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Epidemiology of epilepsy in old age – English Version

Johannes D. Lang · Hajo M. Hamer
Epilepsiezentrum, Neurologische Klinik, Erlangen, Germany

Abstract

Background: Epilepsy is a common neurological disease affecting all ages. The increasing frequency of symptomatic epilepsies with age is partly due to cerebrovascular and neurodegenerative diseases. Better knowledge of the epidemiology of epilepsy in old age improves our understanding of the disease as well as the therapeutic and sociomedical challenges for the individual and society.

Objective: What do we currently know about the epidemiology of the epilepsies in old age and how should this be classified?

Material and methods: A MEDLINE search in PubMed was conducted using the terms “epilepsy”, “elderly” and “incidence” or “prevalence” or “epidemiology” and relevant publications were analyzed.

Results: The point prevalence of epilepsy of older age is 0.5–0.8% of the population and affects approximately 500,000 people in Germany. The highest age-adjusted prevalence is reported to lie beyond the age of 75 years. In recent decades, the prevalence climbed further among the 75-year-olds to be twice as high as among the adult working population. The incidence shows a significant increase among patients 65 years and older, reaches its maximum at around 80–85 years of age and is somewhat higher in men.

Conclusion: Reasons for the high incidence and prevalence of epilepsy in old age are the age-related incidence of potentially epilepsy-associated diseases combined with a longer long-term survival for these diseases due to better medical care and an increase in life expectancy. The change in the age pyramid with a higher (and in the coming decades further increasing) proportion of old people, will further increase the rise of epilepsy of older age.

Keywords

Elderly · Aged · Seizures · Incidence · Prevalence

Background

Epilepsy is a common neurological disorder that affects about half a million people in Germany alone. The prevalence and incidence of the disease are higher in advanced age than in younger years. At the same time, there are diagnostic and therapeutic differences to be considered in advanced age. The relevance of knowledge of these differences continues to increase with population trends and the trend of aging societies. This article reviews in more detail the epidemiology of epilepsy in older age.

What is epidemiology?

Epidemiology is the study of the distribution, causes, and consequences of diseases and (health-related) conditions in the population. Unlike clinical medicine, its aim is not the optimal treatment of individual patients, but the study of target populations of different societies. Thus, it contributes to a more comprehensive understanding of diseases. It forms the basis of clinical studies and enables the identification of risk or protective factors for prevention and facilitates health policy decisions as well as the allocation of health care resources.

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The definition of epilepsy

A uniform definition of epilepsy is needed to enable comparability of epidemiological measures. The International League Against Epilepsy (ILAE) has developed a conceptual definition according to which epilepsy is characterized by a persistent predisposition to epileptic seizures and their neurobiological, cognitive, psychological, and social consequences and requires at least one seizure [1]. It primarily enables a clinical diagnosis to be made [2]. In the context of epidemiological studies, operationalization of the definition is necessary. Here, the use of the more conservative definition of at least two epileptic seizures at a time interval of more than 24 h, which was previously valid and established in practice, is still recommended [3, 4]. The advantages of this recommendation lie in the often simpler and more uniform assessment especially for cases in which recurrence is the only available evidence of a persistent predisposition and in the comparability over past decades [4]. With regard to epilepsy in older people (with a higher proportion of symptomatic epilepsy), it is useful to include imaging and electrographic findings. Without these, there is a risk of under-reporting due to the often more subtle seizure semiology in older age [5].

Epilepsy in older adults and persistent epilepsy

Epilepsy in old age includes both new-onset epilepsy and epilepsy that persists into older age. The term “epilepsy in older adults” includes all forms of epilepsy with new onset after the 65th year of life (LY). This distinction is useful in many respects, since *de novo* epilepsy in older age often has different underlying causes than epilepsy of childhood, adolescence, or adulthood. The 65th LY as the cut-off for epilepsy in older people is arbitrarily chosen, since neither incidence nor morbidity increases abruptly at this age, and it is based on the definition of retirement age [6].

Prevalence of epilepsy in old age

Prevalence describes the distribution of an event or characteristic in a spatially or temporally defined population. Since it represents an actual state, it is not useful for assessing etiology or prognosis. On the contrary, it is more suitable for the distribution of resources in the healthcare system.

The number of studies on the prevalence of epilepsy significantly exceeds the number of incidence studies, which is mainly due to their lower effort and costs. To estimate prevalence, most studies include people with active epilepsy, that is, patients who have epilepsy according to the operational ILAE definition and who have had at least one seizure in the 5 years before the survey.

