

Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and Dr. Miller is an oncologist specializing in pain and palliative care. If you would like to join the discussion, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC.

This evening, Dr. Miller is joined by Dr. Evelyn Shatil. Dr. Shatil is the Head of Cognitive Science for CogniFit, a company dedicated to learning techniques to enhance the functions of the brain. Dr. Shatil joins us to talk about chemo brain, a term used to describe memory lapse during and after treatment with chemotherapy.

Miller Evelyn, let us start out by having you tell us a little bit about your background in cognitive research, and about CogniFit.

Shatil I used to work as a learning disability expert at The University of Haifa in Israel, and at that time I was interested in the formation of longterm memories and attention processes in children. We studied the fact that otherwise healthy and intelligent children were not capable of successfully forming memories. They could not acquire very basic skills such as simple arithmetic, facts or word reading skills. Later I became interested in the retention of memories and preservation and maintenance, and in attention and executive processes, in the way we use them and retain them. This has brought me to our present subject of chemo-fog and this is how I became interested in this phenomenon.

Miller Just go back a little bit and think about children who have problems with learning. Tell us a little bit more what executive functioning means.

Shatil Executive functioning is our ability to manage our cognitive processes. It is almost our ability to manage our lives. If you want to understand it, you have to think about being able to see what will happen. There is a lot of prediction. For example, you think "Okay if I want to invite this couple, are they going to talk to this couple; whom am I going to invite?" It is not just, I am going to have a party on the 17th, it is being able to look into the future and go into quite a lot of details. It is planning and being flexible in your planning. It is being able to change your original thought as you are planning because you have identified a problem. It is even being able to monitor what will happen, not only as it is happening, but in the future. You anticipate either a problem or you anticipate a success, and then you continue acting according to what you anticipate. Executive functioning is actually going into the future.

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Miller This sounds like a problem some young people have as students. Tell us a little bit about what chemo-brain, or chemo-fog, is.

Shatil Chemo-brain and chemo-fog are interchangeable terms and actually I think they were coined by people who had undergone chemotherapy treatment, or even just

cancer treatment. It is the term they used to describe what they were experiencing, and they came upon the right term because it is self explanatory. Think about a fog in your brain, a brain that is not very clear, and doctors and researchers have adopted the term and it has become very well known and referred to.

Miller Along those lines, what are the symptoms, what would make someone say to their doctor that they have chemo-fog?

Shatil There are a few symptoms and most of them are related to people experiencing problems in memory or in attention. For example, a lot of patients report not being able to find the right word in a conversation, especially in a spontaneous conversation. What I mean by spontaneous is one that has not been planned ahead like a job interview where you may rehearse your answers, but just a conversation where you grope for the right word. Everyone gropes for the right word from time to time, that is a normal thing, but people who undergo treatment report many instances of this kind of difficulty. That is one instance. Short-term memory problems are a very common thing that patients report. They sit with their doctor and tell them that they could not remember why they went into the next room. They are in the middle of doing something and realize they have forgotten their pen or whatever it is they have forgotten, and go into the next room and do not understand or do not know why they went into the next room. Even this happens to a lot of people, but it happens many more times. The instances are fewer when you have not been sick.

Miller These are memory and word finding. We have talked a little bit about executive function, is that affected?

Shatil Yes, I think it is very much affected. It is one of the common complaints and it is also a little bit frightening for the person because our lives are very complex and we are always involved with doing something that looks very simple, but we must multitask. We have to divide our attention among several little tasks. For example, you could be talking on the phone and you have to remember that you need to leave in another 2 minutes to pick somebody up and at the same time you need to remember not to forget to turn off whatever is cooking. Multitasking requires a lot of divided attention and being aware of what is going on, and every single little part of your task is important. This is why these complaints are more frequent when a person either returns to work, or returns to some kind of fuller functioning, because his or her tasks become more complex and require more division of attention.

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Miller Do you as a scientist, or in general medicine, know what the mechanism is? How does chemotherapy work, or is it just the stress of having had a cancer?

