Quantitative Spectral Electroencephalography in Predicting Survival in Patients With Early Alzheimer Disease

Jules J. Claus, MD, PhD; Bram W. Ongerboer de Visser, MD, PhD; Gerard J. M. Walstra, MD, PhD; Albert Hijdra, MD, PhD; Bernard Verbeeten, Jr, MD, PhD; Willem A. van Gool, MD, PhD

Objective: To determine whether measures of quantitative spectral electroencephalography (EEG) can predict survival in patients with early Alzheimer disease.

Design: Prospective cohort study; median duration of follow-up was 4.4 years in survivors and 2.6 years in non-survivors. Cox proportional hazards models, with adjustment for age and sex were used to estimate relationships between EEG measures and survival. Log relative percentage values of EEG bands were used as predictors.

Setting: Outpatient university memory clinic.

Participants: One hundred one consecutively referred patients with early probable Alzheimer disease according to National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association criteria were studied with EEG at the time of diagnosis. The mean age of the patients was 79.2 years, which was higher than in previous EEG studies.

Main Outcome Measure: Mortality.

Results: Fifty-one patients (50.5%) died during follow-up, with a median survival time in all patients of 4.1 years. The following EEG variables were significantly associated with increased risk of mortality: from parieto-occipital leads, higher theta (hazard ratio, 2.05; 95% confidence interval, 1.15-3.66; \(P<.05\)), lower alpha (hazard ratio, 0.43; 95% confidence interval, 0.25-0.76; \(P<.01\)), and lower beta (hazard ratio, 0.38; 95% confidence interval, 0.22-0.68; \(P<.001\)) activity; and from frontocentral leads, higher theta activity (hazard ratio, 2.07; 95% confidence interval, 1.17-3.66; \(P<.05\)). Stepwise Cox regression analysis showed that loss of parieto-occipital beta (\(P<.01\)) and alpha (\(P<.05\)) power were independent and significant predictors of mortality. Both beta (12.6-35.4 Hz) and alpha (7.5-12.5 Hz) activity remained significantly associated with mortality after adjustment for education, dementia severity, symptom duration, level of cognitive function, presence of extrapyramidal symptoms or hallucinations, presence of vascular risk factors, and presence of leukoaraiosis or local cortical atrophy.

Conclusions: Decreases of beta and alpha activity on quantitative spectral EEG are independent predictors of mortality in patients with early Alzheimer disease. In the clinical context, the use of EEG technology for prediction of survival in individual patients remains to be determined.

Arch Neurol. 1998;55:1105-1111
PATIENTS AND METHODS

PATIENTS

Patients met criteria for probable AD according to National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association criteria\(^1\) and were participants in a prospective study of 200 consecutive first referrals to the outpatient memory clinic of the Academic Medical Center, Amsterdam, the Netherlands.\(^1\) Inclusion criteria were referral for suspected dementia, age 65 years and older, and presence of an informant involved in the care of the patient; patients who were previously investigated for dementia were excluded. At baseline, all subjects were examined with the Netherlands version of the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX-N).\(^1,6,7\) Computed tomography (CT), EEG, and laboratory screening.\(^1\) Of the 200 patients initially referred, 105 were diagnosed as having probable AD, but 4 EEGs were missing because of technical reasons, leaving 101 patients in the study (43 men and 58 women). All patients and legally authorized representatives gave informed consent to participate in this study. Survival data were obtained from general practitioners and were available for all patients. Presence of extrapyramidal signs was defined as having at least 1 of the following signs at neurological examination: tremor, rigidity, bradykinesia, abnormal postural reflexes, or a characteristic parkinsonian gait. Clinical indicators used to define presence of 1 or more vascular risk factors included history of diabetes mellitus, hypertension, myocardial infarction, transient ischemic attacks, or stroke. Presence of delusions or hallucinations was determined by questioning the caregiver according to the standardized interview with the CAMDEX-N.\(^6,12\) Ten patients used benzodiazepines; no other centrally active medication was used.

