Chapter 17

Dementia and cognition in the oldest-old

Kristin Kahle-Wrobleski, María M. Corrada and Claudia H. Kawas

Introduction

Fueled by medical and technological advances, average life expectancy in the USA has increased by more than 25 years over the past century. A consequence of increased longevity and the aging of the "baby boomers" is that the oldest-old (age 90 or older) have become the fastest growing segment of the US population. Currently, there are fewer than 2 million Americans aged 90 and older, but this number will increase to approximately 10 million by 2050.[1] In terms of percentage of the population, those aged 90 and older presently represent 0.5% of the population in the USA, while by the middle of the twenty-first century, they will form about 2.5% of the population[2] as depicted in Fig. 17.1. Moreover, the increases in the oldest-old population are occurring worldwide. Countries including Japan, France, Italy and Germany are expected to have between 3 and 5% of their population aged 90 and over by 2050.[3]

Cognition in the oldest-old: key questions

- What is the prevalence of dementia in the oldest-old?
- What are the causes of dementia in the oldest-old?
- How can we screen for dementia in this population and what challenges must we overcome in the cognitive assessment of this age group?
- What are the clinical–pathological correlates of dementia in the oldest-old?

The rapidly growing population over the age of 90 signals a need to understand aging and age-related conditions in the oldest-old. Many issues require investigation in these pioneers of aging. Estimates of dementia prevalence vary as described in more detail below. More precise estimates and a better understanding of the causes of dementia are crucial for understanding the public health impact of this rapidly growing group. The present chapter presents a brief overview of our knowledge regarding dementia and cognition in the oldest-old and describes preliminary findings from the 90+ Study, a population-based study of individuals aged 90–108 years of age.

The 90+ Study

To address the dearth of information regarding dementia and cognition in the oldest-old, The 90+ Study was established in 2003. The study is composed of survivors from the Leisure World Cohort Study, which was established in the early 1980s when 13 978 residents (8877 women and 5101 men) of a California retirement community (Leisure World, Laguna Woods) completed a postal health survey.[4,5] The cohort is mostly white and well educated. Basic demographic information is summarized in Table 17.1 and a summary of participants' medical histories is shown in Fig. 17.2.

The 90+ Study invited all 1151 members of the Leisure World Cohort Study who were aged 90 years and older on January 1, 2003 to participate in this longitudinal study of aging and dementia. Cohort members were asked to undergo a comprehensive evaluation either at our clinic or their residence, including a neuropsychological evaluation, neurological examination and self-administered as well as informant questionnaires. A list of neuropsychological tests is provided in Table 17.2. Participants are evaluated in-person every 6 months and informant information is updated annually. As of December 1, 2006, information had been ascertained on 948 (82%) of the 90+ Study cohort.

Dementia prevalence

Although estimates of dementia prevalence are reasonably well established for individuals under the age of 85 years, they have not been well defined for those

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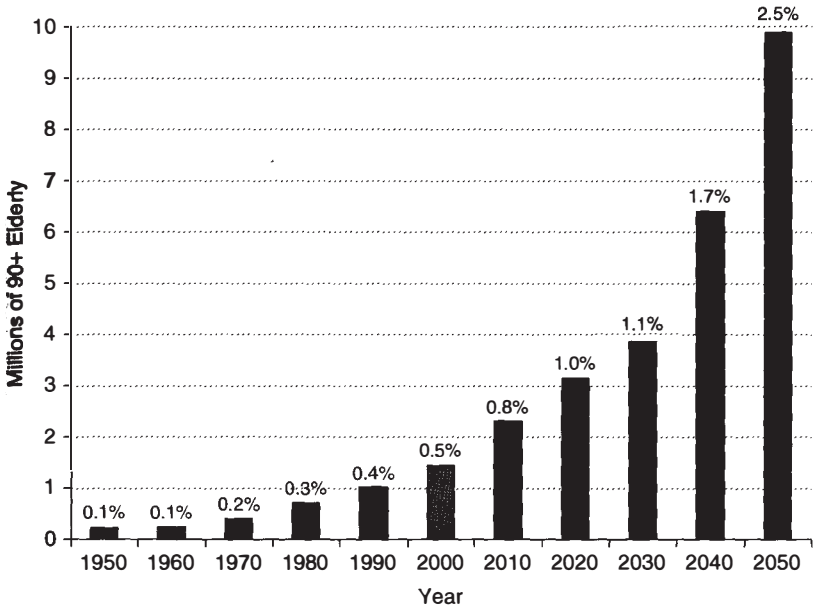

Fig. 17.1. Oldest-old population in the USA from 1950 to 2050. Figures over bars are percentage of US population. (Sources: US Census Bureau 1950–2000[1] and US Census Bureau Population Projections Middle Series, 2002[2].)

