

Prevalence of Epilepsy in the Elderly: The Rotterdam Study

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Summary: We assessed the prevalence of epilepsy in an elderly population in The Netherlands. The study was conducted from 1991 to 1993 as part of the Rotterdam Study, a population-based door-to-door study of all elderly people living in Ommoord, a suburb of Rotterdam, and included 5,559 persons aged 55–95 years. All subjects were screened for epilepsy through direct questions regarding the existence of epilepsy and antiepileptic drug (AED) use, in addition to relevant questions from the World Health Organization (WHO) protocol for epidemiologic studies of neurologic diseases. Further evaluation of screen positives was made by a panel of 1 study physician and 4 epileptologists, who also classified all confirmed cases of epilepsy according to the classifications of

the International League Against Epilepsy (ILAE). The overall prevalence of active epilepsy in our study population was 0.9% including special syndromes and 0.8% excluding special syndromes. The prevalence increased with age from 0.7% for those aged 55–64 years to 1.2% for those aged 85–94 years. The increase with age was detected among men and women both. Our study confirms other findings showing that the prevalence of active epilepsy increases with age in the elderly. The prevalence figures in our study were high as compared with those of other population-based studies. Epilepsy appears to be a major cause of morbidity in the elderly. **Key Words:** Epilepsy—Population studies—Prevalence—Screening—Seizures.

The prevalence of epilepsy in the elderly has been investigated in only a few studies. Hauser and Kurland (1,2) and Tallis et al. (3) reported that the prevalence and incidence of epilepsy increase with age, but this was not confirmed by other investigators (4,5). In a large primary-care-based study of people aged ≥ 60 years in the United Kingdom, Tallis et al. reported an increase in age-adjusted prevalence and incidence figures of epilepsy, making it the third most common neurological disorder (after stroke and dementia) in this age group (3). We wished to assess the prevalence of epilepsy in an elderly Dutch population.

METHODS

Study population

The investigation was conducted as part of the ongoing Rotterdam Study, a prospective follow-up

survey of the total population aged ≥ 55 years in the district of Ommoord in Rotterdam, the Netherlands (6). The baseline survey took place from June 1990 until June 1993. Informed consent and permission to obtain relevant information from treating physicians were obtained from all participants. Throughout the Rotterdam Study, subjects were surveyed in random clusters. Epilepsy screening was incorporated at the time of the 25th random survey in June 1991. The total eligible population consisted of 7,129 persons. Because the number of subjects aged ≥ 95 years was too small to determine an accurate prevalence figure, we excluded this age group from our analysis. Therefore our total eligible population consisted of 7,081 persons, 5,559 (79%) of whom participated in the epilepsy screening.

Screening for epilepsy

The standard Rotterdam Study protocol consisted of a home interview followed by physical examinations in a research center. The screening for epilepsy was conducted during the home interview by a trained research assistant and consisted of one

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question directly inquiring about epilepsy (Have you ever experienced epilepsy or had an epileptic fit?) and three questions regarding possible symptoms of epilepsy that were taken from the World Health Organization (WHO) research protocol for the screening of neurological disorders in developing countries (7), as follows: Have you ever lost consciousness? Have you ever had episodes where you lost contact with your surroundings? and Have you ever had any shaking of your arms and legs which you could not control? In addition, all current drug prescriptions were registered and classified according to the Anatomical Therapeutic Chemical (ATC) classification index (8). We defined as screen-positive for epilepsy all persons who (a) self reported epilepsy or fits, or (b) used antiepileptic drugs (AEDs: ATC-code N03), or (c) answered yes to at least two of the three WHO questions.

Diagnostic workup and classification of epilepsy

For persons who reported having had epilepsy or seizures during their life ($n = 97$), as well as for persons receiving AEDs without reporting epilepsy ($n = 24$), additional information was obtained from general practitioner's and specialists' medical records, including EEG and computed tomography (CT) scan reports. For 22 subjects, no further information was available from medical records and they were contacted by telephone by a specially trained physician who took a detailed medical and seizure history. A similar procedure was used for subjects who gave positive responses to at least two of the WHO screening questions but who neither reported having epilepsy or receiving AEDs ($n = 192$). Persons without a telephone, those who did not answer the telephone on several occasions, and those who were unable to give a reliable history by telephone were invited to an in-person interview, either in their home or at the research center. If the history suggested the possibility of epilepsy, the subject

was reinterviewed by 1 of 4 epileptologists (Drs. D. J. Beintema, C. A. E. H. van Oorschot, A. van Wieringen, and J. M. de Wilde-Ockeloen), and additional information was obtained from the general practitioner and other medical records.

