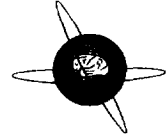# The future of electroencephalography in assessing neurocognitive functioning

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Abstract

High temporal resolution is necessary to resolve the rapidly changing patterns of brain activity underlying mental function. Additionally, simple, non-intrusive equipment is needed to routinely measure such functions in doctors' offices, at home and work and in other naturalistic contexts as people perform normal everyday activities. When compared with all other modalities for measuring higher brain functions, EEG is unique in that it has both these attributes. Two factors are limiting the further development and application of EEG for measuring cognitive functioning: a technical one that is easy to overcome and a sociological one that is more problematic. The technical limitation is that traditional EEG technology and practice provides insufficient spatial detail to identify relationships between brain electrical events and structures and functions visualized by magnetic resonance imaging (MRI) or other modalities. Recent advances overcome this problem by recording EEGs from more electrodes, by registering EEG data with anatomical information from each subject's MRI, by correcting the distortion caused by volume conduction of EEG signals through the skull and scalp, and by computing hypotheses about the sources of signals recorded at the scalp. The sociological limitation is that clinical EEGs are mostly performed by neurologists with no particular special interest in cognitive brain function, while cognitive research using EEG is largely done by psychology professors and their graduate students with no clinical ambitions. The diminishing clinical role of traditional EEGs in localizing lesions in the brain, and the obvious and insistent medical need for inexpensive and accessible tests of cognitive brain functioning may serve to soon dissipate this sociological obstruction. This will lead to a golden age of EEG in which Hans Berger's vision of the EEG as a window on the mind will be realized. Rather than slowly fading into obsolescence, EEG will retain its role as the primary means of measuring higher brain function when the purpose is not 3D localization per se, and will serve as an invaluable complement to functional MRI in those instances when both high temporal and high spatial resolution are required. © 1998 Elsevier Science Ireland Ltd.

Keywords: Attention; Cognition; Electroencephalography; Functional neuroimaging; Language; Magnetic resonance imaging; Memory

1. Introduction

The neurophysiology of cognition involves rapid coordination of processes in widely distributed cortical and subcortical regions. The electrical signals which accompany higher cognitive functions are subtle, spatially complex, and change both in a tonic multisecond fashion and physically in subsecond intervals, in response to environmental demands and internal representations of environment and self. No one brain imaging technology is currently capable of providing both near millimeter precision in localizing regions of activated tissue and subsecond temporal precision for characterizing changes in patterns of activation over time. However, by combining several technologies, it seems possible to achieve this fine degree of spatiotemporal resolution. High-resolution EEG is especially well suited for monitoring rapidly changing regional patterns of neuronal activation accompanying purposive behaviors, while functional magnetic resonance imaging (fMRI) seems ideal for precisely determining their three-dimensional (3D) localization and distribution. It is a topic of current research to figure out how to combine EEG and fMRI data from the same subjects doing the same tasks.

The exquisite sensitivity of EEG to changes in mental activity has been recognized since Berger (1929) reported a decrease in the amplitude of the alpha rhythm during mental arithmetic. Additionally, evoked potential (EP) measurements are well suited for measuring subsecond component processes of sensory, motor and cognitive processes

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(Hillyard and Picton, 1987; Regan, 1989). Measurements of the correlation, coherence, crosspower or covariance of EEG time series from different electrode sites help generate hypotheses about the functional networks which form between different cortical regions during the sensory, cognitive and motor processes which comprise performance of simple tasks. These features would seem to make EEG an ideal tool in itself for measuring higher brain functions, or as a complement to fMRI when both high spatial and high temporal resolution are needed. However, the spatial detail of conventional EEG recordings has been so coarse that it has only been possible to meaningfully interpret them with respect to underlying functional neuroanatomy at the level of entire cortical lobes, if at all. Although the ability to infer the 3D distribution of electrical sources in the brain from scalp EEG (or magnetoencephalography, MEG) recording has fundamental physical limits, the amount of spatial information that can be recovered from the scalp-recorded EEG is frequently underestimated. Indeed, the very low level of spatial resolution obtained from conventional EEGs reflects the fact that activity is only measured at a small number of scalp sites during most routine recordings; moreover, modern spatial signal enhancing methods have not often been applied. Recently, several laboratories have been recording EEGs from more than 100 locations, performing post-processing of the resulting data to increase its spatial detail, and in some cases registering this data with other images of brain structure and function. These developments are producing dramatic improvements in the utility of the EEG as a neuroimaging method for higher brain functions, both as a stand-alone modality and in combination with fMRI.

