Carbohydrates and Depression

Several related behavioral disorders recognized in the past decade are characterized by disturbances of appetite and mood. One of the best-known is seasonal affective disorder, or SAD

by Richard J. Wurtman and Judith J. Wurtman

On May 16, 1898, the intrepid Arctic explorer Frederick A. Cook made the following notation in his journal: "The winter and the darkness have slowly but steadily settled over us.... It is not difficult to read on the faces of my companions their thoughts and their moody dispositions.... The curtain of blackness which has fallen over the outer world of icy desolation has also descended upon the inner world of our souls. Around the tables... men are sitting about sad and dejected, lost in dreams of melancholy from which, now and then, one arouses with an empty attempt at enthusiasm. For brief moments some try to break the spell by jokes, told perhaps for the fiftieth time. Others grind out a cheerful philosophy; but all efforts to infuse bright hopes fail."

We now know that the members of the Cook expedition were suffering from classic symptoms of winter depression, a condition related to a recently described psychiatric disease known as seasonal affective disorder, or SAD. As the journal entry makes clear, recognition of the association between depression and the onset of winter is not new. But in recent years there has been growing interest in SAD and in two behavioral disorders, carbohydrate-craving obesity (CCO) and premenstrual syndrome (PMS), that share some of its symptoms. The symptoms include depression, lethargy and an inability to concentrate, combined with episodic bouts of overeating and excessive weight gain; they tend to be cyclic, recurring at characteristic times of the day (usually late afternoon or evening in CCO), month (just prior to menstruation in PMS) or year (generally fall and winter in SAD).

Over the past decade a wealth of information has emerged that casts light not only on the clinical expressions of this group of mood and appetite disorders but also on the disturbed biochemical processes that underlie them. It now appears that these disorders are affected by biochemical disturbances in two distinct biological systems. One system involves the hormone melatonin, which affects mood and subjective energy levels; the other involves the neurotransmitter serotonin, which regulates a person's appetite for carbohydrate-rich foods. Both systems are influenced by photoperiodism, the earth's daily dark-light cycle. Indeed, photoperiodism appears to be the basis for the cyclic patterns of all three disorders.

At high latitudes in the Northern and Southern hemispheres SAD appears in the late fall or early winter and lasts until the following spring. Once expressed, it tends to recur annually unless the patient moves to a place where day length does not decrease significantly in fall and winter. Sufferers complain of episodic bouts of depression combined with profound cravings for carbohydrate-rich foods. They go to sleep early and stay in bed for nine or 10 hours, unlike patients with nonseasonal depression, who have difficulty sleeping. Their sleep, however, is intermittent and not fully refreshing; during the day they are often drowsy and have trouble concentrating. Once spring arrives SAD patients are full of energy and creativity; they are almost manic in their zest for life. At the same time their craving for carbohydrates lessens and most lose the weight they had gained over the winter.

The following case history typifies many SAD sufferers. Patient M, a 53-year-old teacher, stands five feet four inches tall and weighs 181 pounds. She is unhappy about her weight and over the years has spent a lot of money on short-lived diets. "I know my problem is carbohydrates: when I'm on a diet I stay away from bread, potatoes and sweets and I always lose weight. But when I'm not dieting I get anxious and tense in the midafternoon and I'm unable to concentrate on what I'm doing. I want to eat something to calm myself, so I buy crackers or donuts and nibble on them. At home sometimes I just keep eating until I go to bed." Shortly after Thanksgiving, Patient M experienced two months of feeling tired and depressed. "I told my husband to leave me alone and assigned my pupils problem sets so I wouldn't have to talk to them at school. The house was a mess. I stopped eating except for bread and pasta, but I still gained weight. Finally when spring came I felt better—perhaps because the school year was ending and summer was about to begin."

The symptoms described by Patient M are virtually the same as those associated with CCO and PMS, except that carbohydrate cravers are affected daily, typically in the late afternoon and early evening, and PMS sufferers are affected monthly, during the luteal phase of the ovarian cycle, which lasts for two weeks prior to the onset of each menstrual period.

Interest in seasonal mood disorders was sparked in the early 1980's, when Peter S. Mueller, a psychiatrist at the National Institute of Mental Health,

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reviewed data on a 29-year-old woman he had been treating for cyclic bouts of winter depression. Over the course of several years the patient moved to a number of different cities. Mueller maintained contact with her and observed that the farther north she lived, the earlier she became depressed in the fall and the longer she stayed depressed in the spring. On two occasions when the woman traveled to Jamaica in midwinter her depression disappeared within a couple of days of arrival.

