

# Leisure activities and the risk of dementia in the elderly

## Results from the Three-City Study

T.N. Akbaraly, PhD  
F. Portet, MD, PhD  
S. Fustinoni, MSc  
J.-F. Dartigues, MD, PhD  
S. Artero, PhD  
O. Rouaud, MD, PhD  
J. Touchon, MD, PhD  
K. Ritchie, PhD  
C. Berr, MD, PhD

Address correspondence and reprint requests to Dr. Tasnime N. Akbaraly, INSERM U888, Hôpital La Colombière, 39 Avenue Charles Flahault, BP 34493, 34093 Montpellier, Cedex 5, France  
tasnime.akbaraly@inserm.fr

### ABSTRACT

**Objective:** There is accumulating evidence that involvement in leisure activities may be related to risk of dementia; however, there is no consensus concerning the underlying mechanism of this association. Hypothesizing that leisure activities may contribute to cognitive reserve (CR), we examined the association between leisure activities and risk of incident dementia and its subtypes within a general population sample, categorizing leisure activity as stimulating, passive, physical, and social. The possibility that these associations may be driven by other proxies of CR was also examined.

**Methods:** Analyses were carried out on 5,698 dementia-free participants aged 65 and over included in the Three-City cohort study in Dijon and Montpellier (France) in 1999–2001. Hazard ratios (HR) were calculated for incident dementia and its subtypes (mixed/vascular dementia and Alzheimer disease) in relation to category of leisure activity.

**Results:** Stimulating leisure activities were found to be significantly associated with a reduced risk of dementia ( $n = 161$ , HR = 0.49, 95% confidence interval [CI]: 0.31; 0.79) and Alzheimer disease ( $n = 105$ , HR = 0.39, 95% CI: 0.21; 0.71) over the 4-year follow-up 1) independently of other proxies of CR, 2) after adjusting for vascular risk factors, depressive symptoms, and physical functioning, and 3) independently of other leisure activities. Furthermore, no significant association was found with other leisure activities and dementia after controlling for the potential confounders.

**Conclusion:** Our findings support the hypothesis that cognitively stimulating leisure activities may delay the onset of dementia in community-dwelling elders. *Neurology*® 2009;73:854–861

### GLOSSARY

**AD** = Alzheimer disease; **CI** = confidence interval; **CR** = cognitive reserve; **DSM-IV** = *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition; **HR** = hazard ratio; **MMSE** = Mini-Mental State Examination.

During the past decade, prospective epidemiologic studies report an association between high rates of leisure activities in old age and lower cognitive decline and reduced risk of dementia or Alzheimer disease (AD).<sup>1</sup> Several pathways have been proposed to explain this relationship. One mechanism is based on cognitive reserve (CR) theory. Participants with a higher CR are postulated to have more efficient neuronal networks or may use alternate networks more effectively after neurologic insult, thus delaying AD incidence.<sup>2,3</sup> Regarding this hypothesis, it is important to determine which type of leisure activities are the most powerful contributor to CR. Proxies of higher CR include higher education levels or higher occupational attainment, which have also been consistently associated with reduced risk of AD<sup>4–6</sup>; as leisure activities may reflect socioeconomic advantages gained earlier in life, it is also possible that the association between late-life activities and risk of dementia may be explained by education level or occupational attainment. Two other underlying mechanisms relating leisure activity to reduced risk of dementia involve on one hand the social network and on the other physical conditions. Some studies suggest that maintain-

From the INSERM, U888, Pathologies of the Nervous System: Epidemiological and Clinical Research, Montpellier, and University Montpellier 1 (T.N.A., F.P., S.F., S.A., J.T., K.R., C.B.), Montpellier, France; Department of Epidemiology and Public Health (T.N.A.), University College London, UK; CMRR Languedoc Roussillon (F.P., J.T., C.B.), CHU Montpellier; INSERM, U897 (J.-F.D.), Bordeaux; Université Victor Segalen Bordeaux 2, and INSERM, U708, Hôpital de la Salpêtrière (O.R.), Paris, France.

*Disclosure:* Author disclosures are provided at the end of the article.

ing social ties and frequent social participation may help to prevent cognitive decline and the onset of dementia.<sup>7,8</sup> Furthermore, frequent physical activity has been associated with a reduced risk of cognitive decline and dementia.<sup>9-13</sup> Finally, leisure activities are also related to health status, and may thus constitute a confounding variable.

Based on the hypothesis that leisure activities as a contributor to CR are associated with a decreased risk of dementia and AD, we aimed to examine in a large general population the association between leisure activities and the risk of incident dementia during a 4-year follow-up period. We also focused on examining whether these associations are driven by other proxies of CR such as education level or occupational attainment.

