

used words, such as *grandeur*, that Professor Thorndike had only rarely encountered in the literature of the early part of the twentieth century. This suggested that the healthy sisters had a richer vocabulary in early life and may have read a more diverse selection of literature as children.

These data intrigued us, but they raised as many questions as they seemed to answer. Was it the words the sisters used or the combinations of words that best revealed their cognitive skills? Maybe it was the complexity of the sentences that we should analyze. Should we be counting clauses? Verbs? Conjunctions? A grant application to study these questions led us to someone who could guide us through this maze.

The National Institute on Aging, which funds most of our work, supports academic investigators whose grant proposals fare the best when reviewed by scientists working in the same field. During this peer-review process, the researchers who evaluated our proposal suggested that we needed a language expert to help us determine whether the autobiographies truly held valuable information about our subjects' cognitive or linguistic abilities or whether they simply offered intriguing glimpses into the past. The grant reviewers even went so far as to suggest a specific researcher: Dr. Susan Kemper, a psycholinguist with specialized knowledge about the impact of aging on language skills.

When I read Kemper's publications, I realized that there were an astonishing number of tools to analyze language that we had never considered. In addition to vocabulary, she and her associates assessed such odd-sounding parameters as morphemes, left- and right-branching sentences, embedded clauses, verb phrase infinitive complexes, conceptual propositions, lexical repetition, and anaphora. After I phoned her and described the project, she agreed to look at a few autobiographies. A few weeks later we had an enthusiastic new collaborator.

Smart scientists, like experienced mechanics or carpenters, not only have amassed many tools, but also have a knack for selecting the best tools for the job at hand. Kemper suggested that the most powerful way to quantitatively gauge linguistic ability in these autobiographies was to measure idea density and, separately, grammatical complexity. Kemper defined idea density as the number of propositions (individual ideas) expressed per ten words. Grammatical complexity classified sentences on a scale that ranges from 0 (a simple one-clause sentence) to 7 (complex sentences with many forms of embedding—grammatical units nested within larger units—and subordination).

Kemper explained to me that idea density reflects language processing ability, which in turn is associated with a person's level of education, general knowledge, vocabulary, and reading comprehension. Grammatical complexity, on the other hand, is associated with working memory capacity. In order to write a complex sentence, Kemper pointed out, you have to keep many elements in play, juggling them until they are all properly coordinated. There's always a risk of losing your train of thought before you reach the end of the sentence.

I asked her how a writer such as Ernest Hemingway, who was famous for fashioning simple sentences, might rank in this type of analysis. "I have never claimed that complex sentences or idea-dense sentences make for good literature," said Kemper. But they did, as it turned out, offer us an extraordinary tool in our pursuit of the mysteries of Alzheimer's disease.

**K**emper and her associates would analyze the autobiographies blind, with no knowledge of the sisters' current mental or physical condition.

In some cases, striking differences were apparent from the very first sentence.

*I was born in Eau Claire, Wis., on May 24, 1913 and was baptized in St. James Church.*

—Sister Helen

*It was about a half hour before midnight between February twenty-eighth and twenty-ninth of the leap year nineteen-hundred-twelve when I began to live and to die as the third child of my mother, whose maiden name is Hilda Hoffman, and my father, Otto Schmitt.*

—Sister Emma

When we evaluated all ninety-three autobiographies from nuns who were novices in Milwaukee province between 1931 and 1939, Sister Helen had the lowest scores for idea density and grammatical complexity. Sister Emma had the highest.

*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.*

—Sister Helen

*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.*

—Sister Emma

You do not have to be a linguist to notice the differences in the way that these two sisters describe their lives. As a colleague once pointed out to me, it was as though one was a monophonic recording and the other was in high fidelity. For an even more dramatic example, consider the references they make to their siblings.

*There are ten children in the family six boys and four girls. Two of the boys are dead.*

—Sister Helen

*Already two, a brother and a sister, had begun the family which would gradually reach the number of eight. . . . When I was in the fourth grade death visited our family taking one to whom I was very particularly attached, my little brother, Karl, who was but a year and a half old. He was called to his "Home" after three weeks of very much suffering on Good Friday early in the morning. The pastor was willing to have the funeral services conducted before Easter, but I was hoping and praying that my parents would not consent, for I thought since he died on Good Friday he might be in our midst, living, on Easter Sunday. The services were held on Monday morning which I was privileged to attend since we were quarantined.*

—Sister Emma

Or consider how they end their autobiographies.

