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Still Alice (Genova)

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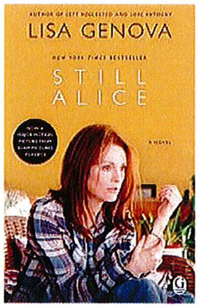

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Still Alice

Lisa Genova, 2007
Simon & Schuster
320 pp.
ISBN-13: 9781439102817

Summary

Still Alice is a compelling debut novel about a 50-year-old woman's sudden descent into early onset Alzheimer's disease, written by first-time author Lisa Genova, who holds a Ph. D in neuroscience from Harvard University.

Alice Howland, happily married with three grown children and a house on the Cape, is a celebrated Harvard professor at the height of her career when she notices a forgetfulness creeping into her life.

As confusion starts to cloud her thinking and her memory begins to fail her, she receives a devastating diagnosis: early onset Alzheimer's disease. Fiercely independent, Alice struggles to maintain her lifestyle and live in the moment, even as her sense of self is being stripped away. In turns heartbreaking, inspiring and terrifying, *Still Alice* captures in remarkable detail what's it's like to literally lose your mind...

Reminiscent of *A Beautiful Mind*, *Ordinary People* and *The Curious Incident of the Dog in the Night-time*, *Still Alice* packs a powerful emotional punch and marks the arrival of a strong new voice in fiction. (*From the publisher*.)

The 2014 film adaptation stars Julianne Moore and Alec Baldwin. Moore won the 2015 Academy Award for Best Actress.

Author Bio

- Birth—November 22, 1970
- Where—N/A

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- Education—B.S. Bates College; Ph.D, Harvard University
- Currently—lives on Cape Cod, Massachusetts

Lisa Genova is an American neuroscientist and author of fiction. She graduated valedictorian, summa cum laude from Bates College with a BS degree in biopsychology and received her Ph.D. in neuroscience from Harvard University in 1998.

Genova did research at Massachusetts General Hospital East, Yale Medical School, McLean Hospital, and the National Institutes of Health. She also taught neuroanatomy at Harvard Medical School fall 1996.

Genova married and gave birth to a daughter in 2000. Four years later she and her husband divorced, and Genova began writing full-time. To hear Genova tell it:

> *When I was 33, I got divorced. I'd been a stay-at-home mom for four years, and I planned to go back to work as a health-care industry strategy consultant. But then I asked myself a question that changed the course of my life: If I could do anything I wanted, what would I do? My answer, which was both exciting and terrifying—write a novel about a woman with Alzheimer's (Cape Cod Magazine* (http://capecodmagazine.com/inspirational-women/) .).

In 2007 she self-published her first novel, *Still Alice*, which went on to became a major best seller and award winning film. Since then, Genova has written three other fictional works about characters dealing with neurological disorders.

Still Alice
Genova's debut novel follows a woman suffering from early-onset Alzheimer's disease. Alice Howland, a 50-year-old woman, is a cognitive psychology professor at Harvard and a world-renowned linguistics expert. She is married to an equally successful husband, and they have three grown children. The disease takes hold swiftly, changing Alice's relationship with her family and the world.

Self-published, Genova sold copies of the book out of the trunk of her car. The book was later acquired by Simon & Schuster and published in 2009. It appeared on the *New York Times* best seller list for more than 40 weeks, was sold in 30 countries, and translated into more than 20 languages.

The book was adapted for the stage by Christine Mary Dunford and performed by Chicago's Lookingglass Theatre Company in 2013.

A 2014 film adaptation starred Julianne Moore as the lead and co-starred Alec Baldwin, Kristen Stewart, and Kate Bosworth. Moore won an Oscar for Best Actress.

Other books
♦ *Left Neglected* (2011)

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Genova's second novel tells the story of a woman who suffers from left neglect (also called hemispatial or unilateral neglect), caused by a traumatic brain injury. As she struggles to recover, she learns that she must embrace a simpler life. She begins to heal when she attends to elements left neglected in herself, her family, and the world around her.

♦ *Love Anthony* (2012)
Offering a unique perspective in fiction, this third novel presents the extraordinary voice of Anthony, a nonverbal boy with autism. Anthony reveals a neurologically plausible peek inside the mind of autism, why he hates pronouns, why he loves swinging and the number three, how he experiences routine, joy, and love. And it is the voice of this voiceless boy that guides two women in this powerfully unforgettable story to discover the universal truths that connect us all.

♦ *Inside the O'Briens* (2015)
In her fourth novel, Genova follows Joe O'Brien, a middle-aged Boston policeman diagnosed with Huntington's. There is no cure, and the disease is progressive and lethal. The story revolves around the fallout on Joe's family, including his daughter who is at risk for carrying the genes.