Shatil This is the \$1000 question. Researchers have been thinking about whether there is a cause, or a relationship; whether chemotherapy is the cause and chemo-brain

is the result. They have been thinking about it since 1974 when the first studies started to come out. As people started to research the problem, they realized that like everything else in life, there is no simple answer. If we have the time I will tell you what the research today says, but as you were suggesting, cognitive decline could occur due to a number of reasons that would have nothing to do with chemotherapy. For example, if you are stressed, and people who have a very serious illness usually are stressed, or if you are depressed, we know depression is also associated with memory problems and cognitive problems. If you are fatigued, we know that multiple sclerosis patients who are very fatigued also report cognitive decline. If you have hormone fluctuation, some women after chemotherapy suddenly go unexpectedly into earlier menopause and the hormone mechanism changes which may affect your cognition and your ability to remember and manage your thinking. There are many, many possible factors. It is very hard for researchers to say today whether chemotherapy is the cause, although the latest studies do point to chemotherapy as one of the possible causes. Also, we must mention that not everybody is affected by cognitive decline or cognitive problems.

Miller We would like to remind you, our listening audience, that if you have questions or things you would like to share, you can e-mail us at www.canceranswers@yale.edu or call 1-888-234-4YCC.

Medial Minute

It is estimated that over 2 million men in the US are currently living with prostate cancer. One in six American men will develop prostate cancer in the course of his lifetime. Major advances in the detection and treatment of prostate cancer have dramatically decreased the number of men who will die from the disease. Screening for prostate cancer can be performed quickly and easily in a physician's office using two simple tests. A physical exam and a blood test. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for prostate cancer. The patients enrolled in these trials are given access to experimental medicines not yet approved by the Food and Drug Administration. This has been a medical minute. You will find more information at www.yalecancercenter.org.

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller and I am very happy and privileged to be here with Dr. Evelyn Shatil who is from Israel and is a researcher doing work on chemo-brain and what she refers to as cognitive rehab. Evelyn, are there certain groups of people being treated for cancer who

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seem to be more likely to have problems?

Shatil There are certain groups that report more problems. We are not sure that they are the people who have more problems though. For example, most of the problems were reported by women who had had breast cancer and were reporting problems

to their doctors in large numbers, but if we think about what research is telling us, I am not aware of groups of people such as more women than men. I've been to conferences where men stood up and told the audience about their problems and women didn't. The latest research tells us about a connection between the intensity of chemotherapy and the strength of the cognitive impairment, and between the duration of chemotherapy and the worsening of cognitive impairment. There was an important Dutch study done. What we know is that higher doses of medication will cause the fog to be more severe. We also know that people who have had several cycles of chemotherapy do not test as well on cognitive neuropsychological tests as people who have had fewer cycles. Our study is to that effect.

Miller What is the natural history? Do most people improve?

Shatil It is quite optimistic because as time passes people report fewer and fewer problems. Sometimes, they report problems that are very subtle. When we use our own batteries they may have limitations because our batteries were originally designed for other purposes. Normal people may actually experience a decline, which the battery is not capable of capturing, but the person is actually experiencing a subtle deterioration and it is accented enough that the person knows and realizes that functioning is not as it used to be. We also know that the drugs, I think they are called "CMF," that were used for breast cancer in the past were more conducive to deterioration than the drugs that are used today. This is very good news, but still the number of complaints is not decreasing. Our studies used to consistently report that 10% to 30% of patients would report problems and score low on neuropsychological. Some studies now are going as high as 45%.

Miller I want to move on to a very important topic in your field which is in a sense helping people sort of restore their functioning. What can we do for people?

Shatil I personally believe in an integrated view of life. As we were saying before, anything that will help a person feel less depressed, more relaxed or happier is good. It is not a recipe-giving thing. We know that some people love to listen to music, some people love to read, some people love to go and visit their grandchildren. Everyone knows what makes them happy so perhaps it is a time for introspection and thinking about oneself what they want to do to make themselves happier and to recover better. That is the first thing where the brain is affected. You are the doctor so you know more about drugs than I do, but from what I know drugs are not really doing the job for restoring memory. We do not

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have the magic drug in cognitive rehabilitation. I believe in cognitive training, otherwise I would not be here.

Miller What does that mean? What is that?

Shatil It means that you stimulate your brain knowingly using tools that were designed for this purpose. I want to explain the difference between a game and a cognitive training program. A game may be excellent for you, it may be fun and it may make you feel very competent because usually people go back to games they know how to play and where they feel successful. You might do this unconsciously. On the other hand, a cognitive training program would start by evaluating your cognitive abilities. It would be done in a friendly way. Knowing what your cognitive abilities are, we would have a record of what cognitive abilities are in very good shape and what cognitive abilities need strengthening or reconstructing. The program would then start working but without a baseline, the program cannot build a tailored regimen of training.

