Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/neurofrontiers/childhood-onset-epilepsy-a-look-into-the-effects-of-aging/14247/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Childhood-Onset Epilepsy: A Look into the Effects of Aging

Dr. Wilner:
In patients with childhood-onset epilepsy, little is known about how the brain changes due to aging, but a new study funded in part by CURE Epilepsy offered some interesting findings on how epilepsy and aging overlap in a unique population-based group.

You're listening to *NeuroFrontiers* on ReachMD. I'm your host Dr. Andrew Wilner, and joining me today are the authors of the study, Dr. Bruce Hermann and Dr. Shlomo Shinnar. Dr. Hermann is an Emeritus Professor at the University of Wisconsin School of Medicine and Public Health, and Dr. Shinnar is a Professor Emeritus of Neurology and Pediatrics at Albert Einstein College of Medicine.

Dr. Hermann, welcome to the program.

Dr. Hermann:
Thanks, Dr. Wilner. I'm happy to be here, and thanks for the invitation.

Dr. Wilner:
And, Dr. Shinnar, thanks for being here.

Dr. Shinnar:
A pleasure.

Dr. Wilner:
So let's just dive right in starting with you, Dr. Hermann. Before this study, what was known about epilepsy and brain aging, particularly with childhood-onset epilepsy?

Dr. Hermann:
Well, what was known was that there was good cause for concern. It's widely appreciated that cognitive difficulties, including memory and language and other cognitive domains, can be adversely affected by both the adult and child epilepsies, and tracking this over time in midlife people with chronic epilepsy, many of whom had early childhood-onset epilepsies, carried a variety of risk factors for abnormal cognitive aging and abnormal brain aging, which has been shown in the broader aging literature. For example, individuals with chronic epilepsy midlife carry abnormalities and quantitative biometric measurements. They have substantial cognitive difficulties and have a variety of health and lifestyle issues that place them at greater risk, as well so being in midlife with a lot of life left ahead of them, the current concern has been what's going to happen going forward. And there's never been a study of a cohort of persons with childhood-onset epilepsy who have been followed to late middle age and followed, as in this case with a lifetime of valuable information.

Dr. Wilner:
Okay. And over to you, Dr. Shinnar, can you tell us how the CURE Epilepsy study was designed?

Dr. Shinnar:
So the overall study is a prospective study of childhood-onset epilepsy that Dr. Sillanpaa started in the '60s and has now been ongoing for over 50 years. The CURE funding helped add imaging and cognitive testing at 50 years out, which is an important addition to this long-term population-based study, which has changed how we view childhood-onset epilepsy.

Dr. Wilner:
So you looked at people who as children had childhood-onset epilepsy 50 years later. Is that right?

Dr. Shinnar:
Yes, but they were identified in childhood and followed from then on, so they were also seen as children.

Dr. Wilner:
Wow. So, Dr. Hermann, do you want to tell us more about this unique population group?

Dr. Hermann:
The cohort got its origins to when Dr. Sillanpaa was working on his MD PhD, and he recruited this cohort of individuals between 1961 and '64. It was epidemiological in nature, and he found everyone under the age of 16 with epilepsy, 99 of whom had uncomplicated epilepsy. And as Dr. Shinnar, mentioned, they have been followed episodically over the decades, and so this has just been a remarkable cohort providing information about the lifespan course of epilepsy, psychosocial outcomes, deaths, and a variety of other information.

Dr. Wilner:
So which countries participated?

Dr. Shinnar:
This is Turku, Finland.

Dr. Wilner:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Andrew Wilner, and I'm speaking with Drs. Bruce Hermann and Shlomo Shinnar about the CURE Epilepsy Study on brain aging in childhood-onset epilepsy.

Okay. So coming back to you, Dr. Shinnar, what were some of the findings?

Dr. Shinnar:
The findings were that the brains of people with childhood-onset epilepsy, particularly if it was still active, showed changes consistent with more rapid aging compared to controls who did not have epilepsy, and that these changes were also associated with cognitive changes, and so this was evidence that ongoing epilepsy even if fairly well-controlled—this was not a refractory epilepsy cohort—was associated with a negative impact on the brain over decades.

Dr. Wilner:
And when you talk about these changes, you mention that neuroimaging was performed and neurocognitive testing. What were some of the changes that you observed?

Dr. Shinnar:
Well, on imaging there were more white spots, if you will, and there was more evidence of amyloid on PET. On the cognitive testing, my colleague Bruce Hermann is the neuropsychologist, so let him describe the cognitive testing.

