Quantitative Electroencephalographic Correlates of Cognitive Decline in Normal Elderly Subjects

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• **We obtained a topographic computer analysis of the electroencephalogram in 53 normal elderly subjects. Normal aging was not associated with an increase in slow (delta) activity. However, cognitive performance correlated positively with fast (beta) activity particularly in frontal leads, even after controlling for age, education, occupation, and medication. Five subjects who showed early signs of cognitive decline, had all a marked reduction in beta activity suggesting that this may be an early indication of intellectual loss.**

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Conventional and quantitative electroencephalographic (EEG) studies of normal aging have produced contradictory results. Some studies suggest that normal aging is accompanied by the gradual development of slow activity in the theta band and a decrease in the frequency and amount of alpha activity.[1,2] Beta activity has been found to increase with age in females but not in males.[2]

Other investigators report that the EEG in normal elderly subjects differs little from that of normal younger subjects.[3-6] Duffy et al[7] have even found that normal aging may be associated with desynchronization, with a decrease in slow activity and an increase in beta activity. Patients with medical illnesses were carefully excluded from this study, which may explain the differences from earlier series.

Work with demented patients has produced less contradictory results. Both conventional and quantitative EEG examinations have suggested that patients with dementia of the Alzheimer type tend to have more delta and theta activity, alpha slowing, and decreased beta activity.[8,9] However, there is no agreement on which change occurs first. Gordon[10] observed that reduction in alpha activity was the earliest change. Johannesson et al[11] and Penttila et al[12] considered that theta increases were the first change seen, whereas Coben et al[13,14] have reported that increased theta and decreased beta were the earliest changes. Few studies have assessed EEG coherence in these patients, but Prichep et al[15] found a general decrease in interhemispheric coherence in patients with dementia compared with normal subjects.

All of these studies examined patients who already were diagnosed as probably having Alzheimer's disease on the basis of clinical examination or psychological testing. The purpose of this investigation was to examine the quantitative EEG of healthy elderly subjects, with particular attention to those who may show evidence of very early cognitive decline. The subjects studied were participating as a control group in a longitudinal study of dementia. We examined correlations between quantitative EEG variables and the Extended Scale for Dementia (ESD), which is a scale sensitive to cognitive decline.[16] In addition to correlations on all right-handed subjects at one point in time, we reviewed quantitative EEG findings in those subjects who demonstrated a decline in their ESD values over time but who still had values in the normal range.

SUBJECTS AND METHODS

Subjects

Fifty-three normal elderly subjects were studied. The mean (±SD) age of the men (n = 30) was 73.9 ± 4.0, with a range of 65 to 81 years. The mean (±SD) age for the women (n = 23) was 71.9 ± 8.6, with a range of 41 to 85 years. Forty-nine were right handed and four men were left handed or ambidextrous. Of 26 right-handed men, the mean (±SD) age was 73.6 ± 4.0, with a range of 65 to 81 years. All were participants in a control group for a longitudinal study of dementia at the University of Western Ontario, London.[17] Informed consent was obtained for participation in this study. Each subject underwent a systematic physical and neurologic examination supervised by one of us (V.C.H.).[18] Subjects with significant psychiatric illness, uncontrolled hypertension or diabetes, angina pectoris, myocardial infarction, or neurologic findings were excluded. Values were assigned for previous levels of occupation and education, respectively, on the basis of a Canadian scale of occupations[19] and on years of education. Twenty-two subjects were taking no medication. Twenty-two subjects were taking an anti-inflammatory or antihypertensive agent; one was taking thyroid replacement but was clinically euthyroid; one was taking an oral hypoglycemic agent and one patient was receiving allopurinol. No information was available on medication use in one subject.

Cognitive Measures

The subjects were all being assessed regularly at an approximately 6-month intervals with the ESD. The ESD is comprised of items[20] that measure cognitive decline from mild to severe levels of dementia. The scale has been shown to have a high level of internal consistency[20] and correlates highly with duration of illness and EEG changes in Alzheimer's diseases.[21,22]

In each case, the nearest ESD score to the date of the EEG was used for correlation analysis. The mean time to this point was 0.74 months, ie, less than 1 month subsequent to the EEG. In 49 subjects, all ESD scores were within 6 months of the EEG with the exception of one subject who was scored within 14 months of the EEG. In addition, ESD scores from the earliest to the most recent were reviewed by two of us (P.C.W., H.M.) for signs of decline within the normal range, without knowledge of the individual EEG results.