**METHODS Study population.** Subjects were recruited as part of a multisite cohort study of community-dwelling persons aged 65 years and over from the electoral rolls of 3 French cities—Bordeaux, Dijon, and Montpellier—between 1999 and 2001 (the Three-City Study).<sup>14</sup> The analyses carried on the subcohorts of Dijon (n = 4,931) and Montpellier (n = 2,259) in which data on leisure activities were similarly collected. Of the 7,051 dementia-free participants included in the cohort, 739 participants (214 deaths) did not have the next 2 follow-ups (follow-up rate = 92.3%). The present analyses carried on the 5,698 participants with validated leisure activity questionnaire and complete data for baseline main adjustment variables.

**Standard protocol approvals, registrations, and patient consents.** We received approval from the Consultative Committee for the Protection of Persons participating in Biomedical Research of the Kremlin Bicêtre University Hospital (Paris).

A written informed consent was obtained from all patients participating in the study (consent for research).

**Data collection. Leisure activities variables.** Leisure activities were assessed at baseline, using 2 different self-report frequency questionnaires, 1 questionnaire for daily leisure activities and 1 for monthly. First, participants were asked, “Usually, how much time in a day did you engage for each of the following activities: watching TV, listening to the radio, listening to music, doing odd jobs, gardening, knitting/sewing, going for a walk.” The frequency of participation for each of these activities was rated on a 3-point scale: 0, never or less than 1 hour per day; 1, 1–2 hours per day; 2,  $\geq 2$  hours per day. In the monthly questionnaire, participants were asked about monthly frequency (0, never or rarely; 1, 1–3 per month; 2, 1 per week; 3,  $\geq 2$  per week) with which they engaged in the following usual activities: inviting friends, inviting relatives, visiting friends, visiting relatives, attending organizations (e.g., charity, institution), doing crosswords, playing cards, going to the cinema/theater, practicing an artistic activity. Within each type of frequency questionnaire, the categorization of leisure activities according to their predominantly mental, physical, or social characteristics was drawn from the existing literature.<sup>15,16</sup> At the end, 4 independent

composite scores were built by summing the corresponding items scores as following.

Among the monthly leisure activities, doing crosswords, playing cards, attending organizations, going to cinema/theater, and practicing an artistic activity were grouped in “stimulating leisure activities” (score ranging from 0 to 15, median score: 3), as they were described as cognitive activities in which seeking or processing information played a central role in several reports.<sup>17</sup> The other 4 items—visiting or inviting friends or relatives—were grouped in “social support activities” (score ranging from 0 to 12, median score: 5), as they involved more the social resources of the participants.<sup>18,19</sup>

Among the daily leisure activities, doing odd jobs, gardening, and going for a walk items are outside activities and were grouped together for their common physical characteristics as “physical leisure activities” (score ranging from 0 to 6, median score: 3). Finally, activities such as watching television, listening to the radio, listening to music, and knitting/sewing constitute leisure activities which are less cognitively demanding<sup>16,19</sup> compared to those classified as stimulating leisure activities and were categorized as “passive leisure activities” (score ranging from 0 to 8, median score: 2).

**Screening for dementia.** At baseline, diagnosis of dementia was based on a 3-step procedure.<sup>14</sup> First, trained psychologists administered a battery of neuropsychological tests detailed elsewhere.<sup>14</sup> Second, all the participants in Montpellier were then examined by a neurologist, whereas in Dijon, because of the larger number of participants, only those who screened positive underwent further examination. Finally, an independent committee of neurologists reviewed all potential prevalent and incident cases of dementia to obtain a consensus on its diagnosis and etiology according to the criteria of the *DSM-IV*.<sup>20</sup> Similar procedures were performed at follow-up for incident dementia screening. Cases of AD were classified according to the National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association<sup>21</sup> and cases of mixed/vascular dementia according to the National Institute of Neurological Disorders and Stroke–Association Internationale pour la Recherche en l’Enseignement en Neurosciences<sup>22</sup> criteria.

**Other variables measured at inclusion.** Sociodemographic variables consisted of gender, age, study center, marital status, educational level (no formal education or primary school, lower secondary education, higher secondary education, university degree), and occupational grade (high grade/office-based/manual worker/staying at home). Health status was ascertained by measures of vascular risk factors, depressive symptoms, physical functioning, cognitive impairment, and *APOE* genotype. Vascular risk factors consisted of diabetes (fasting glycemia  $\geq 7.0$  mmol/L or antidiabetic treatment), hypertension (systolic/diastolic blood pressure  $\geq 140$  mm Hg/ $\geq 90$  mm Hg or antihypertensive drug use), hypercholesterolemia (plasma cholesterol  $\geq 6.20$  mmol/L or anticholesterol treatment), history of vascular disease (stroke, angina pectoris, myocardial infarction, and cardiac and vascular surgery). Depressive symptoms were assessed by the Center for Epidemiologic Studies–Depression scale<sup>23</sup> with a 16 cutoff point. Physical functioning was evaluated using the instrumental activities of daily living scale (score  $> 0$ ). Cognitive impairment was defined by a score below 24 on the Mini-Mental State Examination (MMSE).<sup>24</sup> Finally, allele  $\epsilon 4$  of *APOE* was also considered (<http://www.genopole-lille.fr/spip/>).

