RESTING AND P300 AUDITORY RESPONSES IN NORMAL SUBJECTS AND PSYCHIATRIC PATIENTS: ANALYSIS USING DLM AND BRAIN IMAGER

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Equivalent source techniques, including the dipole localization method, are used to analyze both resting auditory evoked responses and the auditory P300 waveform in normal subjects and patients with consistent abnormal electrical patterns detected with EEG/EP mapping techniques. By comparing the data derived from normals and psychiatric patients and relating the theoretical sources to results derived from other assessment procedures, it may be possible to elucidate the subcortical origins of the P300 component.

Introduction

Various aspects of brain morphology and physiology have been investigated in patients with psychiatric disorders. Earlier quantification procedures have relied upon postmortem measurement of brain size, ventricle dilation, left/right differences, gray matter/white matter ratios, etc. More recently, sophisticated in vivo morphological measurements have been possible with contrast CT-scans and magnetic resonance imaging (MRI) techniques. Measurement of more functional properties have been accomplished with conventional and computerized electroencephalographic (EEG) analyses, regional cerebral blood flow measurement (rCBF) and, most recently, with positron emission tomography (PET). Neuropsychological assessment, a behavioral-based method which allows inferential localization of brain dysfunction, has also been used with psychiatric populations.

Recent studies using computerized analyses of brain electrical activity and color display techniques have identified reasonably consistent abnormalities in psychiatric patients, particularly in schizophrenics. In addition to analyzing conventional EEG and resting auditory evoked responses (AER), several studies have focused upon the evolution and topography of the AER P300 waveform. Resting AERs indicate primary and secondary processing of auditory stimuli. In P300 recording paradigms, subjects are instructed to count randomly presented "oddball" stimuli (e.g., a higher pitched tone), and only the responses to the "oddball" stimuli are averaged. The resulting AER shows the usual N1/P2 complex and an additional prominent positive vertex peak beginning around 300 ms (1). The P300 is not affected by variation in the stimuli; rather, it is contingent upon the subject's concentration and attention, and probably reflects the neurophysiological process associated with the updating of working memory.

In schizophrenic subjects, P300 has been shown to be attenuated in the left temporal area (2,3). Research in our laboratory has confirmed the P300 attenuation; however, the attenuation appears more frontally as well, and is more consistent with results from other imaging and neuropsychological evaluations. Moreover, the attenuation appears not only in patients having diagnoses of schizophrenia, but also in related disorders in which there are symptoms of thought disorder (e.g., schizophreniform, schizoaffective, major depression with psychotic features). While the attenuation appears at scalp recordings, it has been hypothesized that the site of abnormality is in the limbic system, and the cortical attenuation reflects underactivation in the ascending aminergic system (2). Depth recordings from limbic structures (hippocampus) have verified the presence of the P300 component, and have demonstrated unilateral attenuation in depth and scalp P300s in patients with complex parietal seizures which are localized to the left or right temporal lobes (4).

A complementary way of analyzing AER components and making inferences about cortical or subcortical origins is to use equivalent source mathematical models. The neural generators of the N1, P2, and particularly the P300 responses are simulated by single current dipoles. The loci and orientations of these theoretical foci and their changes in time are then used to draw conclusions about the actual generators of the scalp-recorded potentials and can be related to results derived from the other assessment procedures described above.

The purpose of this investigation was to use dipole localization methods (DLM) to analyze resting AER and P300 waveforms in normals and selected patients with thought disorder symptoms and left fronto-temporal P300 attenuation. Given a group of patients with abnormal P300s according to EP imaging techniques, we anticipate corresponding differences in the foci and/or orientation of the P300 equivalent source.

Methods and Procedures

Subjects

Ten normal control subjects (six male; mean age 29.6 years; all right-handed) with complete data and minimal artifact recordings were selected from an existing normative data base. Evoked potential data from nine psychiatric inpatients (six male; mean age 32.0 years; all but one right-handed) which met the following criteria were selected: All patients had a minimum amplitude difference of 6-8 μv between homologous fronto-temporal recording sites (F7/F8, T3/T4, FTC1/FTC2) during AER P300 waveforms, with the left fronto-temporal area showing relative attenuation. Amplitude asymmetries also had to exist for a minimum of 20 ms. DSM-III diagnoses of the patient group were: Schizophrenia, paranoid (n=1), chronic (n=2); Schizophreniform (n=3); probable schizophrenia (n=1); Major Depression with psychotic features (n=1); and Atypical Depression with questionable schizophreniform diagnosis (n=1). Inpatients' recordings were originally made for clinical analyses and interpretation.

Apparatus

All electrical recordings were made with a 28-channel NeuroScience Brain Imager, Series III, with full mapping and statistical capabilities. Stretchable caps (Electro-Caps, Inc.) were used for electrode placement. The 10-20 system, with ten additional placements for improved resolution, provided complete coverage of the head.

