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Short- versus long-term prediction of dementia among subjects with low and high educational levels

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Abstract

Background: Using simple measures of cognition and disability in a prospective community-living cohort of normal elderly persons, the main objectives of our study were to distinguish short- and long-term predictors for dementia according to educational level and to propose a tool for early detection of subjects at high risk of dementia.

Methods: Data derived from the French cohort study Paquid (Personnes Agées QUID), which included 3777 subjects, older than 65 years of age, who were followed for a 20-year period. The risk of dementia at 3 years and 10 years was estimated by logistic regression for repeated measures combining data from all the 3- and 10-year windows throughout the follow-up. Predictors included disability assessed by the number of dependent items among four instrumental activities of daily living (IADLs), four neuropsychological tests, five Mini-Mental State Examination (MMSE) subtests, and four items of subjective memory complaints.

Results: Of the 2882 included subjects, the number of IADLs remained a predictor of short- and long-term conversion to dementia for those with low educational level (combined with only one cognitive test) whereas the best predictors for more educated subjects combined subjective memory complaints and memory and executive function tests. The episodic memory subtest was the only predictive MMSE subtest. In the high-education-level group, the areas under the receiver–operating characteristic curve of the selected models were 0.85 for 3-year prediction and 0.78 for 10-year prediction.

Conclusion: Early predictors of dementia are different according to educational level. Among subjects reaching the secondary school level, early detection of those at high risk of dementia is possible with good predictive performance, with a few simple objective and subjective cognitive evaluations.

Keywords: Activities of daily living; Cognition; Dementia; Educational level; Prediction

1. Introduction

Dementia, mostly Alzheimer's disease (AD), has become a major public health concern worldwide, and treatments approved for AD have only shown a modest efficacy [1]. Because it was demonstrated that a long preclinical phase—more than 10 years—is present before the diagnosis of dementia [2], current research is focusing on preventive treatments that could be administered during this phase [3–5]. Early intervention aims at stabilizing the progression of the pathophysiological disease process to avoid or delay the progression to dementia. The main challenge is then to define the target population at highest risk of developing dementia for assessing potential preventive treatments, which depends on reliable procedures to predict the onset of dementia with adequate sensitivity and specificity, and which could be usable and affordable in daily clinical practice. In the absence of such reliable predictors, early intervention trials would inevitably lack the power to prove efficacy of preventive strategies, simply because the prevalence of dementia in the general population older than 65 years is rather low. As an example, the prevalence of dementia for those older than 65 years in

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western Europe was estimated at 7.2% [6]. An early diagnostic procedure would also make a valuable routine tool in primary care settings for large-scale screening aiming at secondary prevention, provided that it is quick to complete, risk free, non invasive, and inexpensive [7]. This is the reason why subjective complaints, and cognitive and functional scores are important candidates in the development of a predictive marker of dementia at the general population level, unlike sophisticated tools such as genetic markers, biomarkers, or medical imaging [8]. A recent article from Alzheimer's Disease Neuroimaging Initiative [9] suggests that neuropsychological tests may well be the best candidate markers for that purpose.

For more than 20 years, several assumptions have been made about the link between memory complaints, cognitive impairment, and dementia. Some studies suggested that subjective cognitive impairment could be a predictor of cognitive decline and dementia [10,11]. In a long-term study [2], a simple score of memory complaints was found to be significantly higher in future patients with AD than in control subjects (matched for age, sex, and education) 8 years before diagnosis. Other findings suggest that episodic memory may be impaired early during the preclinical phase of AD but remains stable thereafter [12]. Based on these results, short- and long-term predictive factors are likely to be different, which led us to consider different periods of prediction.

Earlier work from our group [13] showed that cognitive decline preceding dementia diagnosis differed by educational level. The profile of decline in subjects with a high educational level differed from subjects with a low educational level in two ways, as confirmed later [14,15]: Among subjects with a high education level, a strong acceleration of cognitive decline occurred about 3 years before dementia diagnosis, and consequently their cognitive decline during the late prediagnosis phase was more rapid. This phenomenon may be explained by the cognitive reserve hypothesis, which assumes that more educated people are better able to compensate for progressive brain pathology during a certain period of time [16]. So it makes sense to study low- and high-education groups separately to assess differentially the predictive value of simple clinical tools on the general elderly population.

The objectives of the current work were, therefore, (*i*) to propose a tool for early detection of subjects at high risk of dementia based on objective and subjective measures of cognition and disability, (*ii*) to compare the short-term (3 years) and long-term (3–10 years) predictors, and (*iii*) to distinguish the best predictors according to educational level.

2. Methods

2.1. Population

The prospective cohort study Paquid (Personnes Agées QUID) initiated in 1988 included 3777 elderly people older than 65 years [17]. Subjects living at home in 75 parishes in southwest France were selected randomly from electoral rolls. The subjects were visited at home at baseline in 1988 and 1989 by a trained psychologist, and then were monitored at 1 (V1), 3 (V3), 5 (V5), 8 (V8), 10 (V10), 13 (V13), 15 (V15), 17 (V17), and 20 (V20) years after the initial visit. At each visit, a questionnaire was administered that included information about lifestyle, health characteristics, a battery of cognitive tests, and scales of disability. The diagnosis of dementia was assessed at each visit using a two-stage procedure: According to the neuropsychological evaluation, the psychologist assessed the A (memory impairment), B (impairment of at least one other cognitive function), and C (interference with social or professional life) *Diagnostic and Statistical Manual for Mental Disorders*, 3rd edition, revised (DSM-III-R) criteria for dementia [18]. Subjects that met the three DSM-III-R criteria then underwent a clinical assessment by a senior neurologist who confirmed or refuted the diagnosis of dementia and specified the etiology (AD, vascular dementia, or other types), according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria and Hachinski score. Last, all cases were reviewed by a group of experts to obtain a clinical consensus.

2.2. Sample selection

The objective of the analysis was to find the best combinations of cognitive and disability measures to predict the risk of dementia onset in 3 and 10 years after assessment. The target population was made up of subjects who initially did not have dementia and had a health condition that allowed for valid assessments of cognition and disability (i.e., not blind, deaf or bedridden), leading to a sample of 3510 subjects.

Among them, only 44 subjects without missing values for the predictors measured at V0 were diagnosed as having dementia during the first 3 years of follow-up. This was too few subjects to perform analyses for short-term prediction stratified by educational level. Thus, for each predictive window, data from all the available 3- or 10-year spans were combined, as displayed in Fig. 1, to obtain the 3- and 10-year window samples. The four spans combined for the 3-year window were: V0 to V3, V5 to V8, V10 to V13, and V17 to V20. For the 10-year window, three spans were used: V0 to V10, V5 to V15, and V10 to V20 (V3 to V13 was not considered because one of the cognitive tests was not completed at V3). For the 10-year window, subjects that acquired dementia during the first 3 years of each span were excluded to consider the long-term prediction of dementia and to be able to compare the short- and long-term predictive factors.

Subjects contributed for one span if (*i*) they were free of dementia at the start of the span, (*ii*) they had no missing data for the predictors measured at the start of the span, and (*iii*) they were diagnosed with dementia during the span