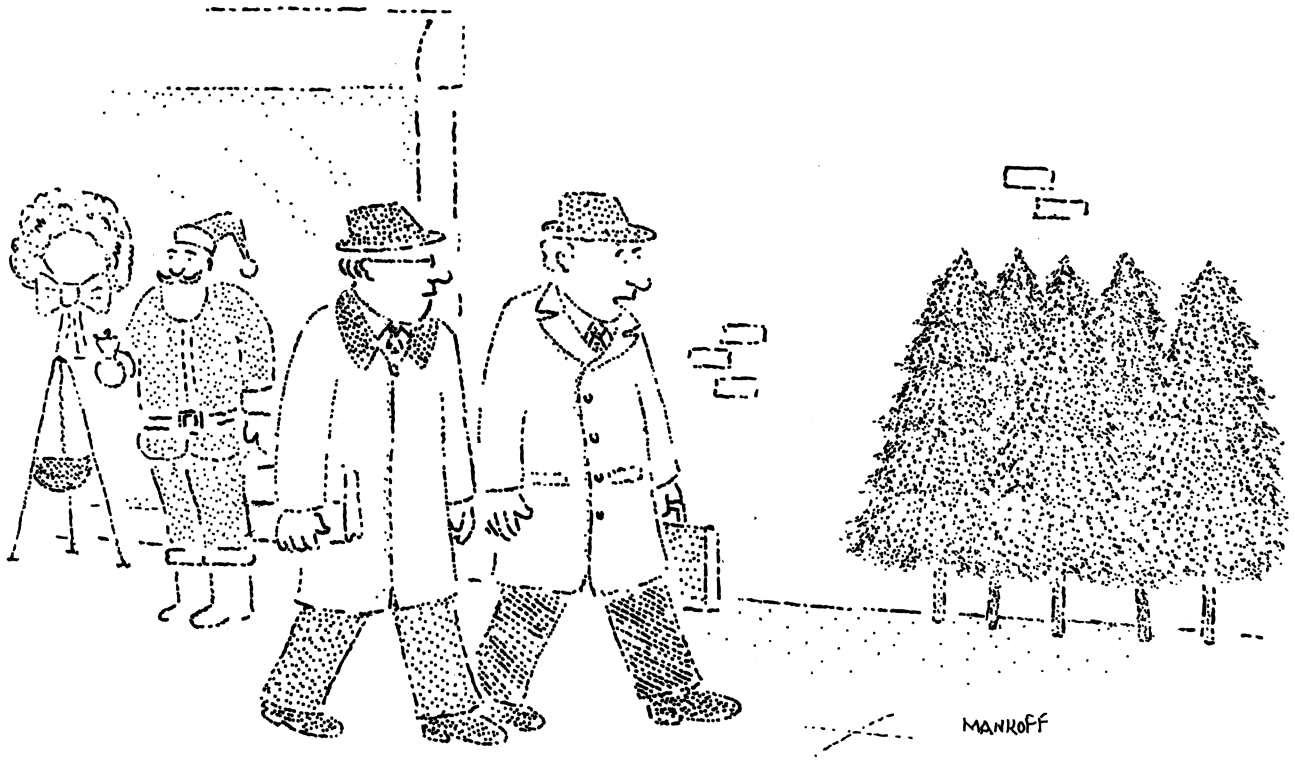
Mueller began to speculate that sunlight (or the lack of it) contributed in some way to the woman's depression and decided to experiment with phototherapy (a form of treatment previously shown to be effective in treating jaundiced infants and psoriasis). On consecutive mornings he exposed the patient to 2,500 lux of supplemental, full-spectrum light. (A lux is a unit equivalent to the illumination cast on a surface by one candle one meter away, which is equal to from one-fifth to one-tenth of a foot-candle.) In less than a week the patient had recovered from her depression.

Mueller's findings came to the attention of Norman E. Rosenthal, Thomas A. Wehr and Alfred J. Lewy, also at the NIMH, who were interested in the various manifestations of clinical depression. They launched a full-scale investigation into the natural history of winter depression, recruiting large numbers of volunteers for observation and treatment. The results were both revealing and intriguing. They confirmed the therapeutic effect of supplemental light in treating winter depression with phototherapy. In addition their data provided the first link between winter depression and carbohydrate craving.

A subsequent study by Steven G. Potkin, Daniel F. Kripke, William Bunney and their colleagues at the University of California at Irvine provided more complete data on the correlation in the U.S. between SAD and latitude. A questionnaire published in the newspaper *USA Today* in March of 1985 provided a description of SAD but omitted any reference to its presumed association with day length. Readers were asked to provide yes or no responses to 15 statements thought to characterize the disease. Those who responded yes to eight or more statements (and thus presumptively had SAD) were asked to send the questionnaire to the authors; 723 did so. The prevalence of SAD in each state was determined by dividing the number of respondents by average daily sales of the newspaper in that state. Results indicated that 100 people per 100,000 in the northern regions of the U.S. are affected by SAD; in the south the incidence is less than six people per 100,000. These estimates, however, are undoubtedly low because people with SAD are less likely to read newspapers and to answer questionnaires than unaffected people.

At about the same time, we began to investigate eating disorders at the Massachusetts Institute of Technology's Clinical Research Center, an inpatient clinic on the university campus. A typical study at the CRC might last for two weeks and focus on carbohydrate consumption among 20 patients in one of two weight groups: moderately obese (from 20 to 39 percent above ideal body weight) and obese (those who are from 40 to 80 percent above ideal body weight).

