

A 5-Year Longitudinal Study of the Mini-Mental State Examination in Normal Aging

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The Mini-Mental State Examination (MMSE) measures global cognitive performance and is often used as a screening test for dementia. This paper presents a 5-year longitudinal study of the MMSE score in a sample of 2,537 non-demented French community residents aged 65 years and older who were participants in the Paquid Study in 1988–1992. Subjects were evaluated at the baseline visit (T0) and 1 year (T1), 3 years (T3), and 5 years (T5) later. Analyses performed with a random effects linear model showed that the score rose between T0 and T1 (by 0.60 points for subjects aged 65 years at T0 to 0.83 points for subjects aged 85 years at T0), then it decreased very slightly between T1 and T5 (by 0.02 points for subjects aged 65 years to 0.57 points for subjects aged 85 years). The improvement during the first year, which was larger for less educated subjects, may be explained by the stress due to the test situation at T0 or by a learning effect at T1. The decline during the last 4 years was more pronounced for older and less well educated subjects. The cross-sectional measure of age effect was larger than the longitudinal measure of time effect. This difference may be explained by a cohort effect or by a practice effect induced by repetition of the test. The authors conclude that the MMSE score declines very slightly in non-demented subjects, thus suggesting that the cognitive processes involved are spared by the aging process. These results may have implications for dementia screening. *Am J Epidemiol* 1997;145:498–506.

aging; cognition; cohort studies; longitudinal studies; Mini-Mental State Examination; missing data

The Mini-Mental State Examination (MMSE) (1) is the most widely used psychometric test to measure cognitive performance (2). The MMSE has been well studied (2, 3) and validated in different populations as a screening test for dementia (4). It provides a brief and objective measure of global cognitive functioning. The MMSE score has been found to be associated with educational level (5) and principal lifetime occupation (6), and it is strongly correlated with age. However, these results are based on cross-sectional studies. Such studies do not make it possible to distinguish between the aging effect and the cohort effect, which may be induced, for instance, by inter-cohort differences in educational and socioeconomic status. Longitudinal studies are better adapted to investigate aging effect and cohort effect, although the relation may be blurred in these studies by test-retest effect.

Longitudinal studies of MMSE have generally been planned to evaluate the progression of cognitive im-

pairment in demented subjects, and are based on the follow-up of small samples during a short period of time (1 or 2 years). For Alzheimer's disease patients, these studies report that the MMSE score significantly declines with time, with an annual change evaluated between 1.8 and 4.2 points (7, 8); however, for non-demented subjects, the course of cognitive change with time is not clear. Recently, Izaks et al (9) gave results of a 3-year follow-up of 134 community residents aged 85 years and over including demented and non-demented subjects. They found a median decline of the MMSE score of four points but their subjects were very old, and initially cognitively impaired subjects were oversampled.

However, cognitive impairment is a frequent symptom in the elderly even in the non-demented population. Cross-sectional studies show that a low MMSE score is a major correlate of dependency as assessed by scales such as the Instrumental Activity of Daily Living, Activities of Daily Living, the Rosow and Breslau scale, or the mobility scale (10). Follow-up studies have also shown that low MMSE score is an independent predictor of dependency (11) and mortality (12). In view of the consequences of cognitive impairment on quality of life, functional disability, and

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mortality, the study of the evolution of cognitive functioning in the non-demented elderly deserves more attention. Moreover, comparison of the progression of cognitive performances in demented and non-demented subjects may give clues for the diagnosis and understanding of Alzheimer's disease and other dementias. The objective of this study was to describe the course of the MMSE score during a 5-year period in a large sample of non-demented elderly subjects, and to examine whether sociodemographic characteristics associated with low score in cross-sectional studies are also associated with the rate of decline.

MATERIALS AND METHODS

Sample

The Paquid research program is a prospective cohort study of normal and pathological cerebral aging. The target population consisted of men and women aged 65 years and older who lived at home at the beginning of the study in two administrative areas of southwestern France (Gironde and Dordogne). This report is based on the follow-up of the sample randomly selected from the electoral rolls of Gironde by a three-step procedure stratified on age, sex, and size of the urban unit. Among 4,050 subjects initially contacted, 2,792 (68.9 percent) agreed to participate in the study. Nonresponders did not differ from responders for age, sex, and educational level. The methodology of the Paquid Study has been detailed elsewhere (13).

Data collection

Subjects who agreed to participate were seen by a psychologist especially trained for home interviews. At the baseline visit, the psychologist collected data on sociodemographic characteristics, health status, and social environment, and evaluated the cognitive level of the participants by a series of psychometric tests including the MMSE (1). The MMSE is a measure of global mental status that consists of 20 questions about orientation to time and place, simple arithmetic (serial subtractions), registration and recall of three objects, simple language tasks, and visuocstructional abilities. The total score ranges from 0 to a maximum score of 30 when all the responses are correct.

