

SCIENTIFIC AMERICAN FRONTIERS PROGRAM

#1402 "Don't Forget"

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Yesterday's Gone

Never Forget A Face

Why Memories Last

When Memory Lies

Keeping Old Brains Young

ALAN ALDA When I was twelve, I went swimming alone in the surf down there. It was rougher than it is today. I was a strong swimmer, and for a while it was fun letting the waves pull me out to sea, and tumble me over and over under the surface and then slam me on the shore. But when I tried to get out, I couldn't, and I started to panic -- I realized I might drown - until eventually I was able to claw my way up the beach, grabbing at handfuls of sand. That was 55 years ago, but I still remember it vividly. I remember the waves pummeling me, taking me under; the wet sand under my fingers; the roar of the waves. I remember the sting of the salt spray. So where - and what - is that memory? How is it tucked away in my brain, ready to flood back in an instant? Tucked way along with, but separate from, hundreds of thousands - probably millions - of other memories? Where is the smell of the salt spray, the grittiness of the sand, the crashing on the rocks? In the next hour, we're going to find out how we create our memories - not just vivid ones like this, but where I left my car keys and the name of the familiar looking person across the room there. And we'll be looking at how our memories are lost, how as we grow older they become slippery and elusive - sometimes vanishing forever, erasing our past and who we are.

Yesterday's Gone

ALAN ALDA (NARRATION) We're starting our exploration of memory a few miles up the coast from La Jolla, with a man whose own ability to create memories vanished almost entirely a decade ago. Ever since, he's been helping researchers from the University of California, San Diego.

E.P. Hi. Good to see you, by golly.

ALAN ALDA (NARRATION) Today, Larry Squire and Jen Frascino are on the latest of many visits the team has made to the man known to memory researchers everywhere as E.P. E.P. We've got nice sun for the camera.

ALAN ALDA (NARRATION) E.P. is now 82. In 1992, retired from a career in electronics, he suffered an acute virus infection that destroyed part of his brain. Most of his thinking skills survived the damage virtually intact. JENNIFER Why should people pay taxes? E.P. To support your country and your counties and states to pay for things. JENNIFER If you were lost in the forest during the day, how would you go about finding your way out? E.P. I would find a river and follow the river down to wherever it may go. JENNIFER M-hm. E.P. Ocean, lake, normally you would pass something possibly.

ALAN ALDA (NARRATION) E.P. can also copy complex drawings... And not only has no difficulty repeating back a list of words - in this case, dog, raccoon, lion and parrot -

E.P. Dog. Raccoon. Lion and a parrot.

ALAN ALDA (NARRATION) But even has a little sly fun with Jen along the way. E.P. What you got to add is about two more. JENNIFER Really? Would that make it tougher?

E.P. Than that would catch 'em. Maybe seven, you know?

ALAN ALDA (NARRATION) E.P. really hits his stride when the testing of his cognitive skills involves Jen's laptop computer. E.P. Having been in electronics over the years, I'm amazed at all this, it's just wonderful, believe me. Little printed circuits, it's just, ah, you can't believe it. Used to be in a six-foot rack and down to this, it's just wonderful. When I was in electronics, this would be in a six-foot rack...

ALAN ALDA (NARRATION) But it's now that something odd about E.P.'s behavior becomes apparent.

E.P. .... oh, just amazing, believe me. When I was in electronics, this would be a six-foot rack. This would be a six-foot rack.... This would be in a couple six-foot racks.... Be in six-foot racks.... This would be in a six-foot rack, and now look at it, down to this, little printed circuits....

ALAN ALDA So he's not aware that he's told us three or four times that he used to be in electronics, that a computer used to fill a room and now it's down to the size of a microchip, he's just not aware that he's said those things several times?

LARRY SQUIRE No, he tells us these same stories again and again. We've heard these stories before and we'll hear these stories again.

E.P. The equipment it takes....

ALAN ALDA How was it? How have you been enjoying this session?

E.P. Oh, I enjoy this. Absolutely.

ALAN ALDA Yeah. It is interesting, isn't it?

E.P. Look at the work you guys are doing. You're getting wonderful, I believe.

ALAN ALDA I'm sorry, I forget her name. What's her name?

E.P. Her name?

ALAN ALDA Yeah.

E.P. I don't remember.

JENNIFER Okay. Jennifer.

ALAN ALDA AND E.P. Jennifer.

E.P. Jennifer. Jennifer. I'm sorry.

ALAN ALDA Have you-- Have you met Jennifer before today?

E.P. I think so. Yes. I'm not positive though. I'm sorry, my mind....

ALAN ALDA That's OK. We all have lapses...

E.P. We all get that way

ALAN ALDA Oh, sure.

ALAN ALDA How much have you worked with him?

LARRY SQUIRE We've probably visited his house 200 times.

ALAN ALDA 200 times? And for him, is each time the first time for him?

LARRY SQUIRE Well, you see, it's yes and no. It's clear that he does have a record of the experiences that are based on the habits and the interactions and the emotional values. The interactions in that they've been positive and not negative. He certainly lets us in the door faster.

JENNIFER Like you saw, he couldn't tell you my name, he couldn't tell you if he saw me before. But there's definitely a rapport there that I think that's been built and he's aware on some level.

JENNIFER I read you some words about 15 minutes ago. Four of 'em. Four words. Do you remember me reading you four words?

E.P. No, I can't recall. I'm sorry.

JENNIFER No, that's okay, no need to apologize.

E.P. My mind's getting old.