Quantitative EEG

The EEG data were acquired on a computer-based system (QSI 9000) from stan-

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Table 1.—Electroencephalographic Power and Coherence at F_3C_3 and F_4C_4 for Right-Handed Subjects*

	F_3C_3	F_4C_4
Power		
Delta	12.1 ± 10.5	10.4 ± 6.8
Theta	10.0 ± 11.0	8.2 ± 8.2
Alpha	13.2 ± 16.4	11.5 ± 11.9
Beta 1	8.1 ± 5.8	8.2 ± 6.8
Beta 2	8.7 ± 5.9	9.2 ± 7.9
Coherence		
Delta	.66 ± .10	.67 ± .09
Theta	.71 ± .08	.72 ± .08
Alpha	.69 ± .12	.69 ± .11
Beta	.49 ± .14	.47 ± .12

*Right-handed subjects (n = 49).

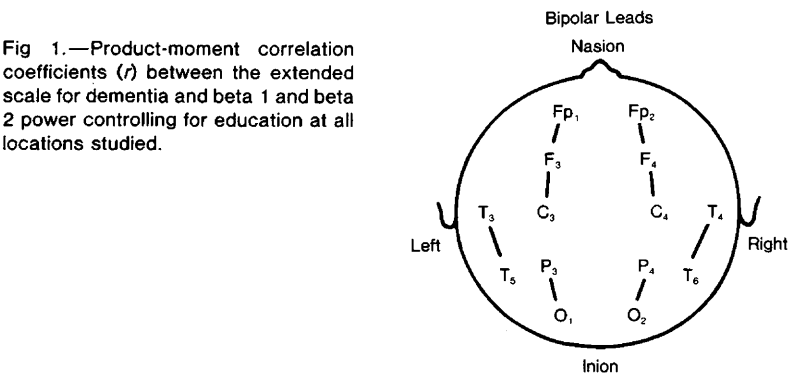
Table 2.—Electroencephalographic Power Differences Between Men and Women

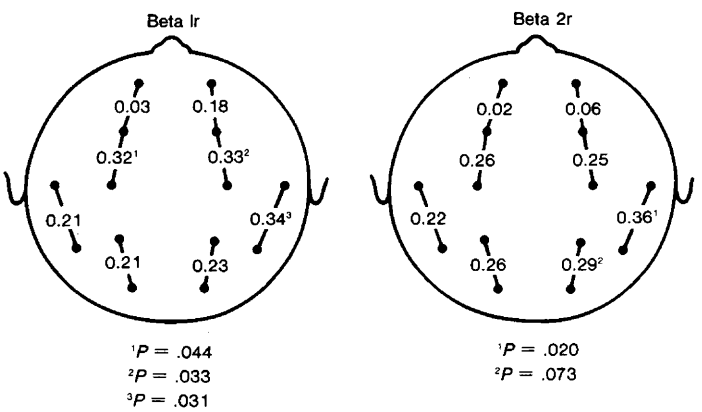
	Men (n = 26)	Women (n = 23)	t	P
F_3C_3				
Beta 1	6.2±5.1	10.3±5.8	−2.66	.011
Beta 2	6.3±5.4	11.4±5.2	−3.35	.002
P_3O_1				
Beta 1	6.3±5.8	11.1±9.1	−2.17	.037
Beta 2	4.3±3.4	6.4±3.2	−2.21	.032
P_4O_2				
Beta 1	6.5±6.2	13.5±12.5	−2.43	.021
Beta 2	4.6±3.7	8.5±10.0	−1.80	.084

Table 3.—Statistically Significant Product-Moment Correlation Coefficients (r) Between Age and Power in Men and Women

	r	P
Males		
Fp_1F_3		
Delta	−.42	.034
Theta	−.49	.010
Alpha	−.42	.032
Fp_2F_4		
Delta	−.40	.045
Theta	−.45	.021
F_3C_3		
Delta	−.39	.046
Theta	−.40	.041
F_4C_4		
Theta	−.43	.028
T_3T_5		
Alpha	−.45	.022
T_4T_6		
Alpha	−.40	.044
P_4O_2		
Beta 1	−.41	.037
Females		
F_3C_3		
Beta 2	−.43	.043
F_4C_4		
Beta 1	−.44	.034
Beta 2	−.60	.003

Fig 1.—Product-moment correlation coefficients (r) between the extended scale for dementia and beta 1 and beta 2 power controlling for education at all locations studied.





