



The Potential to Change the World: The Clinical Memory Disorders Program

In Proust's *Remembrance of Things Past*, tasting a freshly baked madeleine sends him involuntarily reeling into powerful memories of his youth. For Proust, as with many, memory is inextricably linked with identity. Losing one's memory goes beyond the trivial matter of locating the misplaced keys. It strikes at the heart of the self. The dedicated team members of the Clinical Memory Disorders Program have committed themselves to eradicating Alzheimer's disease and other related cognitive disorders. Today they are one step closer to realizing this ambition.

Founded by neurologist Carol Lippa, M.D., in 1996, the program is a highly collaborative effort among neurologists, psychologists, nurses, neuropsychologists, pharmacologists, and basic scientists. It consists of three branches – education, research, and clinical work – each contributing vital insight into the puzzle of dementia and related illnesses. Candidates for the program have a lengthy assessment process where options for treatment, including involvement in the clinical studies, are presented. Carolyn Edwards, R.N., M.S.N., is the clinical research coordinator. A free, NIH-funded program for caregivers, administered by Beth Gonzalez, Ph.D., is also a valuable part of the program. This multifaceted approach to tackling the disease is tenacious and unrelenting, possibly because dementia itself is so merciless.



Carol Lippa, M.D., Professor

While all the research and studies are undeniably important, the work being done in the clinical trials is particularly exciting and potentially life altering at the moment. As Dr. Lippa reveals, "In 18 months or two years, we're going to be analyzing data that could potentially be submitted to the FDA for approval for a vaccine for Alzheimer's. In an optimal scenario, it would change the world."

Up to this point, Alzheimer's therapies have either addressed the symptoms or behavioral aspects of the disease, but not the underlying biology. In terms of combating symptoms, one drug might "give the patient a little bit better focus, [or] stabilize the memory loss so things don't progress for a little while," says Lippa. Similarly, another drug might target behavioral issues, such as "agitation, restlessness, apathy, and anxiety." Yet the patient still has all the underlying causes or manifestations of the disease. It is progressing "underground," so to speak, even while surface problems are being alleviated. "So five years down the road [a patient is] still at the same place they would be without the medicine," she explains.

It is for this precise reason that Lippa and her colleagues at the Clinical Memory Disorders Program are so excited about their current research. The vaccines they're developing in the clinical trials *do* address the underlying biology of Alzheimer's disease.

Alzheimer's is associated with abnormally high amounts of the peptide amyloid in the brain. The vaccines (immunotherapy) in development either clear out the amyloid buildup or prevent it from initially developing in the brain. Lippa says, "The exciting thing about [anti-amyloid therapies] is that they really could potentially impact the course of the disease so that patients get better, or they progress more slowly, or they stabilize."

Both Lippa and her colleague, Yuesong Gong, Ph.D., reveal that scientists do not know precisely how amyloid is connected to Alzheimer's, but there is clearly an important connection between the two. Dr. Gong's research is attempting to discover "what *exactly* leads to Alzheimer's disease development" by examining the relationship between synaptic disintegration and memory loss. Gong and Lippa theorize that amyloid is toxic to the synapse, severing the connection between neurons. "It's like breaking a circuit," illustrates Lippa. "Then you can't think. The hope is that if you can fix the problem, make the circuit stronger, or get the amyloid – stop the factor that breaks the circuit – then you'll be able to slow or prevent [Alzheimer's]. Whereas if you wait until all the brain cells are gone, nothing's really going to help."



Yuesong Gong, Ph.D.,
Assistant Professor

To that end, several therapies are being tested in the clinical trials. Some vaccines are infusions, which make use of the department's infusion suite. Others are subcutaneous injections. One of the vaccines is in Phase Three of its testing, the last stage before the work can be submitted for FDA approval. Alongside these tremendous, groundbreaking advances, Gong is conducting research into herbal compounds that could also be used as an alternative to synthetic drugs. While these immunotherapies are not part of the clinical research yet, they represent the multiple and tenacious ways the program is attacking memory disorders. "There's not much doubt in my mind that someday we're going to have vaccines that can prevent the disease in high-risk people and be of early intervention to people with symptoms," Lippa says. "It's a cool time. Maybe the day [will come] when you get your flu vaccine, and you get your Alzheimer's vaccine [too]. It's a pipe dream at this point but I can see how it could happen in the future."

