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Journal

Cognitive Neurodynamics, 1(4)

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Publication Date

2007

DOI

10.1007/s11571-007-9024-y

Peer reviewed

Cogn Neurodyn (2007) 1:327–340
DOI 10.1007/s11571-007-9024-y

RESEARCH ARTICLE

Topography, independent component analysis and dipole source analysis of movement related potentials

Susan Pockett · Simon Whalen · Alexander V. H. McPhail · Walter J. Freeman

Received: 29 March 2007 / Accepted: 4 August 2007 / Published online: 28 August 2007

Abstract The objective of this study was to test, in single subjects, the hypothesis that the signs of voluntary movement-related neural activity would first appear in the prefrontal region, then move to both the medial frontal and posterior parietal regions, progress to the medial primary motor area, lateralize to the contralateral primary motor area and finally involve the cerebellum (where feedback-initiated error signals are computed). Six subjects performed voluntary finger movements while DC coupled EEG was recorded from 64 scalp electrodes. Event-related potentials (ERPs) averaged on the movements were analysed both before and after independent component analysis (ICA) combined with dipole source analysis (DSA) of the independent components. Both a simple topographic analysis of undecomposed ERPs and the ICA/DSA analysis suggested that the original hypothesis was inadequate. The major departure from its predictions was that, while activity over many brain regions did appear at the expected times, it also appeared at unexpected times. Overall, the results suggest that the neuroscientific 'standard model', in which neural activity occurs sequentially in a series of discrete local areas each specialized for a particular function, may reflect the true situation less well than models in which large areas of brain shift simultaneously into and out of common activity states.

Keywords Bereitschaftspotential · Readiness Potential · Motor Related Cortical Potential · Independent Component Analysis · Dipole Source Analysis · Scale-free · Small-world

Introduction

Even a simple voluntary movement, such as deciding which of three keys to press and then pressing it, involves coordinated activity in a large number of brain areas (Pockett 2006). First, a decision must be made about which key to press. While decision making may sometimes be underpinned by working memory, evidence suggests that working memory (assessed by delayed response tasks) and decision-making (assessed by the ability to select an advantageous response from an array of options) depend in part on separate anatomical substrates. Both lesion studies (Goldman-Rakic 1992; Bechara et al. 1998) and functional imaging of normal human subjects (Jonides et al. 1993; Petrides et al. 1993; McCarthy et al. 1994; D'Esposito et al. 1995; Smith et al. 1995; Cohen et al. 1997; Courtney et al. 1996, 1997) show that working memory tasks involve the dorsolateral prefrontal cortex (BA 46/9).[1] With tasks

Electronic supplementary material The online version of this article (doi:10.1007/s11571-007-9024-y) contains supplementary material, which is available to authorized users.

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[1] Such tasks are also shown to involve additional prefrontal areas (BA8, BA44), the anterior cingulate (BA32), Broca's area (BA44), the parietal cortex (BA40, BA7), the superior temporal gyrus (BA 22/42) the insula, and assorted motor, somatosensory and visual areas (BA1,2,3,4,6,17,18,19). However these observations are usually downplayed over in the interests of presenting a simple story, that working memory occurs in the dorsolateral prefrontal cortex (BA46/9).

that test decision making in isolation from working memory, lesion studies implicate the ventromedial as well as the dorsolateral prefrontal cortex (Bechara et al. 1998; Damasio et al. 1991). When subjects are instructed to pay attention to what the experimenters call their 'intention' to move (Lau et al. 2004), fMRI reveals enhanced activity not only in the dorsolateral prefrontal cortex (DLPFC), but also the intraparietal sulcus (IPS) and pre-supplementary motor area (pre-SMA). The temporal resolution of fMRI does not allow a conclusion about whether the DLPFC activity is causing/influencing the pre-SMA and IPS activity, or monitoring it, or whether the three areas are active simultaneously. However the studies above, together with a large body of similar evidence (for review see Jahanshahi and Frith (1998)) suggest that a number of predominantly frontal brain areas are active during the formation of consciously 'willed' decisions or intentions.

But by definition, decisions or intentions need not be acted upon. The location of the neural activity underlying initiation and execution of whatever voluntary movement a decision or intention dictates is much less understood. It is clear that the last cortical way station before impulses are sent to the spinal cord and muscles is in the contralateral primary motor area, just rostral to the central sulcus (Pedersen et al. 1998). But the progress of neural activity caudally from the pre-supplementary motor area to the primary motor area does not proceed in a neatly linear fashion.

The main complicating factor is that the decision or 'willed intention' to press a particular key has to interface with a 'sensorimotor intention' (Pockett 2006) whch is generated in the posterior parietal cortex, caudal to the motor strip (Andersen and Buneo 2002; Eskandar and Assad 1999; Kalaska 1996). While the frontal 'willed intention' specifies a general motor plan, the parietal 'sensorimotor intention' specifies a particular plan: for example the intention (which may or may not be acted upon) to configure the hand optimally to grasp a particular object. This particular sensorimotor intention is reflected in monkeys by the firing of single cells in the anterior intraparietal area of the cortex (Sakata et al. 1995, 1997). Reversible inactivation of the same area causes deficits in grasping that are reminiscent of problems in shaping the hand for grasping seen in humans with parietal lobe damage (Perenin and Vighetto 1988), and an area specialized for grasping has been identified by fMRI in the anterior aspect of the human intraparietal sulcus (Binkofski et al. 1998). It can be seen that a sensorimotor intention is not merely an abstract entity the existence of which is inferred, after the event, by either the subject or the experimenter. A sensorimotor intention is a specific pattern of neuronal firing in one or more areas of the brain, which correlates with a predictable behavior.

A number of similar temporal, single cell activity maps in the posterior parietal cortex (PPC) have been found to code other varieties of particular motor intention—although it is notable that such maps have been also been found in prefrontal areas, which suggests that an intention may really be a distributed entity that includes, but is not limited to, activity in the PPC (Andersen and Buneo 2002).

To complicate things still further, when sensorimotor intentions are eventually acted upon—which involves their being processed prior to action through the premotor, supplementary motor and primary motor areas of the cortex and various subcortical structures—an efference copy of the sensorimotor intention is also sent to the cerebellum. Here the plan is compared with somatosensory and other feedback generated by the eventual performance of the movement, and if necessary an error signal is computed and fed into the evolving neural activity underlying the movement.

The important point, then, is that before each movement is executed, a complex series of interactions between willed intentions (probably originating in prefrontal cortex), sensorimotor intentions (probably originating in posterior parietal cortex) and error signals (probably originating in cerebellum) must take place. These interactions are probably played out in a series of cortico-cortical and cortico-subcortical loops in the front half of the head, all of which are active in parallel. While the precise details of this looping activity have not been worked out, it is clear that neural communication cycles around the supplementary motor area, the pre-supplementary motor area, the lateral premotor area, the cingulate area, the basal ganglia, the thalamus, the limbic system and the cerebellum (Brunia and Boxtel 2001; Cunnington et al. 2002). When a go-signal finally emerges from all this cycling, it is routed to the primary motor cortex, where it lateralizes to the section of the motor strip appropriate to the body part to be moved, on the side contralateral to movement. The movement is then effected via the spinal cord and peripheral nerves.

