

# LONGEVITY WITH DIGNITY

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Given the choice to live 10 years longer, would you take it? How about if you were offered 20 extra years? 50? How long of a life is too long?

If you lived in, say, the 16th century, you might hold to the concept that one's lifespan is always directly proportional to one's happiness. It is an idea rooted in times before the birth of modern medicine, when people were more likely to die from "accidental" causes like untreated pneumonia than from "wear-and-tear" causes like cancer--and nowadays, it is beginning to be challenged.

In August of 2013, a survey from the Pew Research Center's Religion and Public Life Project showed that the majority of Americans do not want to live past the age of 90 (Pew Research Center, 2013), demonstrating that people have begun to consider whether or not there exists a natural limit to one's age. Among the worries of these Americans was the possibility of lowered life quality in extreme old age. Some, like Ezekiel J. Emanuel, the author of the article "Why I Hope to Die at 75," voice fears that a loss of cognitive function could lead to an undesirable quasi-vegetative lifestyle. Emanuel asserts that cognitive decline in extreme longevity "robs us

group is a small one; the US is home to more centenarians than any other country in the world, yet in 2010, there were less than two centenarians for every 10,000 people in the US (Meyer, 2012). In 2011, the United Nations Population Fund estimated that the global count of centenarians was about 316,000 individuals, projected to increase to 3.2 million in 2050 (UNFPA, 2012).



Gloomy depictions of life in extreme longevity are to some extent justified by the proven link between age-related cognitive impairment and lower odds of survival. A 1996 study, for instance, established that individuals with certain genotypes for apolipoprotein E, a protein that "mediates the clearance of several plasma lipoproteins and likely affects neuronal repair in the brain," are both less likely to experience cognitive impairment and more likely to live longer

(Corder, Lannfelt, & Viitanen, 1996). A 2004 analysis of the Heidelberg Centenarian Study drew similar results, discovering a logarithmic relationship between cognitive status and death in centenarians (Kliegel, Moor, & Rott, 2004). Moreover, the popular "compression of morbidity" hypothesis, developed by Stanford professor James Fries, proposes that the frequency

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of our creativity and ability to contribute to work, society, the world. It transforms how people experience us, relate to us, and, most important, remember us. We are no longer remembered as vibrant and engaged but as feeble, ineffectual, even pathetic" (Emanuel, 2014).

So are the emotional benefits of extreme longevity truly outweighed by the costs of neurodegeneration? Fortunately, evidence that could be used to answer this question can be found by observing the growing number of centenarians, individuals who are at least 100 years old, in the world. This

and severity of chronic diseases, including those of the brain, are compounded with age. Fries posits that since chronic diseases can therefore only be postponed and not cured, longevity past a certain age is simply the postponement of death. (Fries, 2002) Indeed, an analysis of data from the New England Centenarian Study found that centenarians "had compressed age-related diseases into the last 5.2% of their extremely long lives" (Sebastiani & Perls, 2012).

Common among such afflictions are Alzheimer's disease (AD) and argyrophilic grain disease (AGD),

neurodegenerative diseases seen often in centenarians. Alzheimer's is the most frequently seen cause of dementia, while the lesser-known AGD accounts for only 5% of all cases and is named for the small lesions, called argyrophilic grains, that it creates in the brain (Ding et al, 2006, Ferrer et

their extraordinary longevity. If this is indeed true, claims of the poor life quality of the extremely old would be dismissed with proof that centenarians are uniquely suited for long life. Data from the New England Centenarian Study, at least, shows

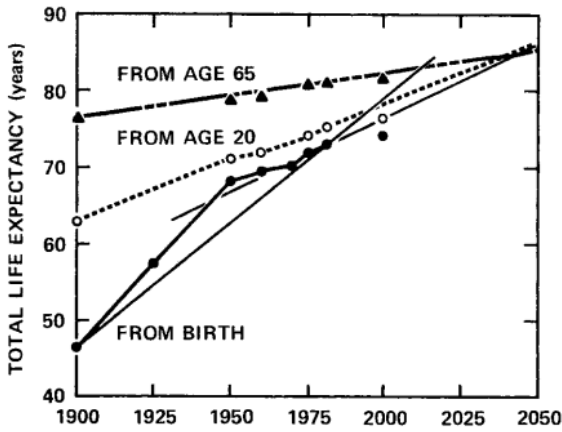


Figure 3. Trends, Limits, and Convergences in Life Expectancy.

