Telemetered EEG in schizophrenia: spectral analysis during abnormal behaviour episodes

JANICE R STEVENS, ARTHUR LIVERMORE

From the Departments of Neurology and Psychiatry, the Oregon Health Sciences University, Portland, Oregon, and the Intramural Research Program, Adult Psychiatry Branch, National Institute of Mental Health, St Elizabeths Hospital, Washington DC, USA

SUMMARY In an attempt to detect electroencephalographic (EEG) changes associated with characteristic clinical signs and symptoms of schizophrenia, power spectra were derived from scalp EEGs of schizophrenic patients recorded by telemetry during free behaviour on their psychiatric wards. Power spectra from EEG epochs coincident with psychomotor blocking, stereotyped automatism or hallucinations were compared with spectra derived during periods of relatively normal behaviour, during performance of specific tasks, and with spectra from control subjects. Ramp spectra, characterised by a smooth decline in power from lowest to highest frequencies, previously found in conjunction with subcortical spike activity of epilepsy were not found in any control subject, but appeared in spectra from schizophrenic patients during catatonic episodes, hallucinatory periods and visual checking. Schizophrenic patients also had more slow activity and less alpha activity in their EEGs than normal control subjects.

A number of similarities between the subjective experiences and stereotyped behaviours of patients with schizophrenia and psychomotor epilepsy suggest that both disorders may reflect abnormal function in limbic structures of the brain.1,2 Amelioration of clinical symptoms by dopamine-blocking agents and dilatation of ventricles revealed by computed tomography provide further evidence that schizophrenia may represent a chronic subcortical encephalopathy.3,4 The scalp electroencephalogram (EEG) of schizophrenic patients is often relatively unremarkable but may show slow or spike activity, especially over the temporal lobes.5,6 As in some patients with psychomotor epilepsy with normal or nonspecific scalp EEGs, intracerebral recordings from patients with schizophrenia reportedly reveal spike and slow activity in deep structures of the limbic forebrain.7-9

Several investigators have reported that evidence of subcortical spike activity could be detected in the coincident spike-free scalp EEG by using specially designed filtering or discriminant analysis programs.9,10 Methods employed by these investigators depended on use of chronic intracerebral electrodes. Because it is rarely possible to record the EEG from indwelling electrodes in schizophrenic subjects, we have attempted to develop non-invasive methods, previously used to detect evidence of subcortical spike activity in the spike-free scalp EEG of patients with epilepsy, to detect and characterise EEG correlates of schizophrenic behaviours. In previous studies using chronic implanted intracerebral electrodes in the study of epileptic foci in animals and man, we found that power spectra averaged from brief epochs of spike-free scalp or dural EEG coincident with subcortical spike activity were characterised by a typical profile which we designated a ramp pattern, manifest by a monotonic decline in power from lowest to highest frequency.11 The log graph of this decline approximates an exponential function. Power spectra from two-second epochs of spike-free scalp EEG of patients with epilepsy tested with a continuous performance task revealed a similar ramp pattern over the site of the epileptic focus during prolonged reaction times. When patients with schizophrenia were tested with the continuous performance task, spectral analysis of EEG epochs during prolonged reaction time revealed ramp patterns from one or more scalp montages in six of 17 patients, and ten patients showed "flat" power spectra, that is a relatively even dispersion of power...
over a broad range of frequencies, during prolonged response latencies.12

The reaction time studies were based on the premise that intermittent long latencies displayed by many patients with seizure disorders or schizophrenia might be associated with episodic cerebral dysfunction detectable by analysis of scalp EEG. However, with schizophrenic subjects, the reaction time test, like other structured activities, often decreased or eliminated the very behaviours we wished to examine, for example, hallucinations, staring, psychomotor blocking, and stereotyped automatisms. To eliminate the intrusion of the reaction-time task, telemetered EEGs were recorded from unmedicated schizophrenic subjects on the psychiatric wards during continuously observed free behaviour. Inspection of these telemetered EEGs—even during episodes of clearly abnormal behaviour—rarely disclosed consistent abnormality.6 To increase the possibility of detecting electrophysiologic disturbances which may be associated with abnormal behaviour states, power spectra were derived from telemetered scalp EEGs of unmedicated schizophrenic subjects during epochs of specified abnormal behaviour and compared statistically with spectra derived during relatively normal behaviours. Spectra derived from the patient EEGs during performance of verbal and spatial tasks were also compared with spectra from normal control subjects recorded under identical conditions.

