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Topographic EEG changes with normal aging and SDAT

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Summary EEG topography was compared in patients with senile dementia of the Alzheimer's type (SDAT), aged normal controls, and young normal controls to assess regional differences. The square root of absolute power was determined for each frequency using a Fast Fourier Transform (FFT). The normal elderly group showed a reduction in all 4 frequency bands, delta, theta, alpha and beta, at each of 32 leads when compared to the young controls. Z-transformation of the data revealed differences in topography. Older normals showed significantly greater mid-parietal and left mid-temporal delta than the younger controls. A similar pattern was seen for theta activity. Elderly controls showed relatively less occipital alpha and greater mid-parietal alpha. Beta activity demonstrated these same significant topographic differences. The elderly/SDAT comparison was significant for delta only. SDAT patients were characterized by a marked delta asymmetry in temporal regions which was not seen in the elderly normals.

Key words: EEG topography; Aging; Senile dementia; Alzheimer-type senile dementia

Although specific changes in the electroencephalogram have been reported to occur with advancing age, the distribution between normal and pathological aging has not been established with precision. Obrist and Busse (1965) described 4 trends in the aging EEG: slowing of the alpha rhythm, increased fast activity, diffuse slowing, and focal disturbances. Over the past two decades, these general trends have been further refined (Obrist 1978) and attempts have been made to associate specific EEG abnormalities with unique pathological developments (Drachman and Hughes 1971; Johannesson et al. 1979; Stigsby et al. 1981; Soininen et al. 1982). With the application of quantitative methods to EEG analysis, investigators have measured the changes in frequency and amplitude of the EEG recording.

The first quantitative report on normals and demented patients (Obrist and Henry 1958) found

increased slow activity in the demented patients; relative power measures showed greater differences than absolute voltages. Matoušek et al. (1967) found decreased EEG power at all frequencies with increasing age; the highest correlation was temporo-parietal delta. Most recent studies have reported relative rather than absolute power and have not found significant differences between younger and older normal controls (Penttilä et al. 1985; Giaquinto and Nolfé 1986), although in a unique longitudinal study Coben et al. (1985) did show delta increases. The visually assessed records of 420 normals (Hughes and Cayaffa 1977) also showed increased slow waves with increasing age, inconsistent with the earlier study of Matoušek et al. (1967).

Obrist and Busse (1965) raised the question of whether EEG changes in senile dementia were merely pronounced aging or a separate and specific pathological process. Niedermeyer (1981) suggests that 'EEG changes ascribed to old age are essentially the result of a variety of pathological developments; there is only a small niche left for old age as such as a causative agent.' This viewpoint is

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supported by recent data (Penttilä et al. 1985; Giaquinto and Nolfé 1986), which did not show normal old/young differences but did differentiate normal old/dementia spectral findings.

Using topographic mapping of computerized EEGs, Duffy et al. (1984) found right temporal slow activity in younger patients with Alzheimer's disease and frontal slow activity in older patients. The new capacity for regional analysis of functional activity offered by positron emission tomography has also been applied in Alzheimer's disease (Friedland et al. 1985; Duara et al. 1986; Miller et al. 1987). They report decreased temporal/parietal metabolic rates without occipital decreases — a pattern consistent with the histopathology and the topographic findings of Duffy et al. (1984). This suggests the importance of systematic regional assessment of EEG in SDAT.

In this study, we have analyzed 32-lead recordings from normal elderly subjects and patients with senile dementia of the Alzheimer's type (SDAT). This study extends earlier studies with higher resolution EEG imaging and explores the effect of reference electrode choice.

Method

Patients

Eight right-handed individuals with SDAT (4 males, 4 females, mean age 70, S.D. 5.1) had EEGs recorded as part of the diagnostic work-up in the Memory Disorders Clinic at UCI. The diagnosis of SDAT was made after the studies were completed by one of us (A.S.) without knowledge of EEG results.

Controls

Elderly controls (8 males, 7 females, mean age 70, S.D. 7.8) were selected from among volunteers at 3 Senior Day Centers in Orange County. They were screened to include only those without neurological or psychiatric disorders, epilepsy, recent drug or alcohol dependence, previous head injury, or those taking psychoactive medications. All were right-handed.

Young controls (5 males, 5 females, mean age 23, S.D. 4.8) were screened with the same criteria as the elderly group; all were right-handed.

