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Interictal quantitative EEG in epilepsy*

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The interictal EEG is often normal in epilepsy patients, particularly with partial seizures of extratemporal origin. Quantitative techniques of EEG analysis may increase the yield of diagnostic abnormality in such patients.

Thirty patients with partial seizures of frontal or temporal origin had EEG recorded from left frontal (F7-C3), right frontal (F8-C4), left posterior (T5-O1), and right posterior (T6-O2) derivations. Four-second epochs were used to compute power in the delta (0.25–4.0 Hz), theta (4.25–8.0 Hz), alpha (8.25–13 Hz), and beta (13.25–30 Hz) bands. The ratio of high (8.25–30 Hz) to low (0.25–8 Hz) power on the left and the right was measured, as was the ratio between the left and the right hemisphere total power. The mean frequency deviation in the alpha band between the left and the right hemispheres was also measured, and spectral mobility was determined in the right and the left frontal regions. These values were also calculated in normal subjects and tension headache patients with normal EEGs. Seizure patients with abnormal interictal EEGs had decreased ratios of high to low power, greater asymmetry of total power and alpha frequency, and reduced spectral mobility on the side of their EEG foci. Epileptics with normal interictal EEGs had lower ratios of high to low power, greater alpha frequency asymmetry, and lower spectral mobility than did headache patients or normal controls.

Power and frequency measurements, and determination of spectral measures such as mobility, can be done with commercially available digital EEG equipment. They may demonstrate otherwise obscure asymmetries in the interictal EEG and thereby aid in epilepsy diagnosis and classification.

Key words: quantitative EEG, spectral analysis, time domain descriptors, epilepsy, seizures.

INTRODUCTION

Theusefulness and appropriateness of quantitative methods of EEG analysis have been the subject of much debate[1]. Early topographic EEG studies showed a broad-band increase of fast and slow activity in the region of an epileptogenic focus[2], and such techniques have been advocated for the identification of obscure seizure foci such as in frontal-lobe epilepsy[3]. Spectral analysis has shown differences in alpha frequency between patients with apparently normal EEGs and nonepileptic controls[4], and between patients on monotherapy with different antiepileptic drugs[5]. Some later studies have shown an increase in diagnostic yield with quantitative EEG techniques[6], while others have reported similar findings in routine and quantitative EEG recordings in seizure patients[7]. Recent observations have suggested a general increase in slow activity in seizure patients[8], an increase in subtle asymmetries with quantitative EEG examination[9], and lateralized asymmetries in frequency spectra on the side of an epileptogenic focus[10]. We applied several generally available methods of quantitative EEG analysis to representative partial-seizure patients with both normal and abnormal interictal EEGs.

SUBJECTS AND METHODS

Thirty patients aged 16–60 years and approximately equally divided between males and females were studied during outpatient visits for previously diagnosed partial seizures of frontal or temporal lobe origin. Their seizures were satisfactorily controlled on monotherapy with carbamazepine or phenytoin, except for four who were also receiving clorazepate dipotassium and two on adjunctive acetazolamide. They had no known structural lesion or encephalopathy, were neurologically normal, and had no other

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significant medical problems except epilepsy. They had no overt toxic symptoms, and anticonvulsant levels, when available, were therapeutic ranges. Thirteen patients had previously had normal interictal EEGs, while interictal EEGs in 17 showed a left or right temporal epileptogenic focus[13] or frontal slowing or epileptiform discharges[4]. These patients were compared with 10 normal controls who were taking no medication and 10 neurologically intact patients being treated for tension headache with over-the-counter analgesics(6), Midrin(4), and butalbital(3).

Electroencephalograms (EEGs) were recorded from gold cup electrodes (Grass AstroMed, E. Warwick, RI) affixed with collodion at International 10/20 System electrode placements. Frequency analysis of the EEG was carried out with the Nicolet Pathfinder II Frequency Analysis Software, version 3.1 (Nicolet Biomedical Instruments, Madison, WI). Fifteen minutes of EEG were recorded from each patient and each control subject in a quiet room with eyes closed but not asleep. Patients and subjects were touched or spoken to every 5 minutes or when they appeared drowsy. Four bipolar electrode derivations were used: left frontal (F7-C3), right frontal (F8-C4), left posterior (T5-O1), and right posterior (T6-O2).