JENNIFER That's okay. I read you four animals and I want you to say "yes", if you think the animal was on the list I read you about 15 minutes ago, or "no" if it was not on the list. Okay? Cat.

E.P. Yes.

JENNIFER How sure are you?

E.P. I feel reasonably sure on that, cat.

JENNIFER Raccoon.

E.P. No. No. I feel no.

JENNIFER Giraffe.

E.P. Yes.

JENNIFER How sure are you that I read that? E.P. I'm real sure on that.

JENNIFER Real sure?

E.P. They're beautiful animals, believe me.

JENNIFER Okay. Lion.

E.P. No.

ALAN ALDA (NARRATION) E.P.'s inability to remember things that happened just a few minutes ago can be traced directly to the damage the virus inflicted on

his brain a decade ago. The areas destroyed were in his temporal lobes - most critically a structure called the hippocampus and the brain tissue immediately around it. Without a hippocampus,

E.P. lives in a permanent present. Anything new that happens to him simply doesn't get recorded.

JENNIFER Do you remember drawing something for me today?

E.P. No.

JENNIFER Drawing something? About 15 or 20 minutes ago?

E.P. No.

JENNIFER Okay.

E.P. No, I'm sorry.

JENNIFER Don't apologize. Thank you for trying. Thank you.

ALAN ALDA (NARRATION) But although

E.P. can't record new memories, old ones from years before his hippocampus was destroyed are remarkably intact. He grew up in Hayward, California.

JENNIFER We're going to take a trip, back to Hayward.

E.P. Okay.

JENNIFER How about your house on Castro Valley Boulevard to the Hayward Theatre. Remember where the Hayward Theater is?

E.P. Yes. I leave the house, turn to the right to A Street. Down A Street to Castro Boulevard, then turn to the left and it's in the middle of the block. Hayward....

JENNIFER And if you didn't go down A Street. If you instead you took another street, what would you do?

E.P. Redwood Road, Redwood Road would run right into it.

ALAN ALDA Unbelievable.

JENNIFER How about the public library? Hayward Public Library. From your house.

E.P. It would be the same thing. Going down A Street. And A you have to go to the left to B, and it's on the corner.

ALAN ALDA He's got that map in his head. He can see all those streets.

LARRY SQUIRE He used to ride his bicycle around.

JENNIFER The last thing I want to talk to you about is the neighborhood that we're in now.

E.P. Here.

JENNIFER How about any of the streets around here? Can you tell me any of the street names in the neighborhood here?

E.P. No I cannot. I cannot.

JENNIFER That's a tough one.

E.P. Yeah. I'm sorry.

JENNIFER You don't need to apologize.

E.P. I know where Castro Valley Boulevard is, but that's where I was born and raised. But right here, I have to say no, I'm sorry. I just live right here ...

JENNIFER Enjoy the world.

E.P. I enjoy the area, right here.

ALAN ALDA You seem to enjoy your life.

E.P. Oh, I have...

ALAN ALDA (NARRATION) The enthusiastic help of amnesics like

E.P. has pinpointed the hippocampus as crucial for recording new memories. At the same time, the fact that

E.P. has vivid memories from years before his hippocampus was destroyed mean it can't be where they are permanently stored. It's to probe more deeply

into how memories are formed that we are meeting another amnesic - but this time a man whose hippocampus, while badly damaged as a result of a heart attack 5 years ago, still struggles to put memories together. MEIKE VERFAILLIE So what I'd like to do is just show you some pictures and ask you, what can you tell me about these pictures? Do they evoke any memory?

ALAN ALDA (NARRATION) Chuck's memory is being studied by Dr Meike Verfaillie. MEIKE VERFAILLIE This is something that you might have seen, oh, in the local newspapers in the last year. MR. O It certainly has something to do with people objecting to the actions, the deeds of...

ALAN ALDA (NARRATION) We're in Boston, where the recent sex abuse scandals in the Catholic Church has received intense media coverage. MR. O ...people who are somehow hurting, abusing, not paying enough attention to others. MEIKE VERFAILLIE Good. Um, is that a picture that looks familiar to you? MR. O I believe this is a picture taken the day or days after the New York, the towers of New York were all --.

ALAN ALDA Chuck? Do you remember where you were when that happened? MR. O Not at all. Um, I remember at the time being especially worried because my son was in New York and...

ALAN ALDA (NARRATION) As Chuck's wife remembers very well, this isn't so. Their son lives in New York today, but didn't on 9/11. Chuck taught English before his illness, and has continued to write since, giving us a unique glimpse into a mind that knows only too acutely what it has lost.

MR. O I cannot remember my wedding day or the celebration surrounding it. I do not recall the birth of my sons, my father's death or who most other family members are. And there are many.

MEIKE VERFAILLIE When you first came in here this morning, we actually started off with looking at some pictures.

MR. O That's right. I knew you were going ask me if I remember them now.

MEIKE VERFAILLIE Do you --

MR. O Can I remember them? Let me think. I'm just getting glimpses, not even any shapes or actual depictions of anything that was there.

ALAN ALDA Is it painful for you to search for memories or ... what are your feelings as you...?

MR. O That's a good legitimate question. Something might happen at night as I'm in bed or falling asleep and I get a thought about something. So I immediately jot it down and show it to my wife the next day, and say, "I've had this thought. Does it have anything to do with anything in our past or anything that you can put together for me?" Then there are times that I have memories that are very, very far-fetched.