After the psychometric evaluation, the psychologist filled in the criteria for dementia from the *Diagnostic and Statistical Manual of Mental Disorders*, third revision (DSM-III-R) (14). Subjects who met these criteria were seen by a neurologist who confirmed the diagnosis of dementia and specified the etiology.

Subjects who were still alive and agreed to participate in the follow-up were reexamined by a psychol-

ogist 1 year, 3 years, and 5 years after the baseline visit. At each visit, cognitive level was evaluated by the MMSE and the same two-step procedure was applied for the diagnosis of dementia. Because our objective was to study the evolution of cognitive level in non-demented elderly subjects, we excluded from the present study all subjects who were diagnosed as demented at any of the four examinations (218 subjects).

Statistical analysis

Model for longitudinal data. Linear regression models for Gaussian longitudinal data are well developed (15, 16). Analyses were performed using a random effects linear regression model. The intra-subject correlation was modeled by a subject-specific random intercept and a subject-specific random slope with an arbitrary covariance matrix. Parameters were estimated by the maximum likelihood method using program 5V of the BMDP statistical software (BMDP Statistical Software, Inc., Los Angeles, California).

To try to characterize the "aging effect" and the "cohort effect," we included in all models the time since the baseline visit, which was denoted by time and took the values 0, 1, 3, or 5, and the age of the subject at the baseline visit denoted by *age*. Differential evolution of subjects according to the baseline age was taken into account by an interaction term *age* × *time*. Other explanatory variables studied were sex and educational level in five classes: no education, did not graduate from primary school, graduated from primary school, high school level, and university level. For all covariates, we studied the association with the mean MMSE and with the slope. The model may be written as follows:

$$Y_{it} = X_{it}^T \beta + \gamma_{1i} + t\gamma_{2i} + \epsilon_{it},$$

where X_{it} is the vector of covariates for subject i at time t including *time* and all interactions with *time*, β is a vector of fixed effects, γ_{1i} and γ_{2i} are the random intercept and random slope, and ϵ_{it} is the intrasubject error with variance σ^2 .

The distribution of MMSE scores was not normal, so we analyzed the square root of the number of errors,

$$Y_{it} = \sqrt{(30 - \text{MMSE}_{it})}.$$

Using this transformed variable, graphical examination of residuals indicated that the hypotheses of normality and homoscedasticity were acceptable. To facilitate the interpretation of the results, we computed the expectation and the variance of the MMSE score using estimated coefficients. Because the transforma-

tion is not linear, the following formula must be used:

$$E\{\text{MMSE}_{ii} = 30 - E(Y_{ii}^2) = 30 - \{E(Y_{ii})\}^2 - \text{Var}(Y_{ii}). \quad (1)$$

$$\text{Var}\{\text{MMSE}_{ii}\} = \text{Var}(Y_{ii}^2) = 2\{\text{Var}(Y_{ii})\}^2 + 4\text{Var}(Y_{ii})E\{Y_{ii}\}^2, \quad (2)$$

where $E(Y_{ii})$ is estimated by $X_{ii}^T \hat{\beta}$ and $\text{Var}(Y_{ii})$ is estimated by the sum of $\hat{\sigma}^2$ and of the t th diagonal element of $Z\hat{\text{Var}}(\gamma)Z^T$, with

$$Z^T = \begin{bmatrix} 1111 \\ 0135 \end{bmatrix}.$$

With our data, the estimated value of the correction factor $\text{Var}(Y_{ii})$ was about 0.6 points, and thus it can not be neglected in equation 1. Because the exact calculation of the variance of the estimate of MMSE expectation was very complicated, the confidence interval of this estimate was approximated by calculating the boundaries of the confidence intervals of the transformed variable Y and then transforming them back and subtracting the correction factor $\hat{\text{Var}}(Y_{ii})$. Thus, the variance of the estimate of the correction factor $\hat{\text{Var}}(Y_{ii})$ was neglected.

Missing data. At each visit, a part of the sample did not complete the MMSE. The major causes of nonresponse were death, refusal to take the follow-up interview, or refusal to complete the MMSE. So, in our study, missing data include both dropouts and intermittent nonresponses.

Excluding from the sample the subjects with intermittent nonresponses, we studied the probability of dropout according to age, sex, educational level, and previous MMSE score. We performed a discrete survival time analysis where the failure time was the time of dropout by using a logistic regression model (17). If we denote p_{it} , the probability that subject i drops out at time t , the model can be written:

$$\text{logit}\{p_{it}\} = \alpha + X_{it}^T \beta,$$

where X_{it} is the vector of covariates for subject i at time t including the previous observed MMSE score and indicator variables for the time of dropout t . Conditional on the previous observed MMSE score and other covariates, repeated observations on a subject are assumed to be independent.

