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EEG Markers of Future Cognitive Performance in the Elderly

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Abstract: This exploratory follow-up study investigated whether EEG parameters can predict future cognitive performance. Forty elderly subjects, ranging from cognitively unimpaired to those with Alzheimer disease underwent EEG registration at baseline and neuropsychological examination at both baseline and follow-up. We assessed relations between EEG measures and future cognitive performance (i.e., global cognition, memory, language, and executive functioning) controlling for age, follow-up time, and baseline cognitive performance. Regression models were constructed to predict performance on the Cambridge Cognitive Examination, a widely used tool within dementia screenings. Baseline EEG measures, i.e., increased theta activity (4–8 Hz) during eyes closed and less alpha reactivity (8–13 Hz) during eyes open and memory activation, indicated lower global cognitive, language (trend significant), and executive performance at follow-up. A regression model combining baseline cognitive and EEG measures provided the best prediction of future Cambridge Cognitive Examination performance (93%). EEG and cognitive measures alone predicted, respectively, 43% and 92% of variance. EEG and cognitive measures combined provided the best prediction of future cognitive performance. Although the “cognition only” model showed similar predictive power, the EEG provided significant additional value. The added value of EEG registration in the diagnostic work-up of dementia should be further assessed in larger samples.

Key Words: EEG, Normal aging, Mild cognitive impairment, Alzheimer disease, Cognitive decline, Longitudinal.

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The prospect of future neuroprotective therapies to slow down or halt Alzheimer disease (AD) underlines the importance of predicting cognitive decline in AD. Of the various possible tools to assess brain function, the EEG has the advantages of being noninvasive and cost-effective.

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Several EEG predictors of future cognitive decline in elderly subjects with various levels of cognitive functioning have been described, mostly obtained during a routine “eyes closed” condition. Pritchep et al. (2006) studied relations between baseline EEG parameters and future cognitive decline in elderly subjects with subjective memory complaints but with normal neuropsychological test results. The following baseline EEG characteristics proved to be associated with a decline on the Global Deterioration Scale (Reisberg et al., 1982) after 7 to 9 years: increased theta power, slowing of mean frequency, and changes in covariance during an eyes closed condition. Other EEG studies assessed progression from mild cognitive impairment (MCI) to AD (Huang et al., 2000; Jelic et al., 2000; Rossini et al., 2006). Those who progressed to AD showed more delta, theta and lower alpha power, lower beta power, slowing of mean frequency, and altered frontoparietal coherence in the baseline EEG than those who did not. Similar changes, i.e., higher theta power, less beta power, and lower peak frequency, were also associated with subsequent cognitive decline on the Cambridge Cognitive Examination (CAMCOG) (Roth et al., 1986) in mildly demented patients with AD (Claus et al., 1998).

The aforementioned studies focused on the eyes closed condition, routinely used in clinical EEG practice. However, other conditions might enhance the degree of abnormality in AD: memory activation has been found to do so in MCI (Hogan et al., 2003; Jiang, 2005; Missonnier, 2006; Pijnenburg et al., 2004; van der Hiele et al., 2007a). To our knowledge only one longitudinal study researched memory-related EEG power changes in progressed versus stable patients with MCI (Missonnier, 2006). In that study, theta event-related synchronization at baseline was significantly lower in those with progressed MCI.

The current exploratory study aimed to examine whether EEG parameters gathered during eyes closed, eyes open, and memory activation can provide markers of cognitive performance after an average time interval of 20 months. We included elderly subjects with various levels of cognitive functioning, i.e., cognitively unimpaired subjects as well as patients with MCI and AD. Their global cognitive performance was assessed, as were memory, language, and executive functions. Finally, we constructed regression models to predict subsequent performance on a widely used global cognitive scale within the clinical dementia screening, i.e., the CAMCOG (Roth et al., 1986).

METHODS

Baseline Assessment

The baseline assessment included 14 patients with probable AD (McKhann et al., 1984) and 20 with amnesic MCI (Petersen et al., 1999) who had been referred to the outpatient memory clinics of the Leiden University Medical Center, the Diaconessenhuis Hospital (Leiden) or the Leyenburg Hospital (The Hague). We included 24 control subjects without cognitive impairment who were recruited through an advertisement in a local newspaper.