Clearly, the fine elucidation of this complex web of cortical and sub-cortical events using scalp EEG recordings, which are generally thought to measure only cortical activity and that with very low spatial resolution, is at best difficult and at worst impossible. Probably the most intensively studied EEG signature of the preparation and initiation of human voluntary movements is the Bereitschaftspotential (BP) or Readiness Potential (RP). This is a slow event-related potential (ERP) first described by Kornhuber and Deecke (1964) and seen when EEG epochs are back-averaged off voluntary movements. The BP/RP waveform is a largely negative-going potential, which can start anything from 2000 ms to <500 ms before the movement. If the ERP starts early, the slope of the waveform increases at about 500 ms pre-movement. Whenever

it started, the waveform peaks at around the time of the movement. It then continues for several hundred ms after the movement has been completed (assuming that one still chooses to call this part of the waveform a BP/RP). The best available localization of the neural sources underlying this evolving waveform suggests that early components are generated in the prefrontal cortex (Singh and Knight 1990) and supplementary motor area (Toro et al. 1993; Praamstra et al. 1999; Cui et al. 2000). Mid-line sources are then thought to be active until the discrete increase in slope that denotes transition from BP1 to BP2 (Deecke et al. 1969, 1976) or BP to NS' (Shibasaki et al. 1980). After that, activity lateralizes in the primary motor cortex to the side opposite the impending movement (Cui et al. 1999). Subcortical sources have been reported to become active as early as the first scalp-recorded potential (Paradiso et al. 2004). However so far, work on neither the 'sensorimotor intentions' (motor plans) known to be generated in the posterior parietal cortex, nor the error signals generated in the cerebellum, has associated these activities with RPs/BPs.

One objective of the present investigation is to determine whether or not localization of the evolving sources underlying scalp-recorded BPs/RPs can be refined by use of independent component analysis (ICA) and dipole source analysis (DSA). Independent component analysis attempts to solve the problem of blind source separation by applying a series of spatial filters to a set of data recorded at multiple sites. While the primary factor influencing separation of components is spatial, the spatial filters are also chosen to produce signals with maximum temporal independence, on the rationale that this isolates components representing functionally distinct, statistically independent information sources in the data. In EEG data, such information sources can have a non-cortical origin (eye movements, muscle noise, line noise), but they can also be the result of synchronous or partially synchronous activity in one or more patches of cortex. Since such cortical patches are relatively discreet, they tend to project into scalp amplitude distributions that match relatively well the projections of single dipole sources. Unlike the standard EEG inverse problem of finding a large number of cortical sources underlying undecomposed EEG, the problem of finding a single equivalent dipole which may generate the scalp map of one ICA component is relatively well posed. Depending on the location and orientation of the active patch of cortex, the calculated dipole location will often not be in the centre of the actual patch, but at least a general location can be inferred for the activity.

These considerations suggest that application of ICA and dipole source analysis to pre-motor EEG may be able to decompose and isolate the series of sequentially active neural sources which, according to a large volume of independent but hitherto largely piecemeal data, may underlie the motor readiness potential. The hypothesis we will investigate in this paper is that the electrophysiological signs of activity in sources active during the early, decision phase of motor preparation should first appear over the prefrontal cortex. Signs of sources active in the middle phase of the pre-motor period should be located over the posterior parietal cortex (caudal to the central sulcus) and also over various locations rostral to the central sulcus, in the area between the frontal cortex and the motor strip. Signs of activity occurring in the few 100 ms before the movement should appear over the contralateral (and to a certain extent the ipsilateral) motor strip. Activity arising in the cerebellum is expected to occur immediately after the onset of movement.

Our approach to testing this hypothesis is first to see how well it fits with a simple topographic analysis of undecomposed pre-motor ERPs. We then split each subject's EEG into independent components using ICA, and for each ICA component (a) do a DSA and (b) reconsitute the event-related potential for that component by back-averaging off movements. On the basis of the starting hypothesis, we predict the time of ERP activity (early, middle, late or post-movement) from the position of the dipole calculated for each ICA component. We then compare these predictions with the actual results.

Methods

Subjects

Results from six male subjects, aged 23–44, are reported. All except JL were right handed. Data were collected at the University of California Berkeley and the study was approved by the UC Berkeley Institutional Review Board. All subjects gave informed consent.

Experimental protocol

Each subject participated in a single 60–90 min session, during which 64-channel EEG data were recorded while a series of paired visual and auditory stimuli were presented. The visual stimuli consisted of a 125 ms flash during which a computer screen positioned in front of the participant's chair turned either entirely red or entirely blue. The auditory stimulus was either a comfortably loud or a much softer 100 ms burst of white noise from two computer speakers positioned to either side of the screen. Three stimulus pairs were delivered at random: Red-Loud, Blue-Soft or Blue-Loud. The subject's task was to learn by trial and error which of three computer keys to press in response

to each of the stimulus pairs. The keyboard was placed on the subject's lap and their hand comfortably supported in such a position that no gross arm movements were necessary in order to press one of the three keys. Keys were pressed with the right hand. As soon as a response key was pressed, feedback ("Correct! Well Done" or "Incorrect. Better luck next time") was presented in white text on a black screen. After 1s this text was replaced by a white fixation cross in the middle of a black screen, which lasted until the next stimulus pair was delivered. Subjects were instructed to maintain their gaze on the location of the fixation cross throughout the experiment and to avoid blinking until the period between key press and the next stimulus. For the first 180 stimulus presentations, positive or negative feedback was delivered at random, so that it was impossible to score 100% correct answers. For the next 200 presentations, "Correct" feedback was delivered if key 1 was pressed for Red-Loud stimuli, key 2 for Blue-Soft and key 3 for Blue-Loud. Most subjects scored 95–100% correct answers after the first 6–10 trials in this second block. For the present analyses, all key presses for a given participant were analysed together. Data related to the covariance of EEG with correct responses (reflecting the ability to categorize stimuli) will be presented elsewhere.

EEG recording

EEG was recorded using BioSemi™ amplifiers with a 64-electrode cap. Sintered Ag/AgCl electrodes were interfaced with the scalp using Signagel (Parker). Approximate postions of the electrodes are shown in Fig. 1. Data were digitized at a sampling rate of 512 Hz, with an analog pass band of DC to 250 Hz. Continuous records were taken, with the times of various sorts of stimuli and responses marked in a 65th recording channel.