All 313 screen-positive persons were subsequently reviewed by a panel consisting of the study physician and the 4 epileptologists. From all available information, the panel then decided whether a subject had epilepsy and, if so, classified the epilepsy according to the classification of the International League Against Epilepsy (ILAE) (9). Single seizures, treated or not, were classified as "epilepsy-special syndromes" according to 1989 ILAE guidelines (9). Active epilepsy was defined as having had a seizure within 5 years of prevalence date, regardless of treatment (10).

Data analysis

Prevalence was calculated by gender and 10-year age groups. We calculated the prevalence of active epilepsy and of lifetime epilepsy, which includes both active epilepsy and epilepsy in remission. Prevalence of active epilepsy was calculated both including and excluding special syndromes. To compare our results with those of other published studies, we also calculated the age-specific prevalences of active epilepsy, defined as having had a seizure within 5 years of prevalence date or current use of AEDs. The proportion of each ILAE subtype of epilepsy was reported by gender.

RESULTS

Table 1 shows the age and gender distribution of the study population and the number of screen-positive individuals. Of the total population of 5,559 persons screened, 313 persons (5.6%) were screen positive. No screen-positive men were in the highest age category. Overall, 97 (1.7%) persons reported epilepsy, 24 (0.4%) received AEDs without

TABLE 1. Age distribution and screening results of the study population

Parameter	Age groups (yr)				Total
	55-64	65-74	76-84	85-94	
No. of subjects	2,125	1,916	1,105	413	5,559
Proportion of women (%)	56	55	65	80	59
No. with self-reported epilepsy (%)	38 (1.7)	37 (1.9)	14 (1.3)	8 (1.9)	97 (1.7)
No. receiving AEDs (%) ^a	19 (0.9)	23 (1.2)	13 (1.2)	6 (1.5)	61 (1.1)
No. of WHO screen positives (%) ^b	97 (4.6)	80 (4.2)	45 (4.1)	15 (3.6)	237 (4.3)
No. of screen positives (%) ^c	121 (5.7)	115 (6.0)	56 (5.1)	21 (5.1)	313 (5.6)

AED, antiepileptic drug; WHO, World Health Organization.

^a Regardless of self-reported epilepsy.

^b Regardless of self-reported epilepsy and AED use: defined as having answered positively to at least two of the three WHO screening questions on epilepsy.

^c Defined as self-reported epilepsy or AED use or WHO screen positive.

TABLE 2. Results of verification for all screen-positive subjects

Screen-positive categories	Final diagnosis			Total
	Epilepsy	No epilepsy	Missing	
Self-reported epilepsy	70	20	7	97
AED use without self-reported epilepsy	4	20	0	24
WHO screen positive ^a without self-reported epilepsy or AED use	11	180	1	192
Total	85	220	8	313

Abbreviations as in Table 1.

^a Defined as having answered positively to at least two of the three WHO screening questions on epilepsy.

reporting epilepsy, and 192 (3.5%) persons were screen positive because of positive answers to the WHO questions even though they did not report epilepsy or treatment with AEDs.

Table 2 shows results after verification of all screen-positive subjects. We confirmed 85 cases of epilepsy, or 27% of all screen positives. For 27 persons (28%) who reported epilepsy, the diagnosis could not be confirmed. Eleven cases showed clear evidence from neurologists' records for a nonepileptic cause of symptoms: sleep apnea, transient ischemic attack ($n = 2$), depression, psychogenic attacks ($n = 2$), muscle headaches, narcolepsy, amaurosis fugax with migraine, nocturnal urinary incontinence, and syncope. For the remaining 16 persons, no information regarding possible epilepsy or other paroxysmal disorder could be detected. Nine of them were reinterviewed by 1 of the epileptologists, who made a specific nonepilepsy diagno-

TABLE 4. Summary of special syndromes in the Rotterdam Study

Etiology (no. of subjects)	Associated condition
Acute symptomatic (7)	Eclampsia, acute CVA, fever, influenza encephalitis, alcohol withdrawal (2), cerebral anoxia
Remote symptomatic (3)	CVA >1 year before seizure, Parkinson's disease, subdural hematoma
Cryptogenic (10)	Abnormal EEG or CT scan; no known antecedent cause (5); no abnormality on EEG or CT scan; no known antecedent cause (5)
Total (20)	

CVA, cerebrovascular accident; CT, computed tomography.

sis. No further information could be obtained in 7 individuals. Of the 24 subjects who received AEDs without reporting epilepsy, we concluded that only 4 had epilepsy. The reasons for treatment with AEDs for conditions other than epilepsy were diverse: 3 persons were prescribed clonazepam for restless legs syndrome, 7 persons received carbamazepine (CBZ) for trigeminal or hypoglossal neuralgia, 1 subject received CBZ for manic-depressive psychosis; 1 was prescribed valproate (VPA) prophylactically after herpes encephalitis without clinical or EEG evidence of epilepsy, 5 persons with mental disorders were long-term barbiturate users, 2 persons were prescribed CBZ for polyneuropathy, and 1 subject could not be verified as an AED user.