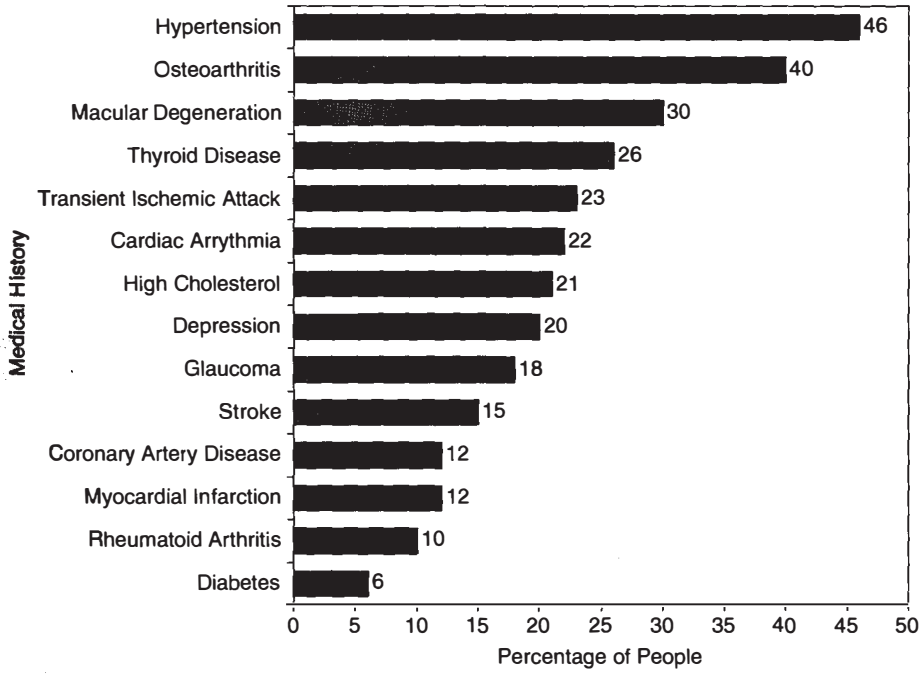

Fig. 17.2. Medical history in the 90+ Study.

in their tenth and eleventh decades of life. It is not clear if the prevalence of dementia, which doubles every 5 years of life between ages 65 and 85, continues this exponential increase in the tenth decade. Figure 17.3 shows available studies of dementia prevalence in people over age 90. Some studies have found that prevalence continues to increase with age after 90,[19,20,22] whereas others suggest that prevalence plateaus in the tenth decade.[23,30] Estimates of prevalence for people over age 90 vary from approximately 30%

Table 17.1. Baseline demographic characteristics of participants in the 90+ Study ($n = 948$)

Characteristic	Percentage
Sex	
Women	77
Men	23
Marital status	
Widowed	76
Married	14
Never married	6
Separated or divorced	4
Education	
High school or less	31
Some college or vocational school	29
College graduate or more	40
Type of residence	
At home alone	28
At home with spouse	11
At home with relatives or friends	7
At home with paid caregiver	10
Nursing or group home	44
Cognitive diagnosis from neurological examination	
Normal	32
Cognitively impaired not demented	34
Demented	34
Use of assistive devices	
None	29
Cane	31
Walker	51
Wheelchair	37
Average age (years [range])	94.9 (90–106)