Data analysis

Stored data were converted offline to Matlab™ format using the BioSig conversion facility available in EEGLAB (Delorme and Makeig 2004). Specified data epochs surrounding individual key presses were then extracted from the continuous record, re-referenced to an average reference, de-trended, locally de-meaned and normalised to the standard deviation of the whole data set, using purpose-written Matlab routines on a Linux platform. For each subject, averaged event-related potentials were computed for each electrode and displayed using Matlab code rewritten from an EEGLAB routine (Fig. 2). Those trials where the stimulus-response time was greater than 1500 ms were then dropped from further analysis[2] and the

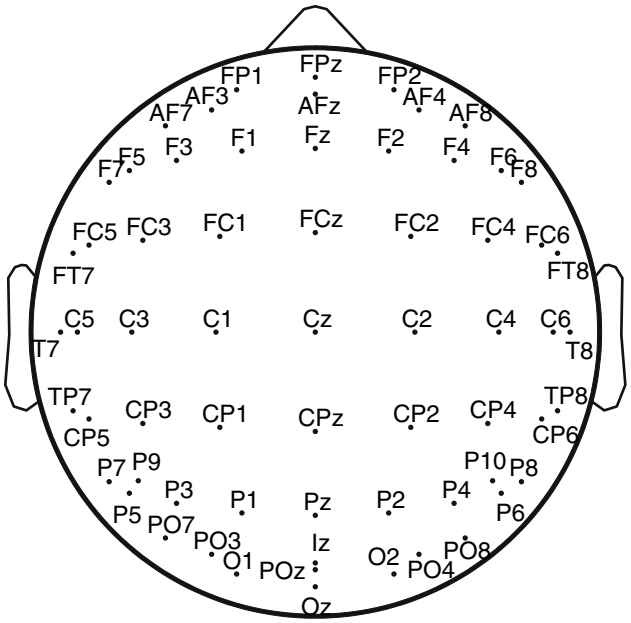

Fig. 1 Electrode locations

remaining data epochs concatenated and run through EEGLAB's version of infomax ICA (Bell and Sejnowsky 1995; Makeig et al. 2002). This initially produced a 64×64 weight matrix, representing the weight of each of 64 ICA components at each of the 64 electrodes. Left multiplication of the original data by the weight matrix produced a component activation matrix, representing the activation of each ICA component over time. For each ICA component, the rows of the component activation matrix corresponding to the other 63 components were zeroed, and then the modified activation matrix was left multiplied by the inverse of the weight matrix to produce a set of 64 time series, each representing the activation the component in question at a particular electrode.[3] These sets of time series were then parcelled up into single trials again and back-averaged off the times of the key presses to

[2] Inclusion of epochs with very long response times was tried, but trouble was experienced fitting dipoles to many of the resulting ICA components. This may have been because the assumption of stationarity underlying ICA was unacceptably violated in very long data segments, resulting in ICA components that could not be not associated with any single dipole. The 1.5 s response time cut-off was chosen as an acceptable compromise between maximization of stationarity (which would presumably be more closely approximated in shorter data segments) and truncation of the BP signal. Use of this constraint resulted in many more successful dipole fits, while preserving what was apparently the full length of the BP.

[3] An alternative description of these operations which may be more readily acceptable to ICA afficionados is as follows. The back-projected time series of each independent component was computed by taking the outer product of the column vector of the mixing matrix with the corresponding row vector of the activation matrix. This gave a matrix time-series of rank 1 for each of the 64 independent components.

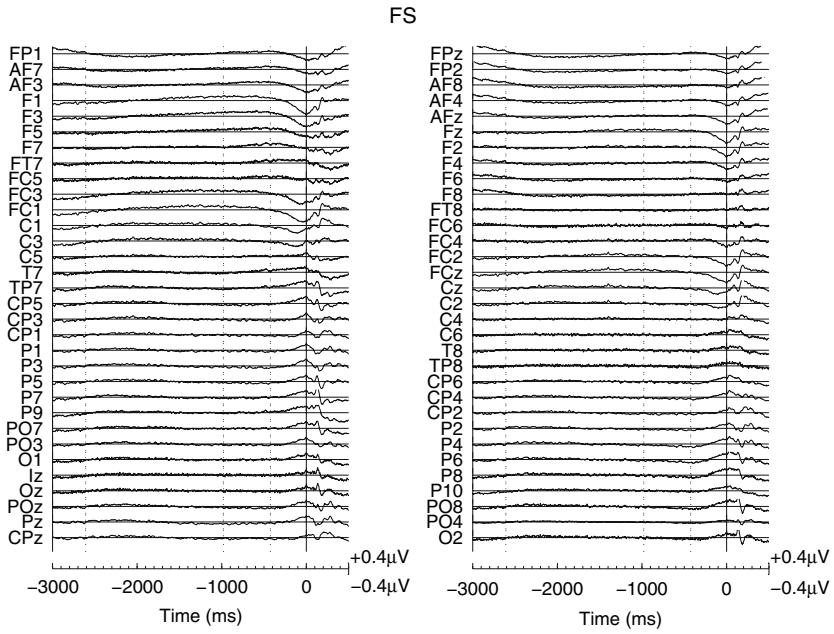

Fig. 2 Topography of ERPs for subject FS. No ICA has been performed on the data in this figure. Average reference. Key press at time zero (solid vertical line). Dotted vertical lines indicate median and range (i.e., earliest and latest) times of stimulus presentation. $n = 390$ trials

produce a set of 64 event-related potentials (one per electrode) for each ICA component. The number of trials included in these averaged event-related potentials (ERPs) varied from 65 to 319 depending on how many trials had been dropped from a particular subject's data because they involved response times >1500 ms, but for most subjects n was several hundred (see figure legends for individual numbers). Finally the 64 ERPs for each ICA component were compared with the dipole fit for that component, calculated using EEGLAB's dipole fitting routine with a spherical head model.

Prediction testing

Predictions of the hypothesis under investigation were that:

(1) Dipoles in the prefrontal region of the head would produce 'early' ERPs. These were defined as waveforms that started and finished well before the key-press.
(2) Dipoles in the middle of the head rostral to the central sulcus would produce 'middle' ERPs, defined as waveforms that started later than the 'early' ones but still returned to baseline before the key-press.
(3) Dipoles caudal to the central sulcus, roughly over the region of the posterior parietal cortex, would also produce 'middle' ERPs (defined as above).
(4) Dipoles lateralised over the region of the central sulcus would produce 'late' ERPs. These were defined as waveforms which departed from baseline just before the key-press and were maximal around the time of the key-press.
(5) Dipoles at the extreme rear of the head would produce 'post key-press' ERPs, due to activation of cerebellar error-correction circuitry.

The accuracy of these predictions was tested by dividing IC dipoles into groups according to their position on the head and seeing whether the ERPs associated with each dipole displayed activity in the predicted time period. A prediction was scored as correct if the ERP departed from baseline only during the predicted time period.