Table 3 summarizes the types of epilepsies for both active and lifetime epilepsy and for men and women. Localization-related epilepsy was the most

TABLE 3. Subclassification of epilepsies according to the ILAE

Epilepsy type according to ILAE classification	Active epilepsy, no. of subjects (%)		Lifetime epilepsy, no. of subjects (%)	
	Men	Women	Men	Women
I Localization-related epilepsies	17 (73.9)	18 (64.3)	19 (55.9)	21 (41.2)
I-1 Idiopathic	0	0	0	0
I-2 Symptomatic	10	8	11	10
I-3 Cryptogenic	7	10	8	11
II Generalized epilepsies	1 (4.4)	2 (7.1)	3 (8.8)	2 (3.9)
II-1 Idiopathic	0	1	1	1
II-2 Cryptogenic or symptomatic	0	0	0	0
II-3 Symptomatic	1	1	2	1
III Epilepsies undetermined whether focal or generalized	0 (0.0)	4 (14.3)	4 (11.8)	16 (31.4)
III-1 With both focal and generalized seizures	0	0	0	0
III-2 Undetermined seizure type	0	4	4	16
IV Special syndromes	5 (21.7)	4 (14.3)	8 (23.5)	12 (23.5)
IV-1 Single seizure, not followed by treatment with AEDs	1	2	3	6
IV-2 Single seizure, followed by treatment with AEDs	4	2	5	6
Total	23 (100%)	28 (100%)	34 (100%)	51 (100%)

ILAE, International League Against Epilepsy; AEDs, antiepileptic drugs.

TABLE 5. Prevalence of lifetime and active^a epilepsy by gender and age [cases per 1,000 (no. of cases)]

10-Year age group	Men					Women		
	No. of subjects	Including special syndromes		Excluding special syndromes		No. of subjects	Including special syndromes	
		Lifetime	Active	Lifetime	Active		Lifetime	Active
55-64	932	13.9 (13)	6.4 (6)	9.7 (9)	4.3 (4)	1,193	16.8 (20)	7.5 (9)
65-74	855	16.4 (14)	11.8 (11)	12.9 (11)	10.5 (9)	1,061	17.0 (18)	7.5 (8)
75-84	390	17.9 (7)	15.4 (6)	15.4 (6)	12.8 (5)	715	9.8 (7)	8.4 (6)
85-94	83	0	0	0	0	330	18.2 (6)	15.2 (5)
Total	2,260	15.0 (34)	10.2 (23)	11.5 (26)	8.0 (18)	3,299	15.5 (51)	8.5 (28)

10-Year age group	Women		No. of subjects	All			
	Excluding special syndromes			Including special syndromes		Excluding special syndromes	
	Lifetime	Active		Lifetime	Active	Lifetime	Active
55-64	12.6 (15)	7.5 (9)	2,125	16.0 (33)	7.1 (15)	11.3 (24)	6.1 (13)
65-74	12.3 (13)	6.6 (7)	1,916	16.2 (32)	9.9 (19)	12.5 (24)	8.4 (16)
75-84	8.4 (6)	7.0 (5)	1,105	12.7 (14)	10.9 (12)	10.9 (12)	9.0 (10)
85-94	15.2 (5)	12.1 (4)	413	14.5 (6)	12.1 (5)	12.1 (5)	9.7 (4)
Total	11.8 (39)	7.6 (25)	5,559	15.3 (85)	9.2 (51)	11.7 (65)	7.7 (43)

^a Defined as at least one seizure within 5 years of prevalence date, regardless of treatment.

common type in both men and women. The second most common type of active epilepsy in men was special syndrome, whereas in women it was both undetermined epilepsy and special syndrome. Generalized epilepsy was relatively uncommon in both sexes.

Table 4 summarizes all special syndromes. Of the 20 cases detected, 7 were acute symptomatic seizures, 3 of which were subsequently treated with AEDs [stroke, alcohol withdrawal (n = 2)]. Three patients with remote symptomatic epilepsy were detected, all of whom received AEDs. The remaining 10 patients had no determinable antecedent cause, but 5 of them had abnormalities on EEG or CT scan; 1 of the 5 patients subsequently was started on AED treatment. Four of the 5 remaining subjects with no abnormality on EEG or CT scan were treated with AEDs.