¹P = .044
²P = .033
³P = .031

¹P = .020
²P = .073

dard 10/20 electrode locations.[23] The EEG was collected with eyes closed and the electro-oculogram was monitored to exclude eye movement. Artifacts due to eye movement, muscle tension, and drowsiness were excluded via an automatic computer rejection program and visual inspection of the record. A minimum of 20 seconds of artifact-free EEG data using averaged 2.5-second epochs were selected. These samples were then digitized at 102.4 samples per second and filtered at 0.5 to 30 Hz for each electrode location. The EEG absolute power and coherence was then calculated for the delta (0.5 to 4.0 Hz), theta (4.0 to 8.0 Hz), alpha (8.0 to 12.0 Hz), beta 1 (12.0 to 18.0 Hz), and beta 2 (18.0 to 26.0 Hz) bands. The EEG coherence was also calculated for the same bands except that the beta band was not divided (12.0 to 26.0 Hz). Bipolar leads Fp_1F_3, Fp_2F_4, F_3C_3, F_4C_4, T_3T_5, T_4T_6, P_3O_1, and P_4O_2 were chosen for analysis.

Analysis

All descriptive statistics are reported as mean ± SD. Correlations for age and the ESD with quantitative EEG variables were assessed using Pearson product-moment correlation coefficients. The effects of age, educational level, and occupation were controlled by partial correlation techniques. Differences between subjects showing decline on the ESD and those showing no decline were assessed with a weighted t test for unequal variances. Two-tailed probability values are presented unless otherwise specified.

There are 40 possible correlations for age with power (eight locations, five wave bands). There are 32 possible correlations for coherence (eight locations, four bands). Similar numbers of comparisons exist for the ESD with power and coherence. In this situation, a Bonferroni correction for multiple comparisons can be expected to reject conclusions that may be valid. We have accepted, as meaningful, those comparisons in which more than 5% were significant at $P < .05$, two tailed, and at least one new finding had $P < .01$. Further, the pattern of change had to be consistent at neighboring electrodes.

RESULTS

Illustrative values for mean power and coherence in right-handed subjects at F_3C_3 and F_4C_4 (n = 49) are shown in Table 1. Values for left-handed subjects (n = 4) were similar so only values for right-handed subjects are presented. The mean ESD value was 244.3 ± 5.5 for right handers and 242.3 ± 7.4 for non-right handers. Test scores may range from a maximum of 250 down to 0 as "untestable."

Statistically significant differences between men (n = 26) and women (n = 23) are shown in Table 2. The only significant difference was a reduction in beta activity in men at F_3C_3, P_3O_1, and P_4O_2. Statistically significant product-moment correlation coefficients (r)