Table 17.2. Neuropsychological assessment battery of the 90+ Study

Domain	Test	Reference
Global cognition	Modified Mini-Mental State Examination (3MS)	6
	Mini-Mental State Examination (MMSE)	7
Language	Boston Naming Test (BNT) 15-item	8,9
	Animal Fluency	10,11
Visuoconstruction	CERAD constructions	11
	Clock Drawing	12,13
Verbal memory	California Verbal Memory Test (CVLT) 9-item	14
Attention/ Executive Function	Digit Span (Forward and Backward) from Wechsler Adult Intelligence Scale, 3rd edn	15
	Trail Making Test A	16,17
	Trail Making Test B	16,17
	Clock Drawing	12,13
	Letter F Fluencies	10,11
Motor speed	Trail Making Test C	18

to approximately 60%, essentially a two-fold difference between estimates. When specifically considering prevalence rates of centenarians, the percentages also vary widely, with estimates ranging from 42% to 88%.[19,31–35] Moreover, the confidence intervals of all estimates in the oldest-old are wide, reflecting the lack of precision of these estimates.

Owing to small numbers, most studies of the oldest-old estimate prevalence for all subjects aged 90 and older as a combined group. Only a handful of publications have reported age- and gender-specific estimates for ages 90 and above.[19,20,22,25] In these studies, estimates for ages 90–94 range from approximately 32% to 48% and increase modestly from approximately 40% to 60% for ages 95+. Although prevalence estimates for women are fairly consistent in terms of magnitude and direction (all appear to increase with age after age 90), the estimates for men are discrepant. When comparing prevalence between ages 90–94 and 95+ in men, one study shows a dramatic increase,[19] another shows a striking decrease[20] and the remaining two studies have similar estimates for the age groups.[19,22] Consequently, precise estimates of the prevalence of dementia have been elusive in the oldest-old, with insufficient numbers of subjects in most studies.

The 90+ Study is to our knowledge the largest prevalence investigation in a population-based sample of those 90+ years of age and, therefore, allows more precise estimates than previously published. Preliminary results obtained from 911 participants show an overall prevalence of all-cause dementia of 41%. Estimates of prevalence were higher in women than in men (45% versus 28%) and continued to increase with age in women but appeared to level off in men (Fig. 17.4). The 90+ Study suggests that dementia prevalence rates, particularly in women, continue to

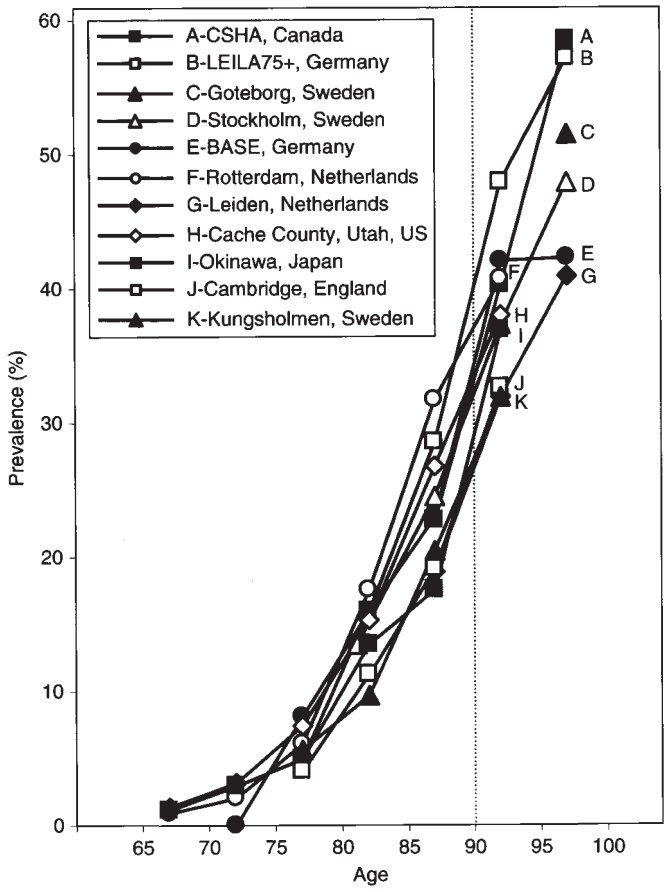

Fig. 17.3. Age-specific prevalence of dementia in studies with subjects aged 90+ years. Studies A-CSHA, Canada;[19] B-LEILA75+, Germany;[20] C-Goteborg, Sweden;[21] D-Stockholm, Sweden;[22] E-BASE, Germany;[23] F-Rotterdam, the Netherlands;[24] G-Leiden, the Netherlands;[25] H-Cache County, Utah;[26] I-Okinawa, Japan;[27] J-Cambridge, England;[28] K-Kungsholmen, Sweden.[29]