Dr. Hermann:
Yeah. Let me just make a couple points as one of the unique aspects of this study is it includes about 75 percent of the cohort has remitted epilepsy, so it's fair to say that at least from a cognitive perspective, 99 percent of what we know is obtained on people who have active epilepsy. So here we have a cohort that includes both those who have remitted epilepsy, sometimes decades later, as well as individuals who have active epilepsy, so we were able to take a look at whether the degree of activity of their epilepsy, if still present or not, had an impact on cognition, imaging, and the grayest measures that were obtained. And what we wanted to do was to merge the epilepsy field with the preclinical AD world, and they are very big on biomarkers, amyloid, tau, and so on, and so we wanted to obtain amyloid imaging on the epilepsy cohort, which was a quite unusual proposition, and it was a very difficult to get funding. And actually, the people who supported us throughout this investigation was CURE Epilepsy, so we initially got an Innovator Award to help support the amyloid imaging, and amyloid at baseline was three times higher compared to the controls in 2012. And you're exactly right. Is this something they carry with them over the decades? Or is this something new? And by bringing them back five years later, that answers the question, and in both groups, amyloid increased. There was a 3-fold increase in the epilepsy cohort, so very important finding, and actually one of the few human amyloid imaging studies.

In way of cognition, it's largely the active epilepsy group that shows the most problems. They showed the most problems in 2012 at baseline, including memory problems, and then over the course of the five years, both the remitted and the active epilepsy patients showed some declines and more significant in the latter group. So in a sense, things are cooking a bit, and I guess that some careful study of these individuals going forward is really warranted.

Dr. Wilner:
And let me ask you, were you able to differentiate between the patients whose epilepsy had been, say, controlled for the last 10 or 20 years? And as far as they knew, they were not having seizures versus those who had active epilepsy? Was there a difference in their imaging and cognitive testing?

Dr. Shinnar:
Active epilepsy does worse. Surprisingly, even those in remission were somewhat worse than controls.

Dr. Wilner:
Let me ask a practical question that affects patients we see in the clinic every day, and that is when we have patients who say they have been seizure-free for a year, two, three, or four and they don't want to take antiepileptic drugs anymore, the tendency has been to stop the treatment because they're not having seizures. Do your findings influence that decision?

Dr. Shinnar:
Well, this has been the topic of my research for over 20 years, and remembering that medications themselves have a negative impact, including on cognition, so I think if you're seizure-free, we would love to get you off the medications. On the other hand, it highlights the importance of making sure you are, in fact, seizure-free and being aggressive with our medication management if you're not.

Dr. Wilner:
Well, before we close our discussion, I'd like to open the floor to each of you to share any final thoughts with our listeners. Dr. Shinnar, do you want to continue? Let's start with you.

Dr. Shinnar:
I think this ongoing study is highlighting the importance of looking longitudinally at epilepsy and all its manifestation and impact beyond

simply that of seizures. And the more we learn about epilepsy, the more folks like me are happy we're going into the business of treating it and highlights the importance of treating it.

Dr. Wilner:
Thanks, Dr. Shinnar. And, Dr. Hermann, I'll give you the final word.

Dr. Hermann:
Sure. Two things—first, I think this study points to the utility of taking advantage of what's known in the general aging and preclinical AD world. There's a lot of push to look at modifiable risk factors to improve cognitive and brain health with aging. There's a huge push on detecting or discovering biomarkers, including serum biomarkers. And I think riding on their coattails will allow practitioners who see people who are aging with epilepsy to detect early adverse changes and make some prescriptive life changes and perhaps, other alterations. The second point is I think more than anything else this points to the highly collaborative nature of research these days. Dr. Sillanpaa was able to put together a remarkable team of coinvestigators in Finland that involved neuroradiologists, neurologists, neuropsychologists, and electroencephalographers, and it really was a remarkable undertaking. And this was very difficult to get funding for initially and maintain funding, and CURE Epilepsy was just instrumental throughout the whole process.

Dr. Wilner:
Well, we've certainly covered a lot of ground today, and I'd like to thank my guests, Dr. Bruce Hermann and Dr. Shlomo Shinnar, for sharing their insights in a wonderful discussion.

Dr. Hermann, Dr. Shinnar, it was a pleasure speaking with you both.

Dr. Hermann:
Thank you.

Dr. Shinnar:
A pleasure.

Dr. Wilner:
For ReachMD, I'm Dr. Andrew Wilner. To access this and other episodes in our series, visit ReachMD.com/NeuroFrontiers where you can Be Part of the Knowledge. Thanks for listening.