The eating habits of our study subjects were closely monitored—both at regularly scheduled meals and between meals. Snack intake was meas-



"Yes, I'm somewhat depressed, but seasonally adjusted I'm probably happy enough."

PUBLIC AWARENESS of seasonal affective disorder, or SAD, has increased in recent years. The spirit of the disorder is captured in this drawing by Robert Mankoff, which appeared in the December 10, 1984, issue of the *New Yorker* magazine.

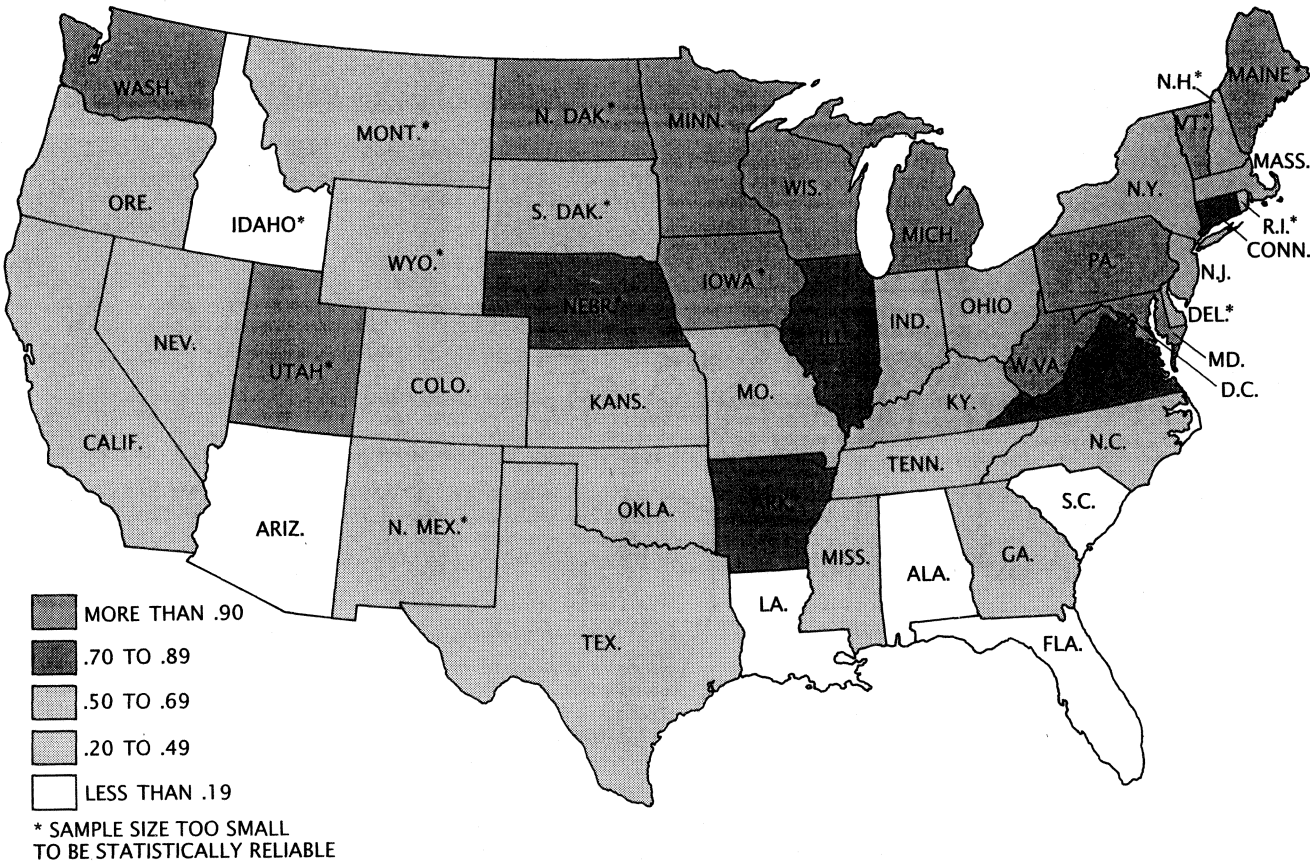
ured by a computer-operated vending machine (based on a design by J. Trevor Silverstone of St. Bartholomew's Hospital Medical College in London) that was available around the clock and contained a variety of snack foods ranging from carbohydrate-rich cookies to protein-rich sardines. All the selections contained roughly equal amounts of fat (six grams, for example) and calories (about 110). The foods could be obtained only by typing a special access number into a keyboard connected to a computer that kept a continuous record of the number and type of snacks selected by each patient. Participants in the study were asked to eat as they normally would and not be embarrassed about their caloric intake; most cooperated, believing the data we obtained would eventually help them to overcome their weight problem.

Food consumption during regular meals was measured by giving participants unlimited portions of food in preweighed, labeled containers that were color-coded and set on a table in the dining room. The different foods, like the snacks in the vending machine, varied in their protein and carbohydrate content and were equal to one another in fat and calories. At the end of each meal a dietitian reweighed the containers (and their leftovers) to determine how much of each food type a person had eaten.