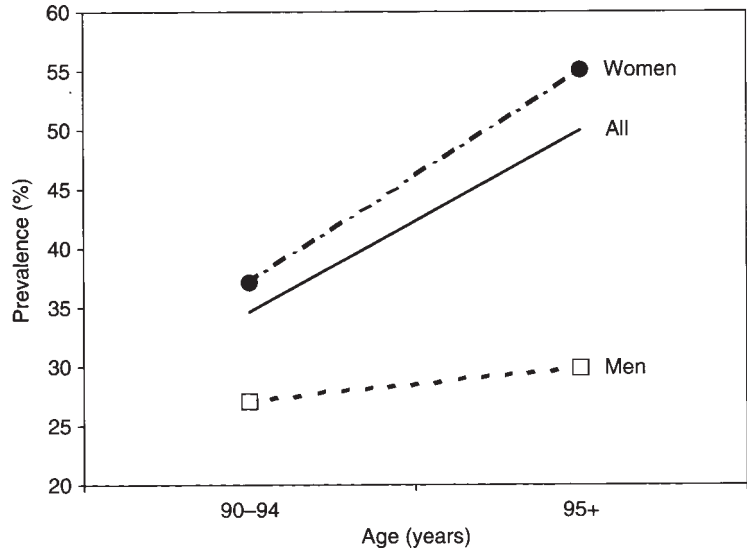

Fig. 17.4. Age- and sex-specific prevalence of all-cause dementia in the 90+ Study.

Table 17.3. Mini-Mental State Examination (MMSE): cutoff scores for dementia by education group in the 90+ Study

Age (years)	High school or less		College or more	
	MMSE cutoff score	Sensitivity/specificity	MMSE cutoff score	Sensitivity/specificity
90–93	≤ 23	0.87/0.94	≤ 25	0.82/0.80
94–96	≤ 23	0.90/0.93	≤ 24	0.85/0.80
97+	≤ 22	0.80/0.76	≤ 22	0.89/0.90

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rise across the tenth decade. Because women make up more than three-quarters of all individuals over age 90, we can expect increasing numbers of persons with dementia in the growing population of oldest-old.

Screening for dementia

With high rates of prevalent dementia in the oldest-old, determining the utility of dementia screening instruments for this age group is essential. Perhaps the most widely used dementia screening instrument, the Mini-Mental State Examination (MMSE),[7] does not have published cutoffs for persons over age 90. Scores on the MMSE generally decline with age,[36,37] and failure to adjust cutoffs for older age groups may reduce the specificity of this instrument,[38,39] resulting in more oldest-old patients or participants inaccurately being labeled as having dementia.

Table 17.3 shows results from the 90+ Study, suggesting the MMSE is an accurate screening tool for identifying dementia in those aged 90+ years when used with age- and education-adjusted cutoff points.[40] Even across the tenth decade, cutoff values need to be adjusted downward with increasing age to preserve the balance between sensitivity and specificity, a crucial first step in characterizing dementia in nonagenarians and centenarians.

Normative neuropsychological data

Limited age-appropriate normative data are available when assessing persons over age 90 for impairments in specific domains of cognition. Common normative datasets, such as those published for the Halstead–Reitan Neuropsychological Battery[41] or the Wechsler Adult Intelligence Scale, 3rd edition[15] do not include adults over the age of 90 in their samples. The Mayo Older Adults Normative Study does include those aged 90+ years but has relatively few individuals (less than 30).[42] One recently published study provided norms on the neuropsychological battery of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) drawn from 196 individuals aged 85 years and older.[43] The authors found a strong effect of education and age on most tests, concluding that norms drawn from younger populations are not appropriate for the oldest-old and might lead to misclassification of participants as demented.[43]