All patients and controls underwent general medical, neurologic, neuropsychological, and brain MRI investigations as part of the standard diagnostic work-up of dementia. Patient histories were reviewed, and diagnoses reached in multidisciplinary consensus meetings. Within 3 months from standard diagnostic work-up, patients and controls participated in an additional EEG examination. Neuropsychological testing consisted of a standardized test battery including tests of global cognition, memory, language, and executive functioning. The CAMCOG (Roth et al., 1986), which incorporates the Mini Mental State Examination (Folstein et al., 1975), was used to assess global cognitive functioning. Memory function was tested with the Wechsler Memory Scale (WMS) (Wechsler, 1945). Language ability was assessed using the Boston Naming Test (BNT) (Kaplan et al., 1978). Tests of executive functioning included the Trail Making Test consisting of a simple (Trails-A) and a complex version (Trails-B) (Reitan, 1958).

Eligible subjects had to be free of psychotropic medication, aged 60 years or above, and without previous history of psychiatric or neurologic disorders or substance abuse. Moreover, they had no abnormalities on MRI other than an incidental small lacunar lesion (≤ 5 mm diameter) or white matter hyperintensities conforming with age or of a nonspecific nature.

Follow-up Assessment

We invited 14 patients with AD, 18 patients with MCI, and 22 control subjects to participate in the follow-up study. Beforehand, we excluded subjects with extremely low EEG voltage ($< 10 \mu\text{V}$) on most leads (two patients with MCI) and drowsiness (two controls) during baseline EEG registration. Thirteen subjects did not participate for various reasons: one patient with AD and two patients with MCI had died, four patients with AD and four patients with MCI refused to participate because they were either too ill or not motivated, one patient with AD could not be traced, and one control subject decided not to participate because of medical reasons. Eventually, 8 patients with AD, 12 patients with MCI, and 21 control subjects participated in the follow-up study.

Follow-up took place after a mean interval of 20 months (range, 15–25) and consisted of a short medical and neurologic check-up, a standardized questionnaire concerning the medical history and cognitive complaints, and a neuropsychological examination including the CAMCOG, WMS, BNT, and Trail Making Test. In a consensus meeting, patient histories and results were reviewed and diagnoses were reached. After medical check-up, one patient with MCI was excluded because of possible brain damage after a fall.

At follow-up, 3 of 11 patients with MCI (27%) were diagnosed with AD. None of the patients with MCI returned to a normal level of memory functioning.

The interval to follow-up did not differ between patients with AD (mean, 20 months; range, 15–25), patients with MCI (mean, 21 months; range, 17–25), and controls (mean, 20 months, range, 17–25). For each cognitive test, we calculated annual change in cognitive performance: $((\text{follow-up score} - \text{baseline score}) / \text{number of months}) \times 12$. A negative value indicated a decrease in performance for the CAMCOG, WMS, and BNT tests, but the opposite applied for the Trail Making Test, as that is described as the time needed to perform the test. Not all subjects underwent all tests at follow-up, except for the CAMCOG test. Seventeen controls, 9 patients with MCI, and 6 patients with AD completed the WMS; 16 controls, 9 patients with MCI, and 5 patients with AD completed the BNT; 17 controls, 9 patients with MCI, and 5 patients with AD completed the Trails-A test. Because Trails-B could not be completed by most patients with AD, this test was excluded from further data analysis. The reason for these divergent subject numbers is that the original research protocol included only the CAMCOG test at follow-up. Furthermore, not all subjects were able or motivated to undergo all additional tests.

The study was approved by the local Medical Ethical Committee. All subjects or their caregivers gave informed consent.

EEG Recording and Analysis

At baseline, EEGs were recorded using a Nihon Kohden 2110 apparatus with 21 Ag/AgCl electrodes placed according to the 10/20 system. Electrocardiogram, respiration, and horizontal eye movement leads were recorded to facilitate artifact recognition. The EEG was band-pass filtered from 0.16 to 70 Hz for display and analysis, but recorded unfiltered. The sample frequency was 200 Hz and the AD precision 12 bits. The average reference montage was used, with the exclusion of electrodes Fp1, Fp2, A1, and A2.