The prevalence figures of epilepsy are shown in Table 5. We noted an overall lifetime prevalence of epilepsy in this 55-95-year-old population of 15.3

cases in 1,000 and an overall prevalence of active epilepsy of 9.2 cases in 1,000. The prevalence of active epilepsy increased with advancing age, but the prevalence of lifetime epilepsy leveled off or even decreased in the highest age groups. When we excluded special syndromes, the overall prevalence for active epilepsy was 7.7 cases per 1,000 persons. When we included subjects treated with AEDs in the definition of active epilepsy, regardless of whether they had had a seizure in the last 5 years, the prevalence figures increased slightly (Table 6).

DISCUSSION

We screened a large elderly population and determined the prevalence of active and lifetime epilepsy in the group. The prevalence figures for active epilepsy were among the highest reported in the literature among elderly persons. Only Hauser et al. reported a higher rate for active epilepsy in persons aged >75 years (2).

TABLE 6. Prevalence of active epilepsy by gender and age (cases per 1,000 persons)

10-Year age group	Men			No. of subjects	Women		No. of subjects	All	
	No. of subjects	Including special syndromes	Excluding special syndromes		Including special syndromes	Excluding special syndromes		Including special syndromes	Excluding special syndromes
55-64	932	8.6	6.4	1,193	9.2	8.4	2,125	8.9	7.5
65-74	855	14.0	11.7	1,061	9.4	8.5	1,916	11.5	9.9
75-84	390	15.4	12.8	715	8.4	7.0	1,105	10.9	9.0
85-94	83	0.0	0.0	330	18.2	15.2	413	14.5	12.1
Total	2,260	11.5	9.3	3,299	10.0	8.8	5,559	10.6	9.0

Active epilepsy defined as at least one seizure within 5 years of prevalence date or antiepileptic drug use.

TABLE 7. Prevalence of epilepsy in elderly subjects: A comparison of recent studies

Country (reference)	Year	Study design	Study size (age, yr)	Age group (yr)	Prevalence (cases per 1,000)		Criteria used to define epilepsy and activeness of epilepsy	
					Active	Lifetime		
Rotterdam, The Netherlands	1994	Population based; WHO screening protocol	N = 5,559 (55+)	55-64	6.1	7.5	11.3	Recurrent seizures, provoked and unprovoked; active defined as having had at least one seizure in the past 5 years regardless of treatment (column 1) or having had at least one seizure in the past 5 years or current treatment (column 2)
				65-74	8.4	9.9	12.5	
				75-84	9.0	9.0	10.9	
				85-94	9.7	12.1	12.1	
Rochester, MN, U.S.A. (2)	1991	Register based; total population of Rochester	N = 56,447 (all ages)	55-64	7.7	9.8	Recurrent unprovoked seizures; active defined as having had at least one seizure in the past 5 years or having had AED treatment in the past 5 years	
				65-74	6.8	8.1		
				75+	14.8	16.9		
United Kingdom (3)	1991	Register based; computerized general practice database	N = 81,727 (60+)	60-69	—	10.9	No distinction between provoked or unprovoked seizures; no distinction between active epilepsy or epilepsy in remission	
				70-79	—	12.0		
				80+	—	13.1		
Ecuador (18)	1992	Population based; study-specific screening protocol	N = 10,948 (50+)	50-59	11.7	21.2	Single or recurrent seizures, provoked and unprovoked, excluding febrile seizures; active epilepsy defined as having had a seizure in the past year and/or receiving AED at the time of the study	
				60-69	6.6	16.4		
				70-98	8.2	14.2		
China (4)	1985	Population based; WHO screening protocol	N = 14,173 (50+)	50-59	—	3.4	Recurrent unprovoked seizures; no distinction between active and lifetime prevalence	
				60-69	—	3.9		
India (13)	1988	Population based; WHO screening protocol	N = 8,071 (40+)	70+	—	2.9	Recurrent unprovoked seizures; active epilepsy defined as having had at least one seizure in the past 5 years regardless of treatment	
				40-59	3.4	3.9		
Nigeria (11)	1987	Population based; WHO screening protocol	N = 18,954 (all ages)	60+	3.5	4.3	Recurrent unprovoked seizures; if previously untreated, having had at least one seizure in the past 2 years and if under treatment having had at least one seizure in the past 3 years	
				35-54	4.5	—		
				55+	4.8	—	Recurrent unprovoked seizures; active defined as having had at least one seizure in the past 5 years or having had treatment in the past 5 years	
Tunisia (12)	1993	Population based; WHO screening protocol	N = 3,460 (50+)	50-59	0.5	—	Recurrent unprovoked seizures; active defined as having had at least one seizure in the past 5 years or having had treatment in the past 5 years	
				60+	3.1	—		
Copiah county, U.S.A. (19)	1986	Population based; study-specific screening protocol	N = 8,925 (40+)	40-59	8.8	13.1	Recurrent unprovoked seizures; active defined if under treatment as having had at least one seizure in the past 3 years and if untreated having had a seizure in the past year	
				60+	5.1	8.4		
Sweden (5)	1992	Register based; multisource medical registers	N = 52,792 (50+)	50-59	6.4	—	Recurrent unprovoked seizures; active defined as having had at least one seizure in the past 5 years or receiving AEDs in the year preceding prevalence date	
				60-69	6.2	—		
				70+	3.2	—		
Italy (20)	1983	Register based; medical and nonmedical registers	N = 45,153 (all ages)	40-59	4.6	—	Recurrent unprovoked seizures; active defined as having had at least one seizure in the last 5 years or receiving AEDs	
				60+	3.0	—		
United Kingdom (21)	1983	Register based; register of one general practice	N = 1,581 (51+)	50-60	— ^a	11.8	Provoked and unprovoked seizures excluding febrile seizures; active defined as having had at least one seizure in the past 2 years	
				61-70		24.1		
				71-80		26.2		
				80+		10.6		