TV and film
Since her first novel was published, Genova has become a professional speaker about Alzheimer's disease. She has been a guest on the *Today Show, Dr. Oz*, CNN, PBS *News Hour*, and the *Diane Rehm Show*. She appeared in the documentary film *To Not Fade Away*. It is a follow-up to the Emmy Award-winning film, *Not Fade Away* (2009), about Marie Vitale, a woman who was diagnosed with Alzheimer's disease at the age of 45. (*Adapated from Wikipedia. Retrieved 4/6/2015.*)

Book Reviews

After I read *Still Alice*, I wanted to stand up and tell a train full of strangers, "You have to get this book."
Beverly Beckham - Boston Globe

Reads like a gripping memoir of a woman in her prime watching the life she once knew fade away....A poignant portrait of Alzheimer's, Still Alice is not a book you will forget.
Craig Wilson - USA Today

Neuroscientist and debut novelist Genova mines years of experience in her field to craft a realistic portrait of early onset Alzheimer's disease. Alice Howland has a career not unlike Genova's—she's an esteemed psychology professor at Harvard, living a comfortable life in Cambridge with her husband, John, arguing about the usual (making quality time together, their daughter's move to L.A.) when the first symptoms of Alzheimer's begin to emerge. First, Alice can't find her Blackberry, then she becomes hopelessly disoriented in her own town. Alice is shocked to be diagnosed with early onset Alzheimer's (she had suspected a brain tumor or menopause), after which her life begins steadily to unravel. She loses track of rooms in her home, resigns from Harvard and eventually cannot recognize her own children. The brutal facts of Alzheimer's are heartbreaking, and it's impossible not to feel for Alice and her loved ones, but Genova's prose style is clumsy and her dialogue heavy-handed. This novel will appeal to those dealing with the disease and may prove helpful, but beyond the heartbreaking record of illness there's little here to remember.

Publishers Weekly

First novel efficiently showcases the experience of developing early-onset Alzheimer's. In 24 months, 49-year-old Harvard psychology professor Alice Howland exchanges the role of high-achieving teacher, wife and mother of three for that of a disoriented, inarticulate, forgetful shell of her former self. Stricken much earlier than most by this progressive, degenerative disease for which there is no cure, Alice loses her profession, independence, clarity and contact with the world with shocking rapidity in a narrative that sometimes reads more like a dramatized documentary than three-dimensional fiction. Genova, an online columnist for the National Alzheimer's Association, has a brisk style and lays out the facts of the disease-statistics, tests, drugs, clinical trials-plainly, often rather technically. The responses to Alice of her three grown-up children, who are also at risk of the disease; the struggles of her equally high-flying husband, a Harvard biologist; and Alice's own emotional responses, including fear, suicidal thoughts, shame and panic, are offered in semi-educational fashion, sometimes movingly, sometimes mechanically. Alice's address to the Alzheimer's Association Annual Dementia Care Conference is an affecting final public statement before her descent into fog and the loving support of her children. Worthy, benign and readable, but not always lifelike

Kirkus Reviews

Discussion Questions

1. When Alice becomes disoriented in Harvard Square, a place she's visited daily for twenty-five years, why doesn't she tell John? Is she too afraid to face a possible illness, worried about his possible reaction, or some other reason?

2. After first learning she has Alzheimer's disease, "the sound of her name penetrated her every cell and seemed to scatter her molecules beyond the boundaries of her own skin. She watched herself from the far corner of the room" (pg. 70). What do you think of Alice's reaction to the diagnosis? Why does she disassociate herself to the extent that she feels she's having an out-of-body experience?

3. Do you find irony in the fact that Alice, a Harvard professor and researcher, suffers from a disease that causes her brain to atrophy? Why do you think the author, Lisa Genova, chose this profession? How does her past academic success affect Alice's ability, and her family's, to cope with Alzheimer's?

4. "He refused to watch her take her medication. He could be mid-sentence, mid-conversation, but if she got out her plastic, days-of-the-week pill container, he left the room" (pg. 89). Is John's reaction understandable? What might be the significance of him frequently fiddling with his wedding ring when Alice's health is discussed?

5. When Alice's three children, Anna, Tom and Lydia, find out they can be tested for the genetic mutation that causes Alzheimer's, only Lydia decides she doesn't want to know. Why does she decline? Would you want to know if you had the gene?

6. Why is her mother's butterfly necklace so important to Alice? Is it only because she misses her mother? Does Alice feel a connection tobutterflies beyond the necklace?

7. Alice decides she wants to spend her remaining time with her family and her books. Considering her devotion and passion for her work, why doesn't her research make the list of priorities? Does Alice most identify herself as a mother, wife, or scholar?

8. Were you surprised at Alice's plan to overdose on sleeping pills once her disease progressed to an advanced stage? Is this decision in character? Why does she make this difficult choice? If they found out, would her family approve?

9. As the symptoms worsen, Alice begins to feel like she's living in one of Lydia's plays: "(Interior of Doctor's Office. The neurologist left the room. The husband spun his ring. The woman hoped for a cure.)" (pg. 141). Is this thought process a sign of the disease, or does pretending it's not happening to her make it easier for Alice to deal with reality?

10. Do Alice's relationships with her children differ? Why does she read Lydia's diary? And does Lydia decide to attend college only to honor her mother?

11. Alice's mother and sister died when she was only a freshman in college, and yet Alice has to keep reminding herself they're not about to walk through the door. As the symptoms worsen, why does Alice think more about her mother and sister? Is it because her older memories are more accessible, is she thinking of happier times, or is she worried about her own mortality?