During recording subjects sat slightly reclined in a comfortable chair, approximately 1.5 m in front of a computer screen. The light in the room was dimmed. Vigilance was monitored constantly by visual inspection of the EEG and video registration. An auditory stimulus was given in case of drowsiness. The EEG of each subject was registered during two conventional rest conditions and memory activation. The first rest condition comprised 10 minutes of being awake with eyes closed and the second a 3-minute period with eyes open. Three artifact-free samples, 4 to 8 seconds in length, were selected visually for further analysis. We used this sample length to enable comparison with EEG samples registered during memory activation, which necessitated a fairly short duration. The memory activation condition concerned picture memory. In a previous study, this particular task was found to be sensitive to EEG abnormalities in patients with MCI (van der Hiele et al., 2007a). During memory activation, 10 pictures of common objects were shown on a computer screen. Each was presented for 2 seconds, and subjects were asked to name the objects aloud and memorize them. After the last picture, subjects had to close their eyes and memorize the

objects for 15 seconds (“memorization period”). They were then asked to open their eyes and name as many objects as they could. This task was performed three times using the same 10 pictures shown in the same order. From each of the three memorization periods, one EEG sample, 4 to 8 seconds in length, was selected for further analysis.

The selection of EEG samples free of eye movements, blinks, and muscle activity was performed blinded for diagnosis by the first author and supervised by an experienced clinical neurophysiologist (A.V.). Frequency analysis was performed using a Fast Fourier Transformation.

For each sample, absolute power was calculated in the theta (4–8 Hz) and alpha (8–13 Hz) bands and averaged over all electrode positions and over the three samples. Lower and higher frequencies were not used because these are easily contaminated with blinks, eye movements, and electromyographic activity, especially in patients with dementia. This resulted in six power values: two for each of the three conditions (i.e., eyes closed, eyes open, and memory activation). Using these power values we calculated the following three parameters: (1) theta relative power during eyes closed, i.e., absolute theta power as a percentage of total power in the 4 to 13 Hz band, (2) alpha reactivity during eyes open, defined as the percentage of decrease in absolute alpha power as compared with the eyes closed condition, and (3) alpha reactivity during memory activation, defined in a similar manner. We chose these parameters from a clinical viewpoint, i.e., easily available, simple EEG measures with known sensitivity to dementia. For similar reasons we chose to avoid delta and beta or higher frequencies, because these may be contaminated by various artifact sources. An alternative would be to filter or detect and counteract such contamination, but the efficacy of such procedures is difficult to determine. A recent study using induced paralysis showed clear effects of EMG activity on high-frequency EEG bands (Whitham et al., 2007).

The choice of global EEG parameters was based on previous research showing global EEG changes in both MCI and AD (Jiang, 2005; Pijnenburg et al., 2004; Stam et al., 2003; van der Hiele et al., 2007a, b). Finally, we chose to use relative parameters because these provide an intraindividual measure and decrease interindividual differences.

Statistical Analysis

SPSS for Windows (release 14.0.1; SPSS Inc., Cary, NC) was used for data analysis. Group differences in sex, age, and years of education were assessed using parametric and nonparametric tests where appropriate. Because the “homogeneity of variance” assumption was violated for several cognitive variables and group sizes were unequal, we used nonparametric tests to compare these outcomes between groups. When parametric tests were possible, we used univariate analysis of variance (ANOVA) with age as covariate, except for the WMS Memory Quotient, which is already age-corrected.

Univariate ANOVA with age as covariate and *post-hoc* Bonferroni tests were used to compare EEG parameters between groups. We then computed partial correlation coefficients, corrected for age, follow-up time, and baseline cog-

nitive performance, to assess independent relations between EEG parameters and follow-up cognitive performance. Finally, we created linear regression models for follow-up CAMCOG score using baseline EEG, cognitive, and demographic variables both separately and combined. The level of significance in this exploratory study was set at $P \leq 0.05$. $P > 0.05$ and ≤ 0.10 were considered trend significant.

