Michigan Society for Medical Research

BioFocus

A Newsletter Exploring Science & Biomedical Research Issues For School Educators

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Our Mission

The Michigan Society for Medical Research (MISMR) is a nonprofit educational organization that supports biomedical research and testing and the judicious use of animals in research, education and testing in the interests of human and animal welfare. Established in 1981, MISMR is made up of the state's leading research universities, teaching hospitals, pharmaceutical companies, voluntary health organizations and hundreds of scientists, educators and students who understand and support the importance of animal research and testing in advancing health care and treatment.

MISMR Educational Projects & Activities

ANNUAL ESSAY CONTEST

Every year MISMR sponsors an essay contest open to all Michigan high school students. Students from well over 500 schools in the state have annually participated in the contest to address the benefits of biomedical research. Prizes are awarded.

SPEAKERS BUREAU

MISMR volunteers visit K–12 schools and civic community groups through out Michigan each year to educate the public about biomedical research and to dispel commonly held myths.

ANNUAL SYMPOSIUM

MISMR's popular annual meetings have often proved to be "standing room only," typically attracting local and national educators and researchers with interactive training workshops and presentations promoting biomedical research.

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The Work of Behavioral Toxicology

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During the early 1950s, the residents of Minimata, Japan were confronted with a strange and terrifying mystery. A "sickness" had beset their neighbors — afflicting them with a dizzying array of behavioral symptoms that included fine motor disturbances (e.g., difficulty fastening buttons, grasping chopsticks, etc.), muscle weakness, tremors, disruptions of speech, and disturbances of sight and hearing. These symptoms gradually evolved to include paralysis, deformity, convulsion and even death. When the sicknesses first appeared, doctors in Minimata believed that a contagious disease had taken hold in their community. However, in July of 1959 (several years after the sicknesses began) a group of scientists from Kumamoto University concluded that the mysterious behavioral syndrome — which has subsequently come to be known as "Minimata Disease" — was a result of exposure to a toxic chemical called methyl mercury. Methyl mercury, which is used in a variety of chemical and manufacturing processes, had been released into the environment by a nearby factory. The chemical had become concentrated in the fish that were living in the local waterways and was subsequently consumed by the citizens of Minimata *(See Fig. 1)*.

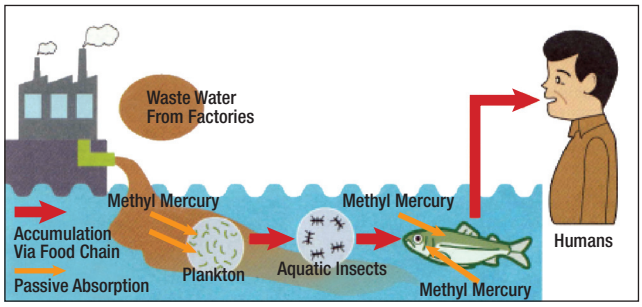

FIG. 1 Accumulation of methyl mercury in the food chain.

In the years that followed, much has been learned about the harmful effects of methyl mercury and laws have been passed to limit the amount of methyl mercury that is allowable in the environment. The research that led to these new discoveries was conducted, in part, by a group of scientists who today would be known as "Behavioral Toxicologists".

Behavioral Toxicology is the study of how drugs, chemicals, or other environmental conditions (generally referred to as "toxicants") change the way in which organisms behave. In Minimata, scientists were able to study these behaviors in human subjects outside of a laboratory setting. In other cases, Behavioral Toxicologist must resort to laboratory "simulations" to study behavioral effects that exist in the real world. Scientists working with the U.S. Food and Drug Administration's National Center for Toxicological Research, for example, have used laboratory-based techniques in Behavioral Toxicology to study effects of drugs proposed to treat motion sickness experienced by astronauts during space flight. As part of this research, motion sickness was induced in human volunteers using a special spinning "chair". Effects of 4 different motion sickness drugs were evaluated to determine which had the fewest adverse effects on mental abilities and behavior. The results of this work have helped to classify these

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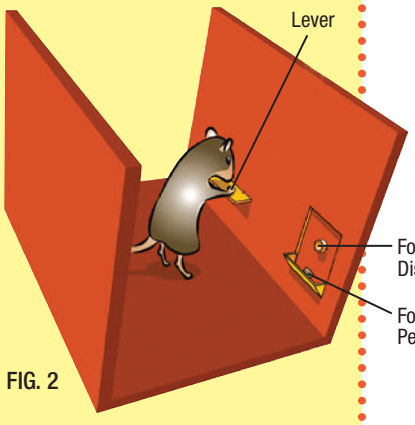

FIG. 2

Behavioral Toxicology... *Continued from page 1*

potential treatments to ensure that drugs used to treat motion sickness in astronauts will not significantly disrupt the cognitive skills required to perform the complex tasks needed for space flight (Paule, et al., 2004).

Although human conditions (such as motion sickness or Minimata Disease) are generally best studied using human subjects, situations often arise wherein the study of Behavioral Toxicology in humans is impractical. In such cases, scientists turn to the responsible use of animals to study the behavioral effects of toxicants. Animals, such as rats, mice, and monkeys can be trained to engage in complex behaviors such as lever-pressing or maze-learning in exchange for food rewards *(See Fig. 2)*. Once these behaviors are well learned, the effects of drugs, chemicals or other environmental conditions can be tested.