MEIKE VERFAILLIE Chuck certainly has severe damage to the hippocampus, but his hippocampus isn't gone completely. So there is still something working to some extent. And what happens is that some experiences, some fragments of experiences may stick, but they're not linked in the correct way. They're not linked to other things that happen. They're not linked to the correct context. Sometimes they're not linked to the correct people. And so, in that way we're left with fragments that are not integrated. Occasionally these fragments will pop up. They may pop up in seeing a picture. But as he described it, he may also have some random thoughts and not know, is this really a memory or is this just a thought I'm having?

ALAN ALDA (NARRATION) Chuck's problem making a whole memory from fragments of his experiences fits with what Mieke Verfaillie and other researchers believe to be the main job of the hippocampus-not itself to store memories, but to link together the bits and pieces of an experience stored throughout the brain - sights, sounds, smells, even feelings - so that they can later be recalled as a coherent whole. MR. O. I am missing pieces of a puzzle. Completely incomplete. I overflow, unfinished, Buzz hour by hour. There is never a way to say All I want to say. Words buzzing around me Miss what should be. Words That hive of an alphabet Stinging me from A to Z.

Never Forget A Face

FRANK FELBERBAUM Let me give you a way to remember my name....

ALAN ALDA (NARRATION) So far we've learned about the role of the hippocampus from people whose memory is dramatically impaired. To probe deeper, we're turning to someone with the memory of a champion.

FRANK FELBERBAUM ...very easy. Something fell.

ALAN ALDA (NARRATION) Frank Felberbaum worked with us a few years ago teaching a class how to put together a name and a face so we'd never forget them.

FRANK FELBERBAUM A bomb, yes, we've got a falling bomb now.

ALAN ALDA (NARRATION) Frank employs a method others in the memory business also use - making up highly visual stories that help glue together someone's name with a distinctive facial feature. FRANK FELBERBAUM What feature would you choose on my face? My nose, I knew he'd say that.

ALAN ALDA (NARRATION) We wanted actually to peer into Frank's brain while he's remembering names and faces and see his memory in action.

FRANK FELBERBAUM ...all over my face. You can imagine that happening.

ALAN ALDA How much time is he going to have in this test to remember names?

RIESA SPERLING He's going to have only two seconds per person.

ALAN ALDA Two seconds? FRANK FELBERBAUM Which is a very short period of time.

ALAN ALDA Can you actually do your thing in two seconds? FRANK FELBERBAUM I've never done it in that short period of time so it's a brand new experience for me. FRANK FELBERBAUM My new designer outfit.... RIESA SPERLING You look stunning. You look fantastic. FRANK FELBERBAUM I'm nude underneath. RIESA SPERLING Well, you don't have to tell me that. All right, so let's go ahead and bring you into the magnet room and make sure you're comfortable.

ALAN ALDA (NARRATION) We've brought Frank to a research scanner at the Massachusetts General Hospital in Boston. RIESA SPERLING He's got a very young looking brain. It's beautiful. This view actually allows us to look at this folded-over gray structure, my favorite part of the brain, which is called the hippocampus. And you can see that in fact he does have what I'll call "plump hippocampi", evidence that these are nice healthy hippocampi for someone whose 66 years old -- that looks great.

ALAN ALDA You got to tell him he has plump hippocampi when he comes out. He's going to really... I mean... he'll just love it.

RIESA SPERLING It'll be a compliment.

ALAN ALDA He won't even care what it means.

RIESA SPERLING Well in this case, bigger is better. This is a size that matters, so his hippocampi look great.

ALAN ALDA (NARRATION) It's Frank's plump hippocampi we're going to be checking on as he lies in the scanner and sees projected on to a mirror over his head a series of face-name pairs. He presses a button if he thinks the name and face go together; but the main purpose of this is simply to make sure he's awake and concentrating -- because the task involves a staggering 455 face-name pairs, shown for only 2-seconds apiece. Meanwhile, the scanner is recording how hard his hippocampus is working.

RIESA SPERLING When you remember this morning and you remember being here outside the scanner and all of us, your hippocampus is putting together all of that information. What it sounded like, what it looked like, who is talking, what you felt like. All of that gets formed in an associative or episodic memory. We're trying here to just tease that associative component out of trying to say things that you haven't seen before, that face and the name, put them together. But that's just an example of what I think the hippocampus is always doing, which is putting together things into a cohesive memory.

ALAN ALDA (NARRATION) So the hippocampus turns out to be like a super-efficient file clerk, noting all the things that go into an experience as they are perceived in specialized regions of the brain, and forming a network of associations between them. The question now is: How well did Frank's hippocampus work?

RIESA SPERLING You feel okay?

FRANK FELBERBAUM It's all right. Can you remove the bolts from my neck?

ALAN ALDA (NARRATION) After a half-hour rest, Frank is put back to work, trying to remember which of two names actually went with the face he saw in the scanner. It's a long, arduous task - and for the first hundred or so faces, Frank seems to be cruising. But as the faces parade by, Frank's success rate declines - after all, he'd had no time to use his own method to match face and name - and in the end he approaches the success rate of most of the subjects Riesa has run in her study - about 75%.

RIESA SPERLING So that's somewhat amazing that you can remember three quarters of the face-name pairs you saw -- 455 -- seeing each one of them for less than two seconds. That's amazing to me the brain can do that.

ALAN ALDA (NARRATION) Even more amazing is what Frank's hippocampus was doing when he was in the scanner. Because it lit up for face-name pairs he would later remember correctly, but stayed dark for those he'd forget. In other words, Riesa could, in theory, look at someone's brain while they are trying to memorize something, and know whether they were going to succeed or not. It

was now my turn to get my hippocampus scanned - this time while wearing goggles that would project face-name pairs directly into my eyes. My task is a lot easier than Frank's

ERIN Here we go.