RESULTS

Baseline Demographics and Cognitive Performance

Data are shown in Table 1. Sex and years of education did not differ significantly between groups. However, patients with AD were significantly older than controls ($P = 0.02$).

Cambridge Cognitive Examination, Mini Mental State Examination, and Trails-A scores differed significantly between groups (Kruskal-Wallis χ^2 30.5, 23.5, and 16.6, respectively; $P < 0.001$). Using Mann-Whitney *post-hoc* tests (with $P < 0.0167$ considered significant) we found that patients with AD scored lower than controls on all aforementioned tests ($P < 0.001$). Patients with MCI scored lower than controls on the CAMCOG and Mini Mental State Examination ($P < 0.001$). Furthermore, patients with AD performed significantly worse than patients with MCI on Trails-A ($P = 0.009$).

Using ANOVA we found that the WMS Memory Quotient differed significantly between groups ($F(2,37) =$

TABLE 1. Baseline Clinical Characteristics

	Controls	MCI	AD
Male/female	7/14	4/7	3/5
Age (years)	70 (5)	73 (5)	77 (9)*
Education (years)	11 (3)	9 (3)	10 (4)
CAMCOG (/106)	95 (3)	80 (5)†	70 (10)‡
MMSE (/30)	28 (1)	24 (2)†	22 (3)‡
WMS (MQ)	120 (10)	90 (7)†	88 (11)‡
BNT (/30)	25 (3)	23 (3)	20 (6)*
Trails-A (seconds) ^a	43 (12)	55 (15)	129 (71)†‡
Annual change in CAMCOG ^b	0.5 (2.2)	-1.3 (2.4)	-8.9 (3.9)†§
Annual change in WMS ^b	5.4 (6.0)	-1.2 (3.3)*	-6.1 (4.3)†
Annual change in BNT ^b	0.5 (1.1)	-1.0 (2.2)	-0.9 (1.9)
Annual change in Trails-A ^c	-1.2 (7.7)	2.5 (9.6)	30.0 (51.8)
Theta relative power (%) (eyes closed)	25 (11)	27 (13)	50 (15)†‡
Alpha reactivity (%) (eyes open)	68 (24)	54 (21)	33 (27)*
Alpha reactivity (%) (picture memory)	37 (29)	16 (36)	-10 (25)†

Values are means with SD in parentheses. *Differs from controls ($P \leq 0.05$); †Differs from controls ($P \leq 0.001$); ‡Differs from patients with MCI ($P \leq 0.01$); §Differs from patients with MCI ($P \leq 0.001$). ^aHigher scores indicate worse performance; ^bNegative scores indicate a decrease in subsequent performance; ^cPositive scores indicate a decrease in subsequent performance. CAMCOG, Cambridge Cognitive Examination; MMSE, Mini Mental State Examination; WMS, Wechsler Memory Scale; BNT, Boston Naming Test.

49.3, $P < 0.001$) in that patients with AD and patients with MCI scored significantly lower than controls ($P < 0.001$). Scores on the BNT also differed significantly between groups (ANOVA with age as covariate, $F(2,35) = 4.2$, $P = 0.02$; the covariate age showed no significant difference). Bonferroni *post-hoc* tests indicated that patients with AD scored significantly lower than controls ($P = 0.02$).

Baseline EEG

Theta relative power during eyes closed differed significantly between diagnostic groups (ANOVA with age as covariate, $F(2,36) = 9.1$, $P = 0.001$; the covariate age showed no significant difference). Bonferroni *post-hoc* tests indicated that theta relative power was increased in patients with AD as compared with controls ($P = 0.001$) and patients with MCI ($P = 0.002$). Because theta relative power depends on both theta and alpha powers (calculated as absolute power in the 4–8 Hz band as a percentage of total power in the 4–13 Hz band), we also tested absolute powers. Absolute theta power (log-transformed) differed between groups at trend significance ($F(2,36) = 3.2$, $P = 0.054$; the covariate age showed no significant difference). *Post-hoc* tests revealed increased theta power in patients with AD compared with patients with MCI at trend significance ($P = 0.07$). Absolute alpha power did not differ between groups.