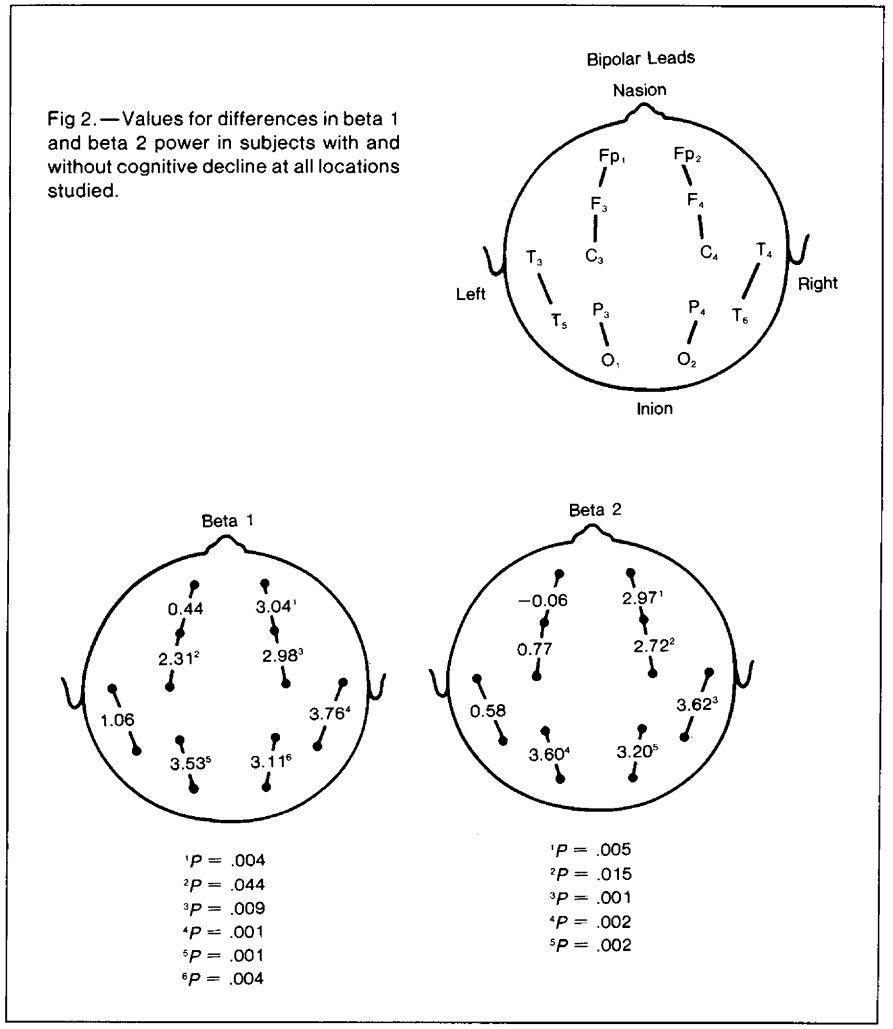


Fig 2.—Values for differences in beta 1 and beta 2 power in subjects with and without cognitive decline at all locations studied.

between power and age for men are shown in Table 3. A general trend to lower delta, theta, and alpha power was seen with age in frontal, temporal, and central leads. A negative correlation between beta 1 power and age was found at P_4O_2. A negative correlation between beta coherence and age was also found in women at F_3C_3 ($r = -.40$, $P = .050$). No other significant correlations were found between age and power or coherence in either group at other locations.

Of 40 correlations between power and age in men, 11 were significant (Table 3). Of 40 correlations between power and age in women, three were significant and one exceeded 0.01. Only an isolated finding was significant for coherence. This suggests a relationship between age and power in both men and women.

Product-moment correlation coefficients between the ESD and beta 1 and beta 2 power (controlling for education) are shown in Fig 1. A positive correlation is seen between the amount of beta activity and performance on the cognitive test at frontal-central locations bilaterally. The correlation reaches or approaches statistical significance at only four of eight locations and positive correlations are seen across the scalp. The ESD also correlated with theta power (r −.31, $P = .045$) and coherence ($r = .31$, $P = .045$) at P_3O_1. No other statistically significant correlations were seen between other power or coherence bands and the ESD after controlling for education.

After controlling for age, significant correlations between beta 1 and the ESD remained at F_3C_3 ($r = .27$, $P = .059$) and F_4C_4 ($r = .30$, $P = .037$). After controlling for occupation, significant correlations between beta 1 power and the ESD also remained at F_3C_3 ($r = .31$, $P = .048$) and F_4C_4 ($r = .31$, $P = .044$).

In summary, five of 40 correlations for power and the ESD (controlling for education) reached P values of <.05, with no values exceeding $P < .01$. The correlations remained significant at the same two locations after controlling for age and for occupation. A trend to positive correlations was also seen in adjacent leads. These findings suggest a possible relationship between beta power and the ESD. To test that relationship, the next comparison was undertaken.

Five subjects were found to show evidence of decline in their ESD scores over time even though their scores remained in the normal range. Three of these subjects were identified independently by the raters and two by consensus. This group had a mean age of 73.1 ± 5.2 and included four men and one woman. The mean ESD of subjects showing decline was still within the normal range (239.4 ± 6.8), but it was slightly less than the mean of subjects not showing decline (mean ESD, 244.9 ± 5.1; $t = 1.76$; $P = .072$, one tailed). The subjects showing decline had considerably less beta power at Fp_2C_4, F_3C_3, F_4C_4, T_4T_6, P_3O_1, and P_4O_2 (Table 4 and Fig. 2). A reduction in alpha power was also seen in subjects showing decline at Fp_2F_4, F_3C_3, T_4T_6, P_3O_1, and P_4O_2 (Table 4). A reduction of delta power in subjects showing decline was found at T_4T_6 and P_4O_2.

Subjects showing cognitive decline had significantly lower delta coherence compared with those not showing decline at F_4C_4 ($t = 3.19$, $P = .019$) and T_3T_5 ($t = 2.95$, $P = .018$). No other coherence differences were seen between the two groups.

There were no statistically significant differences between patients on and off medication on any power or coherence value at any location. Four of five subjects showing cognitive decline were taking medication. One was receiving an antihypertensive; one was receiving thyroid replacement and an anti-inflammatory agent; and two were taking an anti-inflammatory agent alone.