Projection of total life expectancy data into the future shows convergence at the ideal average life span, 85 years, in 2045. Spans of 82.6 to 85.6 years can be calculated from projections from different ages (at birth, at age 20, and at age 65) and different years in this century. (Data are from the National Center for Health Statistics [1977]<sup>10</sup>; values indicated by triangle and circles for the year 2000 are estimates from the Office of the Actuary.)

Figure 1. James Fries's compression of morbidity hypothesis.

al, 2008). When determining the instances of these diseases in centenarians, usually by post-mortem examination of the centenarians' brains, scientists use neurological formations such as argyrophilic grains as indicators of neurological disease. The neuropathological markers for Alzheimer's include senile plaques--extracellular deposits of improperly folded proteins--and neurofibrillary tangles (NFTs)--tangles in the microtubules, or structural components, of neurons caused by deposits of tau protein in the brain (Nussbaum, Seward & Bloom, 2013). Neurological formations are chosen to be neuropathological markers on the basis of their tendency to cause neuronal loss, which on a larger scale is classified as neurodegeneration.

There has been much speculation about the possibility of centenarians having a relatively low risk for neurodegenerative disease, which could explain



that centenarians are not more likely than non-centenarians to have single-nucleotide polymorphisms (SNPs), or natural variants of genes, associated with dementia that would indicate their lower likelihood of contracting neurodegenerative disease. Similarly, multiple studies suggest that the majority of centenarians are affected by dementia. In a study of 27 centenarian brains, senile plaques were found in 23 brains (Mizutani & Shimada, 1992). A study of Danish centenarians found that 51% of the subjects had mild, moderate, or severe dementia (Andersen-Ranberg, Vasegaard & Jeune, 2001); analysis of data from the Heidelberg Centenarian Study, using the mini-mental state examination (MMSE) to score cognitive impairment, also showed that over half of the subjects were moderately or severely cognitively impaired (Kliegel, Moor & Root, 2004). Centenarians unaffected by dementia seem to be rarities; a 1992 study categorized these individuals as "supernormal centenarians." These centenarians' brains appeared to have undergone little senile change, exhibiting a "frequency of hippocampal NFTs...comparable with that in the 80s age group" (Mizutani & Shimada, 1992). Additionally,

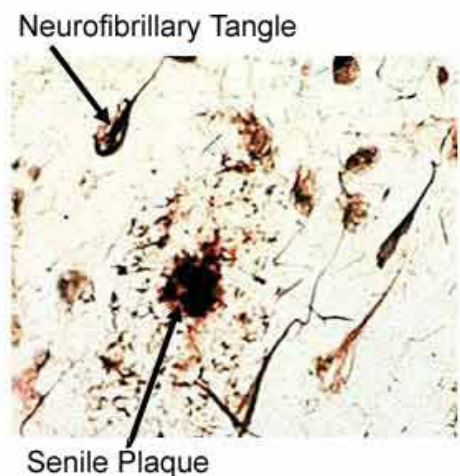
*"Fries posits that since chronic diseases can therefore only be postponed and not cured, longevity past a certain age is simply the postponement of death."*

both the Heidelberg Centenarian Study and another Danish study of centenarians found that about a quarter of the centenarians observed had "virtually no cognitive deficits" (Kliegel, Moor & Rott, 2004, Andersen-Ranberg, Vasegaard & Jeune, 2001).

Even given such external valuations, it is the individual who ultimately decides whether he or she is content or happy. Thus it is

“*[Supernormal] centenarians’ brains appeared to have undergone little senile change, exhibiting a frequency of hippocampal NFTs... comparable with that in the 80s age group.*”

important to take into account the centenarians’ perception of their own life quality. Although according to a 1998 survey, centenarians, when compared to elderly non-centenarians, experience the loss of more functions necessary for activities of daily living, including decline in cognitive function, the same study found that centenarians were “less inclined to complain about their physical condition and, despite greater



functional disability, were no more subject to depression or anxiety than the younger groups [aged 75-85 and 86-99 years]” (Buono, Urciuoli & De Leo, 1998). Survey results were analyzed using the Instrumental Activities of Daily Living Scale and the LEIPAD cognitive function scale. For at least this group of centenarians, loss of cognitive function did not translate to lower perceived life quality.

Barring consideration of the “supernormal centenarian” anomaly, the differences between the nature of neurodegenerative disease in centenarians and that in non-centenarians do not appear to be significant. It appears, then, that the centenarian is like any other elderly individual; over

time, the centenarian mind deteriorates, just as the minds of other aging individuals do. Whether or not the dementia that comes naturally with age can temper the joys of longevity is a highly subjective matter. However, it is worth noting that those mentioned who most fear and condemn the onset of extreme old age are also those who have not yet experienced it.

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#### IMAGE SOURCES

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