Alpha reactivity during eyes open also differed significantly between groups ($F(2,36) = 3.8$, $P = 0.032$; no effect for the covariate age) in that reactivity was decreased in patients with AD as compared with controls ($P = 0.029$).

Finally, alpha reactivity during memory activation differed significantly between groups ($F(2,35) = 8.1$, $P = 0.001$; no effect for the covariate age) in that reactivity was decreased in patients with AD as compared with controls ($P = 0.001$).

Follow-up Cognitive Performance

Table 1 shows that patients with AD and patients with MCI deteriorated with time on all cognitive tests, whereas control subjects improved with time on all cognitive tests. The latter is probably a result of a learning effect.

The mean annual deterioration in CAMCOG scores differed significantly between groups (Kruskal-Wallis $\chi^2 = 19.0$, $P < 0.001$). Using Mann-Whitney *post-hoc* tests (with $P < 0.0167$ considered significant) we found that patients with AD deteriorated faster than both controls ($P < 0.001$) and patients with MCI ($P = 0.001$). Using ANOVA we found that the mean annual deterioration in WMS Memory Quotient differed significantly between groups ($F(2,29) = 12.7$, $P < 0.001$) in that patients with AD ($P < 0.001$) and patients with MCI ($P = 0.012$) deteriorated faster than controls. The mean annual deterioration in BNT and Trails-A scores did not differ between groups.

Three of 11 patients with MCI (27%) converted to AD at follow-up. In the baseline EEG, these MCI “converters” displayed a higher percentage of theta relative power than “stable” patients with MCI [31% (SD = 10) versus 25% (SD = 14) in stable MCI], a lower percentage of alpha reactivity during eyes open [31% (SD = 7) versus 64% (SD = 17) in stable MCI], and a lower percentage of alpha reactivity

