Craving may be at the root of several drug addictions

In spite of differences in withdrawal symptoms, a number of researchers have found that people in the initial phase of trying to kick an alcohol or opiate addiction experience similar changes in brain chemistry that create a craving for drug use. Scientists at Columbia University in New York City report that this craving is also present during cigarette withdrawal and can be suppressed with clonidine, an antihypertensive drug that decreases activity among brain cells containing the chemical messenger noradrenaline.

"Our finding raises many testable questions," says study director Alexander Glassman. "It appears that an addict's craving is a learned response to increased activity in the central noradrenergic system."

In the Nov. 16 SCIENCE, Glassman and colleagues describe their study of 15 volunteers who had been smoking 30 or more cigarettes a day for at least one year. During three 24-hour test periods, each separated by at least three days of smoking as usual, the subjects did not use cigarettes. They randomly received doses of clonidine on one test day, an anxiety-reducing drug called alprazolam on another and a placebo on the third. Various withdrawal symptoms were measured on each day.

Clonidine and alprazolam diminished withdrawal symptoms in 13 of the subjects. The two drugs reduced anxiety, tension, irritability and restlessness equally, but only clonidine, the subjects reported, significantly reduced cigarette craving — thinking about or wishing to smoke. None of the volunteers improved on placebo.

Other investigators have shown that clonidine suppresses the initial withdrawal symptoms of opiates and alcohol. The new results suggest that all three addictions are characterized by an excess of noradrenaline, says Glassman. The most likely site of clonidine's action, he adds, is the locus ceruleus, a small area of the brain where cells that contain noradrenaline are concentrated. These cells are thought to be involved in detecting and responding to strange or dangerous stimuli.

"A person may quiet the activity of the locus ceruleus by using cigarettes, alcohol or opiates," says Glassman. "The locus then overfires [produces too much noradrenaline] on withdrawal."

The data do not suggest, caution the researchers, that clonidine is a cure for tobacco addiction. Volunteers received the treatment over a short period; long-term abstinence was not studied. "We would need at least a year of follow-up to determine the clinical potential of clonidine," notes Glassman.

The investigators, however, are more interested in the theoretical potential of their craving hypothesis. It could explain the observation that stress increases cigarette craving, says Glassman. Stress elevates noradrenergic activity, which in turn could stoke the urge to smoke. In fact, he explains, behaviors that reduce tension and noradrenergic activity, such as binge eating, could be habituating because of a learned craving for the behavior similar to that found with addictive drugs.

"Eating behavior may be hard-wired to control moods among binge eaters," observes Glassman.

A host of environmental factors encourage drug taking, says addiction researchers Mark S. Gold of Fair Oaks Hospital in Summit, N.J., but data on craving support the observation that drug use eventually takes on a life of its own.

In the past, he points out, investigators have often assumed that addictive drugs produce only physical withdrawal symptoms. Psychological concepts such as craving have been largely overlooked.

"Craving is a major cause of relapse after quitting an addictive substance," he says.

"The neurobiological correlates of craving need to be studied, along with underlying commonalities between cigarette smoking and other addictions."

Concludes Glassman, "We now have a model that works across multiple types of addictions and possibly explains their connection to stress and personality factors." — *B. Bower*

Dry developing for printed circuits

Electronic microcircuitry, such as computers use, is made by printing techniques. A substance called a photoresist is coated on a substrate, most often silicon. A mask representing the lines and connections of the circuit is placed on top of the photoresist and exposed to light. Light causes a chemical change in the photoresist. Developing with solvents then gets rid of the unwanted portions of the photoresist, leaving the lines of the desired circuit. Two scientists at Sandia National Laboratories in Albuquerque, N.M., have now found a photoresist that does not need development by solvents. It promises, they say, easier and more accurate manufacture of printed circuits and also more circuitry per silicon chip.

The substance is a polysilane copolymer. The two scientists, John M. Zeigler and Larry A. Harrah, developed it by accident while looking for an insulating material for a nuclear safety program. They irradiated a sample with ultraviolet light to get a spectrum by which they could characterize some of the material's chemical properties. They found that the stuff disappeared on exposure to ultraviolet light. An image of the slit through which the light had come was etched in the film, Zeigler says.

This means that exposure to ultraviolet light through a mask can bring out a circuit pattern in this material without the necessity of development with solvents. Exposure turns the polysilane into gases that are nontoxic and noncorrosive — an advantage over chemical development, as some of the solvent products are corrosive. Solvent development also causes photoresists to swell, and that can lower the resolution and destroy the accuracy of the resultant pattern.

"Thirty percent of all chips that are manufactured have to be thrown away," Zeigler says. Polysilane does not swell under exposure. It is not sensitive to visible light, and so does not need the darkroom and "redlight" procedures that have to be used with other photoresists. The ultraviolet to which it is sensitive has a shorter wavelength than visible light, and that means narrower lines can be etched closer together in it, yielding more circuitry per chip.

Silane has been known since the early 1900s, Zeigler points out, but chemists did not believe it could make a high polymer. Textbooks usually tell you, he says, that silicon is different from carbon, that it will not catenate — that is, form the long chains that are the backbones of high polymers. It turns out, however, that under proper conditions silicon does catenate. Polymer backbones have now been made that string together up to 20,000 silicon atoms. A group at the University of Wisconsin in Madison under Robert West has produced a dimethyl silane copolymer, and the Sandia group now has its phenyl methyl silane copolymer.

The Sandia polymer is also useful in a two-step process. Sometimes the surface of the silicon substrate is not smooth. Undulations in its surface will then reflect light back through the photoresist in many directions, broadening and undercutting the sharpness of the lines. The way around this, Zeigler says, is to lay on top of the photoresist a very thin (1,000-angstrom) layer of a highly absorbent material. This outer layer absorbs the light, and the circuit is printed in it.

Then the whole assembly is subjected to reactive ion etching: a bath of ionized oxygen. The oxygen ions react with both layers, cutting straightwalled channels in the polysilane. Furthermore, the polysilane reacts with oxygen to form a layer of silicon dioxide — exactly what the circuit makers desire.

The industry is conservative, Zeigler says, and may not wish to change its procedures quickly. So he points out that the polymer can also be developed with solvents. — *D.E. Thomsen*