The point prevalence of active epilepsy is approximately 6.4/1000 (95%CI: 5.6–7.3) and varies, sometimes significantly, by country of origin, age, and sex [7]. In a review of European studies, the prevalence across all age groups ranged from 3.3 to 7.8/1000 population [8]. With a proportion of 0.6% of the population (6/1000), approximately 500,000 people in Germany (out of 83 million, as of 2021) suffer from epilepsy. In the EPIDEG study (EPIDemiology of Epilepsies in Germany), the prevalence of treated patients with epilepsy in Germany was recorded for the first time in 1995 on a representative, nationwide sample and again in 2010 in a second study. During this period, the prevalence increased from 4.7 to 5.5/1000 [9], comparable to the prevalence in other European countries and previous studies in Germany. In Europe, the prevalence in adults aged 20–64 years was approximately 5.3–6.3/1000 (1.9 million) and, by comparison, in children and adolescents it was in the range of 3.2–5.1/1000 (0.9 million). In older adults, prevalence data vary even more (3.0–7.6/1000; 0.6 million in those over 65 years of age; [8]). Using prescription data in Germany in 2009, another study found a period prevalence of 9.1/1000 for medication prescriptions due to epilepsy. In older adults (≥ 65 th LY), it was significantly higher (12.5/1000) than in children and adolescents (< 18 th LY, 5.2/1000) and higher than in adults (8.9/1000; [10]). In

Iceland, an increase from 6.7/1000 in those aged 55–64 years to 7.3/1000 in those aged 85 years and older was described, while a Danish study showed an increase from 7.1 to 12.1/1000 for the same age groups, and values up to a maximum of 20/10,000 were described in England and Germany [11].

Underestimation of seizures in old age

As a reason for the lower prevalence in older age in some studies, an incomplete identification of people with active epilepsy and thus an underestimation in this age group can be assumed. In four homes for older adults in the Erlangen area, epilepsy was found in 2.8% of 389 residents aged 82.5 years (66–105 years) surveyed, whereas only 1.8% had been diagnosed before the study began [5]. In addition, 30% of all people over 60 years of age in Germany live alone, and by 2040 this will be 33% [12]. At 80 years of age, half of women (56%) and 22% of men live alone [13]. Therefore, it is likely that seizures in this age group often go unobserved. In addition, seizures with subtle semiology occur more frequently in older ages [5].

Incidence of epilepsy in old age

Incidence describes the relative frequency for the occurrence of a disease or characteristic in a population over a defined period of time. In a meta-analysis of 48 incidence studies, the annual cumulative incidence was 67.8/100,000/year [7]. The incidence rate, the proportion of newly diseased individuals, averaged 61.4/100,000 person-years (PY; [7]). Both ratios differ, sometimes significantly, depending on the event studied and the characteristics of the sample. Important influencing variables include age, sex, and country of origin (e.g., industrialized or developing country; [14, 15]).

Age dependence of incidence

Epilepsy is a disease of all age groups. However, its incidence shows a U-shaped course, with the highest incidence rates in the youngest and oldest individuals

[7]. Until the early 1980s, epilepsy was considered primarily a disease of childhood [5]. The shift of the highest incidence to old age is a result of better medical care (prevention of perinatal complications) and increasing life expectancy (see below). In a prospective study between 1984 and 1987, 25% of patients with new-onset epilepsy were younger than 15 years [16]. In children, the incidence varies from around 80 to 130/100,000/year, with the highest rate in the 1st LY [17, 18]. After the 1st–9th LY, the incidence is around 50–60/100,000/year [17] and then decreases to the adult level of just under 20–40/100,000/year by the 17th LY [17, 19, 20]. Here it remains stable (about 30/100,000/year or less) between 20 and 65 LY [8]. With increasing age, the incidence increases again until it peaks around the 85th LY with up to 180/100,000/year [17].

Risk factors for epilepsy in older adults

The main reason for this second peak is the increasing incidence of cerebrovascular disease with age (40%; [5]), by far the most common cause of seizures in this age group, as well as toxic-metabolic processes, neurodegenerative diseases, tumors, and traumatic brain injury. Thus, increased longevity inevitably leads to an increase in the at-risk population [14], despite likely underdiagnosis at older ages [5]. Beyond the age of 85, the incidence decreases again due to increasing mortality in old age.