As a practical matter, an obvious but often unappreciated feature of EEG technology is worth mentioning, namely its extreme compactness and simplicity. This fact has important economic considerations, which frequently fail to be considered in scientific discussions of brain mapping technology. It also means that, unlike all other functional neuroimaging modalities which require massive machinery, large teams of technicians, and complete immobilization of the subject, EEGs are easily recorded, even from an ambulatory subject who is literally wearing the entire recording apparatus. In addition to providing inexpensive medical tests that can be performed in the doctor's office, this feature of EEGs will facilitate research into the as yet uncharted territory of how brains think when performing everyday activities in the real world (Gevins et al., 1995b).

2. Improving the spatial detail of EEGs

Better spatial sampling is the first requirement for extracting more detailed information about cognitive processes from scalp-recorded EEGs. Often only 3 electrodes are used in cognitive EP studies. The 19 channel 10–20 electrode montage commonly used in clinical and research EEG recordings has an interelectrode distance of about 6 cm on a

typical adult head. This spacing may be dense enough for detecting signs of gross pathology or for differentiating the gross topography of EP components, but is insufficient for resolving the finer topographical differences that are important in studying cognitive brain function. By increasing the number of electrodes to over 100, average interelectrode distances of about 2.5 cm can be obtained on an average adult head, which is within the range of the typical cortex-to-scalp point spread function (i.e. the size of the scalp representation of a small, discrete cortical source; Gevins, 1990).

The usefulness of such increased spatial sampling remains limited by the distortion of neuronal potentials as they are passively conducted through the highly resistive skull. This distortion amounts to a spatial low-pass filtering, which causes a blurring of the potential distribution at the scalp. In recent years, a number of spatial enhancement methods have been developed for reducing this distortion. The simplest and most widely accessible of these methods is the spatial Laplacian operator, usually referred to as the Laplacian derivation (LD). It is computed as the second derivative in space of the potential field at each electrode. The LD is thought to be proportional to the current entering and exiting the scalp at each electrode site (Nunez, 1981), and is independent of the location of the reference electrode used for recording. It is relatively insensitive to signals that are common to the local group of electrodes used in the computation, and thus relatively more sensitive to high spatial frequency local cortical potentials. A simple method of computing the LD assumes that electrodes are equidistant and at right-angles to each other, an approximation that is only reasonable at a few scalp locations, such as the vertex. A more accurate approach is based on measuring the actual 3D position of the electrodes and using 3D spline functions to compute the LD over the actual shape of a subject's head (Le et al., 1994). The main shortcoming of the LD is that it unrealistically assumes that the skull has the same thickness and conductivity everywhere on the head, which limits the amount of improvement in spatial detail that the method can achieve.