12. Alice and the members of her support group, Mary, Cathy, and Dan, all discuss how their reputations suffered prior to their diagnoses because people thought they were being difficult or possibly had substance abuse problems. Is preserving their legacies one of the biggest obstacles to people suffering from Alzheimer's disease? What examples are there of people still respecting Alice's wishes, and at what times is she ignored?

13. "One last sabbatical year together. She wouldn't trade that in for anything. Apparently, he would" (pg. 223). Why does John decide to keep working? Is it fair for him to seek the job in New York considering Alice probably won't know her whereabouts by the time they move? Is he correct when he tells the children she would not want him to sacrifice his work?

14. Why does Lisa Genova choose to end the novel with John reading that Amylix, the medicine that Alice was taking, failed to stabilize Alzheimer's patients? Why does this news cause John to cry?

15. Alice's doctor tells her, "You may not be the most reliable source of what's been going on" (pg. 54). Yet, Lisa Genova chose to tell the story from Alice's point of view. As Alice's disease worsens, her perceptions indeed get less reliable. Why would the author choose to stay in Alice's perspective? What do we gain, and what do we lose?
(*Questions issued by publisher*.)

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Books & Authors
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About the Author

Full text biography:

Lisa Genova

Birth Date : 1970

Known As : Seufert, Lisa Genova

Nationality: American

Occupation : Novelist

Table of Contents:

about this author

Personal Information:

Children: one son, one daughter. **Education:** Bates College, B.S.; Harvard University, Ph.D. **Memberships:** Dementia Advocacy & Support Network International, DementiaUSA. **E-mail:** lisa@stillalice.com.

Career Information:

Writer, actor, research scientist. National Alzheimer's Association, online columnist; has performed various scientific research pertaining to molecular etiology of depression, Parkinson's disease, drug addiction, and memory loss following stroke. Also performs on stage and in independent films.

Writings:

- *Still Alice,* Pocket Books (New York, NY), 2008.
- *Left Neglected,* Gallery Books (Bel Air, CA), 2011.

Contributor to the National Alzheimer's Association Web site.

Sidelights:

Lisa Genova studied biopsychology at Bates College, where she earned a bachelor of science degree and graduated as valedictorian. She later attended Harvard University from which she earned a doctorate in neuroscience. Her scientific research interests cover a number of topics, including the molecular etiology of depression, Parkinson's disease, drug addiction, and memory loss in the wake of a stroke. Genova belongs to both the Dementia Advocacy & Support Network International and to DementiaUSA. In addition, she writes a regular column for the National Alzheimer's Association Web site. Outside of her scientific efforts, Genova is also interested in the arts. She performs regularly on stage, primarily in Boston, Massachusetts, and has acted in a number of independent films. Her debut novel, *Still Alice,* was published in 2008.

In *Still Alice,* Genova merges her scientific curiosity regarding Alzheimer's disease with the horror she felt when her beloved grandmother succumbed to the illness in her mid-eighties. When her grandmother was first was diagnosed with the disease, Genova began to research the illness, learning as much as she could about what was taking place inside her grandmother's brain. Much of the scientific material she studied discussed the molecular results of the disease's progress. Beyond that, however, she read more personal nonfiction accounts of living with Alzheimer's, much of which was written either by caregivers or clinicians analyzing the illness. Ultimately, however, her grandmother was too far along in the progression of the disease to tell Genova what she most wanted to know, which was how it actually felt to suffer from Alzheimer's. That burning question and Genova's search for an answer served as the origin for the novel.

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Genova tells the story of Alice Howland, a professor at Harvard University and a high-achiever, who begins to suffer symptoms of Alzheimer's and gradually, over a two-year period, is ravaged by the illness. Genova depicts Alice as a much younger Alzheimer's patient than is typical, having her first begin her decline at the age of forty-nine. This choice serves to show the extremes of the disease, including how it can rob a person of their livelihood, well-being, and self-respect, all within a short period of time. A reviewer for *Publishers Weekly* declared that "it's impossible not to feel for Alice and her loved ones, but Genova's prose style is clumsy." However, a contributor to *Kirkus Reviews* found the book "worthy, benign, and readable, but not always lifelike." Joanna M. Burkhardt, in a review for *Library Journal*, dubbed Genova's effort "realistic and compelling."

Related Information:

PERIODICALS

- *Kirkus Reviews*, November 1, 2008, review of *Still Alice*
- *Library Journal*, May 1, 2009, Joanna M. Burkhardt, review of *Still Alice*, p. 50.
- *MBR Bookwatch*, May 1, 2008, Mary Cowper, review of *Still Alice*
- *Publishers Weekly*, October 20, 2008, review of *Still Alice*, p. 31

ONLINE

- *Lisa Genova Home Page*, http://www.lisagenova.com (July 18, 2009).*

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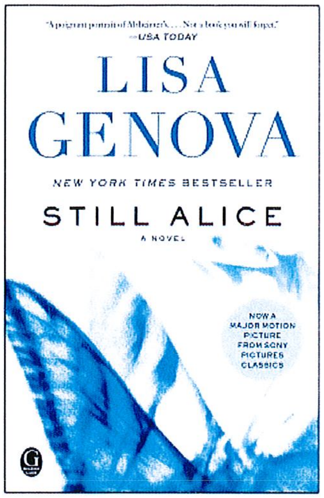

Popularity: ★★★★★
First Chapter

Still Alice (Jan 2009)

Author: Genova, Lisa

Adults Fiction

Description:
Feeling at the top of her game when she is suddenly diagnosed with early onset Alzheimer's disease, Harvard psychologist **Alice** Howland struggles to find meaning and purpose in her life as her concept of self gradually slips away.