Material and methods

Eighteen patients aged 19-44 years, hospitalised for schizophrenia, were studied on the hospital wards with 2-48 hour telemetered EEG (average 20 hrs), electroculeogram (EOG), electromyogram (EMG), and behavioural monitoring. All of the patients had an illness of at least six months duration, with subacute or insidious onset of delusions, hallucinations, stereotypies of thought and action, and incoherent, fragmented, or impoverished thought processes. Eight patients had not received neuroleptic treatment for 1-6 months prior to this study. Eight patients were studied prior to any drug or other physical treatment. One patient was removed from medication one week prior to the study but required a single dose of thioridazine (100 mg) 24 hours prior to recording and one patient was removed from Loxapine (100 mg daily) 36 hours before the recording. Three patients were left-handed, one had mixed dominance, the remainder were right-handed. All patients were socially and mentally impaired by their illness at the time these studies were conducted. Nine normal control subjects (students, aids, and nurses), aged 21-40 years, eight right-handed, one left-handed, were studied under the same conditions and with the same equipment as the patients. Ten patients were in the National Institute of Mental Health Research Unit of Saint Elizabeths Hospital, Washington, DC. Eight patients and nine control subjects were studied on the psychiatric wards of the Oregon Health Sciences University. Patients were diagnosed by consensus of senior staff psychiatrists and met the Taylor and Abrams (1975) modification of the Feighner criteria for diagnosis of schizophrenia. None had a history of epilepsy.

Telemetered EEG, EOG and EMG were recorded on 7-channel FM tape and ink-writing polygraph from a multiplexed 8-channel FM system (Benton Instrument Company). A small (1 x 3 x 4 cm), lightweight (90 gm) transmitter was firmly held on the subject's head by a special cap. Bipolar EEG was recorded from perforated tin or gold electrodes filled with saline conducting paste and attached to the scalp with collodion. C3-P3; C4-P4; T3-T5; T4-T6. (To minimise eye movement and still cover the anterior temporal region, T3' and T4' were placed halfway between the conventional positions of F7-T3 and F8-T4.) Lateral eye movement was recorded between similar electrodes applied to the skin at the outer canthus of the eye. Vertical eye movements and blinks were recorded between electrodes placed above and below one eye. EMG was integrated from activity over 30 cps from T4'-T6 montage.

Subjects were free to walk about the ward or dayroom within a 40-60 yard radius of the receiver antenna, slept in their own beds and generally carried on their usual hospital routine during the recording period. The FM receiver and recording equipment were centrally placed in a hall near the patient's room or the ward dayroom. Except during sleep, the patient's behaviour was observed continuously by a member of the research team or nursing staff who recorded normal and abnormal behaviours throughout the EEG recording period. EEG, EOG, and EMG were continuously taped at 1/2 ips and were monitored by ink-writing polygraph (paper speed 1-1.5 cm/s). Selected portions of the taped EEG were subsequently rewritten from the tape at 3-6 cm/s for detailed examination of periods of particular clinical or physiologic interest. Specific abnormal behaviours (see below), characteristic of each patient, were identified by the senior author in collaboration with the patient's physician and nursing team. Exact time and number of these abnormal events were recorded on one channel of the tape recorder and polygraph by a trained observer, who by pressing a noiseless switch attached to the recording apparatus by a long cord, incremented the first three digits of a time code generator modified to record and number events as well as clock time. A written log of numbered behavioural events was kept by the observer, permitting exact correlations between EEG, EOG, and patient activity.