**Statistical analyses.** In the present analyses, leisure activities were considered as categorical variables. Given the non-normal

**Table 1** Characteristics of the 5,692 participants according to the onset of dementia during the 4-year follow-up

	No dementia (n = 5,537), % or mean (SD)*	Dementia (n = 161), % or mean (SD)*	p
Women	61.0	56.5	0.25
Age, y	73.6 (5.3)	78.0 (5.7)	<0.0001
No academic qualification/primary school	20.8	36.6	<0.0001
Manual worker	18.3	25.5	0.09
Living alone*	34.5	35.4	0.82
Hypertension*	76.6	80.1	0.29
Diabetes*	7.6	10.6	0.16
Hypercholesterolemia*	56.9	52.3	0.25
Vascular diseases*	15.3	29.2	<0.0001
Depressive symptoms*	14.2	24.4	0.0004
APOE ε4 genotype	20.1	33.1	<0.0001
Incapacity measured by IADL*	8.4	28.6	<0.0001
Cognitive impairment (MMSE score)*	4.0	13.7	<0.0001

\*Mean (SD) for continuous variables.

\*Missing values: 16 for marital status, 29 for diabetes, 99 for hypercholesterolemia, 1 for vascular diseases, 61 for depressive symptoms, 140 for APOE genotype, 5 for instrumental activities of daily living (IADL) incapacity, 18 for Mini-Mental State Examination (MMSE) score.

distribution of the dependent variables, they were categorized by tertiles: high (tertile 3), mild (tertile 2), and low (tertile 1) levels of activity being defined for each of the 4 variables. The association between leisure activities and risk of dementia over the 4-year follow-up was determined by a proportional hazards model with delayed entry and age of the participants as time scale.<sup>25</sup> Additionally to the age, analyses were first adjusted for gender, educational level, occupational grade, and study center (model 1) and then adjusted for other sociodemographic and health status variables (model 2). Similar analyses were performed to explore the association between levels of leisure activities and onset of AD cases and mixed or vascular dementia cases. The proportional hazards assumption was verified by adding a time-dependent variable to the model. Interactions between each covariate and each leisure activity were also tested and were found to be nonsignificant.

Results of proportional hazards regressions were expressed as hazard ratios (HR) and 95% confidence intervals (CI). Statistical analyses were performed using SAS software version 9.1 (SAS Institute, Inc., Cary, NC).

**RESULTS** The present analyses were carried out on the 5,698 participants without prevalent dementia at baseline. Compared to dementia-free participants excluded from the analyses (n = 1,353), those participating were younger, with higher education levels and occupational grades. Participants excluded were also more likely to have cognitive impairment at baseline, and low levels in each category of leisure activity.

Over the 4-year follow-up, 161 new cases of dementia (76 diagnosed at the 2-year follow-up, 85 at

the 4-year of follow-up) were diagnosed including 105 cases of AD, 38 cases of mixed (n = 19) and vascular (n = 19) dementia, and 18 other dementia. Characteristics of the participants as a function of the onset of dementia are described in table 1. Factors associated with each leisure activity are given in table 2. Associated factors varied according to type of activity. For instance, a lower proportion of participants with the lowest education level were observed across the tertiles of stimulating leisure activities, while a higher proportion were observed across the tertiles of physical leisure activities. Low education level was also associated with higher levels of passive leisure activities and was not associated with social leisure activities.

Table 3 shows the results from the proportional hazards models designed to estimate the associations between frequency of participation in leisure activity and incidence of all dementia types during the 4-year follow-up. Stimulating leisure activities were associated with a 50% reduction in risk of dementia in participants with high or moderate levels compared to those with the lowest levels after controlling for potential confounders. Similar associations were observed for AD, while no significant association was observed for mixed/vascular dementia.

For passive and physical leisure activities, no significant association was found between levels of participation and risk of any type of dementia.

A significant association was observed between social leisure activities and onset of dementia and mixed/vascular dementia but not AD in the model adjusted for gender, education, occupational grade, and study center (model 1, table 3). However, further adjustment for other covariates attenuates this association, so that it is no longer significant. A step by step analysis showed that the association between social leisure activities and mixed/vascular dementia was shaped by depressive symptoms (results not shown).

Finally, to assess whether the association between stimulating activities and risk of dementia was driven by the other leisure activities, a model in which all the 4 leisure activities variables were included simultaneously was performed. Results showed that stimulating leisure activities were independently associated with risk of dementia and AD (in a full adjusted model, HR 0.50, 95% CI 0.33 to 0.78 for dementia; HR 0.46, 95% CI 0.27 to 0.80 for AD).