This analysis showed that the probability of dropout depends on the previous observed MMSE score. In such a case, maximum likelihood estimators of the linear model ignoring the missing data remains unbiased if the mechanism leading to nonresponses does

not depend on the missing values of the outcome variable and does not depend on the slope (18). Adjusting on the covariates associated with dropout, we assumed that these hypotheses were verified and we used the maximum likelihood method ignoring the missing data.

RESULTS

Study of the missing data pattern

Among our sample of non-demented subjects, 2,537 subjects (98.6 percent) completed the MMSE at least once, and they form the basis of this report. Among them, 563 (22.2 percent), 478 (18.8 percent), 463 (18.3 percent), and 1,033 subjects (40.7 percent) completed the MMSE at one, two, three, and four visits, respectively; 497 participants died during the follow-up. Table 1 gives the proportions of missing data patterns in the sample.

At the baseline visit, the mean age of the participants was 74.4 years (standard error (SE) = 6.8; range 65–101 years), 59 percent were women, 3.9 percent had no education, 27.3 percent did not graduate from primary school, 33.4 percent did graduate from primary school, 29.6 percent had a high school level education, and 5.8 percent had a university level education. The mean baseline MMSE score was 26.1 (SE = 3.1) and 20.2 percent of the subjects had a baseline MMSE score smaller than 24 points.

We performed a logistic regression analysis to study correlates of nonresponse using the subsample of subjects without intermittent nonresponses (2,107 subjects, the four first rows of table 1). The results in table 2 show that the probability of dropout was smaller at T3 and T5 than at T1, as suggested by table 1. According to the model, the odds ratio for the probability of dropout at T5 versus T1 and at T3 versus T1, respectively, were estimated to be 0.70 ($1.057^{75} \times$

TABLE 1. Patterns of nonresponse to the Mini-Mental State Examination: the Paquid Study, France, 1988–1992

Pattern* (T0, T1, T3, T5)†	No.	%
(1, 1, 1, 1)	1,033	40.7
(1, 1, 1, 0)	218	8.6
(1, 1, 0, 0)	308	12.1
(1, 0, 0, 0)	548	21.6
(1, 0, 0, 1)	98	3.9
(1, 0, 1, 0)	64	2.5
(1, 0, 1, 1)	137	5.4
(1, 1, 0, 1)	99	3.9
Other patterns	32	1.3
Total	2,537	100

* 0 = missing response, 1 = observed response.

† Subjects were evaluated at the baseline visit (T0) and 1 year (T1), 3 years (T3), and 5 years (T5) later.

TABLE 2. Odds ratios (OR) for the association of probability to drop out with time, age, sex, and educational level according to a logistic regression model, among subjects evaluated by the Mini-Mental State Examination (MMSE): the Paquid Study, France, 1988–1992*

Variable	OR	95% CI†
Indicator for T3‡	0.02	0.003–0.10
Indicator for T5‡	0.01	0.001–0.09
age	1.01	0.99–1.02
age × indicator for T3	1.05	1.03–1.08
age × indicator for T5	1.06	1.03–1.09
Previous MMSE	0.91	0.88–0.93
Sex (women vs. men)	0.86	0.75–0.99
Education		
No education§	1.88	1.15–3.07
Did not graduate from primary school§	2.02	1.39–2.93
Graduated from primary school§	1.67	1.17–2.40
High school level§	1.39	0.96–2.00

* Analysis performed on the sample of 2,107 subjects without intermittent nonresponses.

† CI, confidence interval.

‡ Versus T1.

§ Versus university level.

0.011) and 0.77 ($1.053^{75} \times 0.016$) for a subject aged 75 years. High baseline age was associated with high probability of dropout only at T3 and T5. The odds ratio for the probability of dropout at T5 for a subject aged 75 years versus 65 years was 1.90 ($1.057^{10} \times 1.009^{10}$). This may be explained by the fact that a larger proportion of dropouts was due to death at T3 (38 percent) and T5 (46 percent) than at T1 (16 percent). Male sex and low educational level led to higher probability of dropout. More importantly, the probability of dropout was associated with the previous MMSE score at all times (interaction with *time* was not significant; results not displayed here). A low MMSE score was predictive of dropout at the next follow-up time.

For five age groups defined by the age at the baseline visit, figure 1 shows the observed mean MMSE scores at each visit computed using all observations (2,537 subjects) or using only complete observations (1,033 subjects). It is clear that subjects with complete observations had a better MMSE score for all the visits, but the evolution of the two samples during 5 years was not very different: the score rose between T0 and T1, then remained nearly stable or decreased very slightly except for subjects aged ≥ 85 years with complete observations, but this group was small (48 subjects). These results suggest that the nonresponse mechanism does not depend much on the slope of evolution of the MMSE.