EEG recording

All recordings were made in the morning in a sound-attenuated room under identical conditions. Subjects were seated in a reclining chair at a 45° angle, with a headrest adjusted to minimize neck muscle tension. They were instructed to keep their eyes closed throughout the session and remain as relaxed as possible. Resting EEGs were recorded with the lights extinguished.

EEGs were recorded in three 30 sec periods. After each recording, subjects were asked if they were drowsy. Records that showed evidence of sleep or excessive movement were discarded. Typically 30–40 2.56 sec blocks were included in the analysis.

Alerted EEG data were obtained from a second set of 3 blocks, recorded while subjects listened to a tape-recorded story.

Electrodes were placed on 32 positions over the scalp surface, using the international 10–20 system plus 5 interpolated leads on each hemisphere and 2 interpolated midline positions with linked ears as reference (see Fig. 1).

Computer analysis

Data were collected with an on-line computer system. EEG activity for spectral analysis was amplified with a 3 dB bandpass of 0.5–50 Hz and digitized for each channel at 200 Hz and recorded in 2.56 sec blocks (512 points). All 32 leads for each epoch were inspected for artifacts, eye blink and movement. Any 2.56 sec epoch containing artifacts was eliminated from further analysis. The amplifiers were calibrated by recording a 10 Hz standard signal through all channels and determining the calibration factor for each channel. Before analysis, each channel was thus proportionally adjusted. A window function consisting of a 10% cosine taper was obtained by weighting the 25 points at either end of each 2.56 sec epoch by a cosine bell. A standard fast Fourier transform was applied to each of the artifact-free 2.56 sec epochs in a recording and the power estimates were computed at 0.39 Hz steps. The transform yielded a value representing the average magnitude, expressed in microvolts (square root of power). This was calculated as the square root of the sums of the squares across the 0.39 Hz steps and yields the

Fig. 1. Placement of 32 electrodes at standard 10–20 system locations, midline and interpolated midline positions in centers of squares formed by the 10–20 system.

sine wave equivalent in microvolts. The bandwidths for each frequency were: delta, 0.8–4.3 c/sec; theta, 4.7–7.8 c/sec; alpha, 8.2–12.9 c/sec; beta, 13.3–19.9 c/sec. In a second analysis, we recomputed all EEG leads based on a digital computer averaged reference and repeated the spectral analysis in exactly the same way.

Topographic mapping

Continuous surface density maps of the entire scalp surface were created from these values, using a 4-nearest neighbor interpolation algorithm (Buchsbaum et al. 1982a, b).

Statistical analysis

Differences between groups were assessed for each frequency band separately using a 3-way ANOVA with the BMDP2V program (Dixon et al. 1981) with repeated measures: lead (1–32) $\times$ group (young, elderly, SDAT) $\times$ sex. Huynh-Feldt reduced degrees of freedom were used to avoid type

I errors caused by falsely inflated df in repeated measures ANOVA. Where significant ($P < 0.05$) lead $\times$ group interactions were found, the ANOVA was repeated, using values normalized with a z -transformation to correct for a possible multiplicative effect produced by differences in source strength (McCarthy and Wood 1985) and to eliminate differences due to overall reduction in EEG power. This was done by calculating the mean and standard deviation across the values for the 32 leads and then reexpressing each lead as (lead value – mean)/standard deviation. The z -transformed frequency bands yielding significant lead $\times$ group interactions were selected for further analysis, consisting of the calculation of group means and t tests at each of the 32 leads, using the BMDP3D program (Dixon et al. 1981).

Lastly, it should be noted that our major hypothesis based on the PET results of Friedland et al. (1985), an increase in delta in the temporal/parietal region, is tested statistically by the application of only one statistical test, the group $\times$ lead ANOVA interaction. This was followed by post-hoc t tests on each lead. Figures showing these contrasts were developed. Multilead t values are used to exhibit the effect graphically and each EEG frequency band is reported systematically as exploratory analyses for literature comparison and replication. These post-hoc t tests are presented only to illustrate the regional effects of statistically confirmed lead interactions.