*I prefer teaching music to any other profession.*

—Sister Helen

*Now I am wandering about in "Dove's Lane" waiting, yet only three more weeks, to follow in the footprints of my Spouse, bound to Him by the Holy Vows of Poverty, Chastity, and Obedience.*

—Sister Emma

When we opened our records and discovered who had written which autobiography, we discovered that the sisters' fates differed as much as their writing styles. The sisters in our sample had started out on the same educational footing. Both Sisters Helen and Emma had twelve years of education at the

time they wrote their autobiographies. Both went on to receive their bachelor's degrees. Sister Helen also earned an M.A. When they were first assessed for the Nun Study in 1992, Sister Emma had a score of 30 on the Mini-Mental State Exam, the highest possible score for this test of overall cognitive function. Sister Helen, however, scored a 0. A year later Sister Helen died, at age eighty, and Markesbery's autopsy confirmed the diagnosis of Alzheimer's disease. Sister Emma was still alive and fully mentally intact.

Despite the obvious contrast between these two writing samples, it did not take on any real scientific meaning until Susan Kemper had quantified all ninety-three autobiographies and we compared those results to the scores on the battery of cognitive tests that the sisters had taken every year. What we found astonished us.

The level of idea density in the autobiographies was strongly associated with the scores from our cognitive tests. Grammatical complexity was also associated with the test scores, but the relationship was weaker. This led us to focus our analysis on idea density.

We classified sisters as having low idea density if their scores fell in the bottom third of the group. The remainder of the group—the top two-thirds—were classified as having high idea density. For each cognitive test, the prevalence of impairment was dramatically higher in those with low idea density. For example, 35 percent of those with low idea density had scores on the Mini-Mental State Exam that suggested mental impairment (scores of less than 24 out of a possible 30). In contrast, only 2 percent of those with high idea density had scores this low.

On average, these sisters were twenty-two years old when they wrote their autobiographies and eighty when we assessed their mental function. Somehow, a one-page writing sample could, fifty-eight years after pen was put to paper,

strongly predict who would have cognitive problems. We ruled out the possibility that this finding might have reflected the level of education or occupation in one group versus another: Fully eighty-five of the ninety-three sisters whose autobiographies we studied were college-educated and worked as teachers.

Jim Mortimer had hypothesized that intellectual stimulation throughout adulthood might be the key to keeping aging brains sharp and preventing Alzheimer's—an expansion of his idea of brain reserve. Here, however, this was clearly not a factor. "To me it was the most bizarre finding on earth," he later told *New York Times* reporter Gina Kolata. This study convinced him that Alzheimer's disease might well reflect a lifelong process, one that progressed very slowly and caused symptoms only when a certain level of damage was reached.

Our growing bank of brains allowed us to take this inquiry to the next level—confirmation in the laboratory. At the time of this analysis in 1995, fourteen of the ninety-three sisters—including Sister Helen—had died. Based on the count and location of tangles in their brains, Bill Markesbery concluded that five of the sisters had pathologically-confirmed Alzheimer's disease. Sister Helen had such extensive tangles in both her hippocampus and her neocortex that Markesbery rated her a Braak stage VI, indicating the most severe form of Alzheimer's. All five of the sisters with Alzheimer's had low idea density. The other nine autopsied brains that appeared healthy all belonged to sisters who had high idea density.

These results stunned us—but we did not completely trust them because we had so few brains to analyze. So we searched for handwritten autobiographies from other convents and uncovered eleven more from sisters whom Markesbery had autopsied. When they were added to our original sample, we had a total of twenty-five autobiographies from our autopsy pool,

ten of whom had confirmed Alzheimer's. An amazing 90 percent of the women with Alzheimer's disease had low idea density in their autobiographies, as compared to only 13 percent of the healthy sisters.

This was a huge difference, and it suggested that within 85 to 90 percent accuracy, we could predict who would get Alzheimer's disease *about sixty years later* and who would not—simply by evaluating their autobiographies. Several years after this first study, after seventy-four sisters with early-life autobiographies had been autopsied, the power of idea density in predicting Alzheimer's disease in late life was about 80 percent—still an incredible level of accuracy.

I do not know why low idea density early in life predicts so strongly who will develop Alzheimer's. Conversely, I can only speculate about why high idea density seems to protect people such as Sister Emma. One potential explanation is that low idea density early in life indicates that the brain is already compromised in some way. This is corroborated by the Braaks' work on the staging of Alzheimer's disease pathology in the brain: Based on autopsies of the brains of 887 people who ranged in age from 20 to 104, the Braaks and their colleagues concluded that the tangle pathology of Alzheimer's is present in some twenty-year-olds and that the tangles develop over approximately fifty years.

In the end, we faced a chicken-and-egg dilemma. Did neuropathological changes early in life compromise a person's linguistic ability? Or did the low linguistic ability somehow speed up the development of plaques and tangles in mid- and later life?

In 1995 we submitted a paper to the *Journal of the American Medical Association* that described these findings—and these perplexing questions. While I was at lunch one day, a secretary gave Lydia Greiner the reply from the journal's editors. When I returned, I found a fantastic gift waiting for me

on my desk: the open acceptance letter taped to a bottle of champagne.