Book Appeal Terms: Definition of Appeal Terms

Genre: Books to movies; Mainstream fiction

Tone: Moving; Reflective; Sobering

Writing Style: Jargon-filled

Persistent link to this record (Permalink):

http://search.ebscohost.com/login.aspx?direct=true&db=noh&tg=UI&an=294

Database:

NoveList

Booklist:

In a highly readable form of bibliotherapy, first-time novelist Genova, who holds a doctorate in neuroscience, meticulously traces the downward spiral of a woman suffering from early-onset Alzheimer's disease. In September of 2003, 50-year-old Alice Howland leads a very busy, productive life as a psychology professor at Harvard, the spouse of a biology professor, and the mother of two grown daughters. But a series of memory problems, ranging from forgetting where she put her Blackberry to becoming disoriented on her daily run, sends her to the doctor. She learns that she is suffering from Alzheimer's, and the subsequent months and years see a steady decline in her abilities. By September of 2005, the accomplished professional can barely remember her own daughters' names. StillAlice, however, is far from bleak as it depicts both the unalterable course of the disease and the various ways family members can cope with it. Clearly explaining the testing, treatment options, and symptoms of the disease within the context of an absorbing family drama, Genova has written an ideal primer for anyone touched by Alzheimer's. -- Wilkinson, Joanne (Reviewed 11-15-2008) (Booklist, vol 105, number 6, p27)

Publishers Weekly:

Neuroscientist and debut novelist Genova mines years of experience in her field to craft a realistic portrait of early onset Alzheimer's disease. Alice Howland has a career not unlike Genova's—she's an esteemed psychology professor at Harvard, living a comfortable life in Cambridge with her husband, John, arguing about the usual (making quality time together, their daughter's move to L.A.) when the first symptoms of Alzheimer's begin to emerge. First, Alice can't find her Blackberry, then she becomes hopelessly disoriented in her own town. Alice is shocked to be diagnosed with early onset Alzheimer's (she had suspected a brain tumor or menopause), after which her life begins steadily to unravel. She loses track of rooms in her home, resigns from Harvard and eventually cannot recognize her own children. The brutal facts of Alzheimer's are heartbreaking, and it's impossible not to feel for Alice and her loved ones, but Genova's prose style is clumsy and her dialogue heavy-handed. This novel will appeal to those dealing with the disease and may prove helpful, but beyond the heartbreaking record of illness there's little here to remember. (Jan.) --Staff (Reviewed October 20, 2008) (Publishers Weekly, vol 255, issue 42, p31)

Kirkus:

First novel efficiently showcases the experience of developing early-onset Alzheimer's.In 24 months, 49-year-old Harvard psychology professor Alice Howland exchanges the role of high-achieving teacher, wife and mother of three for that of a disoriented, inarticulate, forgetful shell of her former self. Stricken much earlier than most by this progressive, degenerative disease for which there is no cure, Alice loses her profession, independence, clarity and contact with the world with shocking rapidity in a narrative that sometimes reads more like a dramatized documentary than three-dimensional fiction. Genova, an online columnist for the National Alzheimer's Association, has a brisk style and lays out the facts of the disease—statistics, tests, drugs, clinical trials—plainly, often rather technically. The responses to Alice of her three grown-up children, who are also at risk of the disease; the struggles of her equally high-flying husband, a Harvard biologist; and Alice's own emotional responses, including fear, suicidal thoughts, shame and panic, are offered in semi-educational fashion, sometimes movingly, sometimes mechanically. Alice's address to the Alzheimer's Association Annual Dementia Care Conference is an affecting final public statement before her descent into fog and the loving support of her children.Worthy, benign and readable, but not always lifelike. (Kirkus Reviews, November 1, 2008)

ALZFORUM
NETWORKING FOR A CURE

EARLY ONSET FAMILIAL AD

Interview with Lisa Genova

Lisa Genova

Still Alice Book Cover

"In examining disease, we gain wisdom about anatomy and physiology and biology. In examining the person with disease, we gain wisdom about life."—Oliver Sacks, The Man Who Mistook His Wife for a Hat.

Within the pages of this bestseller she had read as an undergraduate, Lisa Genova found something more profound than a set of intriguing neurological case histories. She found tales of humanity. "That's everything right there," Genova, 37, said of the quote from Sacks's book, which propelled her toward a doctorate in neuroscience. "That's what I hope to do with my writing, both fiction and non."

Last summer—nine years after finishing her Ph.D.—Genova published Still Alice, in which she tells the story of a fictional 50-year-old Harvard professor who develops early onset Alzheimer disease. To write Still Alice, Genova read every book she could find on Alzheimer's and interviewed neurologists (one of whom she shadowed for two days at the Massachusetts General Hospital Memory Disorders Unit), general practice physicians, research scientists, genetics counselors, and social workers. While working on the book, she exchanged e-mails daily with people around the world living with early onset dementia, whom she had met through the Dementia Advocacy and Support Network International (DASNI) and DementiaUSA. "They were my litmus test," Genova said, "letting me know if what I'd written rang true."

