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Eight Undergrads Probe Alzheimer's Disease

IWU's Research Project into Memory-Robbing Illness Links Up with Researchers at Harvard, Abbott Labs & Albert Einstein College of Medicine

Editor's Note: Gregory Tinkler, a sophomore, majoring in psychology, from Normal, Ill., is a member of IWU's Alzheimer's Disease research team.

BLOOMINGTON, Ill.--Eight Illinois Wesleyan University students and the head of the campus' psychology department are working with scientists at Harvard, Abbott Laboratories, and the Albert Einstein College of Medicine, trying to unlock the mysteries of Alzheimer's Disease, the memory-erasing malady afflicting an estimated two-to four-million Americans.

Initial findings from experiments conducted by IWU students and faculty were presented last November at an international neurological science meeting in Washington, D.C. A scientific journal, based in the United Kingdom, published an article last November, detailing IWU's preliminary findings.

"The type of work these students are doing as undergraduates at a small liberal arts campus closely resembles my duties when I was a research associate at the University of California, Los Angeles, a major research center," said Wayne Dornan, assistant professor, chairman of IWU's psychology department, and head of IWU's Alzheimer's research project. "No other undergraduates that I am aware of are doing this type of work."

Dornan has a personal stake in the research project since his mother suffers from Alzheimer's Disease.

The researchers from industry and academe IWU linked up with are Dr. Tony Giordano, a research associate in the Department of Neuroscience at Abbott Laboratories, the international pharmaceutical manufacturer, based in North Chicago, Ill.; Dr. Neil Kowall, a member of the Department of Neurology at Boston's Massachusetts General Hospital, who also is affiliated with Harvard University's School of Medicine; and Dr. Peter Davies, who is at the Albert Einstein College of Medicine in New York.

In the summer of 1991, Kowall and a Harvard colleague reported that when a protein, beta amyloid, is injected into the brains of rats, it causes neural cells to die in a way very much like what is seen in Alzheimer's patients.

The effects of beta amyloid on memory in rats is a key target of IWU's experiments.

Giordano and a group of biochemical researchers at Abbott Laboratories have purified a beta amyloid protein for the purpose of injecting it into the brains of laboratory animals to see if the substance can mimic the neuropathology observed in Alzheimer's Disease.

Undergraduate Research Team

Eight IWU undergraduates are working on the Alzheimer's research project:

- Steven Bond, a junior, majoring in biology, from Roscoe, Ill.
- Laura Chapman, a junior, double majoring in biology and psychology, from Dundee, Ill.
- Lesley Hickman, a sophomore, majoring in psychology, from Woodridge, Ill.
- Alex McCampbell, a junior, majoring in biology, from St. Johns, Mich.
- Jason Pequette, a senior, majoring in psychology, from Park Forest, Ill.
- Anthony Peterson, a junior, majoring in psychology, from Frankfort, Ill.
- Gregory Tinkler, a sophomore, majoring in psychology, from Normal, Ill.
- Harinie Wijeweera, a senior, double majoring in business administration and psychology, from Sri Lanka.

Dornan Background

Dornan's mother, Leah, a woman in her late '70s, was diagnosed with Alzheimer's Disease about five years ago. Since then, she has lived in a nursing home in Ontario, Canada, geared to dealing with the special needs of Alzheimer's patients.

In an article, "Alzheimer's Pioneers," which appeared in the fall, 1993, edition of *Illinois Wesleyan University Magazine,* Dornan said of his mother: "She isn't doing well. She has no cognitive ability left. She can walk, eat, drink, and chat meaninglessly. She doesn't recognize me."

Alzheimer's Disease is the No. 1 killer among people older than age 70. It attacks the brain, robbing people of the ability to think, cope, and even remember their children's names. Unless science comes up with a cure, some experts forecast that 20-30 million Americans may be afflicted by it by 2040.

Dornan earned a bachelor of arts degree in psychology from Concordia University in Montreal, Quebec, Canada, in 1982, and a master of science degree and doctorate in physiological psychology/behavioral neuroscience in 1984 and 1989, respectively, from Memorial University of Newfoundland. He participated in a post-doctoral training program in reproductive neuroendocrinology and neuroanatomy in 1987-89 in the Department of Anatomy and Brain Research Institute, School of Medicine at the University of California, Los Angeles. He joined the IWU faculty in 1989.