EEG METHODS

As described previously,\(^6\) EEG recordings were performed at baseline with the use of an on-line 20-channel EEG system, with the international 10/20 system and silver-silver chloride electrodes. The impedance of the electrodes was always lower than 5 k\(\Omega\). The high-frequency cutoff was 35 Hz (−3 dB, 12 dB/octave), and the time constant was 0.3 seconds. The EEG was recorded under vigilance control with the patient’s eyes closed under resting conditions. With visual inspection to rule out segments with artifacts, such as electromyogram or electrocardiogram activity or eye movement, only artifact-free periods were used for quantitative analysis. Computerized spectral analysis was performed by means of fast Fourier analysis after sampling at a rate of 70 Hz on 6 bipolar frontocentral and parieto-occipital derivations: F3 to C3, T5 to O1, F4 to C4, T6 to O2, P3 to O1, and P4 to O2. After fast Fourier analysis was performed on an epoch of 3.36 seconds with a bin width of 0.298 Hz, the power spectrum of this epoch was calculated and an average power spectrum was computed as the mean of 30 successive epochs. Subsequently, this average power spectrum was then filtered with a 3-point triangular symmetrical filter. This filter did not influence the frequency value of the peak. Leakage of power to other frequencies caused by the triangular window did not significantly influence the power within a spectral band, as the spectral bands consisted of at least 12 points and leakage was restricted to only 1 point. The frequency bands were set as follows: delta, 0.3 to 3.5 Hz; theta, 3.6 to 7.4 Hz; alpha, 7.5 to 12.5; and beta, 12.6 to 35.4 Hz. Since absolute values may suffer from large variability, relative values (percentage) were calculated for frontocentral and parieto-occipital regions, since no differences between homologous left and right measurements were observed (Table 2). Fifty-one patients (50.5%) died during the follow-up period, with a median (± SD) survival time of 4.1 ± 0.2 years. The following variables were statistically significantly associated with increased risk of mortality: higher age (per 5-year increase, hazard ratio [HR], 1.26; 95% CI, 1.01-1.57; \(P<.05\)), male sex (HR, 1.92; 95% CI, 1.12-3.23; \(P<.05\)), lower score on the cognitive test from the CAMDEX-N (HR per 10-point decrease, 1.43; 95% CI, 1.19-1.69; \(P<.001\)), lower score on the Mini–Mental State Examination\(^26\) (HR per 5-point decrease, 1.47; 95% CI, 1.19-1.82; \(P<.001\)), and more severe dementia (HR, 2.18; 95% CI, 1.19-3.99; \(P<.05\)), but not education (HR, 1.07; 95% CI, 0.89-1.28; \(P=.58\)) and symptom duration (HR, 1.0; 95% CI, 0.99-1.01; \(P=.54\)).

Higher parieto-occipital (\(P<.05\)) and frontocentral (\(P<.05\)) theta activity, and lower parieto-occipital

Some subject characteristics are presented in Table 1. Relative power EEG values in percentage of delta, theta, alpha, and beta band, respectively, are shown in Table 2. Means of combined right and left EEG variables were calculated for frontocentral and parieto-occipital regions, because of technical reasons, leaving 101 patients in the study. Survival data were obtained from general practitioners and were available for all patients. Presence of extrapyramidal signs was defined as having at least 1 of the following signs at neurological examination: tremor, rigidity, bradykinesia, abnormal postural reflexes, or a characteristic parkinsonian gait. Clinical indicators used to define presence of 1 or more vascular risk factors included history of diabetes mellitus, hypertension, myocardial infarction, transient ischemic attacks, or stroke. Presence of delusions or hallucinations was determined by questioning the caregiver according to the standardized interview with the CAMDEX-N. Ten patients used benzodiazepines; no other centrally active medication was used.