This shortcoming of the LD can be ameliorated by using a realistic model of each subject's head to locally correct the EEG potential field for distortion resulting from conduction to the scalp. One such method is called finite element deblurring, or Deblurring® for short. It provides a computational estimate of the electrical potentials that would be recorded near the superficial cortical surface by using a realistic mathematical model of volume conduction through the skull and scalp to downwardly project scalp-recorded signals (Gevins et al., 1991, 1994b; Le and Gevins, 1993). Each subject's MRIs are used to construct a realistic model of his or her head in the form of many small tetrahedral elements representing the tissues of scalp, skull and brain. By assigning each tissue a conductivity value, it is possible to calculate the potential at all finite element vertices by using Poisson's equation. Given that the actual conductivity
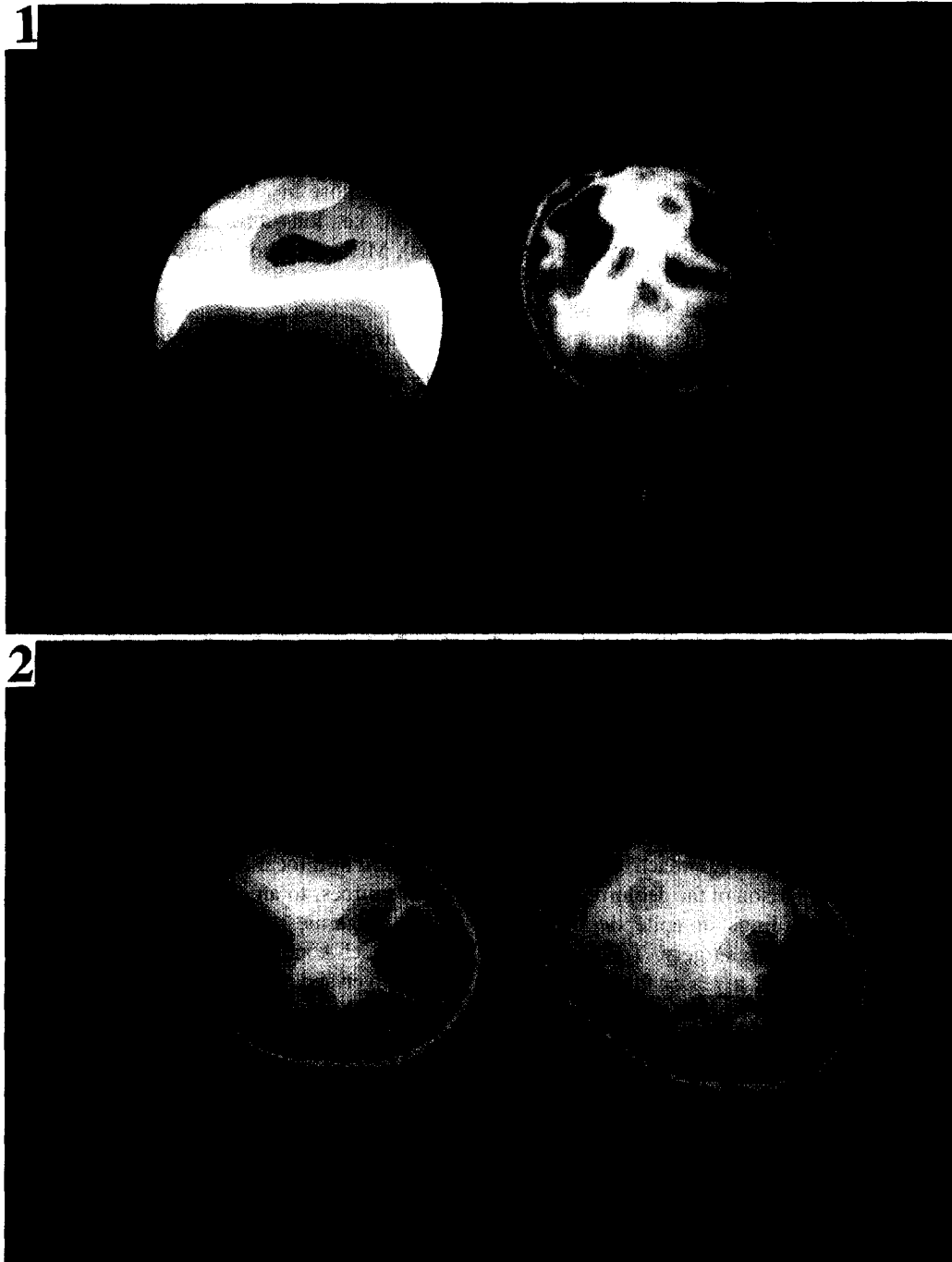
Fig. 1. High-resolution EEG mapping of somatosensory cortex activation. The image on the right is a 124 channel, deblurred topographic map of the potentials evoked by repetitive electrical stimulation of the left middle and right index fingers. The scalp-recorded EEG data have been spatially enhanced and projected down to just above the superficial cortical surface of the subject's brain which was reconstructed from his MRI. It is clear that localized areas of the left and right cerebral cortex have been activated, corresponding to the stimulation of right and left hand fingers. The image on the left shows a conventional, 18 channel, linked mastoid reference topographic EEG map (nose at the top) evoked by the same stimuli.

Fig. 2. Deblurred EPs during reading. The processing of syntactic (grammatic) words differs from the processing of content (semantic) words. The image on the right shows the result of deblurring an EP that reached peak amplitude about 445 ms after presentation of pronouns that were the subject of a short sentence. It had a focus of activity over the left lateral frontal operculum, and a duration of about 200 ms. The image on the left illustrates the deblurred EP elicited by presentation of content words at the same time point. Both classes of words show common activation over the left parietal region and over calcarine cortex during this interval.

