P3b cluster) sources, casting strong doubt on the specificity of the LPC peak at Fz for indexing frontal function.

As in our previous report (Makeig et al., 2002a), partial phase resetting of ongoing intermittent alpha and theta EEG processes does contribute to early visual ERP features in these data. However, partial phase resetting is not a sufficient model for the lower-frequency LPC features, since phase locking of the LPC to the button press (as assessed by ITC) was high and, unlike in the case of alpha

ringing, was associated with an increase in single-trial spectral power and whole data variance (not shown).

**Cluster localization.** The equivalent dipole localization of the P3b cluster mean scalp map (Fig. 9) does not correspond directly to the cortical areas noted to generate P3b-like potentials in implanted pre-surgical epileptic patients by Halgren and colleagues (1995ab) -- parts of the superior parietal lobule, inferior frontal and temporal cortices, as well as the limbic medial temporal lobe. However, in general it is difficult to infer the cortical distribution of generator cortex from equivalent dipoles and clearly, more sophisticated methods of ICA component source localization fit to actual subject cortical geometry (Dale and Sereno, 1993) may be useful for further research. However, it is not clear whether 'hot spots' in local cortical fields recorded from sparsely implanted intracranial electrodes necessarily dominate the scalp EEG dynamics, which might also arise from more spatially diffuse activity in other areas.

The localization and scalp map of the CM cluster strongly resembles that of the P3a and P3novel components seen, for example, when unexpected and unique stimuli are included in a randomly alternating sequence of target and nontarget stimuli (Polich and Comerchero, 2003). However, here this cluster makes only a small contribution to the stimulus-locked ERP (Fig. 10A) and, notably, shows tight theta-band phase-linkage to the FM component cluster during the post-stimulus theta-burst.

**Functional significance of the post-motor theta bursts.** Local bursts of theta band-activity are widely distributed on the human cortex (Kahana et al. 1999) and associated with cognitive functioning (Caplan et al., 2003). In hippocampus, an association between theta phase and high-frequency 'sharp wave'

activity has been observed in animals (Csicsvari et al., 2003). In turn, high frequency activity can index organization of spike timing of similarly-tuned neurons into brief near-synchronous volleys more likely to trigger further spikes in common target neurons (Fries et al., 2001; Salinas & Sejnowski, 2002).

Following nontarget stimuli in this experiment, frontal midline components exhibited weak ‘theta-ringing’ (partial post-stimulus theta phase locking) not accompanied by increased theta power (Makeig et al., 2002a), while here, following targets, a two-cycle period of increased theta activity appeared, phase-locked to the motor response and phase coherent between midline frontal, parietal and motor areas. Coherent theta activity might enhance the speed, salience, and reliability of spike-based communication between these and other brain areas connected with them, including hippocampus and connected limbic structures (Seidenbacher et al., 2003). The result might be facilitation of information transfer about the event and its anticipated consequences to and from memory structures, and selective retuning of attentional states in relevant cortical areas based on anticipatory evaluation of the consequences of the cued motor response, including readjusted sensory and motor expectancies.

The theta bursts seen here following correct speeded responses appear highly similar to the ERP feature with strong theta-band energy that follows highly speeded manual (or foot) responses in the Erickson flanker task (Holroyd et al., 1995). Luu and Tucker (2001) have suggested that the so-called error-related negativity (ERN) in the response-locked ERP following responses the subject knows immediately to be in error largely represents partial phase-locking of enhanced theta-band energy in frontal midline and other sources following known-error responses (Luu, Tucker and Makeig, submitted). A similar ERP feature has been reported following negative feedback whose valence is not known in advance (Ruchow et al., 2002).

Elbert and Rockstroh (1987) have proposed that cortical surface positivities in general index periods of relative neural depolarization and concomitant insensitivity ('disfacilitation') of the involved

cortex to distal input, possibly explaining the concurrent attentional blink (McArthur et al., 1999; Kranczioch et al., 2003) and amplitude decrease in the auditory steady-state response (Rockstroh et al., 1996). Thus, the post-motor LPC or P300 and the theta burst response may have complementary functions: decrease in ‘bottom-up’ environmental sensitivity and concurrent increase in ‘top-down’ processing and memory (learned/remembered ‘context’) updating, respectively, following goal-directed actions.

