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ABSTRACT — Although anecdotal references commonly presume that seizures eventually occur in patients affected with dementia of the Alzheimer type (DAT), no previous American study has documented the rate of new onset, unprovoked seizures in DAT patients. There are few documented cases of the occurrence of myoclonus in autopsy-proven DAT. In a series of 83 autopsy-proven DAT cases, medical records were scrutinized for the presence of any seizure or myoclonic activity. Final evaluations were made by a neurologist. Of the 83 cases, 8 had experienced one or more unprovoked seizures after the onset of DAT. Based on age-specific incidence rates from a population study of Rochester, Minnesota, the expected number was 0.80 ($p<.01$). Eight patients developed myoclonus during the dementing illness. (No appropriate general population study exists that would make comparison of rates of new onset myoclonus possible.) There was no overlap between those who developed myoclonus and those who developed seizures. These data suggest that individuals with DAT have a tenfold greater risk of developing seizures than an age-matched control, but that seizures cannot be considered a universal sign of DAT. Whether this increase in risk is uniform, or whether seizures or myoclonus define unique subgroups of DAT types remains to be explored.

Introduction

Primary senile dementias have only come to be recognized as true disease states since 1956 when data from the National Institute of Mental Health (NIMH) Human Aging Study challenged the notion that "senility" was an inevitable result of normal aging (1,2). Neuropathological studies during the past 15 years have now established that senile dementia of the Alzheimer type (SDAT) accounts for over 60% of the cases of primary dementia occurring in people over 65 (3). Alzheimer's Disease is clinically and pathologically the same disease except that, by historic and arbitrary definition, onset occurs before age 65 (2,3,4). Unless specifically stated, Dementia of the Alzheimer's Type (DAT) will be used here to indicate all affected persons regardless of the age of initial onset.

DAT victims progress from barely perceptible lapses in recent memory to increasingly handicapping and dehumanizing losses in judgment, emotionality, and physical function. This inevitably lethal decline is without remission and usually lasts for 8 to 10 years after onset of symptoms. There is no cure, no effective treatment, and no practical, positive, pre-mortem diagnosis (4).

Coupling these facts with current and projected numbers of cases, it is understandable that scientific interest in Alzheimer's Disease is rapidly increasing. The proportion of older persons in the general population will continue to climb rapidly well into the 21st century, and it is this numerically increasing group that is at risk for DAT (Figure 1) (5). While there is as yet no definitive study of the prevalence or incidence of DAT (6), it is estimated that DAT currently affects about 1.5 million people in the U.S. alone and causes or contributes to the death of 100 thousand older Americans per year (1,7).

The primary rationale for study of seizures in patients with DAT is two-fold. First, there is a clinical need for correct information. Scientific literature and neurology textbooks commonly disagree on seizure rates. Some conclude that seizures are rare or unlikely. Meanwhile inferences are commonly made, both orally and in print, among both lay persons and clinical professionals, that seizures are so common in patients with Alzheimer's Disease that they may in fact be inevitable. Because many DAT patients and their loved ones find this prognosis especially anxiety provoking, any exaggeration of risk should not be viewed as harmless misinformation. Yet no previous American study has documented the rate of new onset, otherwise unprovoked seizures in patients affected with DAT (8). However, a Finish study of clinical findings in dementia noted that 6 out of 71 non-autopsy proven DAT cases had seizures (9). There are documented cases of the occurrence of myoclonus in autopsy proven DAT, but no appropriate age specific control rates are available for comparison (10,11).

The second rationale involves basic scientific inquiry. Because secondary cases of DAT are present in about 33% of the families located through one affected person (proband), both familial and sporadic cases appear to occur. The percentage of familial cases rises to about 43% if only those probands who were affected before the age of 65 are considered (12). Any marker such as seizures or myoclonus occurring in one DAT group but not in another would be of interest, since such differences might signal different underlying biochemical or physiological changes.

Methods

Medical records, death certificates, and family interviews

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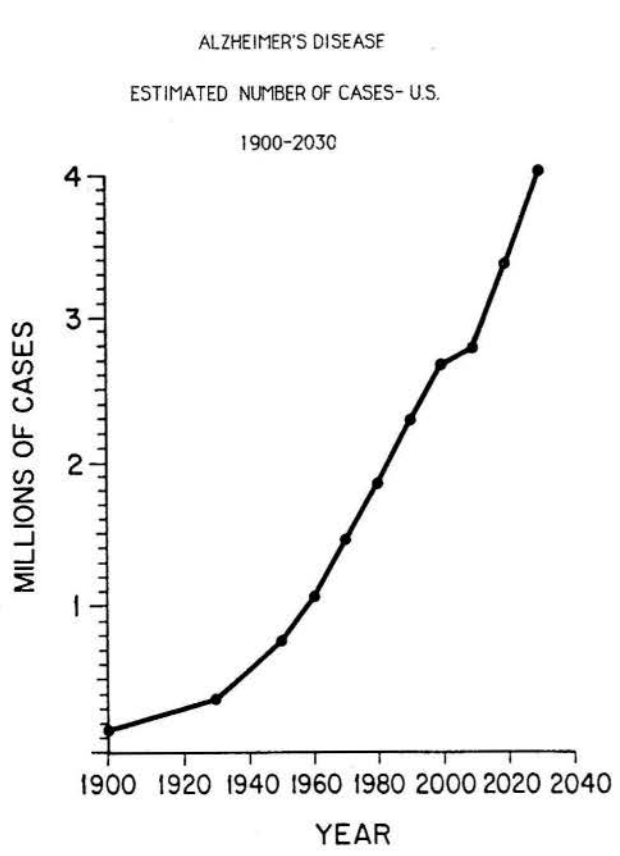