Our studies at the CRC have enabled us to test and discard a number of myths concerning obesity, specifically with regard to carbohydrate craving. Most prominent among them, perhaps, is the notion that all obese people overeat anything that is tasty, whenever it is available. Instead it appears that those who are carbohydrate cravers overeat only carbohydrates and do so only at characteristic times of the day. At mealtime they behave like normal eaters, consuming a total of some 1,940 calories per day. (An average adult female consumes a total of from 1,500 to 2,000 calories, a male from 2,200 to 2,700 calories.) Toward the late afternoon or early evening, however, the volunteers begin to snack, often consuming an additional 800 or more calories per person per day. A similar pattern has been observed among women with PMS: they increased their snack intake by about 460 more calories per day than women at the same stage of the menstrual cycle who are not affected by PMS.

We were also intrigued to discover (with the help of the computer-run vending machine) that patients almost invariably underreport their consumption of snacks. It seems that a snack, if eaten quickly, is easily forgotten, as if it somehow "doesn't count." Yet for those concerned about their weight, snacks do count. In some cases they provide 30 percent or more of an individual's caloric intake.

Moreover, we found that most of the snacks consumed by CCO and PMS patients are carbohydrates. We observed, in fact, that more than half of the carbohydrate-craving obese people at the CRC never select a protein snack, although most will readily eat proteins at mealtime. A possible (but still unproved) explanation for such selective eating behavior is that in carbohydrate cravers the ability to regulate nutrient intake is impaired in the late afternoon or early evening. In a noncraver the desire for something sweet is infrequent, noncyclic and readily appeased, say by eating a cookie or two; in a carbohydrate craver, however, the desire may continue unabated



PREVALENCE OF SAD in the U.S. varies with latitude. In a northern state such as Minnesota, SAD affects more than 100 people per 1,000, whereas in Florida it affects fewer than six people per 100,000. Asterisks indicate a sample that is too small to be reliable. The data were collected by Steven G. Potkin and his associates at the University of California at Irvine.

until nine or 10 cookies are eaten. This suggests there is a malfunction in the feedback mechanism by which the brain knows carbohydrates have been eaten. Another possibility is that carbohydrate cravers snack not because they are hungry but because carbohydrate-rich foods improve their mood.

Why snacking takes place at certain times of day for CCO patients is not clear; its cyclic occurrence, which is monthly in PMS or seasonal in SAD, may reflect the actions of ovarian hormones or melatonin on the brain, but no such relationship has been established for CCO. It is clear, in any case, that carbohydrate snacks tend to exacerbate obesity because they are often rich in fat and thus in calories.

It appears that carbohydrate craving is a multifaceted disorder. As many as two-thirds of all obese people are carbohydrate cravers, but not all carbohydrate cravers are obese; many control their weight by exercising, eating low-calorie meals or satisfying their craving with such low-fat carbohydrates as popcorn (without butter) or candies such as jelly beans. Conversely, not all obesity is linked to carbohydrate craving. Some obese people show no preference for carbohydrates, and some overeat chiefly at mealtime, consuming snacks infrequently.

Our research also focused on mood fluctuations among carbohydrate cravers. When these people were given standardized psychiatric tests based either on an interview (the Hamilton Scale) or a written questionnaire (the Beck Depression Inventory), a high susceptibility to clinical depression was revealed. When carbohydrate cravers were asked why they succumb to foods they know will exacerbate their obesity, their explanation sounded much like the one provided by SAD sufferers. It almost never had to do with hunger or with the taste of the food; instead most said they eat to combat tension, anxiety or mental fatigue. After eating, the majority reported feeling calm and clearheaded. We wondered whether the consumption of excessive amounts of snack carbohydrates leading to severe obesity might not represent a kind of substance abuse, in which the decision to consume carbohydrates for their calming and antidepressant effects is carried to an extreme—at substantial cost to the abuser's health and appearance.

With the help of Harris R. Lieberman and Beverly R. Chew of M.I.T., one of us (Judith Wurtman) set out to test the relation between carbohydrate snacking and mood. Forty-six volunteers, including both carbohydrate cravers and noncravers, were given standard psychological tests before and after eating a carbohydrate-rich, protein-free meal. The carbohydrate cravers were significantly less depressed after snacking, whereas noncravers experienced fatigue and sleepiness. These findings suggest that carbohydrate cravers may eat snacks high in carbohydrates in order to restore flagging vitality, much as some people will pour another cup of coffee when they feel that their energy level or attention span is flagging.

The discovery that one's carbohydrate craving, like SAD, has a distinct periodicity led us to believe photoperiod might in some way be linked to the cyclic manifestations of appetite and mood disorders. We knew from work carried out some 25 years ago that the secretion of melatonin follows a distinct circadian rhythm coupled to daily and seasonal changes in light, which seems to match, at least conceptually, the rhythm most associated with SAD.