To establish a set of normative data for the oldest-old using the largest number of subjects to date, data were compiled from 339 non-demented participants in the 90+ Study. These norms are available in the public domain[44] and include age-specific means, standard deviations, and percentiles for several standardized and widely used tests, listed in Table 17.2. When comparing mean scores of our oldest-old participants with previous studies of younger individuals, age effects are easily noted (Figure 17.5). The oldest-old performed less well, on average, than their younger counterparts on both timed and untimed tasks. Further analyses within our group aged 90+ years showed that cognitive test performance was inversely related to age.[44] Tests with an age effect included the Modified Mini-Mental Status Examination (3MS), Boston Naming Test – 15 item, Animal Fluency, California Verbal Learning Test, Trail Making Tests A and B, Clock Drawing Test, and Digit Span Backward. As seen in Figure 17.5, cognitive performance across age groups for those aged 90+ decreased at nearly twice the magnitude as differences across the younger age groups. For example, mean time to complete the Trail Making Test A was nearly 30 seconds slower for the 95+ age group than in the group aged 90–91 years. In contrast, the mean time to complete the test in the group aged 76–85 years was only 10 seconds slower than completion time for the group aged 71–75 years. Results from the 90+ Study suggest that the performance of non-demented nonagenarians and centenarians continues to decline and