Cognitive impairment occurs in elderly persons many years before dementia onset and commonly leads to a reduction in activity level due to an increasing dynamic of fear of incompetence. As this phenomenon might clearly explain the current findings, we repeated the above analyses after excluding suc-

**Table 2** Factors associated with levels of each leisure activity at baseline

	Leisure activities															
	Stimulating				Passive				Physical				Social			
	Low	Mild	High	p	Low	Mild	High	p	Low	Mild	High	p	Low	Mild	High	p
No.	2,148	1,837	1,713	2,223	1,285	2,190	2,591	1,373	1,734	2,485	1,833	1,380	2,485	1,833	1,380	
Women, %	52.0	63.1	69.8	* 45.7	57.9	79.1	* 69.4	60.3	48.7	* 57.2	61.0	67.5	* 57.2	61.0	67.5	*
Age, mean ± SD	74.3 ± 5.6	73.7 ± 5.4	73.0 ± 4.9	* 74.0 ± 5.6	73.8 ± 5.5	73.4 ± 5.1	* 74.2 ± 5.7	73.7 ± 5.3	73.0 ± 4.8	* 73.9 ± 5.5	73.5 ± 5.2	73.7 ± 5.4	* 73.9 ± 5.5	73.5 ± 5.2	73.7 ± 5.4	
Low education level, %	30.1	18.1	13.2	* 20.5	19.6	23.0	* 18.74	21.4	25.4	* 21.3	20.6	22.0	* 21.3	20.6	22.0	
Manual worker, %	26.5	15.5	11.7	* 19.7	19.2	16.8	* 13.8	19.1	25.0	* 19.6	17.7	17.5	* 19.6	17.7	17.5	*
Living alone, %	29.5	35.0	40.4	* 24.8	32.7	45.6	* 38.0	34.2	29.6	* 33.2	32.5	39.7	* 33.2	32.5	39.7	*
Hypertension, %	78.7	77.5	73.2	* 76.7	76.2	76.9	75.9	76.0	78.4	75.4	78.2	77.0	75.4	78.2	77.0	
Diabetes, %	8.4	7.7	6.7	7.7	7.9	7.5	7.1	8.9	7.8	7.3	8.3	7.7	7.3	8.3	7.7	
Hypercholesterolemia, %	54.3	55.8	60.8	* 53.0	58.0	59.7	* 57.0	58.4	55.1	54.9	57.8	58.6	54.9	57.8	58.6	
Vascular diseases, %	18.3	15.2	12.7	* 17.4	15.7	13.8	* 16.7	15.2	14.5	16.4	16.5	13.3	16.4	16.5	13.3	*
Depressive symptoms, %	17.7	13.6	11.2	* 14.8	13.6	14.5	16.9	13.0	11.9	* 17.5	12.8	11.1	* 17.5	12.8	11.1	*
APOE ε4 genotype, %	20.6	19.7	21.0	21.1	20.7	20.0	20.1	21.5	20.1	20.4	21.2	19.4	20.4	21.2	19.4	
IADL incapacity, %	13.4	7.9	4.6	* 10.0	8.9	8.0	11.2	8.1	6.5	* 10.1	8.6	7.5	* 10.1	8.6	7.5	*
MMSE deficit, %	7.8	2.3	1.9	* 3.6	5.1	4.5	3.6	3.9	5.7	* 4.3	3.8	4.9	* 4.3	3.8	4.9	

Missing values: 16 for marital status, 29 for diabetes, 99 for hypercholesterolemia, 1 for vascular diseases, 61 for depressive symptoms, 140 for APOE genotype, 5 for instrumental activities of daily living (IADL) incapacity, 18 for Mini-Mental State Examination (MMSE) score. Frequency of mentally stimulating activities was categorized as low (score <3), mild (score = 3, 4), and high (score >4). Frequency of passive leisure activities was categorized as low (score <3), mild (score = 3), and high (score >3). Frequency of physical leisure activities was categorized as low (score <2), mild (score = 2), and high (score >2). Frequency of social leisure activities was categorized as low (score <5), mild (score 5, 6), and high (score >6).

\*p ≤ 0.05.