Melatonin was discovered in 1958 by Aaron B. Lerner and his colleagues at the Yale University School of Medicine, who isolated it from the pineal

SNACK MACHINE at the Massachusetts Institute of Technology's Clinical Research Center Research has provided data on the food preferences of both carbohydrate cravers and noncravers. The machine contains snacks that have equal amounts of fat and calories but are either rich in carbohydrates or rich in protein. To get a snack a person enters an access code into the machine, which is connected to a computer. The types of snacks and the time they are taken are recorded for each person.

glands of cattle and found that it lightened excised pieces of tadpole skin. Five years later Julius Axelrod and one of us (Richard Wurtman), then at the NIMH, suggested that melatonin was a hormone in mammals, based on its ability to suppress gonadal function when injected into rats. Subsequently we found that melatonin synthesis decreased when rats were exposed to light and that this effect was mediated by interactions among the retina, the brain and special sympathetic nerves that innervate the pineal gland [see "The Pineal Gland," by Richard J. Wurtman and Julius Axelrod; SCIENTIFIC AMERICAN, July, 1965].

At about the same time, Wilbur B. Quay of the University of California at Berkeley demonstrated that melatonin levels in the pineal gland of rats exhibit a daily rhythm, rising at night and falling during the day. A few years later Russell Pelham and his colleagues at the University of Pittsburgh described similar fluctuations of melatonin in the plasma of humans. Soon thereafter one of us (Richard Wurtman) and Harry J. Lynch of M.I.T. found that melatonin levels in human urine exhibit pronounced time-dependent fluctuations in samples taken from the same subjects: they are at least five times higher at night than they are during the day.

In order to prove that the timing of melatonin rhythms in humans is affected by the day-night, light-dark cycle, David C. Jimerson of the NIMH, Lynch and one of us (Richard Wurtman) examined the effects of abruptly shifting a person's photoperiod. We recruited a number of volunteers, monitored their plasma and urinary melatonin rhythms and then changed their photoperiod. We kept them indoors and on the test day left the lights on until 11:00 A.M., shifting the daily dark period 12 hours—to between 11:00 A.M. and 7:00 P.M.

We found it took four or five days for the subjects to reentrain and adjust physiologically to the new light cycle by secreting melatonin when it was dark and suppressing its secretion when it was light. Thus we showed that melatonin secretion follows a circadian rhythm in humans, as it does in other mammals, that the rhythm is endogenous (generated by a clock somewhere in the brain) and that it is entrained by the light-dark cycle.

Neither we nor other investigators were able to demonstrate in humans, however, what Axelrod and one of us (Richard Wurtman) had shown more than a decade earlier in rats: that melatonin secretion is acutely suppressed if subjects are exposed to light during the dark part of the cycle. Perplexed, we concluded that the pineal gland of humans was inexplicably insensitive to the effects of light.

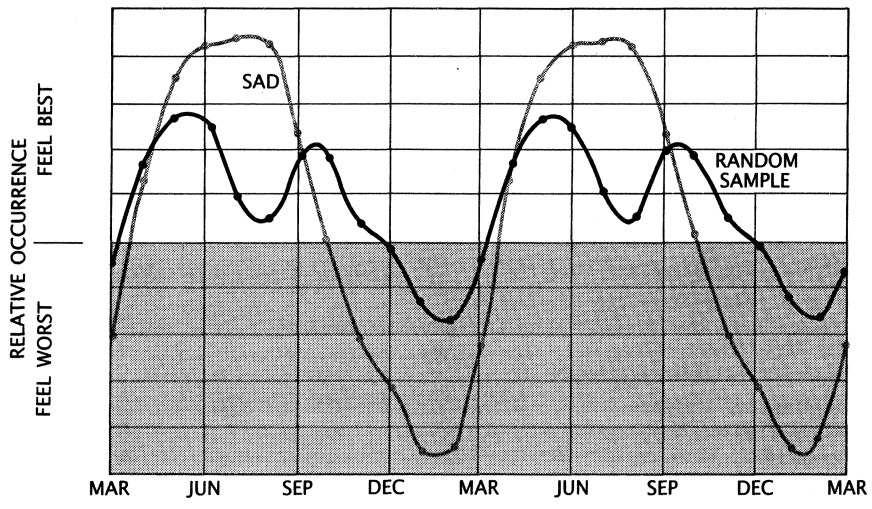
It was not until 1980 that Lewy discovered that melatonin secretion in humans can be acutely suppressed by light—if the light is of sufficient intensity. When the participants in his study were awakened at 2:00 A.M. and exposed to 2,500 lux for one and a half hours, their plasma-melatonin levels declined abruptly. Thus light has two effects on melatonin rhythms in humans, just as it does in rats. It can either reentrain the melatonin rhythm (as when daytime was artificially reversed in our experimental study) or suppress melatonin secretion entirely (if the dark period is eliminated). Either action or both could underlie light's therapeutic effect on SAD.