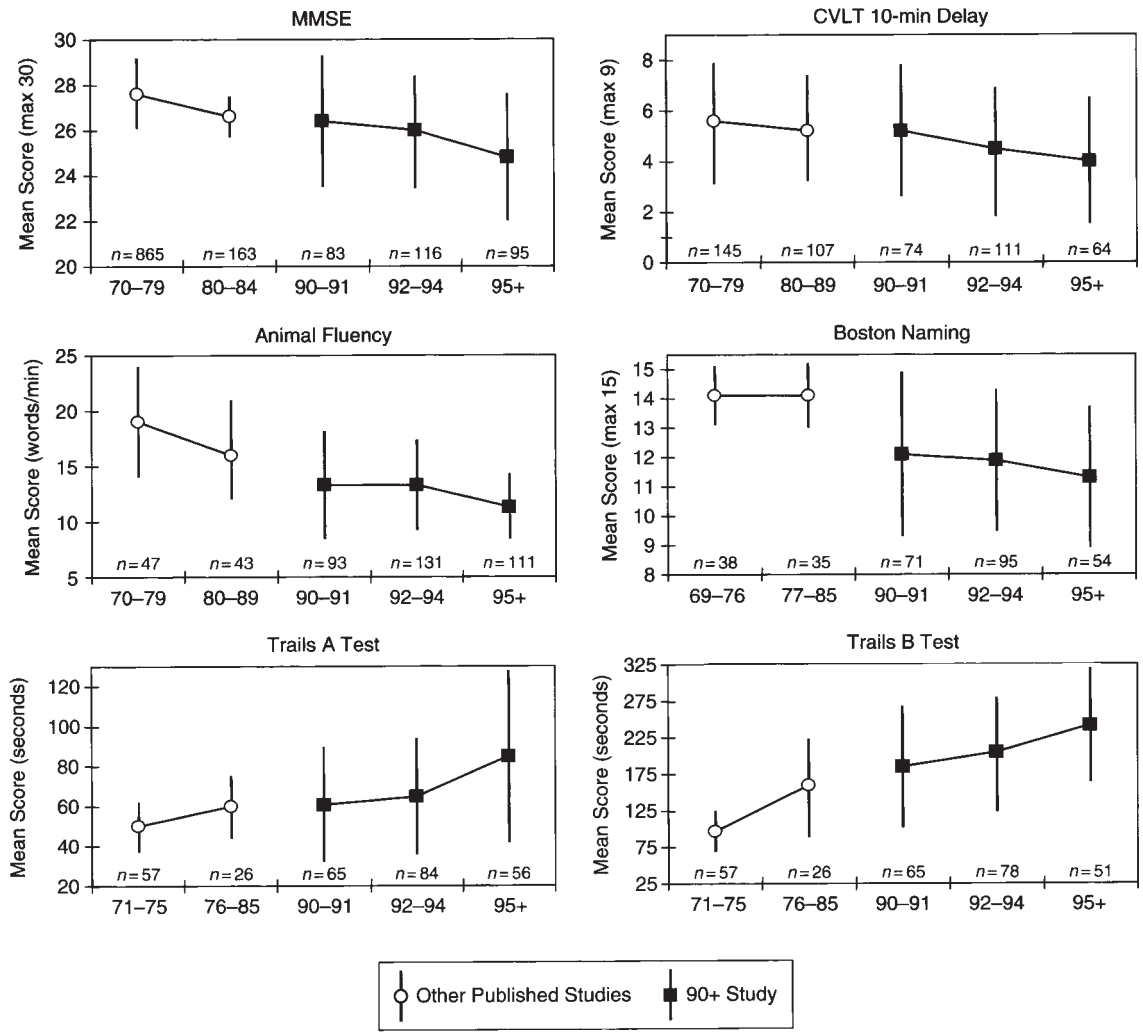

Fig. 17.5. Mean cognitive test scores from the 90+ Study compared with published studies of younger elderly. Vertical bars represent ±1 standard deviation. MMSE, Mini-Mental State Examination; CVLT, California Verbal Learning Test; BNT, Boston Naming Test. Source for other published studies: MMSE,[37] CVLT,[14] Animal Fluency,[45] BNT,[46] Trail Making Tests A and B.[47]

possibly even accelerates past the age of 90. Whether these findings reflect latent disease processes or other age-associated processes requires further investigation.

Challenges in the cognitive assessment of the oldest-old

Factors affecting validity and reliability of clinical assessments are magnified when working with the oldest-old. In particular, sensory deficits, fatigue and motor limitations influence how cognitive tests must be administered and interpreted in studies such as the 90+ Study. A majority (72%) of the participants in the 90+ Study had significant hearing loss, vision loss, or both. Some sensory limitations are overcome with personal devices, such as hearing aids and eyeglasses. However, degenerative conditions such as macular degeneration and glaucoma lead to untreatable visual loss and affect the choice and presentation of neuropsychological tests, as well as interpretation of results.

In addition, our experience shows that fatigue is a pressing concern when working with individuals over the age of 90. Frequent breaks are required and subjects often are slow to complete procedures. Although the cognitive assessment battery of the 90+ Study does not usually take more than 45 minutes to complete, approximately 20% of participants omit at least one test because of fatigue.

Fatigue in those aged 90+ may be attributable to a wide variety of factors. For some participants, sensory deficits may demand additional effort to perceive the stimulus. For instance, participants with macular degeneration often report during the examination that their eyes are tired from the strain, and visually based tests such as the Boston Naming Test or Trail Making Tests cannot be completed. Other likely sources of fatigue include comorbid medical conditions, medications and frailty.

Diagnostic considerations

The effects of sensory deficits, fatigue and medical comorbidities present a challenge for determining if dementia or cognitive impairment should be diagnosed in a person aged 90 or older. For individuals who cannot complete cognitive testing, it is often challenging to determine the nature and extent of cognitive difficulties. Against a background of medical illnesses and sensory losses, it is frequently difficult to determine if functional losses have occurred as a result of cognitive loss. Moreover, informant reports are constrained by different individual and cultural notions of what impairment or decline looks like in the oldest-old. In addition, current diagnostic criteria for dementia were developed with populations under the age of 90, somewhat limiting their applicability to the oldest-old.

Assigning a diagnosis of dementia or mild cognitive impairment is difficult in the oldest-old, and identifying an etiology is a further challenge. The effect of medical comorbidities on cognitive test performance or on the brain itself is not well understood in this advanced age group. Careful consideration must be made of the medical history and medication usage, with an understanding that nonagenarians and centenarians may have less reserve energy and an increased sensitivity to medication interactions and side-effects compared with younger adults.

Neuropathology of dementia in the oldest-old

The association between clinical dementia and neuropathological features is inconsistent In the oldest-old, unlike younger age groups where the association between cognitive functioning and β-amyloid plaque and neurofibrillary tangle neuropathology has been well established.[48] Approximately half of nonagenarians have clinically diagnosed dementia without any measured neuropathology generally associated with dementia.[49,50] The inverse has also been found in the oldest-old: individuals with no significant cognitive impairment have sufficient neuropathology meeting criteria for Alzheimer's disease.[50–52]

Consistent with previous reports, approximately half of the participants in the 90+ Study diagnosed with dementia on clinical evaluation subsequently did not meet pathological criteria for Alzheimer's disease or other known conditions associated with dementia.[53] Yet the study has also identified several individuals with no cognitive impairments but very high levels of plaque and tangle pathology.[54] If amyloid deposition is not related to cognitive loss and dementia in extreme aging, anti-amyloid therapies currently under development may have little utility in our oldest citizens. The development of therapies and neuropathological diagnostic criteria in this age group requires considerable research before we can understand the substrates of cognitive loss in the oldest-old.

