# Clues to nicotine's memory, plaque impact

Low concentrations of nicotine in the blood tend to boost volunteers' performance on tasks that require them to retain and interpret recently acquired information. This memory assist may stem from nicotine's ability to enhance the transmission of chemical messengers in a brain structure known as the hippocampus, according to a new report.

Unrelated, preliminary findings suggest that nicotine may also slow plaque formation in the brains of people with Alzheimer's disease.

Nicotine activates a class of receptors on hippocampal cells that typically responds to the neurotransmitter acetylcholine, explains neuroscientist Richard Gray of Baylor College of Medicine in Houston. Like naturally occurring acetylcholine, externally administered nicotine induces these so-called nicotinic acetylcholine receptors to bolster the actions of other neurotransmitters that facilitate memory, Gray and his colleagues assert.

Alzheimer's disease may derive, at least in part, from an inactivation of these hippocampal sites, known as alpha 7-type receptors, Gray's team theorizes in the Oct. 24 NATURE.

The new findings serve as "an important step toward [recognizing] nicotine as a powerful modulator of memory," state neuroscientists Daniel S. McGehee of the University of Chicago and Lorna W. Role of Columbia University in an accompanying commentary.

Nonetheless, the activation of nicotinic acetylcholine receptors represents only one of many still poorly understood steps that underlie nicotine's effects on thinking and behavior, McGehee and Role contend. Controversial research has indicated that although low concentrations of nicotine aid performance on relatively simple memory tasks, high concentrations interfere with complex mental operations (SN: 1/16/93, p. 46).

Gray's group first established that low concentrations of nicotine, comparable to those observed in the bloodstream after a smoker has consumed a single cigarette, enhance the rate of nerve-impulse transmission in rat hippocampal cells preserved in the lab. Nicotine also increases calcium concentrations in these cells, the researchers contend.

Their results support the theory that the alpha 7-type receptors activated by low doses of nicotine induce the release of calcium, which in turn leads to increased transmission of the neurotransmitter glutamate, they maintain.

Properly timed nicotinic acetylcholine receptor activity may ensure the success of this transmission process, the investigators propose. In people with Alzheimer's disease, the same receptors may fail to coordinate their diminished activity with the arrival of nerve impulses, the team suggests.

A separate investigation, published in the Oct. 22 BIOCHEMISTRY, provides preliminary evidence that nicotine may slow or prevent the formation of the plaque found in the brains of individuals with Alzheimer's disease.

These results may lead to the design of less toxic, nicotinelike compounds to prevent and treat the disease, asserts biochemist and study director Michael G. Zagorski of Case Western Reserve University in Cleveland.

In laboratory experiments, Zagorski and his coworkers examined the effect of high nicotine concentrations on a synthetic version of beta-peptide, a major precursor of plaque. Scientists suspect that various forms of beta-peptide orchestrate chemical reactions that result in the plaque deposits that characterize Alzheimer's disease.

Nicotine attaches to the synthetic beta-peptide and disrupts the chain of events thought to lead to plaque formation, Zagorski holds.

Researchers do not know whether nicotine retards plaque formation in Alzheimer's disease patients, he notes.

*— B. Bower*

# One singular electrochemical sensation

There's no such thing as being too sensitive when it comes to analytical chemistry. Available techniques can readily detect trace elements in concentrations as low as parts per trillion, but picking out a lone molecule in the presence of many others is a much more difficult challenge.

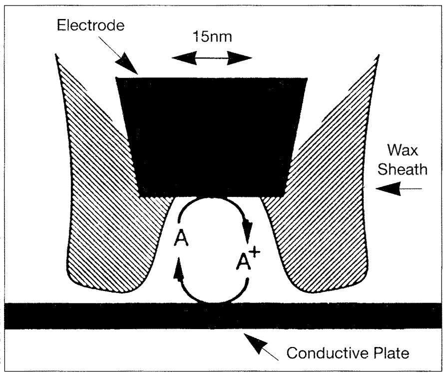
Last year, Fu-Ren F. Fan and Allen J. Bard of the University of Texas at Austin demonstrated a method of detecting the tiny electrochemical current produced by a single molecule in solution. Now, along with their collaborator Juhyoun Kwak of the Korea Advanced Institute of Science and Technology in Taejon, the researchers have measured that current even more precisely. The group's findings appear in the Oct. 9 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

Improved sensitivity is the goal of much research in analytical chemistry. "The ultimate detection in analytical chemistry is the single molecule," says Maryanne M. Collinson of Kansas State University in Manhattan. She regards the approach of Fan and his colleagues as valuable. Such electrochemical techniques, for example, could be used someday to detect extremely low concentrations of trace contaminants in water.

Moreover, isolated molecules may have different physical and chemical properties from ensembles of the same molecule and show greater variation in behavior, Fan says. Scientists may obtain a clearer understanding of those properties by looking at individual molecules instead of many molecules in a solution.

Fan and his colleagues conducted their experiments with a solution of an iron compound that can undergo an electrochemical reaction. Since a small molecule requires a comparably small sensor, the team used a platinum-iridium electrode with a diameter of only 15 nanometers to measure the current.

A sheath of insulating wax surrounded the electrode tip, so it trapped a minuscule volume of solution—one-millionth of a trillionth of a milliliter—when it was lowered onto a conducting disk of indium-tin oxide. The researchers adjusted the concentration of the solution so that the volume trapped beneath the electrode would most likely contain just a single molecule of the iron compound.




Fan *et al.*/JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

*The single-molecule detection system. A wax sheath surrounds the tip of an electrode and, when lowered onto a conductive plate, seals off a small volume of solution. The volume contains a single molecule (A) of an iron compound; the molecule repeatedly gives up an electron to the electrode (becoming A+) and picks up one from the plate, thus producing a tiny, but measurable, current.*

As this molecule shuttled back and forth between the electrode tip and the conductive disk, the researchers detected a current of less than a trillionth of an ampere. The technique is about 60 times more sensitive than conventional electrochemical detection methods, Fan says.

Next, the group would like to try detecting the luminescence of a single molecule. Last year, Collinson and R. Mark Wightman of the University of North Carolina at Chapel Hill were able to detect the light given off by individual molecules undergoing chemical reactions. "If we could combine those experiments, that would be very interesting," Fan says. "Photodetection is usually much faster."

*— C. Wu*