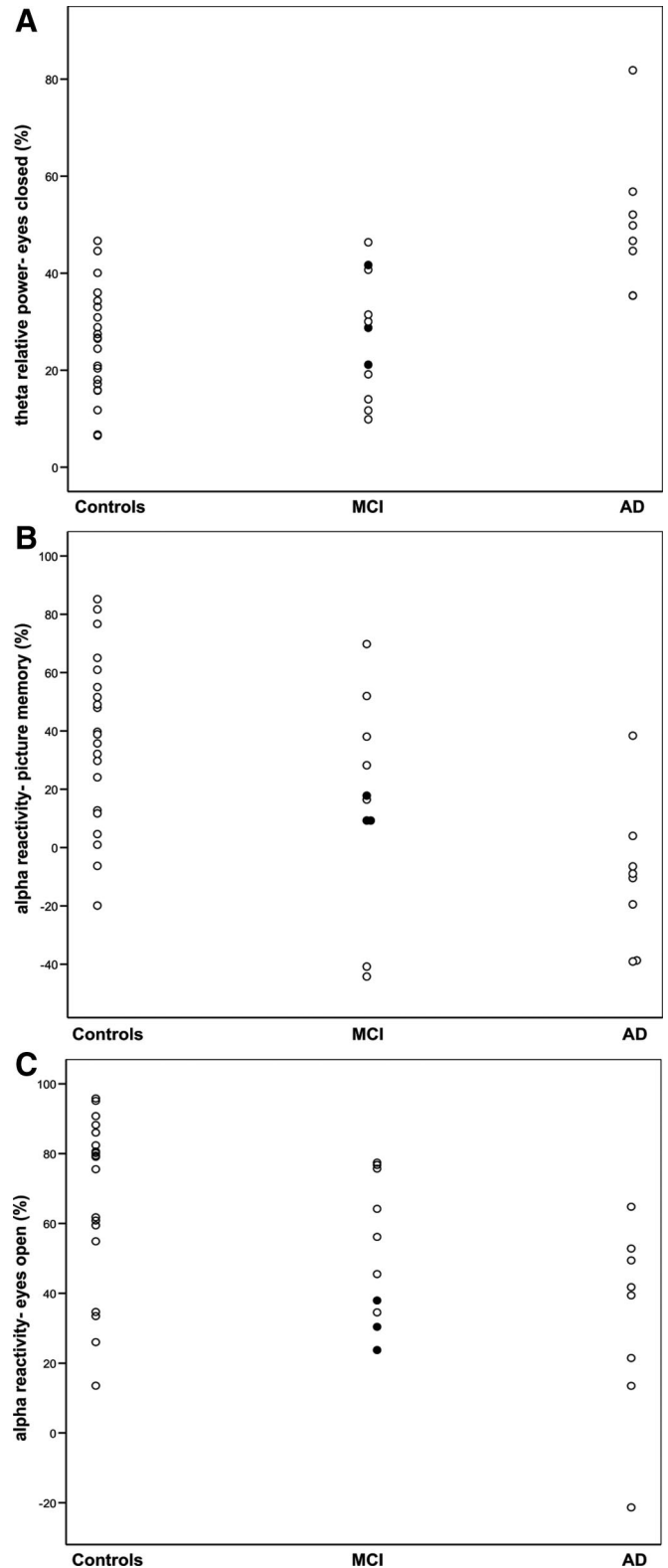


FIGURE 1. Scatterplots of individual EEG values per diagnostic group. **A**, Theta relative power during eyes closed. **B**, Alpha reactivity during picture memory. **C**, Alpha reactivity during eyes open. The black dots indicate those patients with MCI who converted to AD at follow-up examination.

TABLE 2. Correlations Between Follow-up Cognitive Test Scores and Baseline EEG Parameters

	Theta Relative Power (eyes closed)	Alpha Reactivity (eyes open)	Alpha Reactivity (memory activation)
Follow-up CAMCOG	-0.42*	0.22	0.32†
Follow-up WMS	-0.05	0.01	0.30
Follow-up BNT	-0.11	0.38†	0.17
Follow-up Trails-A	0.44‡	-0.33†	-0.16

Partial correlation coefficients controlling for age, follow-up time, and baseline cognitive performance. † $P \leq 0.10$; ‡ $P \leq 0.05$; * $P \leq 0.01$. Significant correlations are printed in bold. CAMCOG, Cambridge Cognitive Examination; WMS, Wechsler Memory Scale; BNT, Boston Naming Test.

during memory activation [12% (SD = 5) versus 17% (SD = 44) in stable MCI]. In view of the small group size, statistical tests were not performed. In Fig. 1, scatterplots display individual EEG values for controls, patients with MCI, and patients with AD. Mild cognitive impairment converters are identified separately; their values for theta relative power (Fig. 1A) do not show systematic differences from the other patients with MCI, but are at the low end of the distribution for alpha reactivity during eyes open (Fig. 1B) and memory activation (Fig. 1C).

EEG Relations With Follow-up Cognitive Performance

We performed correlation analysis with age, baseline cognitive performance, and follow-up time as covariates to assess relations between follow-up cognitive performance and EEG variables (Table 2). Generally speaking, higher theta power and less alpha reactivity in the baseline EEG indicated lower cognitive scores at follow-up. For higher theta relative power during eyes closed, the changes concerned lower follow-up performance on the CAMCOG ($r = -0.42$, $P = 0.01$) and Trails-A ($r = 0.44$, $P = 0.02$) tests. At trend significance, less alpha reactivity during eyes open

indicated lower follow-up scores on the BNT ($r = 0.38$, $P = 0.053$) and lower scores on Trails-A ($r = -0.33$, $P = 0.08$). Finally, less alpha reactivity during memory activation indicated lower subsequent performance on the CAMCOG at trend significance ($r = 0.32$, $P = 0.054$). Within the control group we observed similar relations between higher theta relative power during eyes closed and lower subsequent performance on Trails-A ($r = 0.60$, $P = 0.023$). Because the number of subjects was limited, we did not perform correlation analysis within the AD and MCI groups.