To summarize, for each ICA component (i.e., for each of the 64 ICA components that were calculated for each of the six subjects) we produced (a) one dipole (in cases where a dipole could be fitted) and (b) 64 ERPs—one per electrode. In other words, for each subject we produced up to 64 dipoles and 4096 ERPs. Then for each subject we grouped the dipoles according to their position on the head, as specified above. Finally we checked all of the 64 ERPs corresponding to each dipole to see whether the waveform occurred at the time predicted by the dipole's head position.

Results

Topography of event-related potentials not decomposed by ICA

Figure 2 shows overall ERPs at each electrode, averaged over all 390 trials completed by subject FS. The data are converted to an average reference, partly because the dipole fitting routine employed in later analyses uses an average reference and thus a valid comparison of ERPs

with dipoles requires that the ERPs also be average referenced, and partly in an attempt to lessen the influence of volume conduction, which tends to spread activity from deep or very strong neural sources to all electrodes. In common with standard cellular neurophysiological practice (although not with many previous RP/BP studies), negative voltages are plotted downwards. The time of the key press is indicated by a solid vertical line at time zero. The median and range of the stimulus times for the epochs included in the ERP (where range means the earliest and latest times of stimulus presentation) are indicated by the three dashed vertical lines in each panel. Supplementary Figures S1–5 show similar plots for the other five subjects.

As shown by the positions of the median and range lines, most subjects showed a skewed distribution of response times, with relatively few long latency keypresses. Only TB showed predominantly long response times (which seriously affected the number of trials remaining in that subject's data in later analyses where trials with response times longer than 1.5 s are omitted). The fairly wide distribution of response times for any given subject indicates that the time of the decision about which finger to move—and thus the shape of the waveform of any ERP component reflecting this decision—can be expected also to be quite widely spread.

Figure 2 shows that for Subject FS, the earliest evidence of event-related activity appears—as predicted by the hypothesis—in prefrontal leads. A slow negative-going potential occurs between –2300 and –1100 ms at electrodes FP1, FPz, FP2, AF8 and AF4. This waveform lasts slightly longer on the right side of the head at AF8, and does not appear at all at AF7. Not predicted by the hypothesis is the fact that a second negative-going waveform also appears at all of these electrodes, starting around –200 to –300 ms and continuing to about 300 ms post keypress. This later waveform is more prominent in the left prefrontal area (FP1, AF7, AF3) than the right (FP2, AF4, AF8).

Moving caudally, the earliest activity in the left frontal area (F1, F3, F5) is a positive-going waveform starting at around –1750 ms and continuing till about –300 ms. This waveform does not appear on the right side of the head (F2, F4, F6, F8). It is visible but not pronounced at Fz and starts progressively later at F3, F5 and F7, suggesting an origin in the left medio-frontal area. These results tend to confirm the predicted medial origins of the middle latency waves. However, again there is a second negative-going waveform at all the medial frontal electrodes (but not at the lateral F6, F7 and F8), this time starting at about –200 ms and finishing at about 200 ms after the keypress.

Further caudally still, activity at FC1, FC3 and to a certain extent FCz and FC2 (but not FC5, FT7, FC4, FC6 or FT8—again suggesting an origin slightly to the left of centre) begins with a positive going waveform starting around –2100 ms and finishing around –500 ms. Again this waveform both starts and finishes earlier than the waveform seen at more rostral leads, in contradiction to the hypothesis. This time there is also a very prominent negative-going waveform at FC1, FC3, FCz, FC2, smaller at FC4, starting -350 to -400 ms, peaking around –30 ms and finishing around 200 ms post keypress.

Activity at the vertex (Cz) begins with a negative-going waveform starting about 350 ms before the keypress and ending about 100 ms after it. This activity is slightly larger at C1 and C3, slightly smaller at C2 and non-existent at C5, C4. At electrode T7 it reverses to become a positive-going ramp starting at –600 ms and peaking at the keypress. This reversal of sign is repeated at C6 and T8, but with a much later onset at around –250 ms. These results probably reflect the predicted lateralisation of activity to the left (contralateral to the right handed keypress) in the motor strip.

Caudal to the central sulcus, electrodes CP5 and CP6 show relatively large positive-going waveforms beginning at about –300 ms and ending about 200 ms. The amplitude of these waveforms decreases and their time of onset becomes later more medially (CP1, 2, 3 and 4). Over the parietal cortex both the waveform and the trend towards its being larger at lateral sites are similar (with the exception of P10). Waveforms at the extreme rear of the head tend to show very little activity at all before the keypress, but some activity after the keypress (as predicted by the hypothesis).

In general, these observations tend to confirm the hypothesis that activity starts in the prefrontal cortex on both sides of the head, progresses caudally in the midline (slightly to the left of centre), then lateralizes somewhat to the contralateral side in the motor strip. However, there is some lack of temporal sequentiality in the progression from prefrontal to motor strip leads, and activity in the posterior parietal cortex, which was predicted to occur in the early to middle timeframe, does not seem to start until close to the keypress.

In a further departure from the predictions of the hypothesis, most electrodes record activity that starts a few 100 ms before the keypress and continues for a few 100 ms after the keypress, in addition to whatever earlier activity they might display. In the rostral half of the head, this activity is largest at midline electrodes and decreases towards the lateral leads, but in the caudal half of the head it is more or less independent of electrode location.

Figures S1–S5 show that the other five subjects produced waveforms largely similar to FS's at leads around and rostral to the vertex—with the exceptions that (a) subjects JL (Fig. S2), KK (Fig. S3) and ZY (Fig. S4) did not show the predicted early activity at prefrontal leads and (b) subjects JL (Fig. S2), KK (Fig. S3) or TB (Fig. S5) did not show standard, late, BP-like activity at Cz or any of the lateral C electrodes.

Middle time waveforms at leads caudal to the vertex varied greatly between subjects. Subject CJ (Fig. S1) showed clear mid-range activity over the left posterior parietal cortex (a positive-going waveform at CP3, CP5, P7 and P9, starting at around -850 ms). Subject JL (Fig. S2) showed mid-range activity over the right posterior parietal cortex (a negative-going waveform at CP6 and CP4 starting at around –1700 ms and ending around –350 ms and also a positive-going waveform starting around –850 ms in POz and Oz). Subject KK (Fig. S3) showed clear mid-range posterior parietal activity on both sides: at P1, P3 and P5 a negative-going wave starting about –1700 ms and returning to baseline about –400 ms, and a similar waveform at CP2, CP4, P2, P4, P6 and P8 starting around –1700 ms (slightly later at P6 and later still at P8) and returning to baseline around –400 ms. Subject ZY (Fig. S4) showed considerable, rather complex mid-range activity over all electrodes caudal to the vertex. Subject TB (Fig. S5) had negative-going waveforms starting at around –1500 ms and ending around –450 ms on leads PO7, PO3, Poz and also similar sites on the right of the head.