Procedure

Selected recordings from a standard protocol combining AER and VER averaging during resting and P300 condition, with replication, were analyzed. For this study, one resting AER and one AER P300

recording were chosen. Resting AERs were based on 64 1-kHz tones, 50 ms duration, with ISI = 1 sec (low filter = 1.05 Hz, high filter = 40 Hz, automatic rejection of sample with amplitude >|±115|μv). AER P300 recordings were based upon responses to 32 2-kHz tones randomly presented among the more frequent 1 kHz, with a probability of occurrence = 20% (other parameters identical). All AERs were analyzed over a 600 ms epoch, with a resolution of 2 ms.

Dipole Localization Method and Results

Selected resting P300 recordings for each patient and each normal control were analyzed using DLM. The details for implementing DLM can be found in Sidman, 1988 (5). The following figures show collected results for each group of subjects. Figure 1 shows the DLM analysis of the average data for the ten normal cases. The power maxima occur at those latencies where there is maximal underlying synchronous neural activity, the latencies of the N1, P2 and P300 components. The pictures at the right show the dipole source for each of these components. Figure 2 depicts these results for the nine psychiatric cases.

The resting AERs give similar results for both groups. Latencies for the N1 component for the normal group and patient group are 122 ms and 130 ms, respectively; for the P2 component the latencies are 216 ms and 212 ms. Power amplitudes are comparable in each case as are the locations and orientations of the various equivalent dipoles.

The latencies, amplitudes and equivalent dipoles for N1 and P2 for both groups are similar; however, the P300 latencies are 346 ms and 372 ms, respectively, and the power amplitudes are 38 μv and 21 μv, respectively. Briefly, there is a significant increase in latency and a significant decrease in amplitude for the P300 component in the patient group. Individually, P300 dipole sources from normal controls are clustered tightly around the X, Y, Z center coordinates. P300s from patients are much more scattered and are located away from the X, Y, Z center.

In this presentation we shall discuss the significance of these results, examine the individual cases that comprise these averages, and relate these findings to conclusions inferred from EEG/EP imaging evaluations.

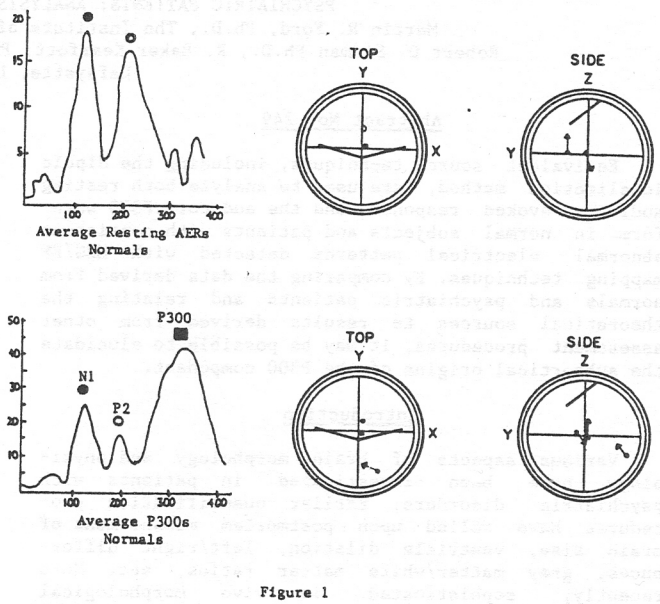

Figure 1

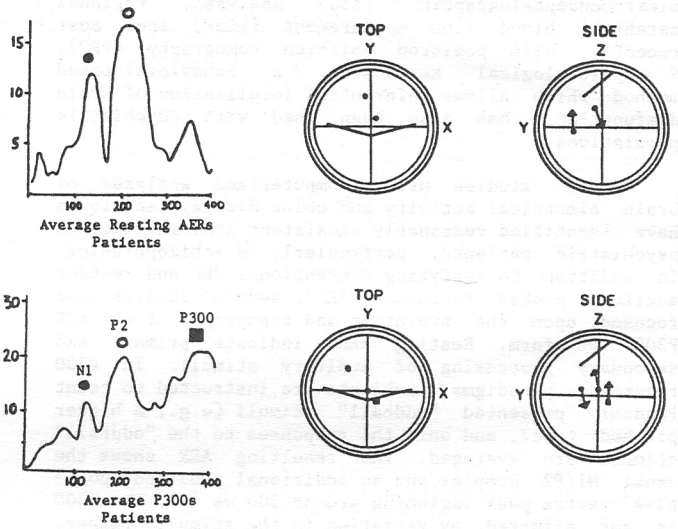

Figure 2

Acknowledgement

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