Regression Models of Follow-up Cambridge Cognitive Examination Score

We created regression models of follow-up CAMCOG score using baseline EEG, cognitive, and demographic variables both separately and combined. For the combined model we used stepwise regression analysis to help select the most useful predictors while removing redundant ones. The model combining baseline cognition (i.e., CAMCOG and Trails-A) and EEG (i.e., theta relative power) provided the best prediction of follow-up CAMCOG score (93%), directly followed by the model with only cognitive variables (92%), then the model with only EEG variables (43%), and finally the model with only demographic data (30%) (Table 3). In the combined model, theta relative power provided significant additional power to the model as compared with a model including only baseline CAMCOG and Trails-A score (F change (1,36) = 7.2; $P = 0.01$).

DISCUSSION

The main findings of this follow-up study in the elderly are twofold. First, baseline EEG measures were related to follow-up performance on tests of global cognition, language, and executive functions. Second, a combination of baseline EEG and cognitive measures provided the best prediction of global cognitive performance at follow-up.

TABLE 3. Regression Models of Follow-up Cambridge Cognitive Examination Score

	Combined Model	Cognition Model	EEG Model	Demographics Model
Explained variance (R^2)	93%	92%	43%	30%
Age				-1.1 (0.4)*
Education				2.1 (0.8)†
Global cognition (CAMCOG)	1.2 (0.1)‡	1.3 (0.2)‡		
Memory (WMS)		-0.09 (0.08)		
Language (BNT)		0.4 (0.3)		
Executive functioning (Trails-A ^a)	-11.6 (5.1)*	-11.5 (5.3)*		
EEG theta relative power (eyes closed)	-15.8 (6.2)*		-52.2 (23.5)*	
EEG alpha reactivity (eyes open)			7.5 (13.2)	
EEG alpha reactivity (picture memory)			11.4 (7.5)	

Values in the table are unstandardized regression coefficients (standard error). It should be noted that the variable "time to follow-up" did not contribute significantly to any of the regression models, and was therefore not further considered. Empty cells indicate those variables with a nonsignificant contribution to the (stepwise) combined model, or those variables not included in the cognition, EEG, or demographics models. * $P \leq 0.05$; † $P \leq 0.01$; ‡ $P \leq 0.001$; ^aLog-transformed values were used. CAMCOG, Cambridge Cognitive Examination; WMS, Wechsler Memory Scale; BNT, Boston Naming Test.

EEG Relations With Follow-up Cognitive Performance

In general, we found that slowing and decreased reactivity of the baseline EEG indicated worse follow-up performance on tests of global cognition, language (at trend significance), and executive functions. This relation was found independent of baseline cognitive performance, age, and time to follow-up. Interestingly, the EEG measures obtained during eyes closed and eyes open complemented each other as each measure was related to follow-up performance in a specific cognitive domain. Higher theta activity in the baseline eyes closed EEG indicated decreased follow-up performance on a global cognitive test (i.e., CAMCOG) and decreased speed on an executive test (i.e., Trails-A), whereas less alpha reactivity in the “eyes open” EEG indicated worse subsequent performance on a language task (i.e., BNT) at trend significance. Unexpectedly, the EEG during memory activation did not show additional relations with follow-up performance in any specific cognitive domain. Less alpha reactivity during memory activation did, however, indicate worse follow-up global cognitive performance on the CAMCOG, albeit at trend significance. Because the use of memory activation during EEG registration revealed abnormalities in patients with MCI in an earlier study (van der Hiele et al., 2007a), we had expected to find relations with memory decline. By including larger patient samples or by looking into specific rather than general memory functions, such relations might be revealed. We therefore continue to encourage further study into the combination of rest and activation conditions during the EEG and their relations to cognitive decline, specifically in patients with MCI.

Relations between theta activity in the rest eyes closed EEG and subsequent cognitive decline have been described previously. These EEG studies used follow-up performance on tests of global cognition, i.e., CAMCOG and GDS, or conversion to AD as endpoints. Consistent with the current study, increased theta activity was linked with subsequent cognitive decline in elderly with subjective memory complaints, patients with MCI and patients with AD (Claus et al., 1998; Huang et al., 2000; Jelic et al., 2000; Pritchep et al., 2006; Rossini et al., 2006). A new finding in the current study is that increased theta activity was also linked with subsequent slowing on Trails-A. This observation warrants further research, especially because executive dysfunctioning has previously been linked with functional disability in older adults, which is one of the hallmarks of dementia (Cahn-Weiner, 2002).