RESULTS

ARCH NEUROL/VOL 55, AUG 1998 1106

©1998 American Medical Association. All rights reserved.
patients had relatively high delta power in parieto-
ter adjustment for all possible confounders examined in
relationships between parieto-occipital beta and alpha ac-
amic ability (P < .01) and parieto-occipital beta (P < .001) ac-
tivity were statistically significantly associated with in-
creased risk of mortality, adjusted for age and sex (Table 3). Stepwise Cox regression analysis showed that
parieto-occipital beta activity was the strongest predic-
tor of survival in AD (P < .01), while parieto-occipital alpha
power was retained in the model with additional pre-
dictive ability (P < .05). Thus, both parieto-occipital beta
and alpha power were used for further analyses. The re-
relationships between parieto-occipital beta and alpha ac-
tivity and survival remained statistically significant af-
ter adjustment for all possible confounders examined in
this study and after exclusion of subjects with a history of
temporary ischemic attacks or stroke. Since our pa-
tients had relatively high delta power in parieto-
occipital leads and delta power may increase with ad-
vancing age,1 the relatively high age of our study
population might suggest that delta is a marker of de-
mentia severity, independent of the CAMDEX-N demen-
tia severity marker used in our study. However, delta
power was statistically significantly associated with gen-
eral level of cognitive function, both the cognitive test
of the CAMDEX-N (P < .01) and the Mini–Mental State
Examination (P < .01), as well as dementia severity
(P < .05). Further, the association between beta and al-
pha power and survival was not changed with the addi-
tion of parieto-occipital delta power to the Cox regres-
sion model as correction factor, with the use of multiple
linear regression analysis with adjustment for age and sex.
The possibility that we included patients with Lewy body
dementia was considered, since this subgroup of pa-
tients appears to have more abnormal EEGs than pa-
tients with only AD.25 However, no patient in our study
satisfied clinical criteria for Lewy body dementia.28 Fur-
ther, there were no significant differences in alpha (P > .50)
or beta (P > .80) power between groups with or without
extrapyramidal symptoms, or in alpha (P > .30) or beta
(P > .20) power between those with and without delu-
sions or hallucinations, by means of multiple linear re-
gression analysis, with adjustment for age and sex. After
a mean of 5.4 years of follow-up, Kaplan-Meier survival
curves for groups dichotomized according to the me-

STATISTICAL METHODS

Data analysis was performed with SPSS, version 7.0 for Win-
dows, a commercially available statistical package (SPSS Inc,
Chicago, Ill). Cox proportional hazards multiple regression
analysis was used to estimate the effects of baseline
variables on survival. Hazard ratios (HRs) with 95% con-
fidence intervals (CIs) are presented as estimates of these
relationships. Statistical analysis was performed in several
segments. Predictors of survival, the log relative percent-
age values of the 4 EEG bands, were entered in the regres-
sion model as independent variables, with adjustment for
age at entry and sex. Then, using statistically significant
predictors from these analyses, we used stepwise Cox pro-
portional hazards regression analysis to identify the best
predicting variable or a combination, adjusted for age and
sex. The next step was to investigate whether the relation-
ship between a significant predictive EEG variable from this
stepwise analysis could be explained by confounding with
other factors. This would be the case if the association were
to disappear when a putative confounder was added as ex-
planatory factor to the model. We examined the possible
confounding effect of education, and clinical and neuro-
imaging features, by adding these variables to the regression
model as independent variables, for each variable in a
separate analysis. Clinical variables included dementia se-
verity, symptom duration, level of general cognitive func-
tion as measured with the overall score on the cognitive
test from the CAMDEX-N, presence of extrapyramidal symp-
toms, presence of delusions or hallucinations, and pres-
ence of vascular risk factors. Neuroimaging variables in-
cluded anterior and posterior horn index, bicaudate index,
width of the third ventricle, presence of cortical or sub-
cortical infarctions, ratings of local cortical atrophy, and
presence of leukoaraioysis. With the EEG variable that was
most strongly associated with survival after these adjust-
ments, we constructed survival curves by the Kaplan-
Meier method with dichotomized groups according to the
median of the distribution. Log rank tests were performed
to assess differences between survival curves. Proportion-
ality of the hazard was visually inspected from log minus
log survival curves,25 stratified by the variable of interest
and adjusted for the other variables, from plots of weighted
Schoenfeld residuals vs time,24 and from the interaction
between variables and log(time). Linearity of the log
(hazard) with prognostic variables was tested from plots
of deviance residuals against the variables23 and from im-
provement of the fit by adding quadratic terms.