Testing of predictions of the hypothesis using ICA and dipole source analysis

Correct predictions

Figures 3 to 8 show the positions of the fitted dipoles and the time-course of the ERPs for selected ICA components where it *was* possible to predict more or less successfully from the position of the dipole on the head what the general shape of the ERP would be. The specifics of the predictions tested are described in "Prediction testing."

Figure 3 represents components with roughly prefrontal dipoles, which predict "early" ERPs. Given that FS was essentially the only subject for whom the non-decomposed ERPs indicated any early activity at all, it is perhaps remarkable that ICA decomposition does allow the isolation of components which show both prefrontal dipoles and some degree of early activity. Figure 4 shows one example from each subject of components with dipoles taken as predicting mid-time activity. Most of the dipoles in this category are oriented vertically, which may implicate loops of cortico-subcortical activity. Figure 5 illustrates a set of components with dipoles taken as predicting mid- to late activity. Figure 6 shows components with dipoles predicting late activity. Figure 7 shows dipoles over the region of the posterior parietal cortex, which predict mid-time activity. Figure 8 shows dipoles at the extreme back of the head, which were taken to predict cerebellar activity occurring after the keypress.

However convincing these figures may or may not be, they depict not 'typical' but the best available examples. Table 1 shows that, even employing the eye of faith necessary to accept some of the predictions illustrated in Figs. 3–8 as correct, a relatively small proportion of dipoles for each subject could be categorized as correctly predicting the temporal features of their ERP.

Incorrect predictions

There were several varieties of incorrect prediction.

(a) Overall about 15% of ICA components isolated what were clearly sources of muscle or other types of noise.

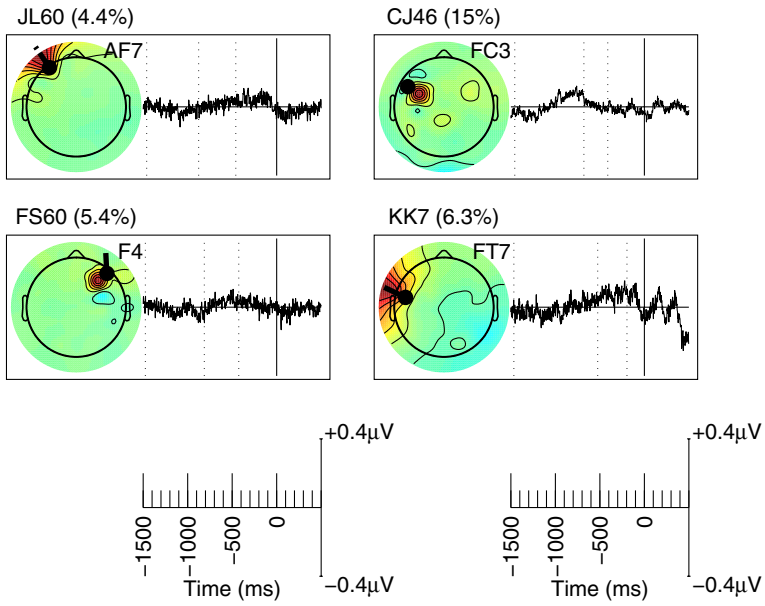

Fig. 3 Dipoles and ERPs for components where dipole position predicted early ERP activity. Percentages in brackets are % of component activity not accounted for by the dipole. Number of trials included in ERP averages are: JL60 = 220, CJ46 = 182, FS60 = 208, KK7 = 316

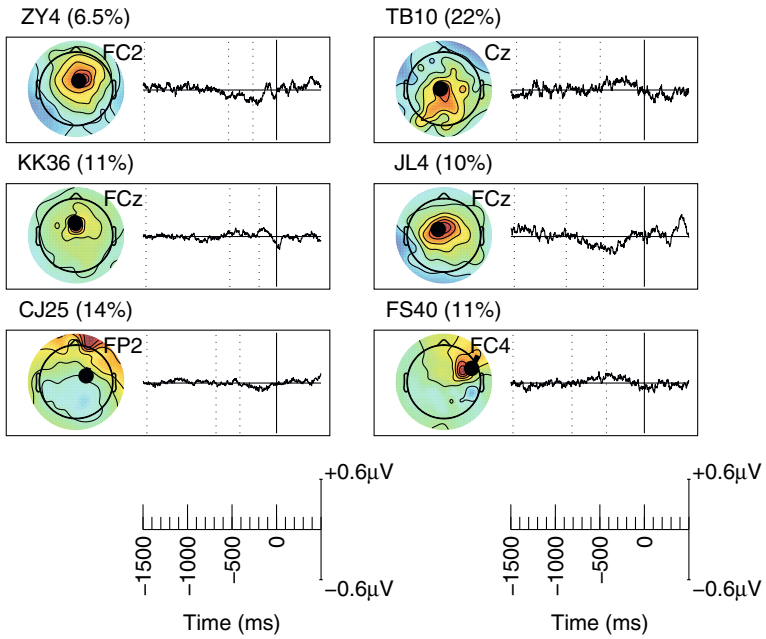

Fig. 4 Dipoles and ERPs for components where dipole position predicted middle-time ERP activity (frontal dipoles). Percentages in brackets are % of component activity not accounted for by the dipole. Number of trials included in ERP averages are: ZY4 = 269, TB10 = 65, KK36 = 316, JL4 = 220, CJ25 = 182, FS40 = 208

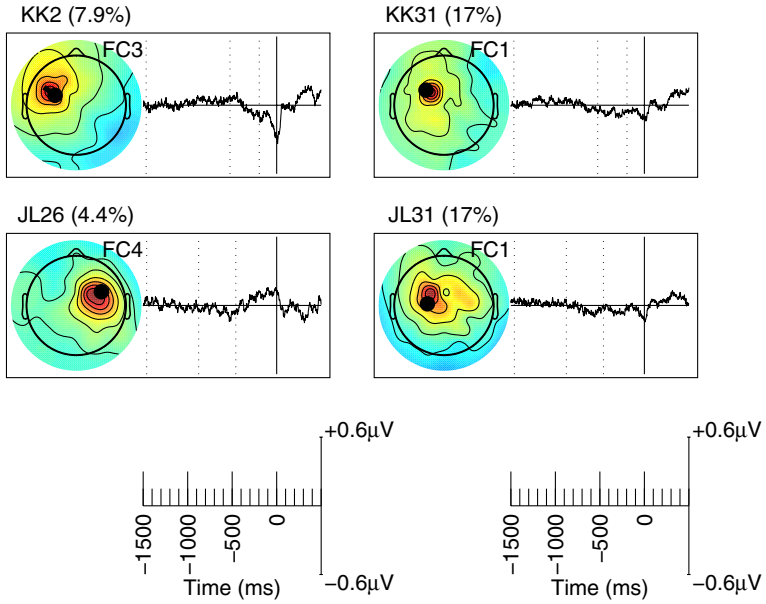

Fig. 5 Dipoles and ERPs for components where dipole position predicted mid-late ERP activity. Percentages in brackets are % of component activity not accounted for by the dipole. Number of trials included in ERP averages are: KK2 = 316, KK31 = 316, JL26 = 220, JL31 = 220

(b) A number of ICA components had ERPs showing activity that did occur at the time predicted by the position of their dipoles, but also occurred at earlier and/or later times. For example, 26 predictions of middle-timed activity arising from the area rostral to the motor strip were categorized as incorrect because the actual (as opposed to predicted) activity in the ERP did occur during the middle time period, but also occurred during late and/or post key-press time periods.