**Table 3** Association between leisure activities and risk of dementia

	All dementia <sup>a</sup>				Alzheimer disease <sup>a</sup>				Mixed/vascular dementia <sup>a</sup>			
	Model 1		Model 2		Model 1		Model 2		Model 1		Model 2	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
<b>Stimulating leisure activities</b>												
Low (tertile 1: score <3)	1		1		1		1		1		1	
Mild (tertile 2: score 3, 4)	0.43	0.29; 0.64	0.49	0.32; 0.75	0.42	0.26; 0.70	0.45	0.26; 0.77	0.39	0.17; 0.93	0.59	0.24; 1.45
High (tertile 3: score >4)	0.44	0.28; 0.68	0.49	0.31; 0.79	0.36	0.20; 0.64	0.39	0.21; 0.71	0.51	0.21; 1.22	0.64	0.23; 1.81
<b>Passive leisure activities demanding lower cognitive activity</b>												
Low (tertile 1: score <3)	1		1		1		1		1		1	
Mild (tertile 2: score = 3)	0.92	0.61; 1.37	0.89	0.59; 1.36	1.09	0.68; 1.75	1.02	0.62; 1.69	0.68	0.28; 1.65	0.87	0.35; 2.21
High (tertile 3: score >3)	0.81	0.55; 1.18	0.75	0.50; 1.12	0.73	0.45; 1.18	0.68	0.41; 1.13	0.78	0.37; 1.67	0.82	0.36; 1.85
<b>Physical leisure activities</b>												
Low (tertile 1: score <2)	1		1		1		1		1		1	
Mild (tertile 2: score = 2)	0.83	0.55; 1.25	0.91	0.59; 1.39	0.87	0.52; 1.47	0.87	0.50; 1.51	0.76	0.34; 1.71	1.03	0.42; 2.48
High (tertile 3: score >2)	1.08	0.74; 1.57	1.09	0.73; 1.63	1.45	0.93; 2.28	1.29	0.80; 2.09	0.67	0.30; 1.53	0.77	0.29; 2.04
<b>Social leisure activities</b>												
Low (tertile 1: score <5)	1		1		1		1		1		1	
Mild (tertile 2: score 5, 6)	0.93	0.65; 1.32	1.03	0.71; 1.50	1.04	0.67; 1.61	1.06	0.67; 1.68	0.66	0.32; 1.34	0.87	0.40; 1.87
High (tertile 3: score >6)	0.64	0.42; 0.99	0.70	0.45; 1.09	0.76	0.45; 1.27	0.70	0.41; 1.21	0.21	0.07; 0.72	0.38	0.11; 1.20

Model 1: adjusting for gender, educational level, occupational grade, study center. Model 2: model 1 + adjusted for marital status, hypertension, diabetes, vascular diseases history, hypercholesterolemia, depressive symptoms, APOE genotype, incapacity in daily life activity, and cognitive impairment assessed by the Mini-Mental State Examination.

<sup>a</sup>For all cause dementia, model 1 was performed on 5,698 participants with 161 incident cases of dementia; model 2 was performed on 5,447 with 147 incident cases of dementia.

<sup>b</sup>For Alzheimer disease, model 1 was performed on 5,642 participants with 105 incident cases; model 2 was performed on 5,394 with 97 incident cases.

<sup>c</sup>For mixed and vascular dementia, model 1 was performed on 5,575 participants with 38 incident cases; model 2 was performed on 5,330 with 33 incident cases.

HR = hazard ratio; CI = confidence interval.

cessively 1) the 262 participants with cognitive impairment at baseline assessed by MMSE, 2) the 76 incident cases of dementia at the first follow-up, and 3) the 2,204 participants with MCI at baseline. The classification of MCI in our study was fully detailed elsewhere,<sup>26</sup> using the revised criteria,<sup>27</sup> which required evidence of impairment in at least one cognitive domain in the absence of dementia. Results of these analyses showed stimulating leisure activities to be significantly associated with the onset of dementia after controlling for gender, age, examination center, education, and occupational grade (table 4, model 1). Similar trends were observed in the fully adjusted analyses (table 4, model 2).

**DISCUSSION** The present report, carried out on a large elderly general population sample, showed that persons engaging in stimulating activities at least twice a week (doing a crossword puzzle or playing cards, attending organizations, going to the cinema/theater, and practicing an artistic activity) had a 50% reduced risk of developing dementia over the 4-year

follow-up compared to persons who engaged in such activities less than once per week 1) independently of education level, occupational attainment, and cognitive functioning of participants at inclusion; 2) after adjusting for vascular risk factors, depressive symptoms, and physical functioning; and 3) independently of other leisure activities.

Our findings thus suggest that stimulating activity may have a protective effect in relation to dementia. Our results are consistent with previous prospective studies showing a lower incidence of cognitive decline, amnesic mild cognitive impairment, dementia, and AD in participants with higher levels of mentally stimulating leisure activities.<sup>17-19,28-32</sup> Nevertheless, there is no consensus regarding the underlying mechanism involved. Our analyses explored multiple hypothetical pathways and appear to support the notion of protective role of leisure activity as a component of CR. Furthermore, the significant association observed even after controlling for education level, occupational attainment, and cognitive functioning suggest that stimulat-

**Table 4** Association between stimulating leisure activities and risk of dementia and Alzheimer disease (AD) after excluding successively participants with Mini-Mental State Examination (MMSE) deficit, incident cases of dementia at 2-year follow-up, and participants diagnosed with mild cognitive impairment (MCI) at inclusion