In between diaper changes, school drop-offs, and book events, Genova—mother of two young children—writes an online column for the national Alzheimer's Association. She is working on a new book with the working title Living Alzheimer's—a collection of stories about people with early onset Alzheimer disease who are living well. Genova generously made the introductory chapter available to Alzforum for a sneak preview.

ARF: Before you wrote this book, you had completed a Ph.D. in neuroscience at Harvard. Why did you write Still Alice?

LG: While I was in graduate school, we discovered that my grandmother had Alzheimer disease. She was in her mid-eighties at the time, and she'd probably been living with the disease for a while. It's sort of accepted in our culture that 80-year-olds forget things. My grandfather had died,

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and she was living alone. I think she, her children, and grandchildren looked the other way for a while. So by the time we figured out that she had Alzheimer's, she was pretty far along in the disease. I was around a lot while she was sick and being cared for. She has nine children and a lot of grandchildren. We cared for her, but there was little we could do but watch this disease systematically disassemble the woman I knew as my grandmother. She didn't know her kids' names. She didn't even remember that she had any children. She didn't know where she lived. She couldn't remember to go to the bathroom when she needed to. I would watch her looking at her own face in the mirror and not understanding the image she saw reflected back. She would care for these little plastic dolls as if they were real babies. It was heartbreaking.

At the same time, as a neuroscientist I found it fascinating. We could see the results of the destruction of her brain, and I wondered about the events that were going on inside—the molecular mechanisms that had gone wrong to produce these deficits. I wondered what it must feel like when those parts of the brain that house your personal history—your sense of self and identity—start to deteriorate. What sort of compensatory mechanisms might be going on? And what does it feel like to go through that? Unfortunately, my grandmother was too far along in the disease to be able to communicate what was going on. I thought it would be interesting to talk to someone about his or her own Alzheimer's who is at the very beginning stages. I understood at the time that this wouldn't be a conversation with someone in their eighties. This would be someone with early onset Alzheimer's. And to my knowledge, the story of people with early onset AD hadn't really been told.

ARF: Were you already aware of this population, the early onset folks?

LG: Yes. I didn't do Alzheimer's research myself, but Rudy Tanzi and his lab were right down the hall from mine at Mass General at the time. So I would sit in on lab meetings and talks and hear about what was going on in Alzheimer's research.

As scientists, we like to tell stories of pathology from the beginning. For example, what molecular events go wrong to then trigger a cascade of events that then leads to something that manifests as disease? I thought it's also interesting to think about the story of Alzheimer's from the very beginning in terms of the manifestations of those molecular events gone wrong. What does Alzheimer's really look like from the beginning? As a culture, we don't see that. When we hear the word Alzheimer's, we tend to think of the aged grandparent in the end stages of disease, the vacant-eyed person, not remembering anyone. But there's a whole beginning stage to this that we don't typically think of. I was interested in understanding that.

But I didn't write the book at that point. I wasn't a novelist. It was just an idea. I kept my eyes and ears open about early onset Alzheimer's for a couple of years while I was working at Health Advances, a strategy consulting firm focusing on the healthcare industry, and when the opportunity arose to take some time off work I decided to write this story.

ARF: Your novel begins in a rather curious fashion, telling us about the neurons in Alice's head that were "being strangled to death" yet "unable to warn her of what was happening before they died." This was occurring at least a year before the appearance of cognitive symptoms. What were you trying to suggest here about the order of events in AD?

LG: I wanted to get across that a lot goes wrong, that it takes a while before people notice they've got something out of the ordinary. Let me give you two ways of thinking about this. Let's say you've got a piece of information that you're trying to recall, that you own in your brain, that's already been encoded. If you have 10 ways of getting to that piece of information—different associations and ways of understanding it—if you have 10 neural pathways that get there, then you can lose one or two of those synapses, or neural connections, and still have eight or nine ways of getting the piece of information recalled. But if you only have one way of getting to that piece of information, if you only have one synapse, once that synapse is blocked, then the information is forgotten. For a lot of people with early Alzheimer's, especially younger or very intelligent people, they lose one or two synapses here and there, but still have another way to get there.

It's like a roadblock. If you need to get to the store and the road is blocked, but you're familiar with the area, you probably know another road to take. Likewise, you may not recall the piece of information immediately, but you can still get the piece of information. So you may forget something like, "I can't remember so and so's name." But you give it some time, and your brain ultimately finds the target. The point is, even though there may be some destruction or blockade going on through Alzheimer's in someone's brain, one can still function and get to the information one needs. The other reason I wanted to present the idea that things are going wrong for quite a while before the disease becomes so disruptive that Alice can no longer do her job is that for some time, people usually pass off these symptoms to I'm not getting enough sleep, I'm overstressed, I'm multitasking too much, maybe I'm depressed, maybe I have menopause. There's a list of things that can cause cognitive problems similar to Alzheimer's, and people will go on functioning for some time at a suboptimal level thinking that their memory lapses and disorientation are due to the very high demands that we have in our culture these days. There are many people today walking around in the beginning stages of Alzheimer's who don't know yet that they have it, i.e., they haven't been diagnosed, and think they're overtired. That's just how the disease presents itself initially.