(c) For another subset of ICA components, the prediction was simply wrong. For example, in a total of 24 components over all subjects the prediction from the dipole position was that the ERP activity would occur early, when in fact it occurred late and/or post key-press.

Possible reasons for incorrect predictions

(a) One possibility is that not enough trials were included in the analysis for the ICA and dipole fitting algorithms to work properly. Table 1 shows that data from the subject for whom all but 65 trials were excluded because they involved stimulus-response times >1.5 s

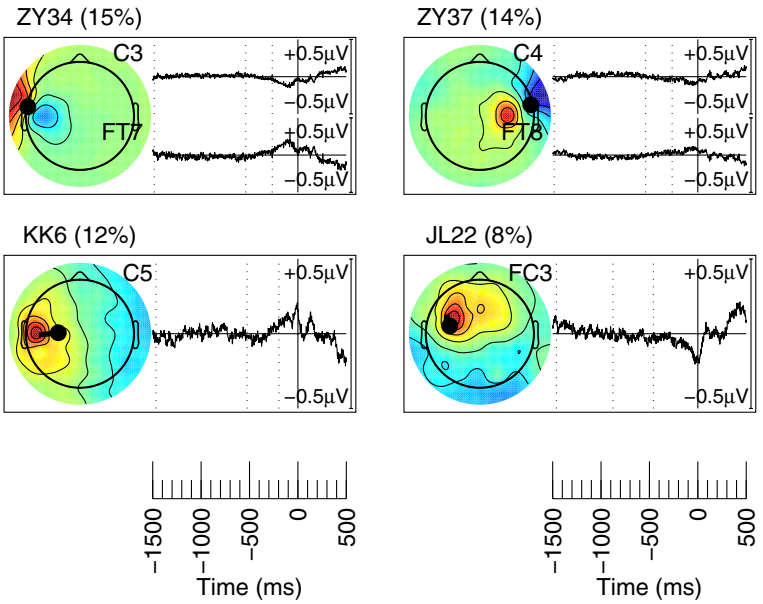

Fig. 6 Dipoles and ERPs for components where dipole position predicted late ERP activity. Percentages in brackets are % of component activity not accounted for by the dipole. Number of trials included in ERP averages are: ZY34 = 269, ZY37 = 269, KK6 = 316, JL22 = 220

did show easily the lowest number of correct predictions. This was at least partly because a large proportion of the components for this subject could not be fit by single dipoles at all. However above a certain threshold, Table 1 shows that the number of trials included in the analysis was not related to the proportion of correct predictions.

(b) Since so many different neural sources are predicted to be active during the period under study and only 64 electrodes were used, the ICA algorithm may have failed to isolate components representing neural sources adequately described by a single dipole. This possibility was tested by correlating number of correct predictions for each subject with the number of components in which a large percentage of the variance was accounted for by the dipole fitted. Taking the conservative figure of <6% residuals (i.e., >94% of the variance of the component accounted for by the dipole), Table 1 shows that there is essentially no relationship between the number of correct predictions for any given subject and the number of ICA components that are very well described by a single dipole. Increasing the acceptable proportion of residuals to 12% still does not produce a linear relationship between the number of correct predictions and the number of components where ≥88% of the variance is described by a single dipole.

Discussion

The main aim of this study was to investigate the hypothesis that the signature of neural activity underlying a decision about which computer key to press and the consequent pressing of that key starts bilaterally in the prefrontal area of the brain, then appears in medial frontal and posterior parietal areas, progresses to the midline of the motor strip and finally lateralizes to the contralateral primary motor area. Various separate parts of this hypothesis are confirmed by a considerable amount of already published data, but the whole progression of activity has not previously been studied in individual subjects.

Topographic analysis

Initial results of the present study show that a simple topographic analysis of ERPs from data not decomposed by ICA tends partly to confirm the starting hypothesis, but already reveals significant deficiencies in it. This analysis shows that in three out of six subjects (FS, CJ and TB), the peak sign of activity preceding a voluntary key press does, as predicted, begin in the prefrontal cortex.[4] No early activity is seen in the other three subjects, but this could easily be because variability in the time of decision making washes signs of its underlying activity out of the averaged ERP. In all subjects the peak sign of activity then moves (although not precisely in the linear rostral-caudal progression predicted by the hypothesis) through frontal sources distributed bilaterally across the midline in the middle time period, with variable middle time contributions also from the posterior parietal cortex. The predicted

[4] Strictly speaking, the presence of a waveform only at prefrontal leads is at best suggestive of the presence of neural activity in the prefrontal cortex.

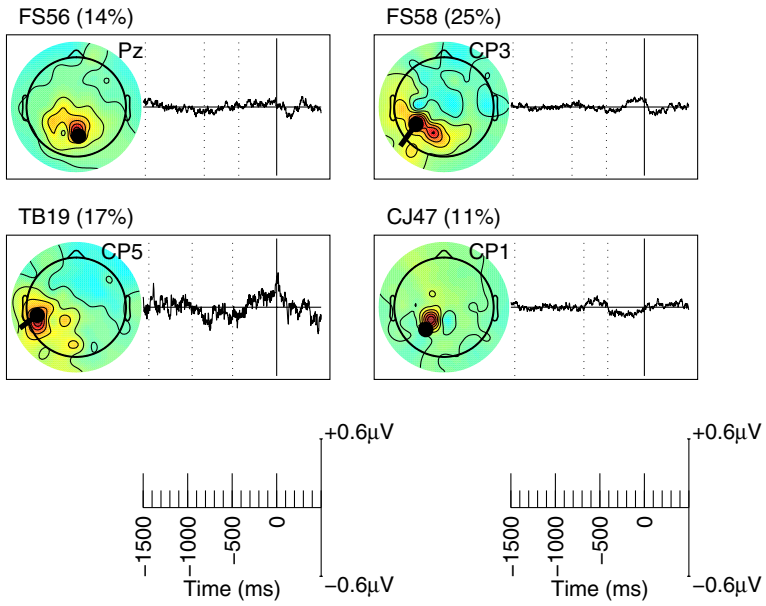

Fig. 7 Dipoles and ERPs for components where dipole position predicted middle-time ERP activity (parietal dipoles). Percentages in brackets are % of component activity not accounted for by the dipole. Number of trials included in ERP averages are: FS56 = 208, FS58 = 208, TB19 = 65, CJ47 = 182

