Food Affects Human Behavior

The effects are subtle, but a number of scientists are finding that people do react to what they eat

Research on whether food and nutrients affect human behavior is gaining serious attention these days. On 9 November, the Center for Brain Sciences and Metabolism at the Massachusetts Institute of Technology (MIT) held a meeting to bring together reputable investigators who are studying this subject.* "To my knowledge, this is the first meeting on this subject that was not held by and for the true believers," says Richard Wurtman of MIT, who was the conference organizer.

The problem is that serious researchers have tended to steer away from this field which has, Wurtman notes, "a dubious reputation." Yet there is good biochemical evidence that, in laboratory animals at least, changes in diet can change the amount of various neurotransmitters synthesized in the brain and can thereby alter behavior. As was apparent at the meeting, there is strong preliminary evidence that the same phenomena occur in humans.

The effects of nutrients on human behavior are subtle, however, and are not necessarily the effects so avidly believed by many members of the general public. The folk wisdom, for example, is that refined sugars and carbohydrates cause children to be hyperactive and cause criminals to act aggressively. In fact, the more likely effect of a junk food diet is to make people sleepy.

The studies of the effects of food on brain biochemistry began about 10 years ago when Wurtman and his associates initiated animal experiments. Since then, they and others have firmly established that half a dozen nutrients can alter the synthesis of the neurotransmitters serotonin, dopamine, norepinephrine, acetylcholine, histamine, and glycine.

These neurotransmitters are precursor-dependent. The rate at which brain enzymes synthesize the transmitters is limited by the availability of precursors that derive from food and are transported into the brain by carrier molecules.

The most often-cited case is that of serotonin and its dependency on tryptophan. Serotonin is made directly from tryptophan, and the body's only source of this amino acid is dietary protein. When protein is digested, tryptophan enters the blood and joins a pool of amino acids available for transport to the brain. But the carrier molecule that transports tryptophan transports eight other neutral amino acids as well. The nine amino acids compete for the carrier. Thus the more tryptophan in the blood relative to the other competing amino acids, the more tryptophan enters the brain and the more serotonin is made.

High protein meals do not increase brain serotonin because they do not increase the relative amount of tryptophan in the blood. High carbohydrate meals, on the other hand, do. After a high carbohydrate meal is eaten, insulin is released and this hormone facilitates the uptake into body tissues of all the amino acids except tryptophan.

Serotonin neurons participate in a wide range of behaviors, including sleep, feeding, locomotor activity, aggression, and pain sensitivity. Dietary manipulations that alter brain tryptophan concentrations can, in animals, affect many of these behaviors.

> ". . . this is the first meeting on this subject that was not held by and for true believers."

Similarly, other dietary precursors of neurotransmitters seem to have the predicted effects in animals. For example, tyrosine is a precursor for dopamine and norepinephrine, which play a role in regulating motor activity and mood. (Tyrosine concentrations in the blood and brain increase after a high protein meal.) Tyrosine causes an increase in motor activity in animals.

Based on these animal studies, it seems at least plausible that diet may affect human behavior. But the question of whether it actually does so is especially difficult to answer because it is not at all clear how to elicit behaviors in normal humans nor how to measure them. Thus it is somewhat surprising that investigators at the meeting found even subtle effects. But many of these studies with humans have been incomplete—researchers have given subjects an amino acid or a high carbohydrate or high protein meal, for example, and then tested their behavior. Unfortunately, however, they generally have not measured changes in plasma amino acids to see if these correlate with the observed changes in behavior.

The best studied behavioral effect of nutrients in humans is sleepiness. Animal studies have clearly established that serotonin is used in the regulation of sleep. When investigators destroy neurons of the midbrain raphe where the cell bodies of many serotoninergic neurons lie, animals' sleep time is significantly decreased. When they give animals a substance that blocks serotonin synthesis, the animals sleep even less.

As early as 1963, Ernest Hartmann and his associates at Tufts University School of Medicine began testing tryptophan as a possible inducer of sleep. More recently, Hartmann gave subjects high carbohydrate or high protein meals to see how this affected sleep.

In his review at the MIT meeting of these and dozens of similar studies by other researchers, Hartmann concluded that tryptophan in doses of at least 1 gram (which is in the range that can be supplied by diet) does make mildly insomniac patients fall asleep more quickly and wake less frequently during the night. Normal good sleepers tend not to be affected by this amino acid and neither do seriously ill insomniacs. Hartmann proposes that since it takes a good sleeper only about 10 minutes to fall asleep, and since these people do not wake in the night, it would be hard to detect much of an effect from tryptophan. Mild insomniacs take about 30 minutes to fall asleep, and tend to wake in the night, so it is easier to observe tryptophan's effects.

When Hartmann tested the effects of a high carbohydrate evening meal as compared to a high protein meal, he found that subjects who eat the carbohydrates are significantly sleepier 2 hours afterwards then those who eat the protein. Perhaps the optimal way to use tryptophan would be to give even lower doses along with a carbohydrate meal, Wurtman advises. High doses of any large, neutral amino acid, including trypto-

*The papers from the conference, "Research Strategies for Assessing the Behavioral Effects of Food and Nutrients," will be published in the *Journal of Psychiatric Research*.

0036-8075/82/1217-1209$01.00/0

phan, will nonspecifically lower the amounts of all the other large neutral amino acids in the brain. So there is good reason to keep the amino acid doses as low as possible.