Longitudinal study of MMSE

Table 3 presents results of the linear regressions with random effects for the square root of the number of errors. With this transformed variable, a positive coefficient indicates that the mean MMSE score decreases when the value of the covariate rises, or, for interactions with *time*, that the decline of the MMSE score with *time* is stronger for high values of the covariate. The evolution according to *time* was correctly modeled by a linear term in *time* and a binary indicator for T0 to account for the poor score of the subjects at the first interview. A quadratic term in *time* was not useful according to the likelihood ratio test.

Model 1 shows that the MMSE score declined with time except between T0 and T1, but the improvement between T0 and T1 was much larger than the subsequent decline between T1 and T5. Between T0 and T1, the square root of the number of errors decreased by 0.205 (0.015–0.220), whereas it increased by only 0.06 ($4 \times 0.015 = 0.06$) between T1 and T5. Baseline age and educational level are highly correlated with the mean MMSE score. More importantly, the regression coefficient for baseline age (0.033) appeared twice as large as the regression coefficient for *time* (0.015); thus, longitudinal and cross-sectional measures of the aging effect were different. This may be explained by a cohort effect which remains after adjustment on educational level or by a practice effect due to the repetition of the same test in the same subjects. The cohort effect should lead to an overestimated coefficient for *age* whereas the practice effect should lead to an underestimated coefficient for *time*.

Model 2 shows that the baseline age interacts with *time*. The increase in the number of errors between T1 and T5 was higher for older subjects (interaction *age* × “indicator for T0” was not significant and is not presented in table 3). Figure 2 presents the MMSE scores estimated by model 2 using equation 1 and the approximate confidence intervals of these estimates. Using equation 2, the standard errors of the MMSE scores were estimated to be 2.4 at T0 and 2.0 at T1, T3, and T5 for subjects aged 65 years at the baseline visit, and 3.5 (T0), 3.2 (T1), 3.3 (T3), and 3.4 (T5) for subjects aged 85 years. Table 4 presents the predicted difference in the MMSE scores between T0 and T5 or between T1 and T5 according to the baseline age. The mean MMSE score was globally improved during the 5 years for all ages, owing to the improvement between T0 and T1. During the last 4 years, the MMSE score decreased very slightly by 0.02 points for subjects aged 65 years at T0 to 0.57 points for subjects aged 85 years at T0.

Model 3 of table 3 shows that educational level was not only predictive of the mean MMSE score but also