	All dementia*				AD cases*			
	Model 1		Model 2		Model 1		Model 2	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
<b>Analysis 1: After excluding the 244 participants with MMSE deficit</b>	N = 5,436/139 cases		N = 5,219/126 cases		N = 5,386/89 cases		N = 5,175/82 cases	
Low (tertile 1: score <3)	1		1		1		1	
Mild (tertile 2: score 3, 4)	0.40	0.26; 0.62	0.47	0.29; 0.74	0.42	0.25; 0.72	0.41	0.23; 0.73
High (tertile 3: score >4)	0.40	0.25; 0.64	0.47	0.28; 0.78	0.32	0.17; 0.61	0.32	0.16; 0.63
<b>Analysis 2: After excluding the 76 incident cases at the first follow-up</b>	N = 5,622/85 cases		N = 5,373/76 cases		N = 5,587/50 cases		N = 5,297/45 cases	
Low (tertile 1: score <3)	1		1		1		1	
Mild (tertile 2: score 3, 4)	0.42	0.24; 0.73	0.52	0.29; 0.96	0.43	0.21; 0.88	0.43	0.19; 0.98
High (tertile 3: score >4)	0.43	0.23; 0.78	0.62	0.33; 1.17	0.73	0.18; 0.94	0.48	0.21; 1.10
<b>Analysis 3: After excluding the 2204 participants diagnosed with MCI at inclusion</b>	N = 3,399/49 cases		N = 3,263; 46 cases		N = 3,380; 30 cases		N = 3,246; 29 cases	
Low (tertile 1: score <3)	1		1		1		1	
Mild (tertile 2: score 3, 4)	0.30	0.14; 0.65	0.36	0.16; 0.81	0.27	0.10; 0.74	0.28	0.09; 0.86
High (tertile 3: score >4)	0.37	0.18; 0.79	0.49	0.23; 1.06	0.35	0.13; 0.91	0.39	0.15; 1.04

Model 1: adjusting for gender, educational level, occupational grade, study center. Model 2: model 1 + adjusted for marital status, hypertension, diabetes, vascular diseases history, hypercholesterolemia, depressive symptoms, APOE genotype, incapacity in daily life activity, and cognitive impairment assessed by the MMSE. HR = hazard ratio; CI = confidence interval.

ing leisure activities contribute to CR independently from other well-known proxies of CR. This finding is in accordance with the finding from the WHICAP cohort study, in which greater participation in intellectual leisure activities was associated with faster cognitive decline in 283 patients with AD,<sup>15</sup> supporting the hypothesis that the disease course in AD may vary as a function of CR, sustaining the “use it or lose it” concept.<sup>33</sup>

We also examined whether the practice of less cognitively demanding leisure activities had an impact on onset of dementia. While one prospective study carried out in an elderly Chinese elderly population (n = 5,437) showed that watching television was associated with an increased risk of cognitive impairment over 5 years,<sup>19</sup> our finding showed no association between the practice of passive leisure activities—including watching television—and the risk of dementia. This result was consistent with findings from several prospective studies<sup>15,34,35</sup> and suggests that passive leisure activities do not contribute to CR in the same way as cognitively stimulating activities.

Impaired physical functioning and more specifically incapacity in activities of daily living have been shown to be associated with onset of dementia in several cohorts.<sup>36-39</sup> Based on this evidence, the hypothesis of a

protective role for physical leisure activities and dementia onset was proposed.<sup>9-12</sup> Our report did not show evidence of an association between doing odd jobs, gardening, and going for a walk and onset of dementia and are consistent with several prospective studies<sup>15,17,19,29-32,34</sup> suggesting that the practice of physical leisure activities in old age is perhaps not a good marker of physical functioning.

In this report, we also showed that social leisure activities such as visiting or receiving friends and relatives were significantly associated with a reduced risk of mixed/vascular dementia, but this association is confounded by depressive symptoms, which perhaps explains previous conflicting findings.<sup>7,8,16-19,34</sup> We observed this association only with mixed/vascular dementia and not with AD, which is consistent with the vascular dementia hypothesis. In this case it may be postulated that vascular changes causing dementia also give rise to depressive symptoms which in turn lead to social withdrawal. However, we were unable to further explore this hypothesis due to small numbers.

Several limitations of the present study should be noted. Our principal concern relates to the measurement of our exposure. First, leisure activities were assessed using 2 different self-report frequency questionnaires which were then categorized according

to their predominantly mental, physical, or social characteristics, resulting in the construction of 4 composite scores. However, leisure activities may simultaneously embody one or more of these 3 components so that it is impossible to derive a pure classification. Additional models were performed, in which the 4 leisure activities variables were entered simultaneously. We still observed a persistent and strong association between leisure activities considered a priori to be cognitively stimulating and risk of dementia, suggesting that although approximate measures, this group of activities is clearly distinct from the others. Secondly, for each leisure activity, we defined 3 arbitrary levels according to the tertile distribution of the composite scores, making comparisons of our results with the existing literature difficult to interpret. To our knowledge, there is no standardized well-validated leisure activity frequency scale for elderly populations which provides a normal distribution permitting more robust statistical analysis and cross-study comparisons.

The length of follow-up is a crucial issue as limited leisure activity might represent a manifestation of early dementia rather than a premorbid risk factor. The relatively short follow-up time—4 years—constitutes the second limitation of the study. To address this issue, we carried out supplementary analyses. No change in the magnitude or in the significance of the association were observed after excluding participants with cognitive impairment, classified as having MCI at baseline, or after excluding incident cases of dementia at the 2-year follow-up. However, it is plausible that apathy and loss of initiative might precede the cognitive impairment by more than 4 years, and thus our results could reflect early symptomatic behavioral changes of dementia.