*Since I am 74 years old and getting older, I have often wondered what miracle has spared me from Alzheimer's disease. Now it turns out that simple, direct exposition, unornamented with lush adjectives and adverbs, puts one at high risk for Alzheimer's.*

*Let me tell you, I have never written a simple declarative sentence in my life. My writing style is complex, prolix, obfuscatory. It is as unfathomable as that of a doctoral candidate in sociology, or maybe even a psycholinguist's—if that is possible.*

*I am trying to hold my prose on a tight leash right now, but believe me, eschewing the tortured phrase is hard. Even as I write this, I feel myself getting more and more "idea dense"—so idea dense you couldn't separate one of my thoughts from another with a blow torch. I may live to be 150 before Alzheimer's gets me.*

—Gordon Carlson, letter to the editor, *The New York Times*, February 24, 1996

When our paper appeared in the February 21, 1996, issue of the prestigious *Journal of the American Medical Association*, it attracted intense media coverage—and some intense scrutiny from both the public and our colleagues. The journal itself subsequently ran two critical letters to the editor. One suggested that we had made "a potentially important omission": the emotional content of the autobiographies. Perhaps, this writer suggested, emotionally expressive people fare better.

Actually, this was one of the first hypotheses that Lydia Greiner and I had come up with. The low-idea-density writers

tended to be what we called “listers,” in contrast to the more “emotional,” “sensuous” high-density writers. However, additional analysis had revealed no relationship between emotional expression and cognitive function. Still, the stylistic difference was so striking that we were determined to return to it in a later study.

The second critic of our linguistic findings correctly noted that the psycholinguistic measures we used originally had been designed for another purpose: to assess how difficult a text was to read or understand. This writer asserted that the ability to comprehend difficult texts may well reflect high linguistic ability, but the ability to write them, he concluded, “reflects just the opposite.” This complaint, similar to the witty letter to the editor of the *New York Times*, missed an important distinction. As we wrote in our reply, there was nothing “wrong” with either the high- or low-density sentences in our study. Both kinds of writers were grammatical, expressed clear ideas, and developed them in a cogent way. The sentences with high idea density are not difficult to understand. Many of them are vivid, almost poetic, in the way they link together complex ideas and events.

Finally we come back to the question I ducked on *Donahue* and which remains one of the most frequently asked questions about our work: How does intelligence relate to the differences we observed, and what do we know about the relationship between IQ and Alzheimer’s? To begin with, we do not have standard measures of intelligence on the sisters during their young adult years; IQ testing did not begin in earnest until World War II. The convent records do, however, contain an indirect measure of intellectual performance: high school grades. Surprisingly, idea density was not related to the sisters’ grades in subjects such as English, Latin, geometry, or algebra. This argues that verbal and analytic intelligence may not be reflected in idea density. Rather, idea density may signify other



SISTER LINDA MARIE BOS

The convent of the School Sisters of Notre Dame in Elm Grove, Wisconsin, was established in 1859. The Nun Study enrolled 678 sisters from seven Notre Dame provinces in the United States.



DR. KATHLEEN R. OMCQUINN

Asking the sisters to donate their brains to the Nun Study was one of the most difficult things I’ve ever done. Sister Loretta Semposki, with whom I’m shaking hands, was one of the first to sign on.



Many of the sisters, like Sister Columbine Kumba, have become part of my extended family.

SISTER LINDA MARIE BOS

Centenarian  
Sister Borgia Leuther.



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Prayer and worship are at the core of the sisters' lives at every age and stage of health. While we cannot directly measure intangibles such as faith and social support, the Nun Study would be incomplete without acknowledging their powerful influence.



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properties of the brain, such as those related to perception, encoding, and memory retrieval. At this point we simply do not know for sure.

The personal impact of this Nun Study data came home to me one afternoon in Bill Markesbery's office as Susan Kemper and I laid out our findings for him. Unexpectedly, Bill didn't ask us technical questions about our statistical and linguistic methods. He looked directly at Susan and said, "What does this mean for our children?"

The question caught me off guard. But when I saw the look on his face, I realized that he was speaking as a father, not a scientist. Bill has three grown daughters, and it was clear he wanted to know whether he and his wife, Barbara, had done the right things as parents.

"Read to them," Susan answered. "It's that simple. It's the most important thing a parent can do with their children."

Susan explained that idea density depends on at least two important learned skills: vocabulary and reading comprehension. "And the best way to increase vocabulary and reading comprehension is by starting early in life, by reading to your children," Susan declared.

I could see the relief spread over Bill's face. "Barbara and I read to our kids every night," he said proudly.

We now know that the brain is capable of changing and growing throughout life, but there is no question that most of its growth comes during our earliest years. Infants' and young children's brains grow exponentially after birth. Before sexual maturity, the brain is sculpted and innumerable connections between nerve cells are formed. This development is powerfully influenced by experience, so there *is* something we can do to increase and direct the brain's capacity.