COMMENT

Our results are in keeping with recent quantitative studies that have indicated that slow activity does not increase with normal aging.[3-7] In fact, we found a fairly consistent decline in delta and theta activity with age in men that was similar to the findings of Duffy et al.[7] There was no significant decline in delta or theta in women with age, but a negative correlation was found between beta activity and age in frontal leads. Some differences also emerged between men and women in resting levels of beta activity. A previous quantitative EEG study[24] has also

Table 4.—Electroencephalographic Power Differences Between Subjects With and Without Cognitive Decline

	No Decline (n = 44)	Decline (n = 5)	t	P
Fp_2F_4				
Alpha	4.8 ± 5.6	2.7 ± 1.2	2.04	.050
Beta 1	4.6 ± 4.8	2.2 ± 0.7	3.04	.004
Beta 2	7.4 ± 9.1	3.0 ± 1.2	2.97	.005
F_3C_3				
Alpha	14.0 ± 17.1	6.8 ± 5.1	2.09	.051
Beta 1	8.5 ± 5.9	5.1 ± 2.6	2.31	.044
F_4C_4				
Beta 1	8.6 ± 7.0	4.3 ± 2.2	2.98	.009
Beta 2	9.7 ± 8.2	5.1 ± 2.5	2.72	.015
T_4T_6				
Delta	12.4 ± 8.0	7.1 ± 1.8	3.61	.001
Alpha	47.2 ± 55.8	21.4 ± 13.9	2.46	.021
Beta 1	13.7 ± 13.9	5.0 ± 2.2	3.76	.001
Beta 2	11.7 ± 12.1	4.5 ± 1.7	3.62	.001
P_3O_1				
Alpha	40.7 ± 53.3	13.1 ± 6.7	3.23	.002
Beta 1	9.1 ± 8.1	4.3 ± 1.2	3.53	.001
Beta 2	5.6 ± 3.5	3.0 ± 1.1	3.60	.002
P_4O_2				
Delta	13.1 ± 9.1	7.2 ± 2.4	3.36	.003
Alpha	38.1 ± 46.0	16.0 ± 8.2	2.82	.008
Beta 1	10.3 ± 10.6	4.6 ± 2.1	3.11	.004
Beta 2	6.8 ± 7.9	2.9 ± 0.7	3.20	.002

reported greater beta power in elderly women compared with elderly men. However, beta activity has been reported to increase with age in women.[2] We found it to decrease, but this might be explained by the older age of our subjects. In keeping with this possibility, a decline in the amount of fast activity has been reported in subjects of advanced age.[1]

Significant correlations between ESD and EEG variables were seen only in the beta and theta bands. The negative correlation between ESD performance and beta power was consistent and remained so even when age, education, occupation, and medication effects were controlled. Fast activity has been associated with superior learning ability in normal elderly subjects.[25] However, a recent quantitative EEG study[7] found a negative correlation between memory ability and fast activity in normal older subjects. Our findings seem to support the earlier conventional EEG study.

The finding of diminished beta activity in the five subjects who showed decline in ESD values suggested beta activity may be associated with early cognitive decline. Diminished alpha activity was also seen in these patients. It is interesting that both diminished alpha activity[10] and diminished beta activity[13-15] have been found in early dementia compared with normals. It is of note that subjects showing cognitive decline also tended to have decreased levels of coherence in the delta band as decreased interhemispheric coherence has been reported in dementia.[15] There is, of course, no way of knowing if these five patients will develop Alzheimer's disease or other dementias until they are followed up for a longer period.

These findings may have been influenced by a number of factors that cannot always be controlled. First of all, the beta activity can be associated with muscle tension and medication. However, the records were carefully edited to exclude muscle tension and we would not expect a correlation between muscle activity and actual ESD score. The effects of medication cannot be completely ruled out but there did not seem to be a relationship between medication users and beta findings. Finally, the possible effects of multiple comparisons must be acknowledged but Figs 1 and 2 demonstrate that findings were widely distributed across the scalp and not just limited to one or two leads.

While the relationship between cognitive performance and beta activity in normal elderly subjects has been suggested before, we believe that this is the first study to link serial cognitive decline with diminished beta activity. Few investigators have examined EEG coherence in the elderly but our study suggests a decrease in delta coherence in subjects showing cognitive decline. We cannot determine yet whether diminished beta or alpha activity or diminished delta coherence may be useful early markers for dementia, but we are continuing to follow up these subjects.

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