Miller You are talking in a sense about a computer program that makes an assessment and then does what with it?

Shatil Yes, exactly. I am talking about home-based training, you can do it in the privacy of your home at a time which suits you. The computer, as you say, evaluates your abilities and then there is a very complex mathematical algorithm at work to create a link between your results on the evaluation and the training you will get. In our program we take great effort to make sure the person is always in their comfort zone. The brain has got to be challenged, that is for sure. If the brain is not challenged, if there is not some effort, then the brain is not working and those synapses are not being created. The effort that you will be experiencing is based on what you can do, as opposed to other programs that are trying to catch some idyllic average that we do not know even exists.

Miller Does it work?

Shatil We do not have research evidence regarding people who have undergone chemotherapy. We have anecdotal testimony, but this is not research evidence. We have people who are very happy to have done it and have felt it has empowered them. We have research evidence with other populations, such as multiple sclerosis, where people who have experienced cognitive decline due to a traumatic brain injury have beautiful results from the studies that are been carried out at Tel Aviv Medical Center in Israel. We have beautiful results being published and that have been published, but regarding the effect of chemotherapy, it is my feeling that it is one of the most promising avenues for treatment. It is fun, it is noninvasive, and as you do the training you say "Oh My Goodness! I am

23:03 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Feb-10-08.mp3 working on my word finding problem." This is clearly a very interesting task of divided attention. You are working on those problems that you were telling your doctor about. This is a very good feeling and it makes you aware that you are becoming self-sufficient, that you are doing something that is specifically geared to this problem you are experiencing.

- Miller In some of the other fields where you have tested this, such as with ageing or multiple sclerosis, are some of the benefits long lasting?
- Shatil We do not know yet, it is a new product. It has taken 5 years to do it in such a way that it could be scientifically based and tested, but lots of studies have been done. We know that programs that are not as systematic as ours, or as long term and are not as tailored and do not give feedback, have long term gains. There are some programs that only test the verbal module. We test all the modules and they have shown long-term results in affecting the quality of life of the people who have been using them. We may generalize that cognitive rehabilitation is probably a good thing to do.
- Miller It does sound wonderful. I see many women with breast cancer who talk about their thinking not being as clear or they are not as quick at word finding. How wonderful it will be to be able to offer something other than a pill or telling people to go do crosswords.
- Shatil The program we have is called, "Back on Track" and it is a cognitive training program that works on the very abilities that are known to be impaired or affected after you have had cancer and treatment with chemotherapy. There is a lot of attention training there and a lot of word finding. There is a lot of planning, predicting, shifting and inhibition which are executive functioning measures. The name of this program is "Back on Track", not "Mind Fit", which is also another program we have.
- Miller The name "Back on Track" makes a lot of sense. For people who go through a cancer experience, it is a feeling that you are off the track.
- Shatil Yes.
- Miller It is bringing things around again. With all the interest in science and different scans that can be done on the brain, in general, when you stimulate people's brains and do work like this, do we know what happens to the brain itself?
- Shatil What happens to the brain is interesting. In most studies, they have had MRI scans, and professor Altmiller at the University of Illinois at Urbana-Champaign for example, has trained older adults and the scans show that before training, several parts of the brain that were usually active in the normal population, he

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was training older people, were not active. It was not an economical way of processing information. After training, there were some specific areas, which we know are identified with that kind of processing, that were activated. He is not the only one, there have been other studies. That is the main finding, that if you trick the brain into believing that he needs that skill by telling the brain, "I need it, I am

doing it", then the brain will say, "Oh! My God, I have got to do it." So, after you stick with it for awhile, you see those areas in your brain have become active. You could have fascinating interviews here on this subject with people who are much more expert than I am.

Miller This has been terrific. I want to thank Dr. Evelyn Shatil, Head of Cognitive Science for CogniFit, an organization that is looking into rehab. Evelyn, thanks for being with us.

Shatil Thank you very much.

Miller I want to thank our audience for joining us. This has been a wonderful program. Until next week, this is Dr. Ken Miller from the Yale Cancer Center wishing you a safe and healthy week.

If you have questions, comments, or would like to subscribe to our Podcast, go to www.yalecancercenter.org where you also find transcripts of past broadcasts in written form. Next week, we will meet Dr. Lynn Wilson who will discuss radiation therapy.