Results

(1) Aging amplitude maps

The normal elderly group showed an overall reduction in EEG amplitude for all frequency bands. This was statistically confirmed with a group effect in all 4 ANOVAs, for delta, theta, alpha and beta. Delta change is shown in Fig. 2 (group effect, $F = 28.2$; $df = 1, 21$; $P < 0.0001$). The decrease was greatest (about 8 μV) over visual cortex (O1) and least (about 2 μV) over left anterior temporal cortex (T3). This was statistically confirmed by ANOVA (lead $\times$ group interaction, $F = 4.82$; $df = 3.46, 72.6$; $P = 0.0027$). Similar significant reductions were seen for theta, alpha and

Fig. 2. Left: mean topographic maps of delta activity in young controls, elderly controls and SDAT patients; scale is in microvolts. Right: map of 32 t values for elderly/SDAT contrast done on each lead as post-hoc tests following significant lead $\times$ group interaction using ANOVA with appropriate reduction in degrees of freedom (see text). Numbers next to scale give lower limit for the gray scale box. Thus t values between -1.08 and -0.68 appear white and t values greater than 2.08 appear black. Black is $P < 0.05$, 2-tailed; SDAT higher than controls.

beta for both group and group $\times$ lead effects. Lead $\times$ lead t tests confirmed an all over significance pattern.

Next, normalized maps were explored because: (1) the amplitude reduction was significant at nearly all leads, obscuring topographic differences, and (2) McCarthy and Wood (1985) have suggested that F ratios for the lead $\times$ group interaction could be spuriously elevated by multiplicative effects produced by change in source strength, and that such biases are removed by normalization.

(2) Aging normalized maps

(a) *Delta*. Both young and elderly subjects showed a predominantly midline distribution (Fig. 3). However, younger subjects had relatively more occipital and right posterior temporal delta whereas older subjects showed higher mid-parietal and left mid-temporal delta. This was confirmed by ANOVA (lead $\times$ group interaction, $F = 4.94$; $df = 6.0$, 126.1; $P = 0.0001$). Similar and significant results were obtained on auditory alerting.

(b) *Theta*. Like delta, theta showed (Fig. 3) a midline distribution, with younger subjects showing increased occipital and decreased posterior temporal activity (lead $\times$ group interaction, $F = 3.25$; $df = 6.9$, 144.8; $P = 0.003$). Again, similar significant results were obtained with alerting.

(c) *Alpha*. An occipital peak for alpha with a left asymmetry is seen in the young group, whereas the elderly show (Fig. 4) a midsagittal distribution (lead $\times$ group interaction, $F = 8.03$; $df = 9.1$, 191.0; $P < 0.0001$). Alerting results were similar and significant.

(d) *Beta*. The midline and occipital beta maxima (Fig. 4) seen in young subjects are diminished in the elderly (lead $\times$ group interaction, $F = 5.73$; $df = 13.4$, 281.4; $P < 0.0001$). Alerting results were similar and significant.

(3) SDAT

A significant lead $\times$ group interaction between the normal elderly and SDAT patients was only found for delta ($F = 7.20$; $df = 8.3$, 158.1; $P < 0.0001$). Whereas the highest amplitudes for the

Fig. 3. Left: mean normalized topographic maps of delta and theta activity in young and elderly normal controls. Scale on the left is in standard deviation units. Black indicates a lead which on the average is 1.3 S.D.s above the mean value for all 32 leads. Thus midline leads, in most subjects relatively high in delta and theta compared to other scalp areas, have values above 0.0. Since not all subjects have maximum at exactly the same lead, highest values average out around 1.3–1.8 rather than 2.0–2.3 expected from a 1 out of 32 deviation. Right: maps of 32 t test comparisons between young and elderly done post hoc following a significant lead $\times$ group ANOVA. Black is $P < 0.05$, 2-tailed, younger controls higher than elderly controls.

SDAT patients occurred frontally, the normal elderly had peaks over the midsagittal plane, at leads FC, CP1 and CP2, and PO1 and PO2. Both groups demonstrated minima over the temporal lobes (Fig. 5), but the SDAT patients' delta amplitudes were higher in a region including the anterior superior areas of the temporal lobes. In addition, the normal elderly had higher delta on a midsagittal line, over the parietal and superior occipital areas. These findings are illustrated with t test maps for normalized data as well as for average reference data (Fig. 6).

Using positron emission tomography to assess regional brain activity in SDAT, Friedland et al. (1985) found a greater hemispheric asymmetry in glucose metabolism in the temporal lobe, which appeared sometimes as right greater than left and sometimes as left greater than right. Because of this finding, we examined asymmetry in our delta values. To assess the asymmetry of the delta increase, we compared the difference between left and right delta amplitudes in the normal elderly and SDAT groups. This difference was computed as the absolute value of the difference so that a