The work of Mueller, Rosenthal and others demonstrated that exposing SAD patients to intense supplemental light for a few hours each morning could eliminate their depression and carbohydrate craving after a few days. Obese carbohydrate cravers have not yet been treated with phototherapy, but a preliminary study by Barbara L. Parry of the NIMH suggests that supplemental light may be effective in treating women with PMS, whose symptoms worsen in the winter.

Michael Terman of Columbia University has found that exposing SAD patients to 2,500 lux for two hours in the morning brings complete remission from both depression and carbohydrate craving in roughly half of them, usually after only a few days of treatment. Most of the remaining patients show some improvement short of full remission. Although his study is not yet complete, Terman thinks it may be possible to enhance the efficacy of treatment by increasing the amount of time patients are exposed to light or by increasing the intensity of the light, say to 10,000 lux. Certainly such levels would more closely approximate sunlight, which ranges from 10,000 lux on a cloudy day in northern Europe to 80,000 lux on a sunny day close to the Equator. Other investigators, however, propose that it is the duration of phototherapy, rather than its timing, that is important in treating SAD. In any case it is now clear that the light must be at least 2,500 lux; customary indoor lights (which range in intensity from 250 to 500 lux) suppress neither the symptoms of SAD nor melatonin synthesis.

Researchers find that light administered in the morning is more effective than light administered later in the day. That finding has been interpreted by Lewy, Terman and others as an indication that light advances a person's circadian rhythm and shortens the dark phase of melatonin secretion. Terman and his associates have noted that the decline in plasma melatonin, which normally occurs early in the morning, is delayed in SAD patients by about two hours. Perhaps high-intensity light induces clinical remission when it is administered in the morning by shortening the daily period of melatonin secretion by several hours.

Is SAD caused by melatonin—either too much of it or when it is secreted for too long? Or is melatonin simply a convenient indicator for another process that underlies the disease? At the moment we cannot answer that ques-



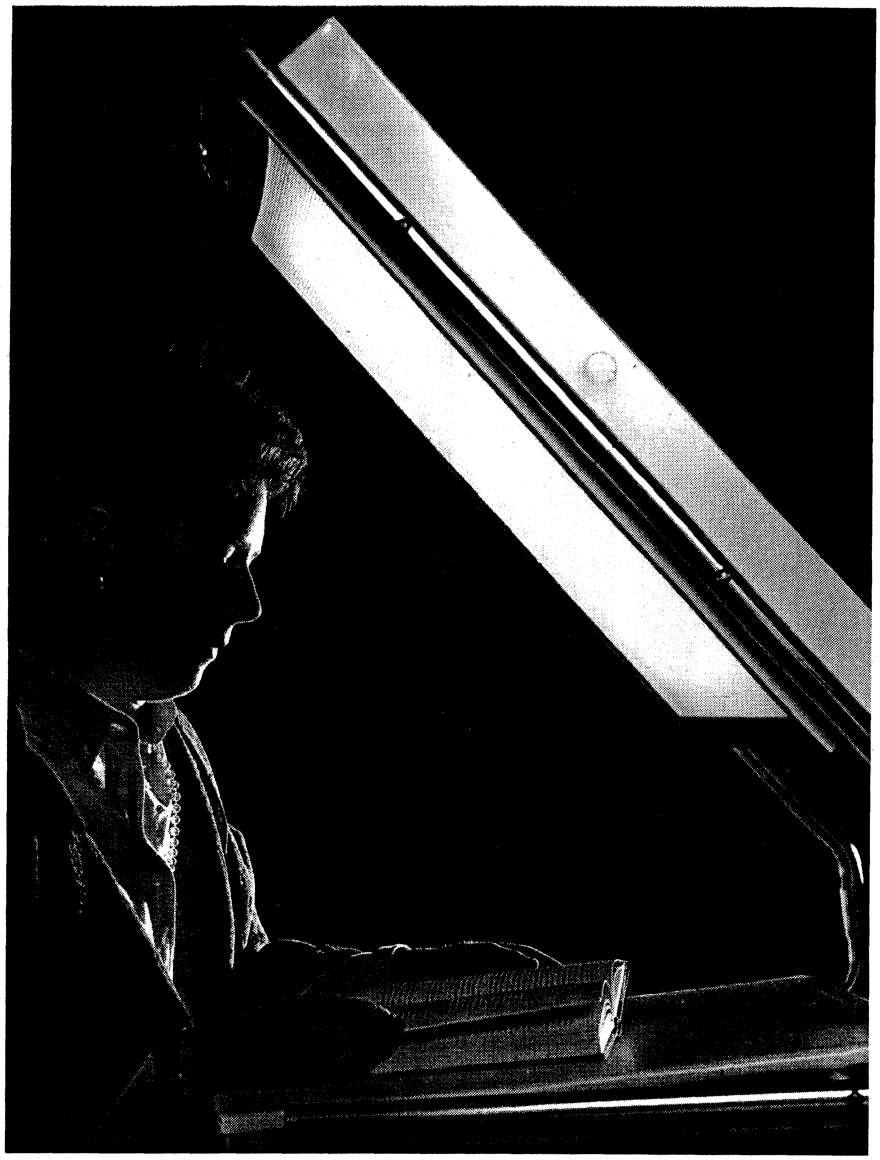
SEASONAL FLUCTUATIONS in mood are common among people in New York City (and in other northern areas) but are severest in patients diagnosed with SAD. The data are from a study by Michael Terman of the New York State Psychiatric Institute.