alpha (P < .01) and parieto-occipital beta (P < .001) ac-

©1998 American Medical Association. All rights reserved.
The frequency bands were set as follows: delta, 0.3 to 3.5 Hz; theta, 3.6 to 7.4 Hz; alpha, 7.5 to 12.5 Hz; and beta, 12.6 to 35.4 Hz.

Table 1. Characteristics of 101 Patients With Alzheimer Disease

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
</tr>
<tr>
<td>Age, y (mean ± SD)</td>
<td>79.2 ± 6.3</td>
</tr>
<tr>
<td>Sex, % M/F</td>
<td>42.8:57.2</td>
</tr>
<tr>
<td>Education† (mean ± SD)</td>
<td>3.2 ± 1.5</td>
</tr>
<tr>
<td>Duration of follow-up, mo (mean ± SD)</td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>41.0 ± 16.1</td>
</tr>
<tr>
<td>Survivors</td>
<td>52.9 ± 6.3</td>
</tr>
<tr>
<td>Nonsurvivors</td>
<td>31.1 ± 51.1</td>
</tr>
<tr>
<td>Medical history, %</td>
<td></td>
</tr>
<tr>
<td>History of TIAs</td>
<td>6.9</td>
</tr>
<tr>
<td>History of stroke</td>
<td>5.0</td>
</tr>
<tr>
<td>Presence of delusions or hallucinations</td>
<td>21.8</td>
</tr>
<tr>
<td>Presence of vascular risk factors</td>
<td>34.6</td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
</tr>
<tr>
<td>Symptom duration, y (mean ± SD)</td>
<td>3.0 ± 2.8</td>
</tr>
<tr>
<td>CAMCOG baseline (mean ± SD)</td>
<td>62.4 ± 16.4</td>
</tr>
<tr>
<td>CAMCOG decline per year (mean ± SD)</td>
<td>9.5 ± 8.1</td>
</tr>
<tr>
<td>MMSE baseline (mean ± SD)</td>
<td>17.9 ± 5.6</td>
</tr>
<tr>
<td>MMSE decline per year (mean ± SD)</td>
<td>3.6 ± 3.3</td>
</tr>
<tr>
<td>Dementia severity, %‡</td>
<td></td>
</tr>
<tr>
<td>Minimal</td>
<td>7.9</td>
</tr>
<tr>
<td>Mild</td>
<td>79.2</td>
</tr>
<tr>
<td>Moderate</td>
<td>12.9</td>
</tr>
<tr>
<td>Presence of extrapyramidal signs, %</td>
<td>25.7</td>
</tr>
<tr>
<td>Computed tomographic findings, %</td>
<td></td>
</tr>
<tr>
<td>Presence of leukoaraiosis</td>
<td>30.7</td>
</tr>
<tr>
<td>Presence of right temporoparietal cortical atrophy</td>
<td>70.3</td>
</tr>
<tr>
<td>Presence of left temporoparietal cortical atrophy</td>
<td>69.3</td>
</tr>
<tr>
<td>Cortical infarctions, silent</td>
<td>4.0</td>
</tr>
<tr>
<td>Cortical infarctions, nonsilent</td>
<td>2.0</td>
</tr>
<tr>
<td>Subcortical infarctions, silent</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* TIA indicates transient ischemic attack; CAMCOG, cognitive test from the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX)16,17; and MMSE, Mini-Mental State Examination.26
† Attained level of education, classified on a 7-point scale that ranges from 1 (primary school) to 7 (university) in accordance with the International Standard Classification of Education (Unesco, Paris, France, 1976).
‡ Severity according to CAMDEX criteria.16,17