AEDs, antiepileptic drugs.

^a Only an overall prevalence figure for active epilepsy was given: 5.3 in 1,000.

Our study has several possible limitations. First, despite our best efforts, we were unable to obtain 100% participation. Although our participation rate was high given the age distribution of our study

population, the prevalence of epilepsy may be different among nonparticipants as compared with participants. A second issue concerns the sensitivity of our screening questions. The screening instru-

ment we used contained direct questions regarding epilepsy and current drug use, in addition to questions that were adapted from the WHO protocol originally designed for neuroepidemiological studies in developing countries (7). Other studies have also used this protocol to screen for epilepsy (4,11–13). Nonetheless, although high sensitivities have been reported, the instrument has never been validated properly (14). We did not include a sample of screen negatives because the prevalence among screen negatives is likely to be much lower than that in the total study population, and to obtain a stable and precise estimate of the prevalence among screen negatives, a very large sample would have been required. Therefore, we may have missed some cases of epilepsy, especially persons with partial seizures. Finally, Alzheimer's disease is a recognized risk factor for late-onset epilepsy (15,16). Because of underreporting of seizures and symptoms in demented patients, we may have missed some patients with both dementia and epilepsy. These various considerations make it likely that our prevalence figures are slight underestimates.

Comparisons among studies must take into account variations in methods and definitions (2). Table 7 compares the results of our study with those of several other recent investigations which provided age-specific prevalences of epilepsy. We classified special syndromes as epilepsy according to the 1989 ILAE classification (9). The rationale of including special syndrome is debatable, however. Most acute symptomatic seizures are clearly not epilepsy, and some subjects who immediately receive treatment with AEDs after a first cryptogenic or remote symptomatic seizure may or may not develop epilepsy subsequently. Furthermore, single seizures that occurred long ago are likely to be underreported. To enhance comparability, we report rates for active and lifetime epilepsy that exclude the special syndromes.

Few investigators have reported age-specific prevalence figures for active epilepsy in the elderly, and those that did generally provided rates considerably lower than those we report. Screening for epilepsy relies on a willingness to report epilepsy or seizures or related symptoms. In the Rotterdam Study, screening for epilepsy was conducted as part of a much larger investigation of other diseases relevant to aging and the participation rate was high (6). This study context may have contributed to our identifying a large number of patients. For lifetime prevalence, however, our estimates are relatively low, in particular as compared with estimates from register-based studies. Because remission rates are estimated to exceed 61% at 10 years after of epi-

lepsy onset (17), population-based studies of the lifetime prevalence of epilepsy may well suffer from recall bias and underreporting, resulting in considerable underestimation, especially in the elderly. Besides, what researchers truly wish to ascertain is the cumulative incidence. Because mortality is increased among subjects with epilepsy, as compared to subjects without epilepsy, lifetime prevalence will always underestimate cumulative incidence.

The results of our study confirm earlier findings indicating that the prevalence of active epilepsy increases with age in the elderly. The prevalence figures in our study were high as compared with those of other population-based studies. Epilepsy appears to be a major cause of morbidity in the elderly.

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