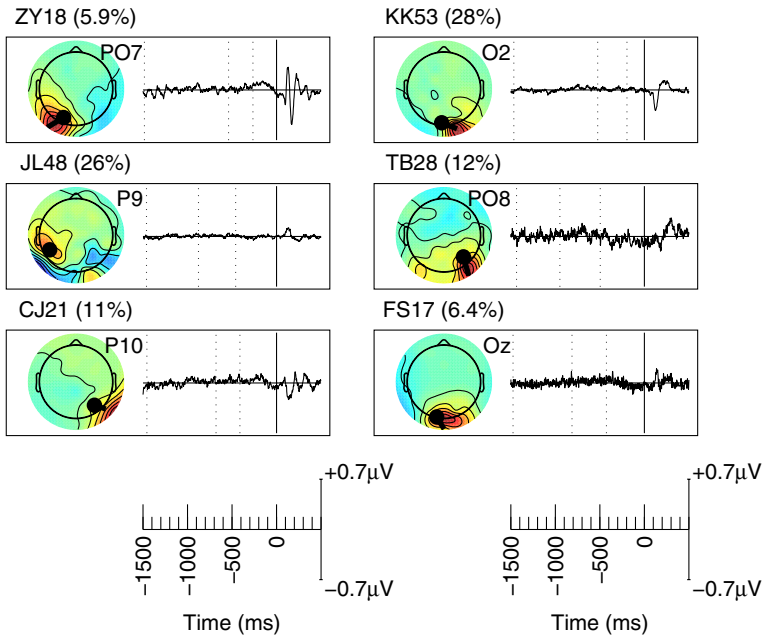

Fig. 8 Dipoles and ERPs for components where dipole position predicted post-key-press ERP activity. Percentages in brackets are % of component activity not accounted for by the dipole. Number of trials included in ERP averages are: ZY18 = 269, KK53 = 316, JL48 = 220, TB28 = 65, CJ21 = 182, FS17 = 208

Table 1 Numbers of correct predictions versus number of trials analysed and goodness of dipole fit

A prediction is a prediction about the shape of the ERP for a particular ICA component on the basis of the position of that component's dipole on the head. A correct prediction is one that fits the hypothesis outlined in the text

Subject	Number of correct predictions (out of 64)	Number of trials analysed	# Dipoles with <6% residuals (out of 64)	# Dipoles with ≤12% residuals (out of 64)
JL	20 (∼31%)	220	12	40
KK	18 (∼28%)	316	3	28
CJ	12 (∼19%)	182	4	27
FS	11 (∼17%)	208	16	45
ZY	11 (∼17%)	269	10	32
TB	7 (∼10%)	65	1	9

late contra-lateralization in the motor strip is seen only in subjects FS, CJ and ZY.

Another finding of the present study that is not predicted by the original hypothesis is that most electrodes, in most subjects, showed post-keypress activity. The hypothesis predicted post keypress activity arising from the cerebellum. However, a little further thought shows that post keypress activity would also be expected to arise from (a) somatosensory activity resulting from pressing the key (signature expected in leads over the post-central gyrus) (b) visual activity from viewing the feedback on the correctness or incorrectness of the key press (signature expected in occipital and parietal leads) (c) cognitive activity related to the construction of hypotheses on the basis of the feedback (signature expected in frontal and prefrontal leads), and even (d) blinks, which the subjects were instructed to hold until after they had pressed the key (signature expected in anterior leads). So this finding really has no significant effect on the underlying tenor of the original hypothesis—it merely adds a few predictions along the same lines.

However, one finding which is not predicted at all by the starting hypothesis, and which must be considered as seriously calling that hypothesis into question, is that most electrodes in most subjects recorded a distinct waveform in the few 100 ms immediately before the keypress, in addition to whatever earlier activity they may have displayed. In the rostral half of the head this waveform was negative-going and in the caudal half of the head it was positive-going. Thus the initial suspicion is that these waveforms might all result from volume conduction of a focus of activity somewhere in the middle of the head. Such a focus might be represented by a tangential dipole in the anterior (motor) wall of the central sulci bilaterally, or perhaps by a deeper, subcortical dipole field, which would tend to spread to all leads by volume conduction. However, this volume conduction explanation is rendered unlikely by two independent observations: (i) most universal volume-conducted activity could be expected to have been removed by the use of an average reference, and, perhaps more tellingly (ii) the shapes of the negative-going and positive-going waveforms are quite different.

An alternative possibility therefore needs to be considered. The only obvious one at the moment would appear to be that coordinated, movement-related, neural activity actually did occur beneath all electrodes during this late time slot. The implications of this possibility will be further discussed in "Local versus global processing in the brain."

The question now arises, can application of the techniques of ICA and DSA add any detail to the picture sketched from direct observation of ERP topography?

ICA and dipole source analysis: possible reasons for low incidence of 'correct' predictions

Our results showed that when the EEG preceding keypresses was decomposed into 64 ICA components for each subject and dipoles were fit to describe the spatial distribution of each component, less than a third of the predictions about the timing of ERP activity that were made by applying the hypothesis under investigation to the dipoles were scored as correct. It is the other two thirds of predictions which might add information over and above that delivered by the topographic analysis.

With regard to the incorrectness of predictions for the other two thirds of components, responsibility could lie either with the techniques of ICA and DSA as applied by us, or with some inadequacy of the original hypothesis. We will begin by considering the possibility that our ICA and DSA methods might in some way be inadequate.

General problems with DSA and ICA

The major problem with DSA is that it requires solution of the EEG inverse problem. Even when the source analysis is performed on individual independent components, each of which presumably comprises a relatively small number of neuronal sources, the inverse problem is notoriously underdetermined. A second general source of inaccuracy in the DSA performed here was the use of a generic, spherical head model rather than a finite element model specific to the individual subjects' skulls.

The method of ICA in general operates on the basis of a number of assumptions that are probably invalid. One is the assumption of independence. Another is the assumption of stationarity. We tried to minimize the problem of stationarity in the present analysis by restricting the length of our data segments, but given that the whole aim of the exercise was to observe a putative flow of activity from one part of the brain to another, lack of stationarity can be expected to have been a significant problem.

Specific problems with ICA and DSA as applied to the present analysis

One feature of ICA (which can probably be regarded as more a strength than a weakness) clearly did contribute to the high percentage of incorrect predictions in the present analysis. ICA is generally accepted as being very good at isolating non-neural artefacts. In our case it did so about 15% of the time.