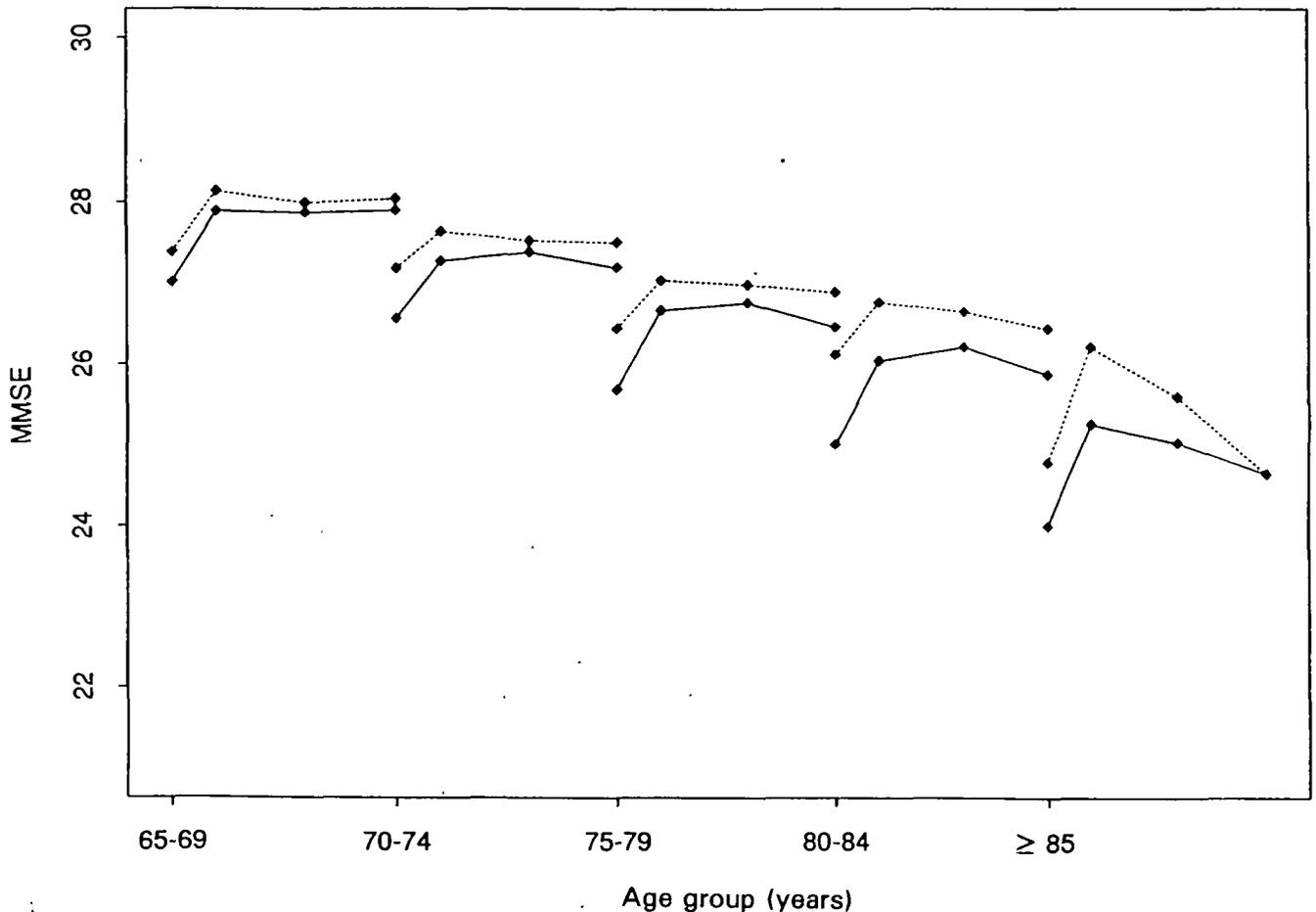


FIGURE 1. Mean Mini-Mental State Examination (MMSE) scores at each visit for five age groups (65–69 years, 70–74 years, 75–80 years, 80–84 years, ≥ 85 years, at the beginning of the study): the Paquid Study, France, 1988–1992. The continuous line represents the mean scores computed using all observations ($n = 2,537$ subjects), while the dotted line represents the mean scores computed using data from 1,033 subjects with complete observations.

of the course of MMSE with *time*. To analyze the interaction with time, we grouped the categories “no education,” “did not graduate from primary school,” and “graduated from primary school” because their coefficients were very close and because the sample size in the category “no education” was small; in the same way, subjects with high school or university level were grouped together in the reference class because they had the same evolution with *time*. Model 3 is the best model according to the Akaike criterion. The improvement of the MMSE score between T0 and T1 was larger for less educated subjects (interaction educational level by indicator for T0 significant, $p < 0.01$). However, the deterioration between T1 and T5 was also larger for these subjects (interaction educational level by *time* was significant, $p < 0.001$). Figure 3 presents the estimated MMSE scores computed with model 3 for five baseline ages and five educational levels. For high school and university levels, the MMSE score did not decline between T1 and T5,

while it did so for the three other educational levels. In figure 3, the inter-cohort differences appear mainly in younger subjects or in subjects with high educational levels. Whatever the educational level and age in the range 65–85 years, the estimated score at T5 remained higher than the estimated score at T0 and the deterioration between T1 and T5 was always less than 1 point in a total score of 30 points.

Sex was significantly associated neither with the mean MMSE score nor with evolution (results not displayed here).

DISCUSSION

The major finding of this study was that after an improvement in MMSE scores in the first year of follow-up, the decline in the MMSE scores with time in non-demented elderly persons was very small. The course of the MMSE depended on baseline age and on educational level, but the latter was much more cor-

TABLE 3. Results of linear regression with random effects for the square root of the number of errors in the Mini-Mental State Examination (MMSE): the Paquid Study, France, 1988–1992*

Variable	Model 1		Model 2		Model 3	
	β coefficient	95% CI†	β coefficient	95% CI	β coefficient	95% CI
<i>time</i>	0.015	0.006–0.025	–0.105	–0.187 to –0.023	–0.114	–0.196 to –0.033
Indicator for T0	0.220	0.184–0.256	0.225	0.189–0.261	0.117	0.059–0.175
<i>age</i>	0.033	0.030–0.036	0.039	0.035–0.044	0.031	0.027–0.035
<i>age</i> × <i>time</i>			0.002	0.0005–0.0027	0.002	0.0004–0.003
No education (NE)‡	1.192	1.044–1.340			1.077	0.917–1.235
Did not graduate from primary school (NPS)‡	0.841	0.738–0.943			0.724	0.606–0.841
Graduated from primary school (GPS)	0.333	0.232–0.433			0.216	0.101–0.332
High school level‡	0.117	0.017–0.218			0.117	0.016–0.218
(NE or NPS or GPS) × <i>time</i>					0.028	0.008–0.047
(NE or NPS or GPS) × indicator for T0					0.171	0.097–0.245

* Analysis performed on the sample of 2,537 subjects who completed the MMSE at least once. Model 1: *age*, *time*, educational level; model 2: *age* and *time* only with the interaction; model 3: the same as model 1 plus the interactions with *time*.