In addition to recordings during free behaviour, 16 patients were studied during a standard interview in which the patient and EEG-EOG were videotaped on a split screen for subsequent examination. Fourteen patients and ten control subjects were recorded during performance to two standard verbal tasks: (1) an “alphabet” test in which the subject was requested to say a word commencing with successive letters of the alphabet as rapidly as possible while the eyes were closed, and (2) subtraction of serial 3s or 7s with the eyes open. Six patients
and nine control subjects performed two standard spatial tasks: the Seguin formboard (eyes closed, both hands) and a jigsaw puzzle (eyes open). Six patients were recorded during a standard interview preceding and during amytal infusion. One patient with acute catatonia received 0.8 mg of naloxone intravenously during the recording. EEG, EOG, and EMG were recorded on the hospital ward from control subjects under the same conditions as the patients. After completion of the recording period, the data were examined visually and the taped record was analysed off-line by a program which sampled and processed simultaneous EEG, EOG, and EMG activity. Power spectra, displayed as the square root, were plotted as discontinuous, compensated spectral arrays (CSA). EMG data were integrated and eyeblinks and lateral eye movements were displayed as interval histograms.

Background EEG (2 s epochs filtered at 0.5-45 Hz), EOG (8 s epochs filtered at 0.5-5 Hz) and EMG (2 s epochs filtered at 30-100 Hz) were digitised (256 samples/s) at 1-5 min intervals. Additional EEG, EMG, and EOG epochs were analysed at the signal of each numbered normal or abnormal behavioural event. To minimise distortion induced by the fast-Fourier analysis due to beginning and ending the sample collection, the first and last 10% of each EEG epoch were shaped with a sine-squared window prior to the fast-Fourier transformation. EEG spectra contaminated by muscle were automatically rejected by the computer when the power in the 35-45 Hz band exceeded the mean background power by five standard deviations. In addition, each sample was edited visually on the computer screen and samples in which ocular or gross body movements occurred were rejected. Following initial processing and plotting of the EEG, EOG, and EMG data from epochs of tagged normal and abnormal behaviour events were averaged, statistically compared (t test, Wilcoxon Signed-Ranks test) and plotted in a format modified from Itil. To eliminate absolute power variation between subjects and thus permit comparison of frequency distributions between subjects and groups, the selected power spectra were normalised by converting absolute power for each frequency to percent of total power, averaged, and compared statistically during “normal” events (E-1) and “abnormal” events (E-2) for each patient and during spatial and verbal tasks for patients and control subjects. To correct for multiple t tests of correlated variables, T values at p = 0.05 were considered significant only if present in two or more adjacent frequencies.

The specified abnormal behaviours were as follows: Psychomotor blocking: arrest of speech, often accompanied by stare (four patients). Hallucinating: muttering to voices (four patients). Lateral eye movements (LEMs): stereotyped rapid darting horizontal saccades resembling ocular searching movements (seven patients). Catatonia: waxy flexibility, motor arrest, mute (three patients).

Finally, spectra from homologous left and right central-parietal (C-P) and temporal regions were compared for predominance of power at each frequency over right and left side during normal and abnormal events, during spatial and verbal tasks, and between patients and control subjects.

Results

Most patients tolerated the procedures without difficulty or complaint although two severely psychotic individuals removed the electrodes or transmitter during their recordings. Inspection of raw EEG data demonstrated focal irregular theta and sharp activity from six patients over one or both temporal lobes.

Although serial power spectra of regularly sampled EEG epochs were an excellent means of reducing the large data base, the CSA display proved a poor method for detection of momentary changes which might be associated with behavioural events (fig 1). Extraction of spectra associated with specific normal and abnormal events or with the specified behavioural tasks gave more information.

Comparison of Patient Spectra with Normal Control Spectra

Summed and averaged normalised spectral patterns from patients and controls from four scalp montages during 2 s epochs of EEG during spatial and verbal tasks are presented in fig 2a. Patients were distinguished by more delta and less alpha than controls during performance of each task with the exception of eyes-open spatial (jigsaw puzzle) task. Recalculation of spectra of individual patients after meticulous exclusion of all epochs containing drowsing or eye movement did not alter this relative delta preponderance and alpha deficit in patient spectra.