ALAN ALDA (NARRATION) I get a full eight seconds instead of two to look at each face-name pair - and Steve and Karen, it turns out, are to become old friends, constantly cropping up among the new faces I'm seeing in the scanner. The idea behind this study is to find out if my hippocampus reacts differently when I'm trying to remember the new faces than it does when I'm confronted with dear old Steve and Karen again. RIESA SPERLING Your hair-do looks great. TECHNICIAN You're a real trooper.

ALAN ALDA How was I?

ALAN ALDA (NARRATION) But first the verdict on my brain. I've been scanned several times before for Frontiers, but you never know what's going to show up. RIESA SPERLING Right here is the hippocampus. You have no space around it. That's good, very plump.

ALAN ALDA Yeah? RIESA SPERLING I'm quite impressed. Whatever you're doing in terms of keeping your brain young. You're doing a good job. It looks great.

ALAN ALDA This is Scott. It's not Sylvester. Maybe it is Sylvester. Wait. Yeah, that's Sylvester. TECHNICIAN That's Sylvester. All right.

ALAN ALDA (NARRATION) When it comes to recalling the names and faces, my plump hippocampi seem to have been working pretty well back there in the scanner.

ALAN ALDA Oh, Jill.

ALAN ALDA (NARRATION) As it turns out, I get most of them right - though I had far more time and many fewer faces than did Frank.

ALAN ALDA Brigitte.

TECHNICIAN Excellent. And that is it. You're all done. Good job.

ALAN ALDA (NARRATION) But the most interesting result again came from the scans. This time, my hippocampus lit up for all the face name pairs. But as time went on, it increasingly failed to respond when Steve and Karen appeared. It's as

if my hippocampus knew I knew them, so didn't bother to make the effort to remember.

RIESA SPERLING This is raw data, so it's quite messy, but if you look at it closely you can see that it started to go up during the first repeated face-name pair, that's it right there, it said, oops, I've seen this before and it falls back down again. My hippocampus doesn't really need to pay attention to this, I've learned this already, and we see this pattern very frequently. Again, it's most pronounced in young folks, and you've got a very young looking hippocampus response there.

FRANK FELBERBAUM Me too!

RIESA SPERLING Absolutely.

Why Memories Last

ALAN ALDA (NARRATION) We've come to the campus of the University of California, Irvine, to meet with one of the giants of memory research, Jim McGaugh. Jim has spent most of his long and distinguished career finding out why - among all the memories we form - some are vivid and indelible. J

IM MCGAUGH I'm sure that all Nobel Prize winners know exactly where they were and what they were doing when they got the news that they won the Nobel Prize and they'll never forget that. I'm equally sure that people who pick up body parts after an airplane crash will remember forever having seen that, and when this is described by them, they call it "It's etched in my mind, It'll be there forever, I'll never forget this, It's engrained, it's welded into my brain." These are the kinds of expressions that are used. So at the extreme, whether it's highly joyful or whether it is terribly disgusting, and annoying....

ALAN ALDA Frightening?

JIM MCGAUGH Frightening, but it doesn't have to be frightening. It can be insulting. I can say to you, which is not true, but I could say, "You know, I read some of your stuff. It's not as good as it used to be. You might give that some thought." Now if you believed that I had said that, you'd remember that forever. What did I do? Was that frightening to you?

ALAN ALDA As a matter of fact, every actor and probably every writer can remember every bad review he or she has ever got word for word. I can tell you word for word my first bad review.

ALAN ALDA (NARRATION) What makes these memories stick is their ability to arouse our emotions.

MALINA Gun.

ALAN ALDA (NARRATION) In this experiment, a volunteer is watching slides while her emotional response to each is measured. MALINA An injured boy.

ALAN ALDA (NARRATION) But the kicker will come after the slide show is over. MALINA A decomposing dog.

ALAN ALDA (NARRATION) The experiment was designed by Jim McGaugh's long-time collaborator, Larry Cahill.

ALAN ALDA What does she know about this experiment? LARRY CAHILL She thinks this experiment is about emotion. So she thinks she's coming to an emotion lab where she's going to be shown a bunch of different slides of varying emotional content. MALINA Snake. LARRY CAHILL Immediately after she watches them, we're going to stick her arm in a tub of ice water. The reason we're going to do that is this is a technique that's well known to activate the body's stress hormone response. And we believe that the body's stress hormone response acts to enhance memory. So by sticking her arm in ice water immediately after she views these slides, we should be able to enhance her memory. MALINA Oh!! Oh!

ALAN ALDA How long can people take this? LARRY CAHILL Many people, myself included, are wimps that can take it for about a minute.

ALAN ALDA You know, what's amazing to me is that you're doing this thing with the ice after she looks at the pictures. She doesn't have to have her arm in there and be getting that burst of hormones during the time she's looking at the pictures. It's afterwards.

LARRY CAHILL Right now she's just recently acquired all this new information, 20 slides, but her brain is busy storing that information: we call it consolidating. Kind of like jello setting. During the setting process, you have the opportunity to activate the body's stress hormone response. And the stress hormones work on the newly forming memory to enhance storage of it.

RESEARCHER Very good, Malina. Just go ahead and put your arm here and rest it. You can take a 3-minute rest period.

ALAN ALDA (NARRATION) Malina endured the ice water for a full three minutes.