Table 2. Quantitative Spectral Electroencephalogram (EEG) Relative Power Values of 101 Patients With Probable Alzheimer Disease

<table>
<thead>
<tr>
<th>Quantitative Spectral EEG Bands*</th>
<th>Delta</th>
<th>Theta</th>
<th>Alpha</th>
<th>Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontocentral left</td>
<td>49.4 ± 17.7</td>
<td>18.4 ± 10.0</td>
<td>18.1 ± 11.7</td>
<td>14.3 ± 9.8</td>
</tr>
<tr>
<td>Frontocentral right</td>
<td>50.9 ± 17.4</td>
<td>17.7 ± 9.5</td>
<td>17.1 ± 10.7</td>
<td>14.4 ± 9.4</td>
</tr>
<tr>
<td>Parieto-occipital left</td>
<td>41.9 ± 16.9</td>
<td>21.6 ± 11.3</td>
<td>27.7 ± 17.6</td>
<td>8.8 ± 7.0</td>
</tr>
<tr>
<td>Parieto-occipital right</td>
<td>40.5 ± 17.3</td>
<td>20.8 ± 10.7</td>
<td>29.4 ± 18.6</td>
<td>9.3 ± 7.2</td>
</tr>
</tbody>
</table>

* Frontocentral was defined as values of leads F3 to C3 (left) and F4 to C4 (right); parieto-occipital, as the average values of leads T5 to O1 and P3 to O1 (left), and of T6 to O2 and P4 to O2 (right). Relative values are defined as absolute value in 1 band/(delta + theta + alpha + beta), expressed as mean ± SD percentages. The frequency bands were set as follows: delta, 0.3 to 3.5 Hz; theta, 3.6 to 7.4 Hz; alpha, 7.5 to 12.5 Hz; and beta, 12.6 to 35.4 Hz.

We studied the relationship between EEG at the time of diagnosis and survival in consecutively referred patients with early AD. Low parieto-occipital beta power was the strongest predictor of mortality, while decrease in alpha power also independently contributed to this mortality risk, although to a lesser extent. The predictive power of the EEG for survival was not explained by differences in demographic, clinical, or CT features. Also, the higher percentage delta power in our patients as compared with that in some previous studies1,19,30 is probably related to the greater age of our study population than in these previous studies, since in healthy older subjects delta activity may increase with age.1 Indeed, delta activity appeared not to be a marker of severity, independent of the CAMDEX-N dementia severity marker used. In this study, we extended our earlier observations that, from all EEG bands, parieto-occipital beta values were the strongest predictor of cognitive and functional decline in patients with probable AD.6 This prognostic value was further specified by the observation that low values of beta on EEG were related to rapidly progressive decline.6

From a methodological viewpoint, our EEG study on survival in AD differs from previous studies in several aspects, including choice of study population, length of follow-up, inclusion of possible confounders, and approach for statistical analysis. In contrast to some reports,3,8,10 we studied consecutively referred patients for evaluation of memory complaints or (suspected) dementia, and these patients were part of a prospective follow-up study.15 None of our patients satisfied any of currently used clinical criteria for dementia with Lewy bodies,28 and alpha and beta power in our study were not different when compared in patients with and without extrapyramidal symptoms, or in those with and without delusions or hallucinations. Electroencephalographic studies in selected groups of patients with AD5 may limit the external validity to clinical practice. Further, in our study 51.5% of the patients died during follow-up, while in some previous studies these percentages varied from 12.5%3 to 27.4%.8 The shorter follow-up in these previous studies may limit the statistical power and may there-
fore explain differences in study results. In the study by Kaszniak et al., 10 45.7% of the patients died, but these were hospitalized patients with dementia. Not all previous reports use analysis of separate EEG bands, 8,10 while the notion that these bands have different regional correlates in the human brain 31,32 suggests the necessity of separate EEG band analysis. Our approach to use a wide selection of clinical and CT variables to identify factors, rather than the EEG alone, that also may account for the observed relationship between EEG and survival was not used in other studies. 3,8-10 Furthermore, we extended our analyses by identifying a subset of independent predictive EEG bands.