ARF: It seems that many of those reasons are legitimate ones in terms of accounting for memory lapses. Is misdiagnosis, or late diagnosis, a serious problem you think could be corrected?

LG: I think it is. I've talked to a lot of people who've been through the process and are now diagnosed with Alzheimer's. It is typically a long and arduous journey to diagnosis, and for lots of good reasons. Of course, people and physicians want to point to something that is curable first. They want to say, "You need to get more sleep." They want to say, "I think you're depressed; we're going to put you on Prozac." They want something that's manageable. But the people I know with Alzheimer's knew a long time before they arrived at diagnosis that this wasn't depression. They'd known depression perhaps earlier in their lives, and this is something different. They've got a good level of energy. Or they aren't just apathetic about things. It's something else. They know they're tired but not unusually so. Or they're going through menopause but the changes that are occurring aren't what's happening to any of their friends. They know that something is not right. And it takes a long time, often, to get the diagnosis because general practice physicians often aren't prepared to ask the right questions or to refer them to neuropsychological testing and a neurologist who can really tease out the problem. (For more on diagnosis, see EOAD Diagnosis and Diagnostic Odyssey Interview.)

People diagnosed with this disease early are spending lots of time advocating for earlier diagnosis because it makes a big difference. First, to get the diagnosis provides a lot of relief for people who've spent maybe a year or more trying to figure out what the heck is going on. So, oddly enough, being told that they're not crazy, that they actually have a reason for the cognitive changes that have been going on—although it's heartbreaking and devastating in some ways, in others I've heard over and over again that it's a relief to finally know what's going on, that they can now do something, which is to get on drugs like Aricept (donepezil) and Namenda (memantine). While these don't cure the disease, people tell me they make a world of difference, especially if taken in the early stages. Over and over again, I hear people say, "If I weren't on these drugs, I wouldn't be able to talk to you right now. I wouldn't be able to recognize the letters on my keyboard to write you this e-mail. I wouldn't be able to dial the numbers on the phone to talk to you."

ARF: How do the drugs work?

LG: Aricept is one of several acetylcholinesterase inhibitors, which means it increases the brain's levels of the neurotransmitter acetylcholine—one of the types of neurotransmission that is diminished with Alzheimer's. It's an important neurotransmitter for learning and memory. It's in a part of the brain called the hippocampus, which is critical for working memory, or short-term memory. It's like the Post-It note section of your brain. When you learn something new, it stays there temporarily. If it's important enough, your brain will commit it into long-term storage, but for now, the information is stored in a sort of short-term space.

ARF: So Aricept doesn't directly target the problem with amyloid-β peptide clogging the synapses, or spaces between neurons?

LG: No, and neither does the other drug, Namenda, which is an NMDA receptor antagonist. Namenda acutely blocks glutaminergic transmission, but chronically it may actually enhance glutamate function. Glutamate is an important neurotransmitter for learning and what's called long-term potentiation. But neither of these drugs gets at the heart of the matter. They don't stop the disease from progressing. They just make the most of what is still functioning.

ARF: Did any of your sources with EOAD have genetic testing done presymptomatically? I mean people who knew their parent had the disease and therefore wanted to get tested right away, before they had symptoms (see e.g., One Man's Forward Approach).

LG: I don't know anyone who had the testing presymptomatically. I know several people who suspected that this was going to be in their future because their mother had it, their mother's father had it, their aunts and uncles all had it, their cousins had it, older brothers and sisters were getting it. I know a couple of people in their fifties where this disease just runs rampant through their family, and since getting the diagnosis, they went ahead and got the screening done. Interestingly, the young adult children of these two people have chosen not to get tested. It's a scary thing to have to face, and denial is a very big player in the lives of people who are first being introduced to this disease.

ARF: Does this population—those who are young and well but know they'll have the disease in the future—have different attitudes about research, compared with patients with late-onset Alzheimer's?

LG: The people I know who are young are very anxious to participate in research, and most of them can't. The vast majority of clinical trials out there have an arbitrarily high minimum age. I've asked neurologists whether there's a reason the minimum age is 60, for instance, in this clinical study, and they say no, we just have to pick an age, and we figured 60. This excludes the 55-year-old who has Alzheimer's without any other medical conditions, who is highly motivated to participate in the trial and to comply and take all the doses and show up to all the follow-up. It's unfortunate. I hope this is in the process of changing to include the younger crowd. (To learn more about why early onset AD families have been excluded from drug trials and how this could change, see EOAD Research essay.)

ARF: A recent study suggests, perhaps contrary to common belief, that a diagnosis of dementia does not make patients more upset but in fact brings a certain sense of relief. Did you find this to be true in the patients you interviewed?

LG: Yes, and I would not have predicted this. But in retrospect, it makes a lot of sense. If you are getting lost on the way home from work, and this is a one-mile commute that you've done for years, and you say, "Gosh, I don't know where I am," or you are forgetting names of people you've worked with for years, or you are forgetting to show up at meetings and that's something you've never done, or you are trying to play a game of chess, your favorite game, and you can only think two moves ahead instead of eight, or you're going to make a cup of coffee, and you're staring at the coffee machine and can't for the life of you figure out how to make the thing work.... You are scared when this is going on. You are worried that you have a brain tumor. You're worried that you're crazy. You can't figure out the checkbook anymore. Bad things are starting to happen. You're not paying the bills appropriately. You're failing at work. This is out of character. Your relationships are at risk. Your status in life is at risk. And you don't know why.