value of each of these finite elements is unknown, a constant value is used for the ratio of scalp to skull conductivity; the conductivity of each finite element is set by multiplying this constant by the local tissue thickness as determined from the MRI. Thus, even though true local conductivity is unknown, the procedure is well behaved with respect to this source of uncertainty, because it successfully accounts for relative conductivity variation due to regional differences in scalp and skull thickness. In initial applications, the deblurring method has been shown to be reliable and more accurate than the LD (Le and Gevins, 1993; Gevins et al., 1994b); of course, at the expense of obtaining and processing each subject's structural MRI. Although the deblurring method can substantially improve the spatial detail provided by scalp recorded EEGs, it doesn't provide conclusive information about the location of generating sources. Nevertheless, the improved spatial detail facilitates formation of more specific hypotheses about the distribution of active cortical areas during cognitive tasks than was previously possible (see below). Exploratory studies of deblurring and other high-resolution EEG techniques focused on the spatial enhancement of sensory EPs, where a great deal of a priori knowledge exists concerning their underlying neural generators (Gevins et al., 1994b). For example, Fig. 1 contrasts the spatial detail obtained for somatosensory stimulation of fingers on each hand using conventional 18 electrode EEG mapping methods with that obtained using 124 electrodes and deblurring. The deblurred somatosensory responses clearly isolate activity to the region of the central sulcus in each hemisphere. Demonstrations of this form serve to verify the plausibility of the approach, but a better validation is obtained by comparison of the deblurred potentials with subdural grid recordings in epileptic patients undergoing evaluation for ablative surgery. To date these validation studies have produced a reasonable degree of agreement between the deblurred potentials and those measured directly at the cortical surface.

The issue of blurring of brain signals by the skull can largely be avoided by recording the magnetic rather than the electrical fields of the brain, because the skull has minimal effects on magnetic field topography. However, this transparency does not eliminate the need for utilizing a high density of sensors to accurately map the spatial topography of brain magnetic fields, and the problems of localizing generator sources are equally severe for MEG as they

are for EEG; when those problems are overcome on average the two techniques produce localizations with approximately equal accuracy. Further, the cost of MEG technology is at least an order of magnitude greater than that required for EEG studies, and the associated infrastructure required to perform MEG studies is more complex and inflexible. Thus, for most laboratories, and for some applications (particularly those in which a subject's head cannot be immobilized, i.e. long-term monitoring or ambulatory recordings), MEG does not provide a viable alternative to EEG.

3. Source generator localization

Neither the LD, nor more advanced EEG spatial enhancement algorithms, nor MEG recordings, provide any conclusive 3D information about where the source of an electrical signal lies in the brain. In some cases, such as when healthy subjects perform difficult cognitive tasks and strong signals are recorded over areas of association cortex (i.e. dorsolateral prefrontal, superior and inferior parietal, inferotemporal and lateral temporal), the hypothesis that EEG potentials are generated in these areas is the most plausible, but counterexamples can always be presented. In addition to visual examination of the potential field distribution, another procedure for generating hypotheses concerning the neuroanatomical loci responsible for generating neuroelectric events measured at the scalp is called 'dipole modeling' (Scherg and VonCramon, 1985; Fender, 1987). Dipole modeling uses iterative numerical methods to fit a mathematical representation of a focal, dipolar current source, or collection of such sources, to an observed scalp-recorded EEG or MEG field. Regardless of which method is used to formulate them, such source generator hypotheses must be independently verified. In rare cases, this can be done in patient populations in the context of invasive recordings performed for clinical diagnostic purposes (Smith et al., 1990). More commonly, another type of imaging modality, such as positron emission tomography (PET) or fMRI, has to be employed.

Since EEG and MEG dipole modeling has become a popular activity in the last few years, it is worthwhile to reiterate that dipole modeling does not, in general, provide a unique and physically correct answer about where in the brain activity recorded at the scalp is generated. This is so,

Fig. 3. Deblurred EPs and ongoing EEG related to focused attention. With EEG it is possible to simultaneously measure both subsecond and multisecond regional brain activity during performance of cognitive tasks. In this experiment, a sequence of increased subsecond EP peaks and waves was observed over frontal (first and second columns) and parietal (third column) cortices during a difficult working memory task, in comparison to control conditions with lower working memory requirements. These subsecond changes in the working memory tasks were accompanied by longer lasting (4 s) increases in ongoing EEG frontal midline theta band power (rightmost column). These EEG findings suggest that various types of attention are associated with neural processes that have distinct time courses in distinct neuronal populations. Amplitude scale is constant across experimental conditions within each column; EP scale is voltage, EEG scale is z-scored spectral power.