IWU's Research Approach

While many researchers have performed Alzheimer experiments using beta amyloid alone, the IWU research team has taken a different approach. For more than a year, it has injected

laboratory rats with beta amyloid, laced with a mild dose of a neurotoxin, to pinpoint whether the protein kills cells directly or is "susceptible to insult," according to Dornan.

"Our work," Dornan explained, "is the first study looking at the protein, beta amyloid, in combination with other toxins."

Dornan and a team of eight undergraduate students are trying to devise an animal model that mimics Alzheimer's disease as a key step in explaining the affliction's origins and developing a treatment.

IWU's Research Accomplishments

IWU's initial findings were published last November in *Neuroreport,* an international referred scientific journal, published in the United Kingdom.

The IWU researchers also reported their preliminary results at the 24th annual meeting of the Society for Neuroscience in Washington, D.C., last November. Kowell and Giordano made presentations at that conference.

"After Tony [Giordano] made his presentation," Dornan said, "I told him about our work at Illinois Wesleyan. We met again in December at a neuroscience symposium near Abbott Laboratories."

A series of follow-up meetings with the Abbott group took place in January, involving biochemical and behavioral scientists.

"We decided," Dornan said, "that the Abbott group would look at one area of the brain and the Illinois Wesleyan team would look at another and compare results."

IWU Experiments

Ongoing IWU experiments in phase one of the joint project involve injecting batches of a dozen laboratory rats with Giordano's purified beta amyloid, sacrificing the animals after two weeks of studies monitoring their behavior.

The IWU undergraduates perform five hours of behavioral testing daily, typically from 7 p.m.-midnight. Rats injected with beta amyloid are placed on a radial maze with eight spokes, resembling a bicycle wheel. Food is placed at the end of five spokes; three spokes have no rewards.

The students record the rats' behavior, for example, how many times a rat goes down a spoke with a reward; how many times a rat makes a mistake, trekking down a spoke without a reward; the time it takes for a rat to make a "spoke" decision; the number of arms a rat traverses before it makes a mistake; and whether a rat opts for a spoke it already has traveled down.

Results of the nighttime experiments are recorded by the students the next day in a 90-minute session.

On Wednesdays, from noon to 1 p.m., the laboratory team meets to review the progress of their experiments.

The rats' brains, surgically removed by the IWU students, are shipped by Giordano to Kowall at Harvard and Davies at the Albert Einstein Medical College for neuropathological study. The goal is to see if the beta amyloid injections resulted in the formation of the trademark Alzheimer clumps and tangles in the rats' brains.

Phase two of the experiment, which is slated to begin in late spring, is likely to involve a series of rat injections involving a stress hormone, cortiosterone.

"Our interest here," Dornan explained, "is to see if stress may trigger the formation of plaques."

IWU Alzheimer's Research Background

IWU's research focuses on a protein, beta amyloid, which evidently accumulates in the brains of Alzheimer patients, presumably leading to the death of brain cells. It appears the protein selectively attacks a few areas of the brain--the hippocampus, basal forebrain, and the cerebral cortex--aggregating into a core and forming a mass, resulting in disruption of neuron functions and perhaps triggering signals that kill surrounding cells.

The hippocampus is deep in the brain and is intricately involved in memory. The basal forebrain, which sends messages to the hippocampus and cerebral cortex, is an area that produces about 80 percent of a neural transmitter chemical--acetylcholine--that plays a role in memory. The cortex, a furrowed outer layer of gray matter, is associated with higher brain functions, including voluntary movement, learning, and memory.

"What we're trying to do," Dornan said, "is take this protein and inject it into the brains of live animals to test animal learning after the protein is in the brain. We're trying to see if the animals develop Alzheimer symptoms--memory loss," in addition to seeing if the beta amyloid protein spreads elsewhere from the hippocampus.

Research into the properties and affects of beta amyloid has been done with tissue cultures. Now, scientists are ratcheting up the complexity of experiments using animals. Some researchers, Dornan points out, have used animals in studies probing for neurotoxic properties of beta amyloid, but none has looked the effects of these injections on memory, something that is profoundly affected in Alzheimer's patients.