ALAN ALDA How did the ice water feel?

MALINA Horrible. Absolutely horrible.

ALAN ALDA So you had an emotional response to it?

MALINA Oh yeah. Yeah.

ALAN ALDA (NARRATION) When subjects in the experiment are tested a week later for their memory of the slides, those who - like Malina - had the ice water treatment remembered the emotional slides better than control subjects. Somehow the stress hormones had helped solidify the memories still forming in her brain.

ALAN ALDA Where does it take place in the brain? What do these stress hormones wash and activate? LARRY CAHILL Well, we've done a lot of work in that regard. And, in fact, there's one region in particular that has been identified as absolutely crucial to these effects. It's a region called the amygdala. This person here would be facing towards you. And his or her amygdala is located about a half an inch in to an inch in either temporal lobe. It's about the size and shape of an almond and amygdala happens to be Latin for "almond".

ALAN ALDA (NARRATION) Most of what we know about the amygdala comes from experiments with rats. JIM MCGAUGH The animal's going to be put in the water for an opportunity to find a platform. It's never been in this water before, so it's going to swim around randomly. It's going to be taken out after a while, and each time it's put back in, it's put back in at a different edge. Okay, so he ran into the platform, but he doesn't know that that's a platform.

ALAN ALDA (NARRATION) From the rat's-eye-view, the platform is invisible. The only way this rat is going to find it is by bumping into it. JIM MCGAUGH No, I'm not going to help you.

ALAN ALDA (NARRATION) Most of the naïve rats spend a lot of time swimming around the edges, looking - in vain -- for a way out. JIM MCGAUGH So, he's going to get a little clue.

ALAN ALDA That's a big clue.

JIM MCGAUGH There is a platform here.

ALAN ALDA When he looks up like that--

JIM MCGAUGH Oh yeah, he's looking.

ALAN ALDA Is he using smell or wind or --

JIM MCGAUGH Oh yeah, he's using everything. He's sampling. He's sampling the environment.

ALAN ALDA (NARRATION) Most rats learn to find the platform within a minute or so. But then some rats get an injection directly into the amygdala of a drug that switches it on just as stress hormones do.

JIM MCGAUGH And now we're going to test for retention. Remember, it took him about 60 seconds on the first trial.

ALAN ALDA Wow.

JIM MCGAUGH There. That's memory enhancement.

ALAN ALDA (NARRATION) So by directly stimulating its amygdala, the drug caused the rat to have the equivalent of a deeply emotional experience, firmly fixing the memory of how to find safety. It's no coincidence that the amygdala - in both rats and humans - is nestled right next to the hippocampus. And it's the hippocampus, of course, that sets up the networks of associations in the brain that constitute a memory.

JIM MCGAUGH The hippocampus is doing its job and the amygdala comes in with a punch and says, "This was important. Do more of what you're doing. Consolidate that more strongly." So, learning can occur without the amygdala. But it's not going to be very strong.

ALAN ALDA And you would remember everything equally? JIM MCGAUGH You would remember everything equally, which is a very bad thing.

ALAN ALDA The death of your mother would be equal to where you put your car keys? JIM MCGAUGH Absolutely.

ALAN ALDA (NARRATION) But it turns out that not even all emotional events are necessarily remembered equally: it may depend on whether you're a man or a woman. Several years ago, Larry Cahill had subjects watch movies of emotionally arousing events. Immediately afterwards their brains were scanned to see how their amygdalas responded. Recently, Larry re-analyzed the results of these experiments - and discovered a puzzling pattern. In men, emotional events turn on only the right amygdala. In women only the left amygdala is activated. Now, there's an old hypothesis that the right brain processes the gist of events, while the left focuses on the details. So...

ALAN ALDA Let's say, I think a man and a woman are having an argument. "Did you pay that bill?" "I did pay that bill." "You never pay bills." "I do pay the bills." Whichever one is saying this about the other. The next day, if they said, let's go over what that was we had a problem with. Is it possible that we might expect the two of them to have a different way of remembering? Either the gist of it or the details of it?

LARRY CAHILL I'd say it was entirely possible that while they were in the middle of that argument, and the emotions were flowing, their two brains were not storing that information in exactly the same way. They weren't using the exact same parts of the brain. And they weren't storing exactly the same information.

ALAN ALDA After the fight... after an emotional fight, regardless of their temperament, after an emotional fight, after they've both been emotional, she'll tend to remember the details, and he'll tend to remember the gist of it.

LARRY CAHILL This is cutting edge stuff. This is the kind of thing that makes people say, really?

ALAN ALDA That's a good definition of cutting edge. "Are you sure about that?"

LARRY CAHILL But the cutting edge is the place I like to be.

When Memory Lies

ALAN ALDA (NARRATION) We're still on the campus of the University of California, Irvine, where - along with her students - Elizabeth Loftus has invited me to a picnic.

ALAN ALDA This looks good.

ELIZABETH LOFTUS This looks very good. Well--.

ALAN ALDA (NARRATION) It's an appetizing spread - but among the choices, one leaps out at me immediately.

ALAN ALDA Deviled eggs. There are the deviled eggs.

ALAN ALDA (NARRATION) Now, to understand why I'm so taken with those eggs, we have to go back a couple of weeks.

ALAN ALDA I hate watermelon.

ALAN ALDA (NARRATION) Elizabeth had sent me a long questionnaire about the foods I like or dislike. Another questionnaire was about things that may or may not have happened to me as a child.