The predictive ability of the EEG for survival in patients with AD was noted by some authors. 3,9,10 but not by others. 8 Our results are in agreement with an earlier study by Kaszniak et al. 10 They examined hospitalized patients, probably more severely demented than patients in our population, with a follow-up period of 1 year and reported that 79% of survivors had either normal EEGs or mild diffuse slowing, contrasting with 13% of the deceased patients with similar EEG findings. 10 Interestingly, they found no differences between survivors and nonsurvivors in baseline demographic and severity of disease characteristics, or in degree of cerebral atrophy on CT. Our results are further supported by 2 other studies reporting that increase of slow activity on EEG is associated with increased risk of mortality. 3,9 In contrast to our observations, Lopez et al 10 found that mean frequency as pooled score from parasagittal derivations was not associated with survival in patients with AD. In this study, however, the HR for increased risk of mortality was in the expected direction. Since 27.4% of their patients died, compared with 50.5% in our study, with similar total patient numbers in both studies, their limited statistical power may render their study sensitive to a type II error. Indeed, age and sex were not significant predictors in the study by Lopez et al, whereas these are well-established predictors of survival. 33-36

Beta and alpha activity were recognized as independent predictors of survival in our study. These results suggest that beta and alpha activity have pathophysiological correlates in the brains of patients with AD and that these correlates are different for both EEG bands. Preclinical and clinical studies show that several brain structures intimately involved in the pathophysiology of AD are linked to beta activity, including the hippocampus, the cholinergic nucleus basalis, and layer II of the entorhinal cortex. 10 Even in patients with very mild AD, there is a marked loss of layer II entorhinal cortex neurons, and synaptic cell loss in the hippocampal formation is an early phenomenon in AD. 71 The observation by Williamson et al 32 that normal elderly subjects with cognitive decline had a marked reduction in beta activity, compared with those without cognitive decline, is intriguing in this context. This observation might have resulted from the incorporation of subjects with unrecognized AD in the sample. Reduction of beta activity in
patients with early AD may thus reflect very early neuropa-thological changes. Further, the predictive ability of decreased beta activity for survival in AD does not simply reflect dementia severity, cortical atrophy, or leuko-araiosis, as suggested by our findings. In analogy with Parkinson disease, where only substantial neuronal loss in the substantia nigra results in clinical impairment, a certain amount of neurons in hippocampus and ento-rhinal cortex may need to degenerate for demonstrable dementia symptoms to be present. The additional predic-tive ability for survival of decreased alpha activity may be explained by the finding that alpha is generated in corticocortical pathways.31

There may be certain methodological limitations to our study. Although we made strenuous efforts to examine the effect of factors that could explain the relationship between EEG values and survival, the possible confounding effect of both clinical and neuroimaging features cannot be excluded. Vascular risk factors and in-dicators of atherosclerosis, recently implicated in the pathogenesis of AD,43 may especially be associated with EEG abnormalities and they may also play a role in the prognosis. We examined leukoaraiosis on CT, but more sensitive assessment of white matter abnormalities and hippocampal atrophy is possible with magnetic reso-nance imaging. Further, we used presence of diseases associated with vascular risk, but no quantified measures of atherosclerosis were used. A recent study suggested that patients with AD homozygous for apolipoprotein E4 allele had selective decreases in functional connectivity, assessed with EEG coherence in the alpha frequency band, compared with those without or with only 1 apolipoprotein E4 allele.44 Although several studies did not find an association between apolipoprotein E genotype and survival in AD,45,46 another study reported that the presence of at least 1 apolipoprotein E4 allele reduced the risk of mortality in AD.37 These results suggest that the role of apolipoprotein E genotype, subclinical vascular disease, and AD progression in relation to EEG findings need further examination. Medication in our patients probably did not play a role, since exclusion of those with centrally active medication yielded similar results. Recent efforts were made to construct prediction algo-rithms based on clinical features, including age at onset, presence of extrapyramidal or psychotic symptoms, and level of cognitive function.46 Since we used these features as correction factors, our results suggest that the EEG should be used as an additional variable in future endeavors to construct a predictor index.