That to people is terrifying, and once they get the diagnosis of Alzheimer's, it's like "now I know what it is; now I can deal with it. And now I know what it's not." Like anything, if we don't know what's happening, there's an anxiety, and once you know, there's a level of control you can have over the situation. And though it sounds bizarre—someone's just told you that you have an incurable, fatal disease—people feel prepared to deal with that rather than the uncertainty. (A woman with whom Genova corresponded while writing Still Alice describes her journey to AD diagnosis in a blog.)

ARF: What practical and logistical concerns do people face upon discovering that they carry a PS1 mutation?

LG: I have not talked to this younger generation yet, but as for the people who currently are symptomatic and diagnosed in their fifties, they worry a whole lot about things like, what does this mean for my health insurance? What does this mean for my life insurance? And it means a lot. People have to wrestle with all sorts of bureaucracy and red tape to make sure their insurance covers them, and trying to plan financially for their future gets tricky. I know a woman who, upon her diagnosis, needed to take a couple of months off to get used to the medication and wanted to return to her job afterward. She revealed at work that she had Alzheimer's but planned on coming back and continuing until she no longer could. But her boss fired her. Of course, this wasn't something he could legally do, and she had to fight it. People face all sorts of obstacles when the public knows about this disease.

If you are in your twenties and you find out you have a PS1 mutation, which means you will definitely develop Alzheimer's, you have to start to think about things like, am I going to have children and pass this gene down? How do you then plan your own life when you're so young?

ARF: One would think that people with early onset Alzheimer's are a population researchers would want to tap into. They're otherwise well and coherent, and eager to participate.

LG: Exactly. Think of all the information you could get out of them. Rather than just taking the drug and going through a series of scans and the simplest of questions like the Mini-Mental State Exam (MMSE)—which is typically not sensitive enough to pick up Alzheimer's in a 50-year-old who has a high IQ and is functioning at a really high level to begin with—you could design more specific tests for these people, such as pencil and paper neuropsychological testing, which is probably the most sensitive indicator of Alzheimer's we have at this point.

Neuropsychological testing has more depth than the MMSE and can last hours to days depending on what combination of tests the clinician chooses. They really get at taxing your short-term memory and your ability to reason and comprehend. I'm finding anecdotally—just from talking to a lot of people who've been diagnosed with Alzheimer's disease early—that it was the neuropsychological testing that revealed the Alzheimer's disease and not an MRI. Sometimes a PET scan, but in my experience most often the thing that took the cloth off the table and revealed what was there was the neuropsychological pen and paper test.

ARF: Were there other obstacles these folks mentioned?

LG: That was the only obstacle mentioned to me. Otherwise this group is very interested in participating in clinical trials.

ARF: It seems that would be an easy thing to change. Why isn't it?

LG: I think there's a lack of opportunity for these two groups to talk to each other. It's the pharmaceutical companies and clinicians running the clinical trials and the access to people with early onset Alzheimer's. There may be the notion that there aren't enough of these people under the age of 55, that this isn't a sizeable enough population. But there are more than 500,000 people in the U.S. diagnosed with early onset Alzheimer's. While this represents only 10 percent of the entire population with Alzheimer's, it's a group that is growing. As more people are less afraid to step forward and get diagnosed and come out of the closet, I think it's an important group to get in clinical trials. They are healthier. They are able to report any changes that they feel are going on. A lot of what the currently available drugs are able to do is improve quality of life. The way to understand improvements in quality of life is to interview the person, and a 55-year-old at the beginning stages of the disease can be interviewed more easily than an 85-year-old in the later stages.

ARF: Is the tide turning? Are researchers realizing these people are the ones to tap into? Or do you think it's still in the future?

LG: I hope it's not way in the future. I don't see a tide turning in the camp of the physicians. I see it turning more in terms of the people with early onset Alzheimer's insisting on being seen and heard—through organizations like the Alzheimer's Association and through the media. More and more in the New York Times, in US News and World Report, on NPR, in PBS's NewsHour with Jim Lehrer, we're seeing people with early onset Alzheimer's showing their faces and voicing what this disease is like when you get it at such an early age. (See also ACT-AD advocacy story and Richard Bozanich Q&A.)

ARF: Is the age limit set high because it's easier to see drug effects in older patients with more drastic symptoms? If the people are younger and don't yet have that many symptoms, you pretty much need to have a preventative agent. Does that have anything to do with the age limit?

LG: Maybe. With the drugs in development now, you want someone who has got a big enough deficit such that if there's improvement, it would be seen as significant. That's what they have to prove. And if there's only a slight deficit to begin with, it's going to be hard to show a significant improvement.

ARF: Still Alice ends with a news report on the Phase 3 trials of Amylex, a drug that binds soluble amyloid-β and prevents its aggregation. What is that?

LG: It's a fictional drug. All the drugs mentioned are real with the exception of Amylex, which is based on a class of drugs that are in clinical trials right now. [Editor's note: for a real-life example, see Keystone meeting report.]