It is well known that alpha reactivity or suppression during eye opening decreases in dementia. The suppression of alpha activity is a response to visual stimulation, but this does not mean that alpha activity or reactivity is exclusively related to visual information. In cross-sectional studies, oscillations in the alpha band have been linked to IQ, memory, and cognition in general (Klimesch, 1999). In a study of cognitive decline in AD it was additionally described that subjects with a deteriorating EEG, including decreased alpha activity, showed deterioration over time on a confrontation naming task similar to the BNT (Helkala et al., 1991). These

findings provide support for the observed relations between EEG alpha reactivity and subsequent cognitive performance. However, it should be kept in mind that it is unlikely that the global EEG variables used in this study provide a direct reflection of specific cognitive processes. Rather, both the EEG and cognitive measures reflect neurodegenerative processes occurring in dementia and its preclinical stages.

Multidisciplinary Approach

In clinical practice, the CAMCOG is a widely used diagnostic instrument for dementia. Its major advantage is the assessment of multiple cognitive domains. We were, therefore, particularly interested in constructing regression models for subsequent performance on this test, and included baseline EEG, cognitive, and demographic variables in regression models both separately and combined. The best model included a combination of baseline EEG and cognitive measures (i.e., baseline theta activity and baseline CAMCOG and Trails-A scores). With this model, 93% of variance in follow-up CAMCOG performance could be predicted. These results might be of clinical interest and should be validated in larger samples. It should be kept in mind, however, that baseline theta relative power did not add that much to the prediction when baseline cognitive measures were already included in the model. Nevertheless, the EEG effect was significant and might become more prevalent in larger samples. It should also be kept in mind that using the CAMCOG at baseline to predict later cognitive performance using the same test almost inevitably results in a strong relationship. It is, therefore, not surprising that its effect is stronger than that of the EEG, which reflects entirely different aspects of cerebral function. Our finding that an EEG variable had any significant effect to add at all should be seen in this light, and speaks in favor of including the EEG in future studies aimed at predicting conversion to AD within a larger sample of patients with MCI.

Future research might also include structural MRI measures in the predictive model. In a previous cross-sectional study by our research group, EEG and MRI measures were each associated with different aspects of cognitive functioning and complemented each other in their relations to psychomotor speed on the Trail Making Test (van der Hiele et al., 2007b).

Advantages and Disadvantages

The application of strict inclusion and exclusion criteria enabled us to restrict the influence of other neurologic and psychiatric disorders or medication on cognitive status. Unfortunately, this also resulted in a limited sample size. In future studies, cooperation with several other memory clinics might help increase sample size. Our follow-up extended over a rather limited time period of 20 months. Larger periods are unfortunately difficult to realize in research with elderly patients.

Concluding Remarks

Baseline EEG measures were moderately associated with follow-up performance on tests of global cognition, language, and executive functions. In the prediction of global cognitive performance, we found that a combination of EEG

and cognitive variables was best. However, a model including only cognitive variables was almost as good in explaining follow-up cognitive performance. This raises the question whether it is worthwhile to include EEG variables when aiming to predict cognitive decline. EEG variables alone provided limited predictive value. However, the amount of slow EEG activity did add to the prediction of future cognitive impairment among the obviously associated cognitive variables, and seems to reflect neurodegenerative processes just as cognitive variables do. We believe that the potential value of EEG variables in the diagnostic work-up of dementia should be further studied in larger samples, particularly in patients with MCI who are at higher risk of subsequent dementia. Eventually, it can be envisioned that the EEG is used in combination with neuropsychological tests and neuroimaging techniques such as (f)MRI, single photon emission computed tomography, or positron emission tomography (Masdeu, 2005; Wolf et al., 2003) to construct a better model of future cognitive performance and AD.

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