Finally, the design of our study—an observational epidemiologic study—does not permit us to conclude that there is a causal link between mentally stimulating leisure activities and the onset of dementia and AD but not with vascular dementia. Furthermore, with only 19 cases of vascular dementia, we may not have the power to detect associations between leisure activities and vascular dementia. However, the longitudinal and multicentric design, the large sample size including more than 5,000 elderly subjects from the general population, the high quality of screening of dementia cases and subtypes of dementia, the low rate of attrition of our cohort, and the full adjustment for a large range of sociodemographic, socioeconomic, and health factors constitute the major strengths of this report.

The observed risk reduction of 50% over 4 years for all dementias in participants engaging at least twice weekly in stimulating leisure activities suggests

that the promotion of these activities in elderly community-dwelling populations may constitute a positive public health initiative without negative side effects which could delay dementia onset.

## AUTHOR CONTRIBUTIONS

S.F. and T.N.A. conducted the statistical analyses.

## DISCLOSURE

The 3C Study is conducted under a partnership agreement between the Institut National de la Santé et de la Recherche Médicale (INSERM), Victor-Segalen Bordeaux-2 University, and Sanofi-Aventis. The Fondation pour la Recherche Médicale funded the preparation and initiation of the study. The 3C Study is also supported by the Caisse Nationale Maladie des Travailleurs Salariés, Direction Générale de la Santé, MGEN, Institut de la Longévité, Conseils Régionaux d'Aquitaine et Bourgogne, Fondation de France, and Ministry of Research—INSERM Programme 'Cohortes et collections de données biologiques.' Drs. Akbaraly, Portet, and Fustinoni report no disclosures. Dr. Dartigues serves on a scientific advisory board for and has received funding for travel from Janssen-Cilag; received a gift worth more than US \$500 from Novartis; holds a corporate appointment with Merck Serono; and has received research support from Novartis and Ipsen. Drs. Artero, Rouaud, and Touchon report no disclosures. Dr. Ritchie serves on scientific advisory boards for the Biomedical Research Centre, King's College London, and London and MRC Strategic Steering Committee (Longitudinal Health and Aging Research Unit); and serves on editorial advisory boards of the *International Journal of Geriatric Psychiatry, Dementia, International Psychogeriatrics, The Journal of Clinical and Experimental Psychogeriatrics, Neuronale, Neurologie-Psychiatrie-Gériatrie, and Gerontology*. Dr. Berr serves on a scientific advisory board for and has received funding for travel from Janssen-Cilag and has received research support from Agence Nationale de la Recherche.

Received February 24, 2009. Accepted in final form June 22, 2009.

## REFERENCES

1. Fratiglioni L, Paillard-Borg S, Winblad B. An active and socially integrated lifestyle in late life might protect against dementia. *Lancet Neurol* 2004;3:343–353.
2. Katzman R. Education and the prevalence of dementia and Alzheimer's disease. *Neurology* 1993;43:13–20.
3. Scarmeas N, Stern Y. Cognitive reserve: implications for diagnosis and prevention of Alzheimer's disease. *Curr Neurol Neurosci Rep* 2004;4:374–380.
4. Evans DA, Hebert LE, Beckett LA, et al. Education and other measures of socioeconomic status and risk of incident Alzheimer disease in a defined population of older persons. *Arch Neurol* 1997;54:1399–1405.
5. Stern Y, Gurland B, Tatemichi TK, Tang MX, Wilder D, Mayeux R. Influence of education and occupation on the incidence of Alzheimer's disease. *JAMA* 1994;271:1004–1010.
6. Alexander GE, Furey ML, Grady CL, et al. Association of premorbid intellectual function with cerebral metabolism in Alzheimer's disease: implications for the cognitive reserve hypothesis. *Am J Psychiatry* 1997;154:165–172.
7. Barnes LL, Mendes de Leon CF, Wilson RS, Bienias JL, Evans DA. Social resources and cognitive decline in a population of older African Americans and whites. *Neurology* 2004;63:2322–2326.
8. Fratiglioni L, Wang HX, Ericsson K, Maytan M, Winblad B. Influence of social network on occurrence of dementia: a community-based longitudinal study. *Lancet* 2000;355:1315–1319.