ALAN ALDA I ate two scoops of ice cream on one cone. That definitely did happen. Of course it happened. Sold chocolate bars for a fundraiser. Definitely did not happen. Ate freshly picked vegetables. No. I'm -- as you can imagine-- fascinated to know what the questionnaire was really about. It wasn't about food, was it? ELIZABETH LOFTUS Actually, we have a very sophisticated computer program that can take all of that information that you gave us about your childhood, about your likes, your dislikes, your habits, your personality--. We have fed it into a computer and --.

ALAN ALDA And you can tell my shoe size from that.

ALAN ALDA (NARRATION) My obvious skepticism here stems from knowing Elizabeth is an expert on false memories -- things we think we remember but never really happened.

ELIZABETH LOFTUS So this is the profile from this very, very sophisticated computer program. And I just would like you to take a look at it and I'm going to ask you a few questions about it.

ALAN ALDA Let's see-- "You disliked spinach as a young child. You enjoyed fried food. You felt sick after eating hard-boiled eggs. Eating chocolate birthday cake made you happy." I can't remember anytime when I ate chocolate birthday cake and actually got happy from it.

ELIZABETH LOFTUS All right. Let me pick one of the other ones. You felt sick after eating hard-boiled eggs.

ALAN ALDA No. No. No.

ELIZABETH LOFTUS When --.

ALAN ALDA I can say with almost cert--. I can't be certain. You can't be certain about anything that happened that long ago but I'm pretty sure that I never got sick after eating hard-boiled eggs. I can't remember a time when that might have happened. ELIZABETH LOFTUS Well, the thing about our childhood is that because it's so long ago and because there is forgetting and because there is childhood amnesia and there are all kinds of things going on, we often don't remember things that are true of us. I mean, you'd accept that, wouldn't you?

ALAN ALDA Yes, yes. Yeah.

ELIZABETH LOFTUS Sometimes when you try to imagine what might have happened, it will tap in to some of those forgotten experiences. So that's why I was trying to think about when you might have eaten chocolate cake or when you might have eaten too many hard-boiled eggs and not felt that great about it.

ALAN ALDA Yeah. I can't remember a time when I might have eaten hard-boiled eggs and have gotten sick from it. I don't remember eating many hard-boiled eggs as a kid, either.

ALAN ALDA (NARRATION) A few minutes later, and I'm again filling out the questionnaire about my childhood experiences with food.

ALAN ALDA Ate a hot dog with onions and sour kraut? No. Ate a candy apple at a state fair? No. Got sick after eating too many hard-boiled eggs? No, but I can't be definitely sure. So 2. Had a cheese pizza delivered. No.

ALAN ALDA Tell me the truth. You don't even have a computer, do you?

ELIZABETH LOFTUS We do. You saw some of our better computers in there. We do.

ALAN ALDA I bet there's a trick.

ALAN ALDA (NARRATION) Well of course there was a trick. Elizabeth was trying to persuade me I remembered something that hadn't happened.

ELIZABETH LOFTUS Okay, Alan, here was the study. A few weeks ago we asked you about your childhood experiences. And asked you if you ever felt ill eating hard-boiled eggs and you said 1, definitely didn't happen.

ALAN ALDA Right.

ELIZABETH LOFTUS Then we gave you feedback from a computer, which of course was bogus. And I know you maybe suspected that. It was bogus, but in the middle of that feedback was the-- from the very smart computer -- we suggested that you as a child had gotten sick eating hard-boiled eggs. And later when we asked you to fill out that sheet about your childhood again, you increased your confidence. You gave it a 2 this time instead of a 1, I believe. So you did show an effect that we're showing in this study. That increased confidence -- that you had the experience that was suggested to you, but was completely made up by us. Now the last step in this process is to see whether the manipulation has any further consequences down the road. I mean, will you avoid hard-boiled eggs?

ALAN ALDA I'm just not that interested in hard-boiled eggs.

ELIZABETH LOFTUS Well people make up all kinds of rationalizations for their behavior.

ALAN ALDA (NARRATION) By claiming that a smart computer had insights into their childhood, Elizabeth Loftus has managed to persuade some 30 percent of the subjects in her study to change their opinion about what foods they like or dislike. In other words, not only is it frighteningly easy to implant false memories in people; you can then get them to change what they think based on those false memories.

ALAN ALDA It's more the potato chips that is at the heart of this somehow, right? A lot of your work has to do with false memories and court cases.

ELIZABETH LOFTUS Right. Little tiny false memories, maybe, that we probably have all the time, don't hurt people very much. But when it comes to people developing these very big false memories of being molested in satanic rituals or assaulted by people who didn't do anything to them. And we know false memories of this sort have been generated, then it does people a lot of harm. Wrong people get prosecuted, innocent people get sued civilly. And so, the false memory problem is a very big problem in society. And we're here really just trying to understand how it is that you can plant a seed of suggestion and out of this a whole false memory can grow.

ALAN ALDA (NARRATION) Well, I intend to pinch one false memory in the bud right now.

ALAN ALDA But I don't eat the yokes. Hmmm...that's good.

Keeping Old Brains Young

ALAN ALDA (NARRATION) Lola Crosswhite is in the early stages of a disease that affects some 4 or 5 million Americans - and is perhaps the one affliction we all fear most. The disease, which begins by robbing us our ability to remember, is of course Alzheimer's.

ALAN ALDA When did you first start to notice that you had a problem with memory?