Four-second EEG epochs were acquired and the power spectra calculated. Four frequency bands were analysed: 0.25–4.0 Hz, 4.25–8 Hz, 8.25–13 Hz and 13.25–30 Hz. High (8.25–30 Hz) and low (0.25–8.0 Hz) frequency bands were compared on the right (F8-C4/T6-O2) and left (F7-C3/T5-O1). The ratio of high to low power on the left (PHLL) and right (PHLR) were determined, along with the ratios between left-sided and right-sided power in the frontal (PLRF) and posterior (PLRP) derivations. The mean frequency deviation between left and right hemispheres in the alpha band was measured frontally (FLRF) and posteriorly (FLRP).

When background activity is predominantly slow PHLL and PHLR approach zero, and they approach 1 when activity is equally distributed over the entire frequency range. When spectral power is symmetric between right and left hemisphere PLRF, PLRP, FLRF, and FLRP remain near zero, but deviate toward -2 when the alpha-band frequency decreases on the left and toward $+2$ when the alpha-band frequency decreases on the right.

Mobility, one of the time-domain descriptors described by Hjorth[11], was calculated for the left frontal (MOLF) and right frontal (MORF) regions. This represents one-half of the average number of zero line crossings per second, and is an indicator of the amount and duration of fast activity.

Because some of the patients with abnormal EEGs had left sided abnormalities, which make measures of power and frequency more negative, and others had right-sided asymmetry, which would make these measures more positive, we neglected the sign of power and frequency asymmetry and instead compared the magnitudes of PLRF, FLRP, FLRF, and FLRP between the groups. We likewise combined patients with left- and right-sided seizure foci and compared high with low power measures ipsilateral and contralateral to the EEG abnormality.

RESULTS

Patients with abnormal EEGs showing a left-sided focus had significantly lower PHLL (1.94 ± 0.35) than did headache patients (5.94 ± 0.69, $P < 0.1$), and PHLL was lower than in normal controls (3.33 ± 0.69), but this did not reach significance. Among the patients with right-sided foci, there was also a significant reduction in PHLR relative to headache patients (1.69 ± 0.38 vs. 7.39 ± 0.97, $P < 0.05$). Again patients showed lower PHLR than controls (5.04 ± 0.53), but this did not reach significance.

Although PHLL and PHLR values were greater among the headache patients than the normal subjects, this difference was not significant. In patients with normal EEGs PHLL and PHLR were both lower than the headache and control groups, but the differences were not significant.

Left to right power asymmetry was significantly greater in the frontal regions among both groups of seizure patients than among the headache patients or normal controls ($P < 0.01$). In patients with abnormal EEG PLRF mean values were 0.48 ± 0.36 and 0.58 ± 0.25 in patients with normal EEG these values were 0.58 ± 0.25, while in headache patients and normal controls these values were 0.045 ± 0.04 and 0.047 ± 0.02, respectively.

This difference was not seen with respect to left to right power asymmetry in the posterior regions, however, PLRP was essentially the same in patients with temporal and frontal EEG foci (0.03 ± 0.01), patients with normal EEG (0.07 ± 0.01), headache patients (0.09 ± 0.04), and normals (0.05 ± 0.01). Left to right alpha-band frequency asymmetry was greater in seizure patients than the headache patients or controls, more markedly in those with abnormal EEGs, but these were not significant.

Spectral mobility in the left frontal region was less in seizure patients with abnormal EEGs (9.47 ± 0.51) and normal EEGs (9.94 ± 0.18) than in headache sufferers (17.93 ± 1.45) or normal controls (17.22 ± 0.83), but these differences did not reach significance. A greater differ-

Table 1: Quantitative EEG measures in normal controls (N), tension headache patients with normal EEGs (HA), and complex partial seizures patient with abnormal (CPS + EEG) or normal (CPS − EEG) in interictal EEGs. High to low power on left and right ratios are shown by PHLL and PHLR, PLRF and PLRP represent ratios of left-sided to right-sided power in the frontal and posterior regions. FLRF and FLRP measure left-right frequency asymmetry measurements in the frontal and posterior areas are shown by FLRF and FLRP, respectively. Left and right spectral mobility are indicated by MOLF and MORF. Details of EEG recording and power spectral computation are given in the text.