Germany's population is aging

From 1991 to 2019, the German Federal Statistical Office recorded an increase in the number of people aged over 65 years from 12 million to 18 million, an increase of 50% in slightly less than 30 years. Due to declining birth rates, the share of this age group in the total population increased from 15% to 22% in the same period. By 2060, it will be around 30% according to the 14th coordinated population projection (06/2019; [21]). Taking into account varying assumptions on birth rates, life expectancy, and population migration, this corresponds to an average increase in the

number of people over 65 to 22–24 million by 2060 [22]. In the medium term, this figure will be about 20 million by 2035 [23]. Due to these developments, knowledge about the specifics of epilepsy in older people will play an increasingly important role in diagnosis and treatment in the future.

Sex

Overall, the majority of studies show a slightly higher incidence rate for epilepsy in men. The difference is mostly explained by the higher incidence of stroke, trauma, and the difference in prevalence of the most common risk factors between men and women [14], despite the fact that women accounted for 56% of those aged 65 years and older in 2019 at 10.2 million (compared with men at 7.9 million, 44%). This represents a relative decline of about 10% compared with the 1990s, when men aged 65 and older accounted for about one third of the age group as a result of the World Wars (1991: women, 7.9 million [66%]; men, 4.1 million [33%]). The same ratio is found in the subgroup of the very old (85 years and older). For both sexes, the distribution follows the U-shaped course of the age distribution.

Incidence by country of origin

A meta-analysis of 33 studies from different countries of origin reported a significantly higher incidence in low- and middle-income countries (LMIC) (approximately 82/100,000/year) than in high-income countries (HIC) (45/100,000/year; [15]). The cause is probably multifactorial. The higher incidence of traumatic brain injury, infections, and parasitic diseases (e.g., malaria or neurocysticercosis) in low-resource regions is discussed. The second age peak has not yet been confirmed for developing countries. The reason for this is probably the lower life expectancy in LMIC.

Incidence of acute symptomatic seizures

Acute symptomatic seizures are particularly common in the first year of life and in older age. The median inci-

dence of acute symptomatic seizure is approximately 30–40/100,000/year [24]. It increases with age and is higher for men (52.0/100,000 PY) than for women (29.5/100,000 PY; [25]). The most common causes of acutely symptomatic seizures are traumatic brain injury, cerebrovascular and metabolic disease, fever, and infection [14]. The RR of epileptic seizures after traumatic brain injury is higher for mild trauma beyond 65 years of age than at younger ages (RR 2.5 vs. RR 1.8 < 65 years of age), but not for severe trauma (RR 10.7 < 65 years of age vs. RR 4.6 > 65 years of age; [26]). Diseases of older age are not infrequently associated with an increased risk of unprovoked epileptic seizures. Strokes, Parkinson's disease, Alzheimer's disease, and other forms of dementia are associated with an increased risk of unprovoked seizures [11]. For example, cellular damage and oxidative stress are discussed as common causes of symptomatic epilepsies and these cerebrovascular and neurodegenerative diseases [27]. Status epilepticus is also mostly acutely symptomatic, and its incidence increases with age [28].

Mortality from epileptic seizures in old age

Mortality from epilepsy is increased by a factor of 2–3 [14, 29]. Compared with the general population, people with epilepsy have an increased risk of premature mortality. The standardized mortality ratio (SMR), an incidence ratio of observed to expected mortality, averages 1.6–3.6 for epilepsy and is increased for all age groups [29]. It depends on the underlying disease and is increased especially in the presence of convulsive seizures and lack of seizure freedom [11]. Beyond the age of 64 years, lower SMRs are reported (1.4–2.6) than in those younger than 45 years (6.4–8.5; [29]), with an increase in competing causes of death at older ages being discussed as a cause [11]. Common causes of death in the elderly include pneumonia (SMR 3.5–7.2; mean age 81.3 years), neoplasms, and cerebrovascular disease [30]. Deaths as a direct consequence of epilepsy or seizures are sudden unexpected death in epilepsy (SUDEP), status epilepticus, or unintentional injury and suicide in 17% [14].

Practical conclusion

- The highest age-adjusted prevalence of epilepsy is in older age at approximately 7/1000 and higher.
- Causes of epilepsy in older adults are mainly cerebrovascular diseases, toxic-metabolic processes, neurodegenerative diseases, tumors, and traumatic brain injury.
- Increasing life expectancy and better medical care with longer long-term survival of underlying diseases will further increase the proportion of people with epilepsy in old age in the coming years.
- Epilepsy increases mortality in all age groups, but especially in older adults. However, pneumonia or the sequelae of the underlying disease are also frequent causes of death.

Corresponding address



Johannes D. Lang

Epilepsiezentrum, Neurologische Klinik
Schwabachanlage 6, 91054 Erlangen, Germany
johannes.lang@uk-erlangen.de

Declarations

Conflict of interest. J.D. Lang and H.M. Hamer declare that they have no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case.

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