## Figure Legends

**Figure 1. Task display.** Subjects fixated a cross above which five boxes were constantly displayed. In each 76-s block, one of these (*grey box*) was colored differently. The location of this covertly attended box varied pseudo-randomly across blocks. Subjects were asked to respond with a thumb button press as quickly as possible whenever a disk presented briefly in pseudo-random order in the five boxes appeared in the attended box.

**Figure 2. Response-time ordered single-trial and mean responses at sites Fz and Pz.** (Left, A,C) Stimulus-locked grand mean response. (Right B,D) Response-locked grand mean response. (Top A,B) Grand mean response at all channels, plus scalp maps at selected latencies. (Bottom, C-F) Grand moving-mean single-trial responses from all 15 subjects, at Fz (C,D) and at Pz (E,F), plotted in ERP-image format (see text) and sorted by subject reaction time (curving dashed trace in left column; vertical solid line in right column, plotted at the mean subject-median response time of 352 ms). ERP-image units:  $z = \mu\text{V}$  divided by RMS  $\mu\text{V}$  in the (-1000 ms to 0 ms) channel baseline EEG of the same subject after removal of eye and muscle artifact components from the data. Vertical smoothing window: 300 trials. Grand mean normalized responses are shown below each image.

**Figure 3. Changes in mean scalp spectral power time-locked to the subject response** (*solid vertical line*, adjusted to the mean subject median, 387 ms). Color scale: dB change from pre-stimulus baseline. Image shows signed-RMS power changes across all 29 scalp channels prior to removal of moderate eye artifacts. Scalp maps show the scalp topography of the spectral power change in dB. Note the broad posterior peri-response theta maximum, the central-lateral post-response beta increase, the bilateral central alpha blocking, and the increase in low-frequency eye artifacts at the end of the record.

**Figure 4. Independent component decompositions for two single trials.** (*Black traces*) Two single target response trials from the same subject recorded at scalp site Pz (*rightmost scalp map*). Stimulus onset was at time 0. Solid vertical lines show stimulus onsets, dashed vertical lines, response times. A large LPC occurred in the top trial, but not in the bottom trial. Single-trial 31-channel EEG epochs time locked to all 561 target stimuli for this subject were concatenated and decomposed by infomax ICA, yielding 31 maximally independent data components. Colored traces show the projections (in  $\mu\text{V}$ ) to this scalp channel of the three (non-artifact) independent components contributing the largest variance to the post-response data window, linked to (individually scaled) maps of their scalp topographies. Component numbers (IC1-IC6) as ranked by total EEG variance accounted for this subject. Cluster membership of the illustrated components (P3f, FM, P3b, R $\alpha$ ) is also indicated.

**Figure 5. Far-frontal component cluster accounting for the pre-response (P3f) positivity.** Each set of four panels in Figures 5-8 shows: A. The mean component scalp map. B. The whole-data and cluster-accounted ERP envelopes (min and max voltage channel values at each time point). Insets show the power spectra of the single-trial EEG (*black*) and averaged response-locked ERP (*red*). The lower edge of the red band shows actual ERP power, the upper edge, the spectrum of phase-incoherent EEG required to produce the observed ERP spectrum by random phase cancellation. The difference between the upper edge and the actual EEG spectrum reflects phase consistency of the single trial evoked response data. C. ERP-image plot of the color-coded response-locked single trials, z-normalized by dividing by the standard deviation of component activity in the 1-s baseline. D. The component mean ERSP showing event-related changes in spectral power in epochs time locked to the response (*solid line*). Median stimulus delivery time indicated by dashed lines.

**Figure 6. Four independent component clusters showing the two-cycle theta response pattern.** A-D. Frontal midline (FM) cluster of components often exhibiting a theta-band peak in their activity spectra. E-H. Central midline (CM) component cluster projecting maximally to the vertex. I-L. Left mu ( $L\mu$ ) component cluster with characteristic circa 10-Hz and 22-Hz peaks in the activity spectrum. Following the button press, this activity is blocked (L). M-P. Corresponding right mu ( $R\mu$ ) component cluster.