In conclusion, decreased beta and decreased alpha activity on EEG are predictors of survival in patients with early AD, independent of demographic, clinical, and CT features, including leukoaraiosis and cortical atrophy. These results suggest that the EEG should be included as an independent variable in survival models of AD. However, the use of the EEG for prediction of survival in indi-vidual patients in clinical practice remains to be de-termined.

Accepted for publication January 16, 1998.

Reprints: Jules J. Claus, MD, PhD, Department of Neu-rology, Academic Medical Center, University of Amster-dam, Meibergdreef 9, 1105 AZ Amsterdam, the Nether-lands (e-mail: j.j.claus@amc.uva.nl).

REFERENCES

1. Cohen LA, Danziger W, Storandt M. A longitudinal EEG study of mild senile demen-tia of Alzheimer type: changes at 1 year and at 2.5 years. Electroencepha-

2. Perilli M, Partanen JV, Soininen H, Riekkinen P.J. Quantitative assessment of oc-


6. Claus JJ, Kva VIH, Teunisse S, et al. Slowing on quantitative spectral EEG is a marker for rate of subsequent cognitive and functional decline in early Alzhei-

7. Kuskowski MA, Mortimer JA, Morley GK, Malone SM, Okaya AJ. Rate of cog-
nitive decline in Alzheimer’s disease is associated with EEG alpha power. Biol Psy-
chiatry. 1993;33:659-662.


troencephalography in Alzheimer patients: preliminary observations. Electroen-

10. Kasznik AW, Fox J, Gandell JL, Garron DC, Huckman MS, Ramsey RG. Predic-


12. Saletu B, Anderer P, Paulus E, et al. EEG brain mapping in diagnostic and therapeu-

13. Lopez OL, Brenner RP, Becker JT, Jungrics C, Rezek D, DeKosky ST. Electroen-
cephalographic correlates of periventricular white matter lesions in probable Alz-


17. Roth M, Huppert FA, Tym E, Mountjoy CG. CAMDEX, the Cambridge Examina-
tion for Mental Disorders of the Elderly. Cambridge, England: Cambridge Uni-

18. Teunisse S, Bollen AE, van Gool WA, Walstra GJM. Dementia and subnormal lev-
els of vitamin B12: effects of replacement therapy on severity of dementia. J Neu-
r. 1996;243:522-529.

19. John ER, Prichop LS, Fridman J, Easton P. Neuroimetrics:computer-assisted dif-


erogeneity of neocortical cerebral blood flow deficits in dementia of the Alzhei-

24. Jacoby RJ, Levy R, Dawson JM. Computed tomography in the elderly I: the nor-

25. Cleland D. Modelling Survival Data in Medical Research. London, England: Chap-
man & Hall; 1994.

The ARCHIVES is available by request to nonfederal physicians in the United States (30 states and Washington, DC) whose official American Medical Association masterfile record shows a primary specialty of neurology or child neurology in an office- or hospital-based practice as a staff physician, resident in training beyond the first year, or clinical fellow.

If you meet the above qualification criteria and are not currently receiving the ARCHIVES and would like to receive it each month, you must complete a free subscription request card. To receive a request card, please write to Kathryn Osten, American Medical Association, Circulation Processing Department, 515 N State St, Chicago, IL 60610 (FAX 312-464-5831). A subscription request card will be sent to you in response. If you are a resident or fellow, please include verification of your training program and a complete mailing address.