Comparison of Patient Spectra During Normal and Abnormal Behaviours

There were a number of differences between pooled average EEG spectra derived from patient EEGs during each of the specified abnormal clinical states compared with spectra during patient’s performance of verbal and spatial tasks. The ramp pattern, a spectral envelope characterised by a smooth decline in power from lowest to highest frequencies, and, as noted above, previously associated with spike activity in deep structures, emerged in 45 to 120 average spectra from patients but in no control subjects. Ramps were almost twice as common during abnormal events as during normal behaviour and were approximately equal in number from C-P and temporal montages and from right and left hemispheres (fig 2b). When classified by the associated behavioural alteration, 3/3 patients with catatonia manifested ramps in the right temporal region. Four of eight patients with chronic paranoid schizophrenia and active auditory hallucinations had left C-P ramps and two of these patients also had temporal ramps; 4/7 patients who displayed frequent visual
checking (LEMs) had ramps (obscured by pooling spectra, fig 2b). Patients also displayed a striking increase in left C-P slow activity and more alpha activity during hallucinatory states than during other behavioural events (fig 2). Comparison of pooled average spectra from all patients during all normal events with spectra during all abnormal events tended to blur these individual differences but disclosed suppression of left temporal alpha during abnormal events (fig 3).

Because of the very large number of spectra generated, it appeared possible that the observed differences between different individuals and tasks might result from chance alone. To test this possi-
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Fig 2 Normalised average power spectra from C-P and temporal regions. (a) During verbal and spatial tasks for all patients and control subjects; (b) During all abnormal behaviours of patients. Although delta peaks are generally prominent in both patient and control spectra, the ratio of delta to alpha activity is clearly larger for patients than controls and much larger for hallucinating patients than for any other group. This does not appear to be due to greater blink or saccade predominance during hallucinations (fig 4b). Ramp spectra, characterised by smooth decline of power from lowest to highest frequencies appear uniquely during the catatonic state.
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Fig 3  Statistical comparison of average power (0-32 Hz) from EEG epochs associated with relatively normal behaviour (Event 1) compared with abnormal behaviour (hallucinations) (Event 2) from same patient and data for which the CSA is plotted in fig 2. Horizontally plotted t tests display differences between E-1 and E-2 for each frequency. Direction of t-test column is toward the band with greater power. Significance is indicated by the double row of lines above and below each t test (p = 0.05, 0.01). Vertically oriented t tests compare relative power predominance between homologous left and right C-P and left and right temporal regions for each one Hz band as in the horizontal display. T test differences in power distribution between the C-P and temporal montages are displayed by the direction of column orientation to the left and right of the midline for each frequency. Note the relative predominance of power over the right C-P montage during both E-1 and E-2, shift of 10 Hz power from left to right temporal montage during E-2 (auditory hallucination). E-1: N = 15. E-2: N = 17.
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RIGGT AND LEFT HEMISPHERE DIFFERENCES DURING TASKS AND ABNORMAL BEHAVIOURS

Although visual inspection of the raw EEG usually revealed relatively symmetrical frequencies over homologous regions of the left and right hemispheres, spectra from brief EEG epochs sampled at 1-2 minute intervals indicated that even at rest, patients and control subjects frequently shifted hemispheric power dominance in all frequency bands between right and left C-P montages and to an even greater degree between right and left temporal regions. Shifts in power dominance between the hemispheres also occurred during sleep (fig 5, top). Pooled data from schizophrenic patients did not appear by simple inspection to differ from controls in this respect, although this point deserves further investigation.