Figure 1. Estimated number of Alzheimer's Disease cases, U.S., 1900-2030.

were scrutinized for an unselected series of 83 probands with autopsy proven DAT who died in Minnesota state hospitals between 1952 and 1972. Any diagnosis of, or reference to, seizures or myoclonic activity were reviewed and classified by a neurologist. All of the seizure activity observed was of a generalized tonic-clonic nature, while a diagnosis of myoclonus was made for cases exhibiting characteristic myoclonic shocklike or jerking movements involving only a subset of muscles.

Using death and medical records as a source of data, like most archival types of research, can be criticized on several grounds: the amount of information available about the proband varies, the cause of death listed may depend on the extent to which the person was studied medically before death, on the certifying physician's familiarity with the patient, and on whether or not an autospy was done; diagnostic labeling and reporting can vary from one area to another in medical practices.

These shortcomings have been largely ameliorated in this study. The probands were all patients who had died in one of three Minnesota state hospitals during a discrete time period, which maximizes the homogeneity of the assessment and reporting methods used by the physicians and support personnel. Moreover, all 83 probands were autopsied, and full autopsy reports were available and studied. All medical information dating from the time of the probands' admission to the state hospitals until death, including reports of previous medical history, was available. This information was further amplified during field interviews with the probands' family members.

Results

Among the 83 DAT probands, 8 (9.6%) had seizures after the onset of DAT. Three of these experienced single episodes, while 5 had recurrent seizures. Based on age-specific incidence rates for combined single and multiple seizures from a population study of Rochester, Minnesota, the expected total is 0.80 (significant, $p<.01$, Poisson) (13). Another 2 probands experienced seizures before DAT onset, both having had seizures during childhood. This result is not significantly different from the .65 expected. A total of 8 probands experienced myoclonus after the onset of DAT. No cases of myoclonus were recorded prior to DAT. Appropriate age-specific incidence rates for comparison are unavailable for myoclonus. There is no overlap between those probands who experienced myoclonus and those who experienced seizures.

The mean age of DAT onset was 71.3 for all 83 probands, 11 of whom were determined to have had an onset prior to age 65 (Table 1). Of the 11 with DAT onset prior to age 65, one had seizures and another had myoclonus (Table 2). The mean age of DAT onset was slightly lower in those who subsequently developed seizures (69 years) than the mean age for those who developed myoclonus (73.5 years). The mean age of seizure onset in those patients with DAT was 75.6 years, while the mean age for myoclonus onset was 79.5 years. The mean duration of illness in the DAT cases who developed seizures, 9.1 years, was slightly longer than those who developed myoclonus, 6.8 years; or neither, 8.3 years. The mean survivorship following onset of myoclonus was 1.1 years (Table 3).

Table 1. Age distribution of Alzheimer's onset.

Age Interval (Years)	Number of Persons
50-59	2
60-64	9
65-69	22
70-79	36
80-89	14
90-99	0
Total	83

Table 2. Myoclonus and seizures by age of Alzheimer's onset.

Age Interval (Years)	Number of Persons in Interval	
	Myoclonus	Seizures
50-59	0	0
60-64	1	1
65-69	2	0
70-74	1	2
75-79	1	3
80-84	1	1
85-89	2	1
90-94	0	0
Total	8	8

Table 3. Age at onset of DAT seizures, and myoclonus.

	Mean Age at DAT Onset	Mean Age at Onset of Seizures or Myoclonus	Mean Age at Death
	(Std. Dev.)	(Std. Dev.)	(Std. Dev.)
DAT alone	71.3 (6.7)	——	79.6 (6.0)
DAT plus seizures	69.0 (8.6)	75.6 (8.0)	78.1 (8.1)
DAT plus myoclonus	73.5 (9.3)	79.5 (7.6)	80.3 (7.7)

Discussion

These data suggest that individuals with DAT have a tenfold greater risk of developing seizures than an age-matched control, but that seizures cannot be considered a universal sign of DAT. Although the lack of an appropriate control study makes the absolute determination of the increased risk for myoclonus impossible, the observed 9.6% who developed myoclonus is probably a significant increase over an expected number. It is not clear whether these increases in risk are uniform or whether seizures or myoclonus occur only in unique subgroups of DAT. In spite of the lowered DAT mean age of onset in probands who developed seizures, the one incidence each of myoclonus and seizures in the group with DAT onset prior to age 65 tends to make this criteria an unlikely condition upon which to separate subgroups. Of more interest for continued research may be the lack of overlap between those probands who experienced myoclonus and those who experienced seizures.

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