tion, but circumstantial evidence does suggest a direct link between melatonin and SAD. Lieberman, Lynch and one of us (Richard Wurtman) found that the administration of rather large doses of melatonin to normal individuals induces sleepiness, decreases alertness and slows reaction time. Perhaps the onset of melatonin secretion in the evening is an important promoter of sleep, sensitizing the brain to other sleep-inducing factors. That may explain why SAD patients are hypersomnic in winter, when the daily dark period is almost twice as long as it is in spring. A link between melatonin and mood is also suggested by the ability of oral melatonin to worsen a patient's depression; unfortunately no drug has been developed that selectively blocks melatonin's production or its actions.

But why do patients with SAD, CCO and PMS have a tendency to crave carbohydrate snacks? Why is it that only some people are vulnerable to CCO? And how is it that the brain normally knows when carbohydrates have been or should be consumed? Inhabitants of developed countries habitually eat from 12 to 14 percent of their calories in the form of protein and about three or four times as much in the form of carbohydrates. Even a bear will eventually forsake honey for an occasional fish. How is such a phenomenon regulated? We now know that the answer to these questions involves serotonin, one of the neurotransmitters: substances that are released from a neuron when it fires and that convey the nerve impulse across the synapse to the next neuron.

Serotonin is a derivative of tryptophan, an amino acid that is normally present at low levels in the bloodstream. The rate of conversion is affected by the proportion of carbohydrates in a person's diet: carbohydrates stimulate the secretion of insulin, which facilitates the uptake of most amino acids into peripheral tissues, such as muscle. Blood tryptophan levels, however, are unaffected by insulin and so the proportion of tryptophan in the blood relative to the other amino acids increases when carbohydrates are consumed. Since tryptophan competes with other amino acids for transport across the blood-brain barrier, insulin secretion speeds its entry into the central nervous system, where it enters, among other cells, a special cluster of neurons known as the raphe nuclei. There it is converted into serotonin.

The level of serotonin in turn figures in a feedback mechanism affecting the amount of carbohydrate an individual subsequently chooses to eat [see "Nutrients That Modify Brain Function," by Richard J. Wurtman; SCIENTIFIC AMERICAN, April, 1982]. When the feedback mechanism is disturbed, as we believe happens cyclically in patients with SAD, CCO and PMS, the brain fails to respond when carbohydrates are eaten, and so the desire for them persists longer than it should.



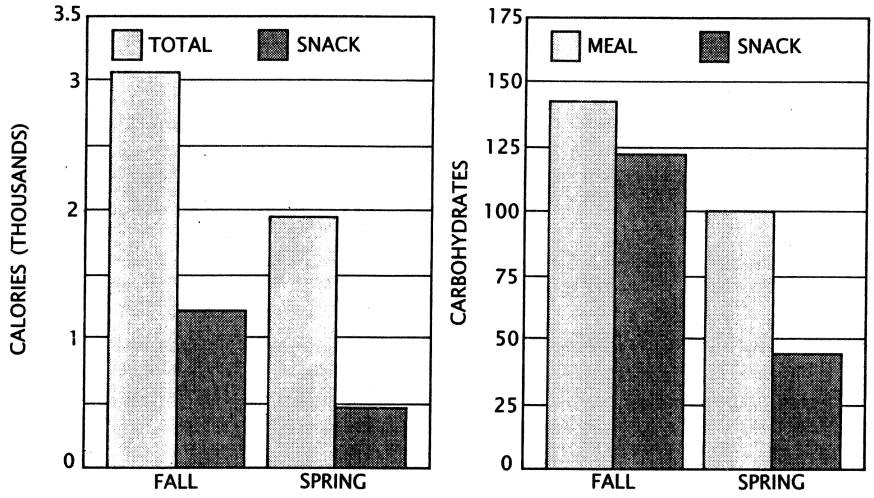
PHOTOTHERAPY is effective in relieving the depression and carbohydrate craving associated with SAD. Patients who are exposed in the morning to between 45 and 60 minutes of high-intensity light improve after only two or three days of treatment.

Serotonin regulates other behaviors too, including mood and sleepiness. Bonnie Spring, now at the University of Health Sciences/Chicago Medical School, found that noncarbohydrate-craving women become sleepy and prone to committing errors following the consumption of a high-carbohydrate lunch (which is expected to increase brain serotonin levels). Similar responses among noncarbohydrate-craving obese individuals were noted by Lieberman and one of us (Judith Wurtman). In contrast, carbohydrate cravers reported feeling refreshed and invigorated after eating a meal rich in carbohydrates.