ARF: What are some promising treatments that are trying to get at the synaptic problems as opposed to just treating symptoms?

LG: There are a bunch of different drugs in clinical trials that aim to attack the disease itself. In Alzheimer disease, there's too much of a protein called amyloid-β42, and this is a peptide that is very sticky. When too much of it is in the synapse, it sticks to itself and forms oligomers, which get in the way of neurotransmission through a complex molecular cascade. So the treatments in clinical trials are aiming to either decrease the production of amyloid-β42, to increase its clearance, to prevent it from sticking to each other, or to rip them apart if they've already formed oligomers. Whether it's the secretase inhibitors (decreasing Aβ42 production) or immunotherapy (increasing clearance), any of these have a shot at stopping the disease from getting worse and clearing up the synapse. If the neurons haven't already died, if they're just clogged—neuron 1 can't talk to neuron 2 because it's got this amyloid-β clog in the middle—if you clear the clog, neurotransmission is restored; at least that's the hope. Then that stored memory can get accessed, or new information can get learned through that pathway, and function is restored for that person. So with Alzheimer's, things aren't irreversible, in theory, if too many of your neurons haven't already died.

ARF: What do you see as the primary barriers to progress in Alzheimer's research these days?

LG: I don't see a lot of barriers to progress. The scientists are highly motivated and passionate about finding a cure for this disease. On the public side, we need a lot of awareness and insistence by Americans that we are facing a crisis. The sheer number of people who will be diagnosed with this disease in the coming years is astronomical. It is going to be a healthcare crisis. And we have a growing number of people in their forties, fifties, and sixties who have aging parents themselves and have young-adult children. They are in a position where they are being diagnosed with Alzheimer's, dropping out of their careers and their financial security while they are expected to care for an older generation and perhaps a younger generation. That is not an equation that will work.

Probably the greatest barrier is making sure scientists have the funds to get the basic research done, to understand the molecular targets for the drug compounds they need to design to cure the disease. Obviously, we want drugs that cross the blood-brain barrier and that are specific enough to the molecular cascade involved in Alzheimer's so that they're safe, well-tolerated, and effective. The NIH needs funding that is appropriate to the millions of people who have this disease. Right now, research is highly underfunded. We need greater awareness so the public understands who has this disease. It's not just the 89-year-old; it's the 50-year-old, the 60-year-old, the 70-year-old. And 70 is younger these days than it was 50 years ago.

Besides drugs, though, it is important to be aware that, both anecdotally and in scientific papers, exercise is probably the single most important thing people with Alzheimer's can do to improve their health and stave off the disease. In studies done with mice, it was shown that mice that exercised all through the night had decreased levels of amyloid-β, decreased plaque load, and improved cognitive function. Exercise seemed to do as well as any drug we currently have for Alzheimer's.

ARF: What kind of exercise?

LG: The mice ran on a wheel. And the people I know with Alzheimer's say that exercise, meditation, staying relaxed, eating healthy, keeping their cholesterol levels down—anything that's good for the heart—is good for your brain. They say exercise and a lifestyle that involves meditation and relaxation—basically taking care of yourself—makes a significant improvement in the symptoms they're experiencing. If they're stressed out, if there's too much going on, if they're not getting enough sleep, then that's when the fog comes in (Teri et al., 2003 and Larson et al., 2006).

ARF: Tell us about your new book, Living Alzheimer's.

LG: It's going to be a collection of stories of people who are living well with early onset Alzheimer's. I've interviewed 10 people. The book is not a list of symptoms or a list of how-to's; it isn't a clinical snapshot. It is an attempt to put a human face and voice to this disease and develop the idea that these people are still living fulfilling lives. They're not in a nursing home, lying in bed and unable to understand anything. These are people who have been diagnosed with Alzheimer's at the beginning stages of the disease. And while they have suffered losses and could continue to as the disease progresses, there is still a lot of life to live. While their cognitive capabilities are diminished, they're not incompetent every minute of the day. Many of these people have gained a wisdom and peace with life that I think everybody strives for.

They have interesting stories to tell in terms of how they adapt to certain problems that arise. It's a tricky disease. People with Alzheimer's are standing on constantly shifting ground. Just when they think they've mastered a way to adapt to what's going on, their symptoms either get worse or new symptoms arise. So they have to stay creative and open and willing to troubleshoot and be positive. They have a lot to offer families who are just entering this terrain. That's what the book hopes to do.

ARF: When will it be done?

LG: By the summer of 2008.

ARF: Of the 10 people who will be featured in Living Alzheimer's, are some of these the same folks you interviewed before writing Still Alice?

LG: I knew half the people through my research for Still Alice; the other half I've met since. It was by understanding what they go through that I saw an opportunity to share more. I didn't plan on writing Living Alzheimer's. It sort of came out of what I learned through writing Still Alice. I wasn't ready to leave writing about Alzheimer's yet. It's just like in any subject. If you're trying to learn about a topic and you read a nonfiction description, it doesn't stay with you nearly as well as if you read a story about that topic. Stories are what we take to heart, what moves us. I think there's an opportunity here to educate people through stories.

ARF: Thank you for this interview.

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