But the effects of carbohydrate and protein meals may be more complicated than Hartmann's data indicate. Bonnie Spring of Harvard University and her associates reported at the meeting on a study in which they gave 184 subjects carbohydrate or protein meals for breakfast or lunch. They then measured these subjects' performance on tests of selective attention and asked them to rate their moods. In the test, called dichotic shadowing, subjects heard strings of words on a "main channel" of a stereo headset. These words were transmitted through only one of the earphones. On the other earphone were distracting words or sounds. Subjects were asked to repeat the main channel words, syllable by syllable. The persons aged 40 and older felt more calm after a carbohydrate lunch but also did worse on the performance test. The younger subjects did worse on the performance test after a carbohydrate breakfast. Spring says she was quite surprised to find any significant effects on performance at all after people ate a single meal. "The fact that we could detect an effect after one meal is quite extraordinary," she remarks.

There is some suggestion that the sleep-inducing effects of tryptophan might apply even to newborn babies. Michael Yogman of Harvard Medical School, Steven Zeisel of Boston University Medical School, and Carolyn Roberts at MIT gave tryptophan or valine (which competes with tryptophan for uptake into the brain) to 2- and 3-day-old infants in a double-blind study. Infants given tryptophan in their bottles of formula entered both quiet and active sleep more quickly than infants that had been given valine.

Intrigued by these results, Yogman now wants to follow up with studies of breast-fed infants. He strongly suspects that the carbohydrate content of breast milk varies according to the mother's diet and thus different breast-fed babies may be getting different amounts of carbohydrates and, possibly, brain tryptophan. This may affect their sleep patterns, Yogman suggests.

A commonly held belief is that carbohydrates, and particularly refined sugars, make children hyperactive. But this effect is inconsistent with the known biochemical actions of carbohydrates, and two studies presented at the meeting failed to confirm it.

Judith Rapoport of the National Institute of Mental Health sought out boys whose parents were convinced that they were immediately made hyperactive by sugar. The children were given, in a double-blind test, drinks with sucrose and saccharin, glucose and saccharin, or saccharin alone. (Rapoport added saccharin to the sugar mixes so as to make the tastes of the three drinks indistinguishable.) The boys wore activity monitors that recorded their physical activity. In addition, trained observers, who did not know whether the children had consumed sugar or just saccharin, assessed their behavior. By both of these measures, the boys were not more active when they drank the sugar mixtures. In addition, when Rapoport analyzed separately the results for the normal and the psychiatrically disturbed boys in the study, she found that each group was significantly slowed down by the sugar, but the slowing effect occurred in 3 hours for the normal group and in 1 hour for the disturbed group.

"There is no longer any real controversy over whether nutrients can affect behavior."

But even the best of these studies of carbohydrates or tryptophan and sleep or performance do not establish that carbohydrates or tryptophan in the diet exert their effects through brain serotonin. Says Hartmann, "Although I and others have assumed that brain serotonin was responsible at least in part, none of the tryptophan studies examined this directly. There have been no studies attempting to block the effects using a specific serotonin receptor blocker."

In animals, increased brain serotonin causes decreased sensitivity to pain. In humans, according to two groups of investigators at the MIT conference, tryptophan causes decreased pain perception. Harris Lieberman and Suzanne Corkin of MIT and their associates conducted a double-blind study comparing tryptophan, tyrosine, and a placebo for their effects on pain sensitivity in normal male subjects. (The test was a standard one used to evaluate drugs that may alter pain perception.) Tryptophan caused the men to be significantly less sensitive to moderate pain but did not diminish their sensitivity to intense pain.

Dorothy Dewart and her associates at Temple University gave tryptophan or placebos to patients with chronic pain of the head or neck. These investigators reported that tryptophan significantly decreased the subjects' reported pain. Of course, tryptophan is hardly a competitor with drugs such as the opiates. "Tryptophan won't put morphine out of business," Wurtman says, "but it looks like the relationship between tryptophan and pain is holding up."

Although most of the studies of nutrients and behavior have focused on tryptophan, the recent discovery that tyrosine also can alter brain biochemistry is leading to studies of that amino acid. Alan Gelenberg of Harvard Medical School and his associates, for example, have begun studies of whether tyrosine can alleviate depression.

One of the theories of depression is that it results from a deficiency of catecholamines, specifically norepinephrine. If this theory is correct, tyrosine might be useful as a treatment for depression.

In a small pilot study, Gelenberg and his associates tested tyrosine against a placebo in depressed patients. They also measured plasma tyrosine and the urinary excretion of a norepinephrine metabolite to see whether the administered tyrosine had the expected biochemical effect. They found that not only did plasma tyrosine concentrations increase 27 percent in the patients taking tyrosine but the concentration of the norepinephrine metabolite increased 24 percent. The clinical results, although not conclusive, are suggestive that tyrosine really is relieving depression, at least in some patients. These investigators have now begun a more definitive study. In any event, says Gelenberg, "We hope that research with tyrosine will be more systematic, rigorous, and therefore conclusive than corresponding work with its sister amino acid tryptophan."

The serious study of the effects of nutrients on human behavior has barely begun but, says Wurtman, it is encouraging that the studies are being done at all and that the results are as positive as they are. One thing that can be said, according to Wurtman, is that now "There is no longer any real controversy over whether nutrients can affect behavior." But researchers certainly could better plan their studies. For example, when they ask whether eating breakfast affects performance, they should specify whether the breakfast is high in protein or high in carbohydrates—something that, up to now, investigators did not always do. Wurtman would also like to see researchers pay more attention to levels of amino acids and other neurotransmitter precursors in the blood in these studies.—**GINA KOLATA**