9. Laurin D, Verreault R, Lindsay J, MacPherson K, Rockwood K. Physical activity and risk of cognitive impairment and dementia in elderly persons. *Arch Neurol* 2001;58:498–504.
10. Yoshitake T, Kiyohara Y, Kato I, et al. Incidence and risk factors of vascular dementia and Alzheimer's disease in a defined elderly Japanese population: the Hisayama Study. *Neurology* 1995;45:1161–1168.
11. Larson EB, Wang L, Bowen JD, et al. Exercise is associated with reduced risk for incident dementia among persons 65 years of age and older. *Ann Intern Med* 2006;144:73–81.
12. Yaffe K, Barnes D, Nevitt M, Lui LY, Covinsky K. A prospective study of physical activity and cognitive decline in elderly women: women who walk. *Arch Intern Med* 2001;161:1703–1708.
13. Lautenschlager NT, Cox KL, Flicker L, et al. Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: a randomized trial. *JAMA* 2008;300:1027–1037.
14. Vascular factors and risk of dementia: design of the Three-City Study and baseline characteristics of the study population. *Neuroepidemiology* 2003;22:316–325.
15. Helzner EP, Scarmeas N, Cosentino S, Portet F, Stern Y. Leisure activity and cognitive decline in incident Alzheimer disease. *Arch Neurol* 2007;64:1749–1754.
16. Karp A, Paillard-Borg S, Wang HX, Silverstein M, Winblad B, Fratiglioni L. Mental, physical and social components in leisure activities equally contribute to decrease dementia risk. *Dement Geriatr Cogn Disord* 2006;21:65–73.
17. Wilson RS, Scherr PA, Schneider JA, Tang Y, Bennett DA. Relation of cognitive activity to risk of developing Alzheimer disease. *Neurology* 2007;69:1911–1920.
18. Wang HX, Karp A, Winblad B, Fratiglioni L. Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: a longitudinal study from the Kungsholmen project. *Am J Epidemiol* 2002;155:1081–1087.
19. Wang JY, Zhou DH, Li J, et al. Leisure activity and risk of cognitive impairment: the Chongqing aging study. *Neurology* 2006;66:911–913.
20. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV*. Washington, DC: American Psychiatric Association; 1994.
21. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;34:939–944.
22. Roman GC, Tatemichi TK, Erkinjuntti T, et al. Vascular dementia: diagnostic criteria for research studies: report of the NINDS-AIREN International Workshop. *Neurology* 1993;43:250–260.
23. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Measures* 1977;1:385–401.
24. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
25. Lamarca R, Alonso J, Gomez G, Munoz A. Left-truncated data with age as time scale: an alternative for survival analysis in the elderly population. *J Gerontol A Biol Sci Med Sci* 1998;53:M337–M343.
26. Artero S, Ancelin ML, Portet F, et al. Risk profiles for mild cognitive impairment and progression to dementia are gender specific. *J Neurol Neurosurg Psychiatry* 2008;79:979–984.
27. Winblad B, Palmer K, Kivipelto M, et al. Mild cognitive impairment—beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *J Intern Med* 2004;256:240–246.
28. Scarmeas N, Levy G, Tang MX, Manly J, Stern Y. Influence of leisure activity on the incidence of Alzheimer's disease. *Neurology* 2001;57:2236–2242.
29. Verghese J, LeValley A, Derby C, et al. Leisure activities and the risk of amnesic mild cognitive impairment in the elderly. *Neurology* 2006;66:821–827.
30. Verghese J, Lipton RB, Katz MJ, et al. Leisure activities and the risk of dementia in the elderly. *N Engl J Med* 2003;348:2508–2516.
31. Wilson RS, Bennett DA, Bienias JL, et al. Cognitive activity and incident AD in a population-based sample of older persons. *Neurology* 2002;59:1910–1914.
32. Wilson RS, Mendes De Leon CF, Barnes LL, et al. Participation in cognitively stimulating activities and risk of incident Alzheimer disease. *JAMA* 2002;287:742–748.
33. Hultsch DF, Hertzog C, Small BJ, Dixon RA. Use it or lose it: engaged lifestyle as a buffer of cognitive decline in aging? *Psychol Aging* 1999;14:245–263.
34. Crowe M, Andel R, Pedersen NL, Johansson B, Gatz M. Does participation in leisure activities lead to reduced risk of Alzheimer's disease? A prospective study of Swedish twins. *J Gerontol B Psychol Sci Soc Sci* 2003;58:P249–255.
35. Fabrigoule C, Letenneur L, Dartigues JF, Zarrouk M, Commenges D, Barberger-Gateau P. Social and leisure activities and risk of dementia: a prospective longitudinal study. *J Am Geriatr Soc* 1995;43:485–490.
36. Barberger-Gateau P, Dartigues JF, Letenneur L. Four Instrumental Activities of Daily Living Score as a predictor of one-year incident dementia. *Age Ageing* 1993;22:457–463.
37. Mathuranath PS, George A, Cherian PJ, Mathew R, Sarma PS. Instrumental activities of daily living scale for dementia screening in elderly people. *Int Psychogeriatr* 2005;17:461–474.
38. Barberger-Gateau P, Commenges D, Gagnon M, Letenneur L, Sauvel C, Dartigues JF. Instrumental activities of daily living as a screening tool for cognitive impairment and dementia in elderly community dwellers. *J Am Geriatr Soc* 1992;40:1129–1134.
39. De Lepeleire J, Aertgeerts B, Umbach I, et al. The diagnostic value of IADL evaluation in the detection of dementia in general practice. *Aging Ment Health* 2004;8:52–57.