† CI, confidence interval.

‡ Versus university level.

related with the mean score than with the amount of change over time. This suggests that high educational level protects against cognitive impairment because the maximum level reached during life is higher rather than because the decline is slower. However, such a conclusion must be made carefully because the small association observed between decline of MMSE and educational level may be explained by the very small change in the MMSE. It is possible that the educational level has a larger effect on the evolution of other psychometric tests.

The longitudinal measure of the time effect was clearly smaller than the cross-sectional measure of the age effect. It is unlikely that this difference was due to differential selection of the subjects in the sample according to their baseline age. Indeed, older subjects were more highly selected than younger subjects because of mortality, but because survival was associated with better cognitive level, this selection should have led to a decrease in the coefficient of *age*. The difference may be explained either by a cohort effect, because socioeconomic status, occupational, or leisure activities in addition to educational level changed with cohorts, or by a practice effect induced by the repetition of the test. To discriminate between these two factors, two samples of the same ages taken at different times have to be compared: this comparison would give a measure of the cohort effect, while longitudinal analyses give a measure of the sum of the age and practice effects and cross-sectional analyses give a measure of the sum of the age and cohort effects.

The improvement of the score between T0 and T1 may be the consequence of the stress due to the test situation at T0 or the learning effect on T1. This improvement has already been observed in test-retest

studies (2) with short time intervals (between 1 day and 2 months), which may indicate a learning effect. However, such a learning effect is less likely with a delay of one year. The assumption of a stress factor raises a methodological problem for longitudinal studies. It is possible that the second assessment provides a better measure of the baseline performances of the subject than the first assessment. Therefore it may be better to perform two assessments with short time intervals at the beginning of the study.

The smaller improvement in the score between T0 and T1 for better educated subjects may be explained by a ceiling effect: at T0, 62 percent of subjects with a high school or university level education had a MMSE score of 28 or more. Another possible explanation is that these subjects were less stressed by the test situation at T0. This latter hypothesis would be confirmed if such a differential improvement according to educational level is found with other psychometric tests that do not give a ceiling effect.

Two previous studies did not report any increase of MMSE over 1 year (19) or 2 years (20), respectively, but these results may be explained by a ceiling effect induced by a higher educational level and a better initial score (means of 28.1 points and 27.7 points, respectively). In another study, Izaks et al. (9) found a large decrease in the MMSE score over 3 years, but their sample included only very old subjects (ages ≥ 85 years) and a large proportion of cognitively impaired subjects (50 percent had MMSE < 24 and almost 25 percent were demented) and these cognitively impaired subjects declined much more rapidly than the general elderly population.

The major drawback of our study is the number of nonresponses. This problem is common with all lon-