"We're hoping that if we can mimic profound memory impairment in rats, then the next phase is to try to alleviate the memory impairment," Dornan said.

Once an animal model is devised, Dornan looks forward to a series of experiments where various chemical transmitters are injected into animals that modulate the activity of acetylcholine--some of which may bring back memory.

Students Deliver Research Paper at Washington, D.C., Conference

Dornan and David Kang, a 1993 IWU graduate, traveled to Washington, D.C., Nov. 7-12, 1993, to present a paper on the Alzheimer's research to the 24th annual meeting of the Society

for Neurological Science, a conclave that attracts about 10,000 scientists from around the world.

Kang, a psychology major from Seoul, South Korea, now is enrolled in a doctoral program in neuroscience with a full fellowship at the University of California, San Diego. Other students who played a pivotal role in the research were Esther Kang, David's sister and a natural science major; and Alex McCampbell, who continues to work on the project.

Article Published in International Science Journal

An article about IWU's Alzheimer research, "Behavioral and Histological Assessment Following Bilateral Intrahippocampal Injections of ß-AP 25-35," was published in mid-November in *Neuroreport,* an international referred journal, printed in the United Kingdom. The journal's editors are from Sweden, United Kingdom, The Netherlands, Canada, Germany, Israel, Japan, Switzerland, and elsewhere. Papers submitted to referred journals are critically reviewed by a panel of experts prior to publication.

"Neuroreport is a journal that specializes in providing a channel for rapid communication of research papers reporting new and important findings in all fields of neuroscience," Dornan explained.

"It is particularly rewarding," he added, "to have this paper accepted for publication in *Neuroreport* since it represents an acknowledgment by experts in the field that this research is important enough to warrant rapid communication. I am very proud of the students who participated in this project."

The article points out the researchers wanted to assess the effects of injections into the hippocampus of beta amyloid; a combination of beta amyloid and ibotenic acid (IBO); and IBO on learning in the rats.

"Bilateral injections of [beta amyloid] into the hippocampus," the article reports, "together with IBO (which by itself has no neurotoxic effects) produced a dramatic disruption in the acquisition of a spatial learning in the rat. Separate injections into the hippocampus of [beta amyloid] or the incubated form of [beta amyloid] alone failed to significantly affect maze acquisition in the rat. Histological examination revealed that only the combination of [beta amyloid] with IBO produced a lesion along with focal deposits in the hippocampus.

"These results suggest," according to the article, "that the beta-amyloid fragment may play a role in the progressive deterioration of cognitive function observed in Alzheimer's Disease."

The article concludes: "It remains to be determined, however, how relevant this approach is to developing an animal model of Alzheimer's Disease. One essential component that remains to be assessed is whether intracerebral injections of [beta amyloid] in the rat mimic the profound impairment in memory characteristic of Alzheimer's patients. Our results, although tentative, strongly suggest they do and, if supported in subsequent research, may provide an essential ingredient toward developing an animal model of Alzheimer's Disease."

National Science Foundation Grant

Last spring, Dornan and his student researchers got a big boost from Washington. The prestigious National Science Foundation (NSF) awarded Dornan and two colleagues--James Dougan, assistant professor of psychology, and Roger Schnaitter, associate dean of academic affairs and a former head of IWU's psychology department--a $259,803 grant.

Under its terms, IWU is adding $389,704, making a total of $649,507, which will be invested in a facility housing laboratory animals used in teaching and research by psychology and biology faculty. The facility--a state-of-the-art research tool with 3,100 square feet of space and accommodations for 300 rats and mice (mammals)--will be located in IWU's new $22.8 million Center for Natural Science Learning and Research. Construction began last summer on the new science building, which is expected to be completed in the fall of 1995.

IWU, founded in 1850, enrolls about 1,800 students in a College of Liberal Arts, College of Fine Arts, and a four-year professional School of Nursing. For five consecutive years, *U.S. News & World Report* has ranked IWU No. 1 in the Midwest among regional colleges and universities in its annual "America's Best Colleges" edition. *U.S. News* also rated IWU as a "best buy" in higher education in its first survey, "Paying for College," published in October, 1993.

Editor's Note: To arrange interviews with Wayne Dornan and/or the IWU undergraduate research team, call Bob Aaron, IWU Public Relations, at 309/556-3181.