**Figure 7. Broad parietal component cluster** accounting for part of the post-response (P3b) positivity. The peri-response energy increase for these processes peaks lower than 5 Hz and does not show the two-cycle theta pattern.

**Figure 8. Three posterior alpha-rhythm component clusters.** A-D. Left posterior alpha ( $L\alpha$ ) component cluster. E-H. Central posterior alpha ( $C\alpha$ ) component cluster with characteristic trapezoidal scalp projection (consistent with a bilateral, peri-calcarine equivalent dipole source), showing prolonged phase resetting following stimulus onset (*curving dashed trace*). I-L. Right posterior alpha ( $R\alpha$ ) component cluster.

**Figure 9. Mean component cluster equivalent-dipole locations.** Each cluster mean scalp map could be well fit by a single equivalent dipole. The figure shows the locations and orientations of these dipoles, as determined by BESA, plotted on the spherical head model, with ellipses showing the spatial standard deviation of the locations of the equivalent dipoles for the individual components of the cluster. Percent residual variance in the cluster mean maps unaccounted for by the dipole model was low (mean, 4.8%).

**Figure 10. Component time courses and summed scalp projections.** Summed projections (A,B) to the grand-mean ERP average of all trials time-locked to stimulus onset (*left*) and to the subject response (*right*), plus (C-H) grand mean normalized activity time courses of each of the nine independent component clusters, scaled and separated into the same cluster groupings as in Figs. 5-8. For comparison with the stimulus-locked responses (*left*), response-locked data epochs (*right*) are shown aligned to the mean subject-median response time (352 ms, cf. *dashed line in left panels*).

**Figure 11. Cluster projections to sites Fz and Pz.** Contributions to the grand mean stimulus-locked and motor response-locked target ERPs at scalp sites Fz (A, B) and Pz (C, D) in  $\mu\text{V}$  (*thin traces*), plus their summed contribution (*thick traces*) to the stimulus-locked and response-locked responses. Although the P3b cluster makes the largest contribution to the evoked response, its contribution does not outweigh the summed contributions of the other clusters.

**Figure 12. Post-response theta-band dynamics.** Frame of an animation representing event-related dynamics in the theta band (three-cycle Hanning data windows, center frequency 4.87 Hz) centered 89 ms after the button press (here aligned to its mean value, 352 ms). Each disc represents the relative location of the equivalent dipole location associated with one component cluster. Log spectral power changes relative to baseline are indicated by solid borders and size of the discs. Colors of the discs index consistent phase locking across trials relative to the button press. Colored arcs between discs indicate significant phase coherence between the within-subject components pairs belonging to the two clusters. Approximate projections of the equivalent-dipole locations (Fig. 9) of the mean cluster component maps are shown on an average MR image (Montreal Neurological Institute).



**Figure 13. Phase-coupling of theta components: time-domain view.** A. ERP-image view of baseline-normalized response-aligned single-trial activity time series of components in the FM cluster sorted by phase at 4.87 Hz in a window centered 89 ms after the button press as in Fig. 12. Vertical smoothing: 400 trials. Units: z, relative to single-trial baseline activity of each imaged component. The curving vertical line (*left*) shows moving-mean stimulus onset time; the vertical line (*central*), the time of the button press. Data band pass in all panels: 0.1-40 Hz. B. Exporting the same trial sorting order (from panel A) to CM cluster components from the same 9 subjects contributing components to both clusters demonstrates the significant partial phase coherence ( $r \sim 0.3$ ) between the two clusters in this time/frequency window. Note the induced (*top-down, left-to-right*) slope of the latency of the two (*red*) positive-going CM-cluster theta wave fronts. C. Phase-sorted ERP-image (as in panel A) of the normalized CM cluster trials. D. FM-cluster trials sorted in the trial order of CM-component phase (as in C). Again, the partial theta-band phase coherence of the two clusters in the post-response period is reflected in the curving (*blue*) negative-going wave fronts of the FM cluster data.

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