PHLL			
N	3.33 ± 0.69	$P < 0.5$	$P < 0.05$
HA	5.94 ± 0.69		
CPS + EEG	1.94 ± 0.35	NS	
CPS − EEG	1.82 ± 0.29		
PHLR			
N	5.04 ± 0.53	$P < 0.1$	$P < 0.05$
HA	7.29 ± 0.87		
CPS + EEG	1.69 ± 0.38	NS	
CPS − EEG	1.55 ± 0.51		
PLRF			
N	0.05 ± 0.01	NS	$P < 0.01$
HA	0.09 ± 0.07		
CPS + EEG	0.48 ± 0.30	NS	
CPS − EEG	0.58 ± 0.25		
PLRP			
N	0.20 ± 0.02	$P < 0.5$	$P < 0.01$
HA	0.06 ± 0.02		
CPS + EEG	1.19 ± 0.26	NS	
CPS − EEG	0.90 ± 0.14		
FLRF			
N	0.07 ± 0.06	NS	$P < 0.001$
HA	0.03 ± 0.01		
CPS + EEG	0.16 ± 0.13	NS	
CPS − EEG	0.12 ± 0.38		
FLRP			
N	0.02 ± 0.01	NS	$P < 0.005$
HA	0.02 ± 0.01		
CPS + EEG	0.08 ± 0.01	NS	
CPS − EEG	0.13 ± 0.04		
MOLF			
N	17.22 ± 0.83	NS	$P < 0.05$
HA	17.93 ± 1.45		
CPS + EEG	9.47 ± 0.51	NS	
CPS − EEG	9.94 ± 0.18		
MORF			
N	18.87 ± 1.23	NS	$P < 0.05$
HA	19.73 ± 0.56		
CPS + EEG	9.65 ± 0.28	NS	
CPS − EEG	9.82 ± 0.28		

ence was found in right frontal mobility between patients with abnormal EEGs (9.65 ± 0.28), patients with normal EEGs (9.82 ± 0.28), and the headache (19.73 ± 0.56, $P < 0.1$) and control groups (18.87 ± 1.73, $P < 0.1$).

In summary, patients with abnormal EEGs had lower ratios of high to low frequency power on the side of their foci, presumably reflecting an increase in slow activity on that side. Patients with normal EEGs showed reduction of these ratios to a lesser degree, suggesting an increase in slow activity relative to headache patients and normal controls. Headache patients had higher power ratios, possibly reflecting more fast activity. In the frontal regions, both groups of seizure patients had greater asymmetry of total power and alpha frequency between right and left hemispheres than either nonepileptic group, but these asymmetries were not evident at the posterior electrodes. Spectral mobility was less in both groups of seizure patients, more markedly in those with abnormal EEGs, and was greater in the headache patients, possibly consistent with more slow and less fast activity in the former groups and more fast and less slow activity in the latter.

DISCUSSION

The literature in the area of quantitative EEG is now substantial and clinically applicable[12]. Limited clinical use of quantitative methods as an adjunct to standard EEG is still the prevailing recommendation[13]. Our findings suggest that measurement of frequency spectra and computation of spectral descriptors may improve the yield of diagnostic abnormality in epilepsy patients with normal or equivocal EEGs.

An increase in power in all frequency bands at the site of an epileptogenic focus has been frequently reported[2], as well as an increase in the beta frequency band in the vicinity of an active spike focus[3].

Partial epilepsies have also been associated with a relative excess of slow activity[7]. Our patients had decreased ratios of high and low power in both frontal and posterior regions and decreased spectral mobility in the frontal regions as compared with normal controls and tension headache patients. This is consistent with a generalized increase in slow activity, as reported by Miyauchi *et al.*[8]. these measures were reduced ipsilateral to the patients' EEG foci when demonstrable, but both patients with abnormal standard EEG and those whose interictal EEGs had been normal had greater degrees of interhemispheric asymmetry of power and alpha frequency than did normal controls or headache patients. This accords with the observations of Tuunainen *et al.*[10], who found lateralizing spectral asymmetry during short-term discontinuation of medications in partial-seizure patients.

Gaches and Gueguen[6] reported an increased yield of focal abnormality in partial-seizure patients with normal imaging studies and standard EEG. In contrast, Nuwer[7] found a strong correlation between quantitative EEG measures and neuroimaging evidence of a focal lesion or standard EEG evidence of a slow focus. In the absence of such findings, however, and in comparison to other test modalities like PET scan or neuropsychological testing, quantitative EEG correlation with focal abnormality was less strong. Our patients with normal interictal EEGs showed a lesser degree of difference from controls and headache patients than those whose standard EEGs had been abnormal. The ratios of high to low power and spectral mobilities were lower and left to right frequency deviation greater in the patients with normal EEGs than in normal controls and headache patients, however, which suggests that these measures may be more sensitive to focal abnormality or background slowing of mild degree.