Fig. 4. Preparatory evoked potential covariance (EPC) patterns preceding Accurate and inaccurate responses. EPCs involving left frontal, midline precentral and left central and parietal electrode sites are prominent in patterns preceding accurate responses (by 0.5–1 s) (left). The number and magnitude of EPCs are smaller preceding inaccurate responses (right).

because solving for the source of an EEG or MEG distribution recorded at the scalp is a mathematically ill-conditioned 'inverse problem' which has no unique solution; additional information and/or assumptions are required in order choose among candidate source models. While some of this a priori information is obvious and harmless (i.e. that the potentials must arise from the space occupied by the brain), other assumptions border on presupposing unknown information (i.e. that the potentials arise only from the cortex, or that the number of active cortical areas is known). One simple, convenient, and possibly clinically useful approach for potentials elicited by simple sensory stimulation is to assume that

the scalp potential pattern arises from a single point dipole source. Although not anatomically and physiologically realistic, such simple models can sometimes be useful, for instance for locating the central sulcus. However, most complex scalp-recorded electrophysiological phenomena are poorly approximated by a single source model, and obtaining estimates of the strength and 3D locations of the underlying neuronal generators when there are multiple, time-overlapped active sources has widely recognized practical and theoretical difficulties (Mosher et al., 1992; Miltner et al., 1994). One promising approach to this issue is to use information about the cortical regions activated by a task as mapped by 3D functional neuroimaging methods such as fMRI or PET to constrain the number and approximate locations of dipole source models, and to derive information about the spatiotemporal dynamics of those sources from EP measurements (Heinze et al., 1994).

4. EEG studies of cognition

Recent developments suggest that high-resolution EEG methods are useful tools in the experimental analysis of higher-order brain functions. For example, spatial enhancement of EEGs related to component processes in reading has yielded results that are highly consistent with current knowledge of the functional neuroanatomy thought to be involved with visual pattern recognition and language functions (Gevins et al., 1995a). In one study, EPs were elicited during a simple cued matching task requiring one of 4 types of matching judgments: graphic (visual identity of unfamiliar non-letter character strings), phonemic (homophonic pseudowords), semantic (antonymy), and grammatic (noun-verb agreement). Each trial of the task began with a cue that indicated which one of the 4 conditions to expect. One second later this cue was followed by the first stimulus, which in turn was followed 1 s later with the comparison stimulus. Several striking between-condition differences were evident in highly localized EP patterns. For example, larger amplitude EP waves occurred in the grammatic condition (relative to the other language tasks) at 445 ms after the first stimulus; the duration of the wave was only about 200 ms. These potentials were largest at scalp locations near the presumed region of Broca's language area in the frontal cortex of the left hemisphere (Fig. 2), and their task correlates are consistent with the postulated functional neuroanatomy of this region. Thus, functional localization of cognitive processes inferred from spatially enhanced and anatomically registered electrophysiological measurements can be compared with the results of lesion studies and other neuroimaging approaches. As a complement to these approaches, the fine-grain temporal resolution of EP measurements, in combination with improved topographic detail, adds valuable insights gained by characterizing both the regionalization of functions and the subsecond dynamics of their engagement.

Modern EEG methods have also been used to study subsecond and multisecond distributed neural processes associated with working memory, the cognitive function of creating a temporary internal representation of information during focused thought (Gevins et al., 1996). In task conditions that placed a high load on working memory functions, subjects were asked to decide if the stimulus on each trial matched either the verbal identity or the spatial location of a stimulus occurring 3 trials previously (about 13.5 s ago). This required subjects to concentrate on maintaining a sequence of 3 letter names or 3 spatial locations concurrently; they had to update that sequence on each trial by remembering the most recent stimulus and could drop the stimulus from four trials back. In two corresponding control conditions, only the verbal identity or spatial location of the first stimulus had to be remembered. Both spatial and verbal working memory tasks produced highly localized momentary modulation of EPs over prefrontal cortical areas relative to control conditions, with deblurred voltage maxima approximately over Brodmann's areas 9, 45, and 46 (Fig. 3). These brief ($\approx$ 50–200 ms) events occurred in parallel with a sustained EP wave, maximal over the superior parietal lobe and the supramarginal gyrus, with a slight right hemisphere predominance. It began $\approx$ 200 ms after stimulus onset, returned to near baseline by $\approx$ 600 ms post-stimulus in control conditions, and was sustained up to $\approx$ 1 s or longer in the working memory conditions. The subsecond EP effects occurred in conjunction with multisecond changes in the ongoing EEG, of which the theta band power focused over midline frontal cortex is shown in Fig. 3 (Gevins et al., 1997). These EEG findings may provide the first direct evidence in a single experiment supporting the idea that the various types of attention are associated with neural processes with distinct time courses in distinct neuronal populations. The increased theta band power may be a marker of the continuous focused attention required to perform the task, and may reflect engagement of the anterior cingulate gyrus (a conjecture supported by dipole modeling). In contrast, the momentary attention required for scanning and updating the representations of working memory may be reflected in increased EP peaks over lateralized regions of dorsolateral prefrontal cortex, while maintenance of a representation of the stimuli being remembered may be reflected in the parietally maximal EP wave and other concomitant changes in the EEG (Gevins et al., 1979, 1980, 1997; Pfurtscheller and Klimesch, 1992).

