

CoNUNdrum

[noun : /kuh-NUN-drum/

a confusing and difficult problem or question]

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The Nun Study was the brainchild of Dr. David Snowdon, that was started in 1986 and has been conducting an ongoing longitudinal study on Alzheimer's disease ever since. Initially, it included 678 catholic sisters of the Notre Dame congregation who were over the age of 75 when the study began. Their medical and personal histories were looked into and the archives of the nuns' personal record files along with handwritten autobiographies served as an excellent insight into their early life.

Dr. Snowdon considered them to be an excellent group for the study of the ageing process because they all had similar lifestyles – free from alcohol consumption and smoking, had uniform backgrounds and economic status which made the nuns great participants for the study.

They were followed up with for over two decades and were regularly given physical checkups and cognitive tests. These cognitive tests focused on memory, concentration, language, visio-spatial ability and orientation to time and space. When these nuns died, their brains were donated for postmortem neuropathological evaluation.

To help you understand how this postmortem evaluation opened up a whole new arena in the study, let us see what goes on inside the brain of an Alzheimer's patient.

There is an abnormal accumulation of a naturally occurring protein, beta amyloid, that clumps together to form plaques in the patient's brain. These plaques collect between neurons and disrupt cell function. Alzheimer's has various neuropathological features but the most important ones that have been identified until now include plaques, tangles and brain shrinkage. Now here's the surprise- when scientists analyzed their brains, they discovered the above manifestations in several nuns which proved undeniably that they had changes related to Alzheimer's in their brains. The nuns to whom these brains belonged had shown no manifestations of this disease while they were still alive! This was proven by the scores on various cognitive tests that were administered.

Researchers believe that this is due to the fact that the nuns possessed a high level of cognitive reserve which is basically the mind's resistance to the damage of the brain. This is influenced by factors like degree of literacy and engagement in mentally stimulating activities which help people with Alzheimer's cross this hurdle. Dr. Snowdon talks about it in detail in his book 'Ageing with Grace'.



The nun study came across some compelling findings. One of the central findings came in 1997, by which time they were in possession of approximately 100 brains for analysis. Dr. Snowdon and neurologist Dr. William Markesbery were fascinated by an idea that strokes and other brain trauma might contribute to the dementia of Alzheimer's disease.

They decided to choose only those brains that belonged to sisters who had acquired a bachelor's degree. They found that in nuns whose brains showed evidence of multiple strokes in addition to pathological evidence of Alzheimer's, inevitably also showed symptoms of dementia. Only half the nuns without strokes were comparably afflicted. This was, indeed, a remarkable finding as it was one of the first studies to look at the cardiovascular element of Alzheimer's disease.

Since the study continued through the progression of the disease in some nuns, relying on them for their life stories headed Dr. Snowdon towards a dead end. An analysis of the autobiographies written by the nuns in their early 20s served as the key that helped him unlock the mystery of the link between the cognitive abilities in early life to the presentation of disease as one ages. That is when he, along with the assistance of a researcher James Mortimer, stumbled across the daunting concept of "idea density" (defined as the number of discrete ideas per 10 words. Idea density served as a marker of a number of linguistic and other cognitive abilities including vocabulary, general knowledge and education).



Two nuns who participated in the study, sisters Maria Mercedes Hartmann and Sister Mary Gilbert Hefe.

(Image) Dayna Smith/The Washington Post/Getty Images

Applying measures such as idea density, vocabulary and grammatical complexity to the sisters' autobiographies, they scored the samples leading to a series of intriguing results.

For instance, one of the lowest-scoring samples, as stated in Dr. Snowdon's book "Aging with Grace", began with: "My father, Mr. L.M. Hallacher, was born in the city of Ross, County Cork, Ireland, and is now a sheet-metal worker in Eau Claire."

In contrast to this was a dramatically different essay portraying similar information: "My father is an all-around man of trades, but his principal occupation is carpentry, which trade he had already begun before his marriage with my mother." Dr. Snowdon used the concept of Idea density to predict Alzheimer's disease with an astonishing accuracy of 85%-90% atleast among the nuns of Notre Dame.

Hence, the study suggests the traits in early, mid and late life have strong relationships with the risk of Alzheimer's disease, as well as the mental and cognitive disabilities of old age.

In conclusion, here's how The Nun study paved a path for the future of diagnosis of Alzheimer's :

A subsequent study was performed by the department of Neurology at the University of California in 2012 with the objective of testing whether idea density measured in late life continued to predict the trajectory of cognitive change.

Results show that lower idea density has been seen to cause a decline in Global Cognition, semantic memory (long term memory that processes concepts not drawn from personal experience) and episodic memory (memory of everyday events). This has a wider application and it was a more practical approach because early age linguistic evidences, as in the case of The Nun Study, are not always available.

This study proves that idea density measured in late life can still act as a reliable index of cognitive reserve which opens up a path for predicting the probability of Alzheimer's disease. Although we have fair knowledge about the construct of cognitive reserve, there are fairly limited means to operationalize it.

These future studies hold promise for identifying underlying mechanisms and mediators that may account for the findings of the original study. This may eventually pave the path to finding a cure or better yet, prevent the onset of Alzheimer's disease altogether.



Sr. Nicolette Welter, SSND, welcomed a special guest, Dr. David Snowdon, to her 101st birthday party.