Advantages associated with the responsible use of animal models include the ability to exquisitely control environmental conditions, the ability to accurately control levels of exposure to potential toxicants, and the ability to evaluate toxicant effects that could not ethically be induced in humans (such as in the case of Minimata disease). Monkeys are an excellent laboratory animal for some Behavioral Toxicology experiments due to their ability to quickly learn new behaviors and their close evolutionary relationship to humans. The use of monkeys in research is complicated however, by the high cost and special facilities required to care for them. Rodents (such as rats and mice) are also used in Behavioral Toxicology experiments, and can be housed much more easily than can monkeys. In practice, scientists often investigate toxic effects in several species simultaneously to take advantage of the useful characteristics of each and to increase their confidence in the experimental results. In either case, steps must always be taken to ensure that the animals used in behavioral toxicology research are cared for in a way that is both humane and ethical.

Neurobehavioral Teratology

An important field of research that is closely related to Behavioral Toxicology is called Neurobehavioral Teratology. Like Behavioral Toxicology, Neurobehavioral Teratology is concerned with the effects of toxicants on behavior. The primary difference, however, is that Neurobehavioral Teratologists study the effects of toxicants that are encountered prenatally (i.e., in the womb), rather than studying the effects of toxicants that are encountered as adults. Effects of toxicants encountered in the womb can differ dramatically from the effects of the same toxicants encountered by adults. The alcohol found in beer, wine, and spirits, for example, has only mild, short-term effects in adults but can produce severe and irreversible effects on organisms developing prenatally. Exposure to alcohol in the womb can result in mental retardation, hyperactivity, motor difficulties, impaired intellectual functioning, and impaired language development as children. Collectively, the toxic effects of prenatal alcohol exposure are known as Fetal Alcohol Syndrome. The behavioral effects of Fetal Alcohol Syndrome are often accompanied by overt physical malformations as illustrated in Fig. 3.

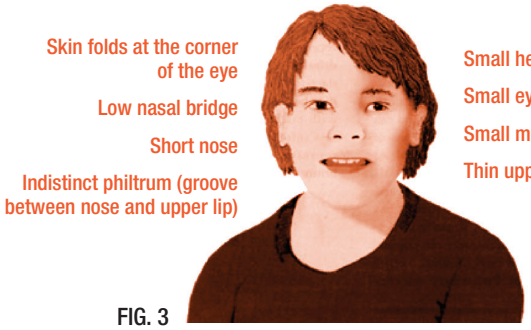

FIG. 3
Children with fetal alcohol syndrome (FAS) may have distinct facial features.

For obvious ethical reasons, controlled studies of Fetal Alcohol Syndrome can not easily be conducted using human subjects. Therefore, animal models are often used. Rats are a preferred animal for use in Fetal Alcohol Syndrome studies due to the large number of offspring in each litter and the fact that the reproductive gestation period of

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BioFocus

WE WANT TO HEAR FROM YOU!

We want to include your stories, comments or questions relating to animals in your classroom in upcoming editions of *BioFocus.* Please email stories to: mismr@umich.edu

Fast Facts...

Minimata Disease

This behavioral syndrome was found to be a result of exposure to a toxic chemical called methyl mercury. Much has been learned about the harmful effects of methyl mercury and laws have been passed to limit the amount allowable in the environment.

Motion Sickness

Behavioral toxicology evaluations of motion sickness drugs helped to ensure that drugs used to treat motion sickness in astronauts will not significantly disrupt their cognitive skills while in space.

Fetal Alcohol Syndrome

The behavioral effects of Fetal Alcohol Syndrome are often accompanied by overt physical malformations. Results also suggest that children who are exposed to alcohol prenatally may be more sensitive to the effects of drugs encountered as adults and therefore, may be more likely than others to abuse them.

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Behavioral Toxicology... *Continued from page 2*

rats is only 22 days in duration. This serves to minimize the number of pregnant female rats that need to be studied and shortens the amount of time that the alcohol needs to be administered. As part of one recent study (Barbier, et al., 2008), pregnant rats received daily doses of alcohol (10% alcohol in drinking water) throughout the duration of their pregnancy. Their offspring (referred to as "pups") were then studied to evaluate the effects that the prenatal exposure to alcohol had on their sensitivity to various drugs as adults. The results were startling in that the rats that were exposed to alcohol in the womb showed a greater sensitivity to the behavioral effects of cocaine and amphetamine as adults than did rats that had not been exposed to alcohol in the womb (even though they had not been exposed to either of these drugs previously). In addition, the rats that were exposed to alcohol in the womb showed a greater tendency to voluntarily consume alcohol when presented with it as adults than did the rats that had not received alcohol in the womb. Together, these results may suggest that children who are exposed to alcohol prenatally may be more sensitive to the effects of drugs encountered as adults and therefore, may be more likely than other people to abuse them.

In a complex society that places heavy demands on an individual's educability, alertness, and emotional stability, even small deviations in behavior are potentially hazardous. The goal of Behavioral Toxicology and Neurobehavioral Teratology is to evaluate behavior changes induced by potential toxicants, investigate their causes, and determine their risks relative to exposure. The comprehensive study of Behavioral Toxicology requires consideration of human and non-human populations examined in naturalistic, as well as laboratory settings. Animal models are useful tools for evaluating the effects of toxicants encountered in the womb.

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