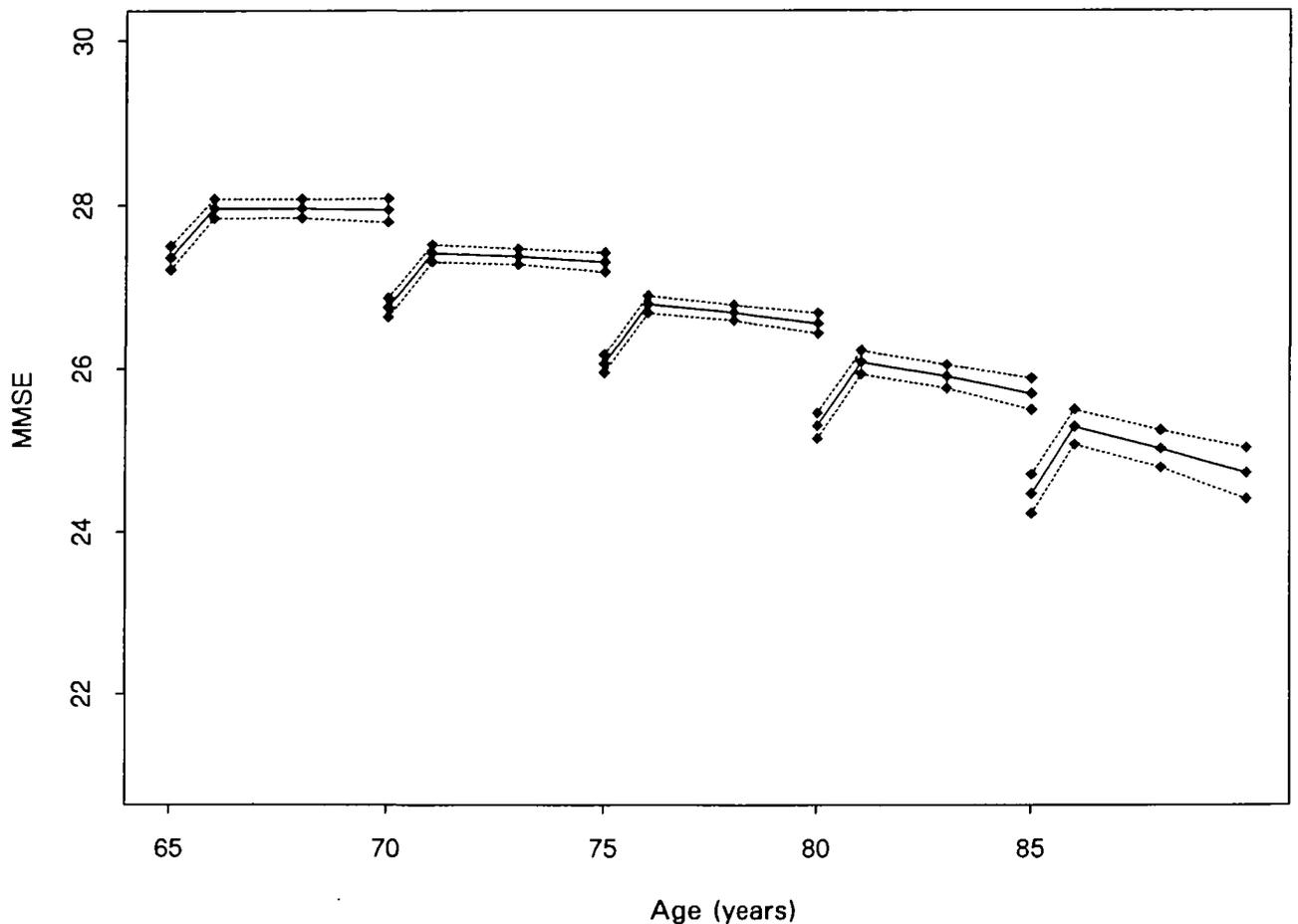


FIGURE 2. Estimated Mini-Mental State Examination (MMSE) scores and 95% confidence intervals computed with model 2 according to age: the Paquid Study, France, 1988–1992. The continuous line represents the estimated MMSE scores, while the dotted line represents the 95% confidence intervals.

TABLE 4. Predicted differences between Mini-Mental State Examination (MMSE) scores at T0 and T5 or T1 and T5 according to the baseline age computed with the linear regression model 2: the Paquid Study, France, 1988–1992

Baseline age (years)	T5–T0	T5–T1
65	0.58	–0.02
70	0.55	–0.11
75	0.49	–0.24
80	0.39	–0.39
85	0.25	–0.57

gitudinal studies and deserves attention. The logistic regression analysis showed that the missing data were not completely random because the probability of dropout depended on the previous MMSE score. This selective nonresponse mechanism was expected: for instance, Liu and Anthony (21) suggested predicting the completion of the follow-up interviews by using the baseline MMSE score. However, the maximum

likelihood method gives valid estimates if the mechanism for missing data depends on observed responses, provided it does not depend on the missing response (17). Diggle and Kenward (22) proposed a model to account for non-ignorable missing data. We used this model in an additional analysis to study sensitivity of our results to hypotheses regarding missing data mechanism, and we obtained very similar results (results not shown here).

Another problem with this study is that subjects who were diagnosed as demented during the 5 years were excluded, but those who became demented after dropout or after the 5-year follow-up were not excluded. Some of the subjects may already have begun to decline and so it is likely that the mean decline would be even smaller if these future demented subjects were excluded.

This study suggests that the decline in cognitive performance as measured by the MMSE is very slow in normal aging. On the other hand, many longitudinal