Another methodological characteristic of both ICA and DSA is that if not enough data are fed into the analyses,

they fail to work well. In our study lack of sufficient data was clearly a problem for Subject TB, for whom all but 65 trials were excluded because they involved stimulus-response times >1.5 s. As shown by Table 1, this subject had easily the lowest number of correct predictions. This was at least partly because a large proportion of his ICA components could not be fit by single dipoles at all. However, each of the other five subjects obviously cleared some threshold in this regard, because among them the number of trials included in the analysis was not linearly related to the proportion of correct predictions.

Another methodological possibility is that, because of the large number of sources likely to be active during the time period under study and the relatively small number of electrodes, ICA failed to isolate components underpinned by single neural sources. If this were the case, it would be expected that incorrect predictions would arise from dipoles that did not account for a high percentage of the variance of their component, while correct predictions would arise from components with low dipole residuals. However, Table 1 shows that goodness of fit of the dipoles calculated for each component was probably not a factor in correctness of predictions. No relationship is evident between the number of correct predictions for any given subject and the number of ICA components where either 94% or 88% of the variance is described by a single dipole.

Of course it is possible that the percentage of a component's variance which can be described by a single dipole is not the best indicator of whether or not that component isolates a single functional neural source. One major reason for predictions' being categorized as incorrect in the present study was that the ERP waveform for the component in question *did* show activity during the predicted time period—but also showed activity in an earlier and/or later period. For example, a total of 26 predictions of middle-timed activity arising from the area rostral to the motor strip were categorized as incorrect because the actual (as opposed to predicted) activity in the ERP did occur during the middle time period, but also occurred during late and/or post key-press time periods. Various possibilities might explain such findings. The ICA components in question might contain activity arising from several different neural sources, each of which is active during a different time period. This might occur because of volume conduction, which contaminates the activity recorded above one neural source with activity generated by its neighbor. Alternatively, such findings might indicate that the component in question does isolate one neural source, but this source is (contrary to the hypothesis) active either repeatedly, or continuously for a longer time than predicted. On present data it is not possible to determine which of these possibilities is correct.

There is, however, a class of components in this analysis which definitely tend to falsify at least part of the original hypothesis. A rich source of incorrect predictions was a series of cases where the predicted ERP shape was simply wrong. For example, in a total of 24 components over all subjects, the prediction from the dipole position was that the ERP activity would occur early, when in fact it occurred late and/or post key-press. This sort of error may be due to non-fatal shortcomings in the hypothesis—in this case, frontal post key-press activity may sometimes be due not to decisions about which key to press in the current trial, but to decisions about the next trial, made on the basis of the visual feedback delivered immediately after the current key-press.

Alternatively, the prevalence of incorrect predictions may reflect some more fundamental inadequacy in the original hypothesis.

Local versus global processing in the brain

The dominant paradigm in neuroscience at present, a largely unarticulated theoretical underlay which is probably ubiquitous enough to be called the neuroscientific 'standard model,' postulates that specific functions are subserved by specific, discrete areas of cortex. Information flows around the brain by means of activation of a number of such areas in sequence, like billiard balls hitting one another, until eventually a particular behavior or cognitive event results. On this model, the task of the experimentalist is to identify the location, extent and activation sequence of the brain areas and the transmission delays between areas based on distances and axonal propagation velocities. The hypothesis under investigation in the present paper is a product of this paradigm.

However, there does exist an alternative model of brain function, a paradigm which has been quietly emerging over the last few decades from work on nonlinear dynamics. The working hypothesis here (Freeman 2004) is that normal brain function is maintained in a stable state by the process of self-organized criticality (SOC, Bak et al. 1987, Jensen 1998). SOC describes complex physical systems as falling naturally into a global state critically poised on the edge of instability, which offers the advantage of allowing large areas of the system to change almost instantaneously to a new state. Thus, in principle, networks exhibiting SOC can support both the spatially segregated or clustered processing of the neuroscientific 'standard model,' and a more globally distributed kind of processing.

The existence in the brain of some form of global processing is certainly supported empirically by a growing number of observations of intermittent long-range synchrony between activity in widely separated areas of cortex

with no detectable delays between them (noted as "zero lag") (Varela et al. 2001; Quian Quiroga et al. 2001; Freeman et al. 2003b; Freeman and Burke 2003; Freeman and Rogers 2003). While most of these studies describe synchrony only between activity recorded at widely separated but discrete sites, Freeman et al. (2003a), using a high density curvilinear array of electrodes, actually find synchrony in the human brain that is continuous over a distance of 189 mm, a significant percentage of the width of the whole brain.

However, although it seems quite likely that the mechanistic basis of such global processing is SOC, at this stage the possibility must be said to remain unproven.

According to Jensen (1998), the hallmark of SOC is the presence of 'scale-free'[5] structure and dynamics, whose signatures are "spatial fractals and temporal 1/f fluctuations" (Jensen 1998 p.12). Temporal power spectral density plots of waking EEG certainly do resemble brown noise ($1/f^{\sim 2}$), at least in the frequency range above about 10 Hz (Freeman et al. 2000, Freeman 2007). But, despite a number of reports that neural systems have 'small-world' topology[6] (Watts and Strogatz 1998; Hilgetag et al. 2000; Strogatz 2001; Bassett and Bullmore 2006; Bassett et al. 2006), the question of whether or not there also exist in individual brains spatial fractals of either structure or functional dynamics is still debatable (Freeman et al. 2000; Freeman 2007).

This brings us back to the possibility mentioned at the end of "Topographic analysis" to explain the major departure of our current data from the predictions of the original hypothesis. In light of the above considerations, it now seems quite likely that the negative-going waveform variously described by others as BP2 (Deecke et al. 1969) or NS' (Shibasaki et al. 1980) actually does occur in a quite widespread area of frontal cortex and associated subcortical structures. If the source of this waveform really is more or less the whole front half of the brain, the activity described by many of the independent components calculated in the present paper would not be strictly localized to a site under particular electrodes, but may extend over much or even all of each hemisphere—possibly bilaterally simultaneously, giving peaks in the midline. The equivalent dipole sources calculated for each component would then be either an approximation of a distributed source—or would possibly correspond to 'hubs' in a scale-free network.

Acknowledgments Thanks to Professor Robert T. Knight for access to hardware, Clay Clayworth for help setting it up and Christina Karns for assistance with stimulus software. Thanks also to Associate Professor Gary Bold for support during the analysis phase of the project.

[5] 'Scale-free' in this context means that the distribution of the parameter under study obeys a power law: i.e., most of the observations fall into the smallest bins of a histogram, with a few instances of very large observations. The distributions in log-log coordinates show a linear relation described as $1/f^{a}$, where the exponent, a, designates the slope. This means that there is no peak in the distribution to provide a characteristic 'scale'.

[6] Small-world topologies are a subset of scale-free topologies which feature dense local connections between neighboring nodes in the network, but at the same time a short path length between pairs of distant nodes due to the existence of a few long-range connections. Such topologies offer obvious possibilities with regard to global processing.

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