Fig. 4. Left: mean normalized topographic maps in young and elderly normal controls. Scale is in standard deviation units. Thus black indicates a lead which on the average is 1.66 S.D.s above the mean alpha value for all 32 leads. For beta, black indicates a lead which on the average is 1.38 S.D.s above the mean for all 32 leads. Right: maps of 32 t test comparisons between young and elderly controls done post hoc following a significant lead $\times$ group ANOVA. Black is $P < 0.05$, 2-tailed, young controls higher than elderly controls.

high value reflected a greater asymmetry regardless of direction (as in the Friedland results). The Alzheimer's patients had a significantly greater asymmetry over temporal cortex (T3, T4) than normals (mean 1.95, S.D. 1.8, vs. mean 0.75, S.D. 0.4; $t = 1.86$, $df = 1, 21$, $P < 0.05$, 1-tailed), but not over frontal cortex (F7, F8) (0.56 and 1.19, respectively, $P = \text{n.s.}$). Using a criterion of 1.7, we identified 4 of 8 patients with SDAT but no normals ($P < 0.05$, Gail-Green test; Gail and Green 1976). Typical EEG tracing is shown in Fig. 7. Similar significant results were obtained during alerting.

Discussion

We have shown some well-delineated local EEG changes that occur in the process of normal aging. Although diffuse slowing has been generally associated with intellectual impairment (Obrist 1978), we found different cortical areas showing different changes — occipital area showing the greatest microvolt decrease with aging and temporal the least. On normalized maps, older subjects had relatively more parietal and temporal delta. This was true of maps using the average reference as well as linked ears, indicating that the low tem-

Fig. 5. Left: mean normalized maps of delta activity in elderly controls and patients with SDAT. Right: *t* comparison map shows significantly higher (white) delta in SDAT in temporal and posterior frontal areas and significantly lower (black) delta in midline areas.

Fig. 6. Left: mean normalized maps of delta activity in elderly controls and patients with SDAT using average reference. Note that the left anterior temporal lobe and left posterior frontal region show relatively more delta activity in patients than the controls. Right: *t* comparison map shows significantly higher (white) delta in SDAT in anterior temporal and posterior frontal areas and significantly lower (black) delta in midline and posterior temporal regions.

Fig. 7. Examples of EEG recorded in 3 patients (S1, S2, S3) with SDAT and 3 elderly controls (C1, C2, C3) for right and left frontal and temporal leads. Top line (S1) is a patient who dramatically illustrates the asymmetry in slow activity in the temporal leads but not frontally. Controls show fair symmetry in all leads. Spectral analysis on the entire sample, on the 90 sec recordings for all 32 leads, revealed that the quantitative shift to greater slow activity in anterior temporal regions was greater in SDAT patients. The difference in regional delta pattern between groups, suggested by the tracings but difficult to identify unambiguously by visual inspection, was confirmed by ANOVA, $P < 0.0001$ (see text).

poral amplitude we observed is not merely due to the use of a linked ear reference close to temporal leads. We have previously noted very similar delta activity distributions with ear and average reference methods (Buchsbaum et al. 1982a).

The localization of increased slow activity to the temporal lobe in aging is often reported (Drachman and Hughes 1971; O'Connor et al. 1979; Torres et al. 1983) and has generally been correlated with the development of pathological processes. Our results show a relative increase in delta over the left temporal lobe in normals without the appearance of clinically significant cognitive impairment. A large asymmetry in temporal delta was a distinctive feature of the group of SDAT patients.

Normal subjects showed a loss of the typical alpha occipital maximum with age, but had dif-

fuse relative increases in alpha amplitude centrally and temporally. No difference in occipital alpha between normal elderly and SDAT was found. This is consistent with the visual sparing reported in SDAT and indicates a qualitative difference between normal aging and the SDAT process.

At the highest frequency analyzed in this study, β_1 , the changes in amplitude with advancing age paralleled those for alpha: the amplitude progressed from the occiput to a central location.

Our lack of significant lead $\times$ group interactions for theta, alpha and β_1 in ANOVA contrasts of the normal elderly and SDAT groups suggests that there may be EEG recording changes that are appropriately associated with age rather than pathology. The one frequency that yielded significant results with ANOVA, delta, had a low amplitude in the SDAT patients in one area of the brain and a higher amplitude frontally, again reflecting a change in distribution that may not be recognized with conventional EEG analysis.

The statistical methods employed to construct the maps allowed us only to depict group effects. However, the group analysis may have obscured pathological changes in the SDAT patients that occurred in different locations for each subject. One approach to this problem was the analysis of absolute values of hemispheric differences which detects gross asymmetries in either lobe even if subjects are equally divided into right and left hemisphere abnormalities.

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