LOLA CROSSWHITE I'd go to the telephone. The telephone would ring and I'd go to take a phone call. And I'm sure I was making all kinds of sense when I was

talking because everything was very easy and that sort of thing. And I realized by the time I would hang the phone up, I hadn't had a clue what had been said.

ALAN ALDA You didn't know what you'd been saying? Did you know... could you remember who you'd been talking to?

LOLA CROSSWHITE Sometimes. And sometimes not.

ALAN ALDA In terms of someone in the early stage of Alzheimer's, what does that mean to them? What do they go through? What's their life like?

MARK TSUZYNSKI What they primarily have, in the early stages, is a problem forming new memories. But everything that they ever were is still there. That judgment, that human being is still there, and is as precious and wonderful as they ever were. But the problem is short-term memory.

LOLA CROSSWHITE That was sort of the first thing. Then it began to be that I would get very confused. I would start to do something, then all of a sudden I kind of like would forget what I was going to do. And then the more I thought about it and the more I agonized about it, the more confused I'd get.

MARK TSUZYNSKI And with time that is joined by other symptoms that include problems sometimes recognizing things, sometimes speech, sometimes problems remembering how to manipulate objects. And by that point we're into the middle stages of the disease. That takes a few years. And after that there is more global decline in cognitive function and the disease really becomes severe.

ALAN ALDA (NARRATION) Mark Tsuzinsky has recently begun a dramatic experiment to try to arrest the damage done by Alzheimer's by injecting genetically engineered cells deep within the brain.

ALAN ALDA How do patients feel when you tell them you're going to stick a needle in their brain? Is everybody okay with that?

MARK TSUZYNSKI Yeah, well... you know, if you were confronted with a disease for which we really don't have an effective therapy, and which you know would ultimately rob you of the essence of our humanity which is really our intellect, you'd probably be willing to take a needle.

LOLA CROSSWHITE I have two very nice little holes.

ALAN ALDA What did they do after they made the holes?

LOLA CROSSWHITE Well, then they go down with very long needles. Then they'd have to take me to the MRI machine and be sure that they were exactly placed in the right place.

ALAN ALDA (NARRATION) Earlier, cells taken from Lola's skin had been genetically engineered to pump out a growth factor vital to keeping brain cells healthy. These skin cells were then injected through the needles to regions where Lola's brain cells were dying. The ultimate goal is to help these brain cells stay alive. But these are very early days, with the emphasis on proving the procedure is safe rather than that it works.

LOLA CROSSWHITE The one thing that was so wonderful --still is -- is I always have this really terrible feeling of confusion all the time. It was just, you know, it was there-- It just kind of ground on me. It's just -- gone.

ALAN ALDA So what do you think? Do you think that's a placebo effect or might something be happening in there?

MARK TSUZYNSKI You know, Alan, I just don't know. It could be a real effect. It could be a placebo. I actually don't know. Hypothetically, what this growth factor would do to these cells -- could do that. It could focus attention actually. That's one of the things it does in the animals' studies. So it's intriguing to hear that kind of thing. But, I don't know. At this stage, with not enough patients, you have to say, it could be the effect and it could be the placebo.

LOLA CROSSWHITE No one has ever said that this is a promised land, you know? It's just that we're... Well, first of all, it's a... O.K., I've lost the word.

ALAN ALDA An experiment? LOLA CROSSWHITE An experiment. So... I'm grateful 'cause I know up to this point I've had some help. I don't know how much longer it will last. But whatever it is it's given me some better time than I would have had. So that's good.

ALAN ALDA (NARRATION) That Lola's hopes rest on a risky experiment highlights her lack of options. Today, there are no proven treatments for Alzheimer's - in part because by the time it is diagnosed, the brain is already badly damaged. These images show what happens to a brain as Alzheimer's slowly conquers it. Blue regions are healthy - white shows where brain cells are dying. One of the real breakthroughs in Alzheimer's research is coming from new technologies to detect the disease much earlier. Here at UCLA, for instance, a technique called Positron Emission Tomography, or PET, is being employed to pick up subtle changes in how well cells in the brain are firing. In a healthy brain, cells firing normally show up color-coded red. In an Alzheimer's brain, the blue

regions are where cells are failing to fire - notably in the memory centers around the hippocampus.

GARY SMALL These scans are so sensitive that in many situations we can diagnose Alzheimer's disease sometimes years before the doctor can arrive at that diagnosis in a clinical setting.

ALAN ALDA That's really fascinating. You can look into a person's head and tell that they're getting Alzheimer's before the symptoms show up? Before the family might be troubled by it?

GARY SMALL It makes sense. Because if you think about it, the brain is a very adaptable organ in the body. We've done other studies where we find that people with very subtle problems, they sort of compensate for this deficit that is there but we otherwise can't see. So this paper and pencil test won't show us anything. But the scans will. And when we do these scans we can see that those cells are not firing as well as they should.

ALAN ALDA (NARRATION) A scan that detects Alzheimer's even before symptoms appear means treatment could begin much earlier, before the brain is ravaged beyond repair. But that, of course, depends on there being effective treatments. And today, there is a growing sense of optimism among Alzheimer's researchers that such treatments are at least on the horizon.

ALAN ALDA When someone has Alzheimer's, what's happening inside their brain?

DENNIS SELKOE They're building up tiny amounts of these nasty molecules that shouldn't be there-that aren't there really, early in life. And that over time, in the 30s, 40s, 50s and 60s start to build up. And the molecule is O.K. when it's just in singlets, if it's just a single unit at a place. When it doubles up and gets into bad company so to speak it gangs up into doublets and triplets and quadruplets, that's when it causes trouble. And we think that that's the cause of the disease.