5. Distributed functional networks

Even the simplest cognitive tasks require the functional coordination of a large number of widely distributed, specialized brain systems. A simple response to a sensory stimulus involves the coordination of sensory, association and other areas that prepare for, register and analyze the stimulus, the motor systems that prepare for and execute the

response, and other distributed neuronal networks. These distributed networks serve to allocate and direct attentional resources to the stimulus, to relate the stimulus to internal representations of self and environment in order to decide what action to take; to initiate or inhibit the behavioral response, and to update internal representations after receiving feedback about the result of the action. In the ongoing EEG, hypotheses about functional interactions between cortical regions are sometimes drawn from measurements of statistical inter-relationships between time series recorded at different sites. These can be quantified by various measures of spectral, wave shape, or information-theoretic similarity, including: spectral coherence (Walter, 1963), correlation (Brazier and Barlow, 1956; Livanov, 1977; Gevins, 1987; Gevins et al., 1981, 1983), covariance (Gevins et al., 1987 Gevins et al., 1989a,b), information measures (Callaway and Harris, 1974; Inouye et al., 1981; Mars and Lopes da Silva, 1987), non-linear regression (Lopes da Silva et al., 1989) and multichannel time-varying autoregressive modeling (Gersch, 1987).

Some of the above methods can be used to characterize the spatiotemporal relationships of subsecond EP components. Since the EP waveform delineates the time course of event-related mass neural activity of a neuronal population, the coordination of two or more populations during task performance should be signaled by a consistent relationship between the morphology of the EP waveforms emitted by these populations, with consistent time delay (Gevins and Bressler, 1988). If the relationships are linear, as they often appear to be, this coordinated activity might be measured by the lagged correlation or covariance between the EPs, or segments of EPs, from different regions (Gevins et al., 1981, 1987, 1989a,b). One such measure of this type of process is referred to as an evoked potential covariance (EPC). (Of course, a significant covariance of this type is only a measure of statistical association, and does not map the actual neuronal pathways of interaction between functionally related populations.) Studies of the neurogenesis of EPCs are still in their infancy (Bressler et al., 1993; Gevins et al., 1994a), and any interpretations of EPCs in terms of the underlying neural processes that generate them must thus be made very cautiously. (It is noted, however, that EPC results to date have been highly consistent with the known large scale functional neuroanatomy of frontal, parietal and temporal association cortices.) In the meanwhile, EPCs have provided fascinating glimpses of the complex, rapidly shifting distributed neuronal processes that underlie simple cognitive tasks.

The EPC technique has yielded its most interesting results as a tool for studying preparatory attentional networks, the changes in brain activity associated with readiness for an impending event or action. For example, subjects in one experiment (Gevins et al., 1987, 1989a,b) performed a task which required graded finger pressure responses with either the right or left hand proportional to visual numeric stimuli from 1 to 9. The hand to be used was cued 1 s before

the stimulus. A 375 ms EPC analysis window spanned the interval preceding the stimulus number in order to measure how EP patterns differed according to the hand subjects expected to use. Fig. 4 shows right-hand preparatory EPCs for 7 subjects for those trials for which the response ($\approx$ 0.5– 1 s later) was subsequently either accurate or inaccurate. The set of subsequently accurate trials are characterized by covariances of the left prefrontal electrode with electrodes overlying the same motor, somatosensory and parietal areas which were involved in actual response execution. (Simultaneous measurement of flexor digitori muscle activity showed that the finger which would subsequently respond was not active during the preparatory interval.) The preparatory patterns preceding inaccurate responses differed markedly from those preceding accurate responses, with fewer EPCs between the left frontal site and other electrodes. Such results suggest that one important role of frontal lobe integrative mechanisms is the anticipatory scheduling and coordination of the activation of those specialized brain regions that will participate in an upcoming cognitive event.

Acknowledgements

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