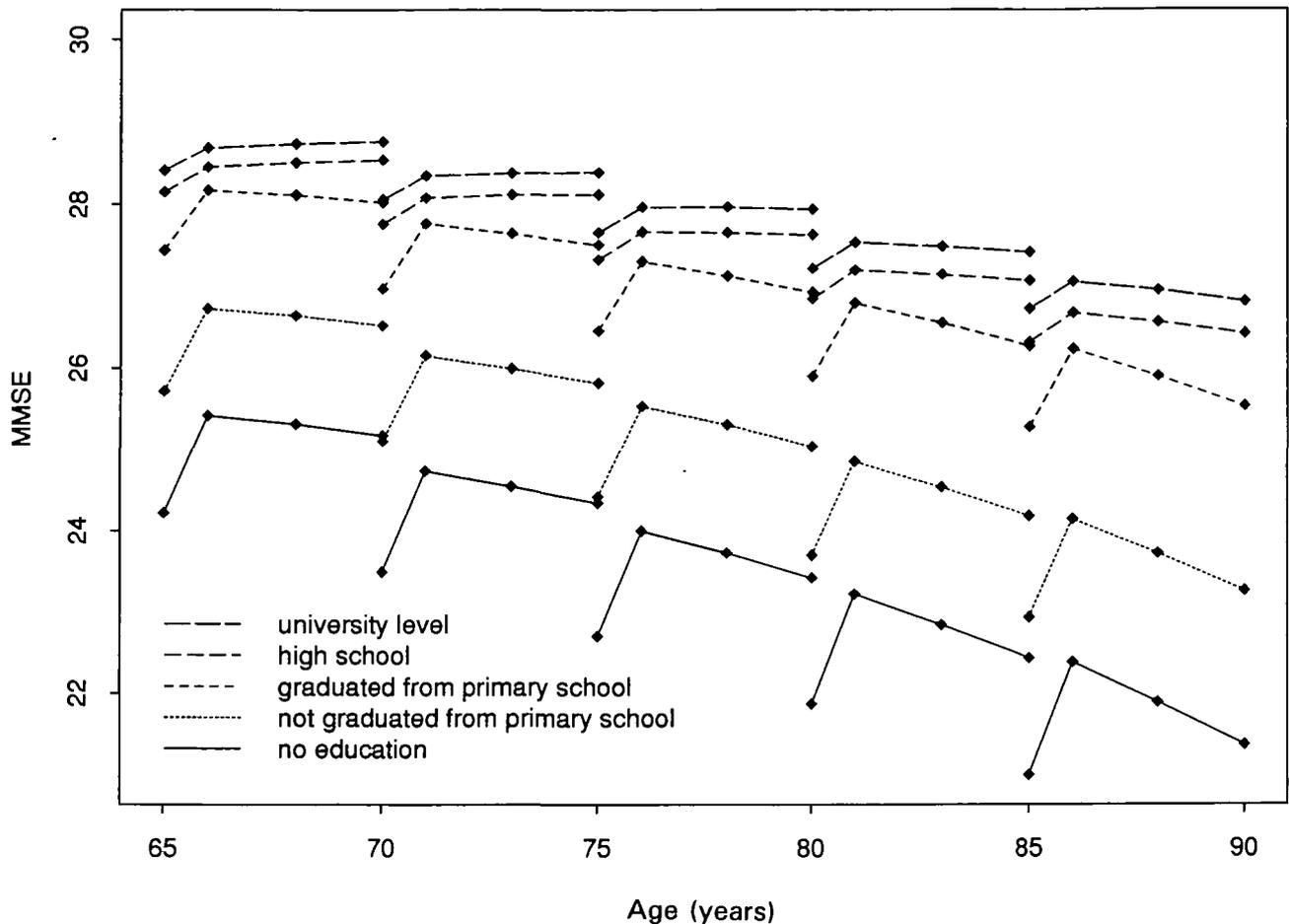


FIGURE 3. Estimated Mini-Mental State Examination (MMSE) scores computed with model 3 according to age and educational level: the Paquid Study, France, 1988–1992.

studies show a clear deterioration of the MMSE score with time for demented subjects (7). The Paquid longitudinal study also gives information regarding the course of MMSE for incident cases of dementia in the years before the diagnosis (table 5). These data show that the decline of MMSE began several years before the diagnosis of dementia and was very large in the 2 years preceding the diagnosis: the mean annual change of MMSE was -3.4 during the previous year (for subjects diagnosed at T1) or during the previous 2

years (for subjects diagnosed at T3 or T5). Thus, these results suggest that a decline of MMSE may be used to detect subjects who have a high risk of developing dementia in the next years. However, the detailed study of the evolution of MMSE as a screening criterion is beyond the scope of this article.

The MMSE is a composite scale including more or less difficult subtests (2) which evaluate different cognitive functions. The lack of decline during 5 years suggests that the different cognitive processes involved in the MMSE are spared by the aging process. However, we can not rule out the possibility that some subscores may improve with time while others decline. Further work is required to study the course of these subtests and also the course of other more difficult psychometric tests. For instance, it seems that the timed tasks decline more rapidly than the MMSE in normal aging (23). However, these future studies require methodological developments which are now underway to account for non-ignorable missing data or to analyze ordinal longitudinal data.

TABLE 5. Mean Mini-Mental State Examination (MMSE) score of the subjects who were diagnosed as demented at T1, T3, or T5 and who completed the MMSE at all the previous visits: the Paquid Study, France, 1988–1992

Date of diagnosis	Mean MMSE score at each visit				No.
	T0	T1	T3	T5	
T5	25.0	25.7	24.4	18.0	22
T3	22.5	23.4	16.2		48
T1	18.3	15.0			19

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