ALAN ALDA The molecule is called what?

DENNIS SELKOE Amyloid beta.

ALAN ALDA (NARRATION) If Dennis Selkoe is right, and it's these killer molecular gangs that destroy brain cells, then are two ways of tackling the problem. Prevent the amyloid beta build up in the first place - perhaps with a drug; or get rid of the amyloid beta before it can reach dangerous levels. This second approach has been dramatically successful - but so far only in mice. These mice have a version of human Alzheimer's disease, and when mice like

them were injected with an antibody that removes amyloid beta, they showed every sign of being cured. DENNIS SELKOE It's like a miracle, basically. There was this one study in a group at Lilly, Eli Lilly and Company and Washington University, where they tested the mice on whether they could recognize objects. And they couldn't - these were Alzheimer's engineered mice. And they gave them one shot of the antibody and tested them again the next morning, and lo and behold, these mice could now distinguish two objects that they couldn't before. They returned the mice from their 23-month old status, which is old for a mouse, down to the level of a 5-month old mouse, which is young. So, we can only hope that such a thing could happen in humans -- maybe get close to that.

ALAN ALDA (NARRATION) But when in 2001 a vaccine against amyloid beta was tried in humans, the trial had to be stopped when one of the patients died from inflammation of the brain. Meanwhile, Dennis Selkoe, working in collaboration with his old friend Howard Weiner, had come up with the idea of giving the amyloid beta vaccine not as an injection, but as nose drops. DENNIS SELKOE They sniff it like a nasal spray, but it's inhaled.

ALAN ALDA (NARRATION) The vaccine works, clearing amyloid beta from the mouse brains. And because there are theoretical reasons to suppose that a nasal or oral vaccine won't cause dangerous brain inflammation, the Harvard team is now hoping to soon begin human trials in a small number of Alzheimer's patients.

ALAN ALDA You're talking about vaccines today that help eliminate a disease once you've got it. Are you hoping to have a vaccine eventually that will help you not get Alzheimer's in the first place?

HOWARD WEINER Conceptually the answer is yes. Because we believe that it's very possible that everybody is accumulating to a small degree or to a larger degree these abnormal proteins, and by giving a vaccine you'll continually be clearing them out. So that if we're lucky, and if the theory holds up, there might be a day that everybody who's a certain age will be getting a vaccine to prevent Alzheimer's.

ALAN ALDA (NARRATION) The idea that a simple sniff or swallow may one day protect us from Alzheimer's is extraordinary, and clearly years in the future. But even today there are preventive measures we can take, if not to avoid the disease, at least to slow its corrosive effects on our brains.

LOLA CROSSWHITE I personally think the more you do and the more you keep on with your life. Like I still ski, I'm going on a photo shoot in Africa. But I do believe that if you sort of set some goals for yourself and keep going, and doing things, I think that helps a whole lot.

GARY SMALL Good morning, everybody. How are you doing? STUDENTS Good morning.

GARY SMALL So we're going to talk about healthy brain aging today.

ALAN ALDA (NARRATION) UCLA's Gary Small has started several community based projects in Los Angeles intended to help keep the brains of the baby boomer generation - now getting to the age when the first subtle signs of memory loss are beginning to nag - in fighting trim.

GARY SMALL In fact, by the time I get done with you today, your memory will be improved almost immediately.

ALAN ALDA (NARRATION) In these programs, Small emphasizes the value to the brain of a healthy diet, stress reduction and physical exercise. But he also teaches mental gymnastics - exercises for the brain to sharpen memory - including putting names to faces.

CINDY My name is Cindy.

ALAN ALDA I'm Alan.

ELEANOR My name is Eleanor.

JACK Jack.

SHERRY I'm Sherry.

JOYCE I'm Joyce.

KEN Ken.

LAUREL Laurel.

NORMA Norma.

NANCY Nancy.

GARY SMALL Visual information for most people is much easier to remember. So what I recommend is, you look, actively observe, create a mental snapshot, you snap and then the last component is connect. Which means you connect up those mental snapshots.

ALAN ALDA (NARRATION) Gary's method, emphasizing linking elaborate visual stories with what you want to remember, is very similar to what we saw Frank Felberbaum do earlier. Here we were asked to memorize a list of unrelated items.

JACK I made up a story. Teddy bear was driving up the road in a truck full of acorns to the bank smoking a cigar, when he ran over a plank kettle and raccoon. And they had the funeral -- which wasn't one of the words -- at the stadium with roses. And at the end a volcano erupted.

GARY SMALL Fantastic. Good for you. That's the fourth time today I've heard that same story.

ALAN ALDA (NARRATION) While there are good reasons to suppose that programs like this will help our brains age gracefully, Gary Small hopes to clinch the case. He plans to scan the brains of some of those who actively practice the program and compare them to brains of a control group - and so demonstrate that how we live can change our brains for the better. Meanwhile, I'm anxious to demonstrate that the lessons of the last hour haven't yet been lost on me.

GARY SMALL So I want you to go home, practice your techniques, and when we meet next time we're going to see if we can remember everybody's name. We're going to work on that next time, okay? Thank you very much for helping us out today.

ALAN ALDA You mean I sat here and remembered everybody's name for nothing! I can name them backwards, forward. And I did that for nothing? I won't be here next time. Nancy, Norma, Laurel, Ken, Joyce, Jerry, Jack, Eleanor and Cindy.

CINDY And Alan.

ALAN ALDA Who?

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