When spectra between homologous left and right montages were compared during normal and abnormal events in a male patient with chronic schizophrenia prior to any treatment, the “normal” right-sided power predominance of his resting EEG was replaced by equalisation of power over both C-P and temporal regions during psychomotor blocking (fig 5, top). A male catatonic patient displayed right temporal delta power predominance during psychomotor blocking. This focal delta predominance disappeared following intravenous naloxone, amytal, or between blocking episodes (fig 5, bottom). For comparison, spectra from a female patient with psychomotor epilepsy and a left temporal spike focus, recorded by telemetry under the same conditions as the patients and controls is presented in fig 6 (top). This woman showed persistent left temporal slow activity which spread to the left C-P montage at rest and was attenuated during the standard interview.

A majority of patients and controls showed distinct right hemisphere predominance of power in all frequency bands at rest. A majority of controls demonstrated a shift of power in the alpha band from right to left temporal montage during performance of spatial tasks and from left to right temporal montage during the verbal task (fig 6, bottom). Patients exhibited a scatter of power without significant lateralised predominance over either temporal lobe during the spatial task. Both patients...
and controls shifted 9-11 Hz power from left to right temporal montage during the verbal task, but patients, in contrast to controls, failed to do so from the C-P montages (fig 7).

Discussion

The purpose of this study was to determine whether the EEGs of unmedicated schizophrenic patients demonstrate changes related to specific abnormal behaviours. More stringently, it was hypothesised that during specified abnormal behaviours, the scalp EEG of patients with schizophrenia might disclose evidence of remote (subcortical) spike or slow activity manifest by the ramp pattern in the power spectrum. This pattern was found in 45 of 120 patient spectra (9/18 patients) and in no normal controls. Ramps were twice as common from epochs of abnormal behaviour (E-2) as during "normal" behaviour (E-1) and were associated with catatonia, auditory hallucinations and visual checking. As previously reported by others, schizophrenic patients also displayed more delta and theta activity and less alpha activity than controls. Patients displayed more delta and theta activity over the right temporal lobe than the left during all abnormal events except auditory hallucinations, during which left C-P delta predominated. Although there were differences in lateralisation of power between patients and controls in this study, no evidence emerged for a specific left temporal abnormality in schizophrenia as proposed by Flor-Henry and Shaw et al.

Brazier was the first to demonstrate that ab-
normal subcortical EEG transients could be detected by analysis of the coincident surface EEG. The interpretations we have made with respect to the possible significance of ramp spectra in relation to subcortical spiking are based on derivation of similar spectra from scalp or dura coincident with subcortical spike activity in epileptic animals and man. Ramp spectra can also emerge from slow transients in EEG and from eye and body movement. Ramp spectra accompanying psychotic behaviours are thus interpreted as consistent with, not diagnostic of, remote spike or slow activity only when movement is meticulously excluded.

In contrast to the relatively persistent patterns of power dominance which emerge from sampling and analysing long samples of EEG (30 s-3 min), analysis of multiple short (2 s) epochs as in this study reveals a much more dynamic, flexible process of continuously shifting power predominance between the hemispheres at the various frequency bands in all subjects. Reporting findings strikingly similar to our own, Kostandov and Serbsky recently discussed the failure of patients with schizophrenia to block right temporal alpha activity during a spatial task, a finding consistent with the absence of left temporal alpha predominance in schizophrenic patients noted by Giannitrapani and Kayton. Schweitzer et al using a very different paradigm for their study, reported similar inappropriate arousal of the left hemisphere of schizophrenic subjects during performance of a spatial task. This interpretation could also be advanced for the significant decrease in 5-2-8-8 Hz power found over left posterior temporal region of schizophrenic patients compared with
controls reported by Shaw et al, who also reported greater intrahemispheric coherence in schizophrenics.

In one of the earliest studies of EEG of schizophrenic subjects, using very few channels and visual analysis, Davis observed that the EEG of patients with catatonic schizophrenia was more abnormal than EEGs of other schizophrenic subgroups, often resembling recordings from patients with convulsive disorder. The findings reported here are consistent with that early report and suggest inappropriate focal cortical arousal, episodic remote spike or slow activity, and slower frequencies in the EEGs of many schizophrenic subjects. These results in turn indicate that schizophrenic thought and perceptual disturbances are probably related to pathologic activity of the brain.

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