Discussing her commitment to eradicating Alzheimer's, Lippa describes a woman she met in her earlier days in a research collaboration associated with the National Institutes of Health. The woman, in her 30s, was a dancer, very fit and healthy. She came to Lippa saying, "I have the same thing as my mother. I know it. I can tell it. I can feel it." Although the young woman appeared healthy, Lippa's team tested her cognitive strength. "She did so well," Lippa explains, "you couldn't say she had dementia. You could hardly say there was much wrong. She might read something, and then she'd have to re-read it. She couldn't quite contain it – these were little, soft things but they were a little worrisome." It was later revealed that the dancer had an aggressive form of early-onset Alzheimer's. "That got me interested," says Lippa, wondering, "What is doing this to these young, vibrant people?"

Gong explains that, from a scientific perspective, we really know nothing about memory formation – how memories are first created and imprinted in the brain. Why and how does some information become embedded, while other events, information, or stimuli float away? Using resources from the College of Medicine's Neurology Brain, Blood and Cerebrospinal Fluid Bank, Gong is looking for "molecular changes, then pathological changes." He demands, "What *exactly* leads to Alzheimer's disease development? We need an answer. Why do we have memory loss?"

Not everyone who seeks the services of the Clinical Memory Disorders Program has acute Alzheimer's disease. There is a range of memory disorders from common "senior moments" to early-onset dementia. Lippa says within the program, the focus is on "maintaining cognitive health" and using that framework for discussions with patients. When a patient first approaches the program, they are evaluated to discern where on the cognitive spectrum they are located and which interventions or clinical trials, if any, may be appropriate.

Edwards, the clinical care coordinator, stresses the importance for candidates to be in otherwise good health, since studies can last up to two years. It is vital for the caregiver to be actively involved as well. "Screening may require MRI, ECG, blood work, PET scan, cognitive testing, activities of daily living questionnaires, and surveys. Once the screening period...is over, subjects may begin the investigational treatment with monthly visits. Visits may include IV infusion, subcutaneous injection, or oral supplements. Clinical trials may range from six months to two years or more...."

Edwards brings up an important point about the caregiver's involvement in the overall process. A unique feature of the Clinical Memory Disorders Program is its special support system for the dementia caregiver. Dr. Elizabeth Gonzalez, through NIH funding, provides an education program free of charge. Lippa states, "It's amazing the stress in the caregiver, and the health issues the caregiver develops because of the stress...financial and energy wise...it's a hard disease to cope with."

Both Lippa and Gong recommend exercise as the best way to combat the advance of Alzheimer's and other memory disorders. While the exact relationship between exercise and a healthy brain is not clear, there is strong evidence to suggest a positive connection. Lippa says, "People who exercise regularly have less amyloid buildup in their brain than people who are couch potatoes...the data is consistent on this." She uses the analogy of cardiac care to describe caring for the brain. "The care of your heart is a package. It's not just a pill; it's a lifestyle. I think the care of the brain as you get older, and maintaining your cognitive and neurological health, is the same thing. It's a package."

Lippa is hopeful that the future of Alzheimer's research will yield life-changing results. She says that at the beginning of her career people were reluctant to seek a "memory specialist," but that folks are now approaching her earlier, rather than later, in the process of memory loss. With the passage of time there has also been an increase in understanding. "Plus the baby boomers," she laughs. "They're not going there with Alzheimer's. They don't want memory loss. They come in. Trends in the future are going to keep bringing people in earlier and earlier."

When those people come to the Clinical Memory Disorders Program, seeking answers and help for themselves or a loved one, Dr. Lippa and her team will be there. Their attack on Alzheimer's is unrelenting. Now, their program is on the cusp of being able to change the world.

For more information about the Clinical Memory Disorders Program, please call 215-762-6915.

For information about the clinical trials, please contact Carolyn Edwards, R.N., Clinical Research Coordinator, at 215-762-7783.