Successfully assessing cognition in the oldest-old

The inherent difficulties of working with a population with high rates of sensory impairment and fatigue, and limited mobility, do not preclude working successfully with the oldest-old. On the contrary, the 90+ Study provides us with a framework for improving our understanding of how best to capture the cognitive status of persons over the age of 90.

Based on our experiences with the oldest-old, we recommend the development of printed instructions to supplement oral instructions. We also suggest using abbreviated versions of tests when available to minimize fatigue and maximize the number of cognitive domains assessed. In considering the diagnostic difficulties of working with the oldest-old, we recommend that assessments include information from informants, medical records and other sources to optimize understanding of cognitive and functional abilities of those aged 90+ years.

Research considerations

With the challenges described above, missing data are frequently unavoidable; such missing data are unlikely to be missed at random. The reasons for non-completion are informative, and research studies should consider coding schemes that can capture reasons for non-completion, such as sensory impairments and fatigue. Order of administration also

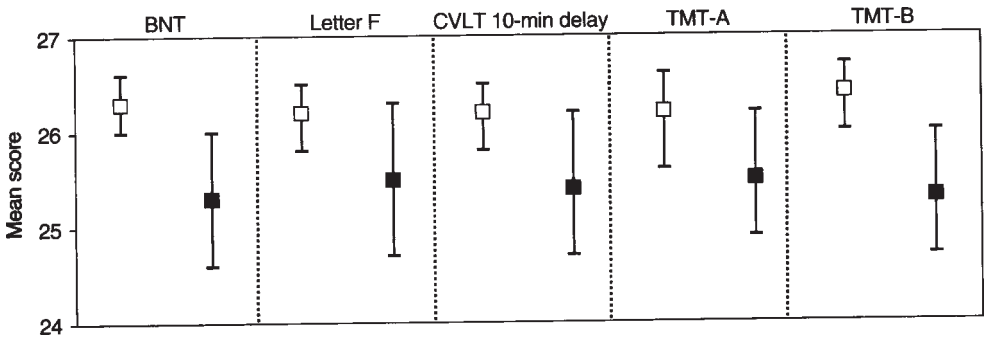

Fig. 17.6. Mean score on the Mini-Mental State Examination for participants who completed (□) or did not complete (■) neuropsychological tests. BNT, Boston Naming Test; Letter F, Letter F fluency; CVLT, California Verbal Learning Test 9-item 10 min delay; TMT, Trail Making Test. Vertical bars indicate 95% confidence interval.

impacts rates of missing data, as does declining cognition. Figure 17.6 demonstrates that those participants who complete a test had a higher global cognition score than non-completers on the same test. As individuals experience cognitive decline, they may be more likely to refuse, may experience fatigue more rapidly in the testing environment and may be less likely to complete some components of the neuropsychological battery.

Conclusions

The oldest-old are the fastest growing segment of the population in most of the world. Age is the primary risk factor for dementia, and the rising number of nonagenarians and centenarians portends an impending crisis for public health. The cost of caring for the rising number of those aged 90+ years who develop dementia in the coming decades will more than double from the approximately US$1 billion currently spent.[55]

Compounding this challenge, the etiology and diagnosis of dementia in this age group is poorly understood. Screening and diagnostic instruments require modifications and present challenges for interpretation. Pathologically, levels of amyloid deposition do not correlate with cognition after age 90, and about half of demented individuals in this age group do not have obvious pathologies, such as amyloid plaques, neurofibrillary tangles or strokes, to explain their cognitive loss. Population studies in the oldest-old, particularly those enriched with clinical pathological investigations, will be essential as we seek to understand the neurobiology of extreme aging.

Investigations such as the 90+ Study are helping to expand our knowledge of dementia and cognitive functioning in our oldest citizens. Determining causes of dementia and identifying risk and protective factors associated with dementia in the oldest-old will be key to the development of successful intervention strategies for this rapidly growing segment of our population.

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