Although our findings accord with recent reports, the differences were less marked than the increased slow activity reported by Miyauchi *et al.*[8] or the lateralized increase in slowing found by Tuunainen *et al.*[10]. This difference may reflect a smaller number of patients, or our exclusion of patients with generalized epilepsy, encephalopathy, or identifiable causative lesion for the epilepsy. We also confined the study to patients on carbamazepine and phenytoin, with very few exceptions, having previously found[5] slowing of alpha-band frequency with phenobarbital and valproate. The patients studied by Tuunainen *et al.*[10] were undergoing short-term medication discontinuation for epilepsy evaluation, whereas our patients were studied during routing outpatient follow up, in order to see whether quantitative measures might increase the yield of routine EEG.

Absolute slow or fast power may be a more accurate measure than ratios, and first-order complexity may be a more sensitive descriptor than spectral mobility. It may also be that alternative quantitative measures now being applied to EEG analysis, such as coherence measures[14], nonlinear dynamical measurements and dimensionality or complexity[15], or measurement of spectral entropy[16] would be more useful in detecting local EEG abnormality in epilepsy.

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REFERENCES

1. Nuwer, M.R. Quantitative EEG. *Journal of Clinical Neurophysiology* 1988; **5**: 1–86.
2. Harner, R.N. Clinical application of computed EEG topography. In. *Topographic Mapping of Brain Electrical Activity* (Ed. F.H. Duffy) Boston, Butterworths, 1986, pp. 347–356.
3. Harner, R.N. and Riggio, S. Interictal EEG topography of frontal lobe epilepsy. In *Frontal Lobe Seizures and Epilepsies, Advances in Neurology*, vol 57 (Eds P. Chauvel, A.V. Delgado-Escueta, E. Halgren and J. Bancaud). New York, Raven Press, 1992: pp. 331–338.
4. Galety, T.J., Burgess, R.J., Drake M.E. *et al.* Computerized spectral analysis of the interictal EEG in epilepsy. *Clinical EEG*, 1986; **16**: 94–97.
5. Drake, M.E., Huber, S.J., Pakalinis, A. and Denio, L. Electroencephalographic effects of antiepileptic drug therapy. *Journal of Epilepsy*, 1990; **3**: 75–79.
6. Gaches, J. and Gueguen, B. EEG mapping in epilepsy. In: *Topographic Brain Mapping of EEG and Evoked Potentials* (Ed. K. Maurer). Berlin, Springer Verlag, 1989, pp. 247–255.
7. Nuwer, M.R. Frequency and analysis and topographic mapping of EEG and evoked potentials in epilepsy. *EEG and Clinical Neurophysiology*, 1988; **69**: 118–126.
8. Miyauchi, T., Endo, K., Yamaguchi, T. and Hagamoto, H. Computerized analysis of EEG background activity in epileptic patients. *Epilepsia*, 1991; **32**: 870–881.
9. Salinsky, M.C., Oken, B.S., Kramer, R. E. and Morehead, L. A comparison of quantitative EEG frequency analysis and conventional EEG in patients with focal brain lesions. *EEG and Clinical Neurophysiology*, 1992; **83**: 358–366.
10. Tuunainen, A., Nousiainen, U., Pilke, A. *et al.* Spectral EEG during short-term discontinuation of antiepileptic medication in partial epilepsy. *Epilepsia*, 1995; **36**: 817–823.
11. Hjorth, B. Physical aspects of EEG data as a basis for topographic mapping. In *Topographic Mapping of Brain Electrical Activity* (Ed. F.H. Duffy). Boston, Butterworths, 1986: pp. 175–194.
12. Duffy, F.H., Hughes, J.R., Miranda, F. *et al.* Status of quantitative EEG (QEEG) in clinical practice, 1994. *Clinical EEG*, 1994; **25**: VI–XXII.
13. American EEG Society statement of the clinical use of quantitative EEG. *Journal Clinical Neurophysiology* 1987; **4**: 197.
14. Gotman, J. Computer-assisted EEG analysis. In: *The Treatment of Epilepsy* (Ed. E. Wyllie). Philadelphia, Lea and Febiger, 1993, pp. 268–277.
15. Fell, J. and Roeschke, J. Nonlinear dynamical aspects of the human sleep EEG. *International Journal of Neuroscience*, 1994; **76**: 109–129.
16. Stam, C.J., Tavy, D.L.J. and Keunen, R.W.M. Quantification of alpha rhythm desynchronization using the acceleration spectrum entropy of the EEG. *Clinical EEG*, 1993; **24**: 104–109.