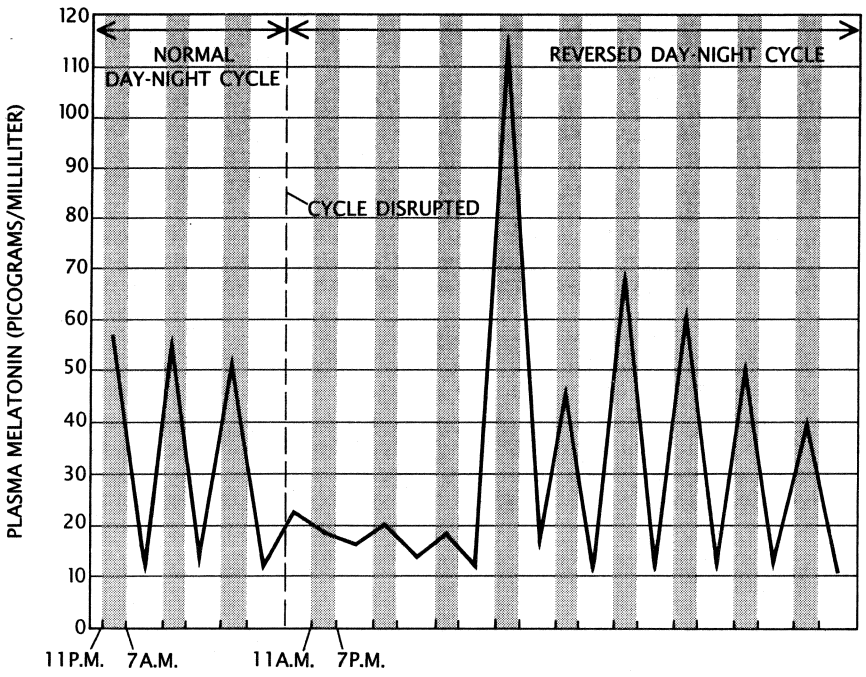
The mechanisms affecting the relative proportions of carbohydrate and protein in one's diet are most apparent when feedback loops are disrupted, as they are when a patient is given drugs that affect serotonin-mediated neurotransmission. Rats that are allowed to choose between two or more synthetic foods containing different proportions of carbohydrate and protein will normal-

ly alternate between them. If, however, the rats are either injected directly with serotonin (into the brain) or given drugs that enhance the effect of serotonin by promoting its release into nerve synapses, prolonging its activity or stimulating its receptors, then carbohydrate intake in experimental rats is selectively reduced.

Drug trials carried out on humans show that a serotoninlike drug, *d*-fenfluramine (which releases serotonin into brain synapses and then prolongs its action by blocking its reuptake into the presynaptic neuron), has a similar effect, selectively suppressing carbohydrate snacking in patients affected by CCO. We also found, while collaborating with Dermot A. O'Rourke, a psychiatrist at the Massachusetts General Hospital, that *d*-fenfluramine can also be effective in treating SAD: it reduces carbohydrate snacking (and its associated weight gain) while simultaneously ameliorating the symptoms of depression. More recently, with Amnon Brzezinski of the Hebrew University-Hadassah Medical School in Jerusalem, we found that *d*-fenfluramine may also be effective in treating similar symptoms in patients with PMS. In 12 of 17 individuals studied, administration of the drug over a six-month period led to a reduction in both carbohydrate craving and depression.



PROPORTION OF CALORIES AND CARBOHYDRATES consumed in the form of snacks by SAD patients varies enormously depending on the season. In the fall patients consume more than 3,000 calories per day, of which about 1,200 are from snacks; in the spring their total caloric intake falls below 2,000, of which fewer than 500 come from snacks (*left*). A similar pattern is apparent for carbohydrate consumption. In the fall almost 50 percent of the carbohydrates eaten per day are in the form of snacks; in the spring the proportion drops to roughly 30 percent (*right*).



MELATONIN SECRETION follows a daily rhythm in humans, as it does in other mammals. During the day (*white columns*) secretion of the hormone from the pineal gland is suppressed and levels of melatonin in the plasma are low. At night (*dark columns*) melatonin is released from the pineal gland and its levels in the plasma are high. If the daily light cycle is abruptly shifted by 12 hours so that the dark period runs from 11:00 A.M. to 7:00 P.M. (instead of 11:00 P.M. to 7:00 A.M.), several days are needed before the new cycle of melatonin secretion reentrains (adjusts) to the new photoperiod. Once adjusted, melatonin secretion again follows a rhythmic pattern.

Another disorder, which we think may be linked to serotonin (and thus to SAD, CCO and PMS), is a form of bulimia that is associated with severe binging, often on carbohydrate-rich foods, but with little or no vomiting. Most such patients are mildly obese women; many are severely depressed and come from families with histories of depression and alcohol abuse. Preliminary studies by G. F. M. Russell of the University of London and Arthur G. A. Blouin of the University of Ottawa suggest that *d*-fenfluramine can be effective in treating such women; those that respond to the antidepressant effects of the drug are most likely to benefit from its effects on appetite suppression.

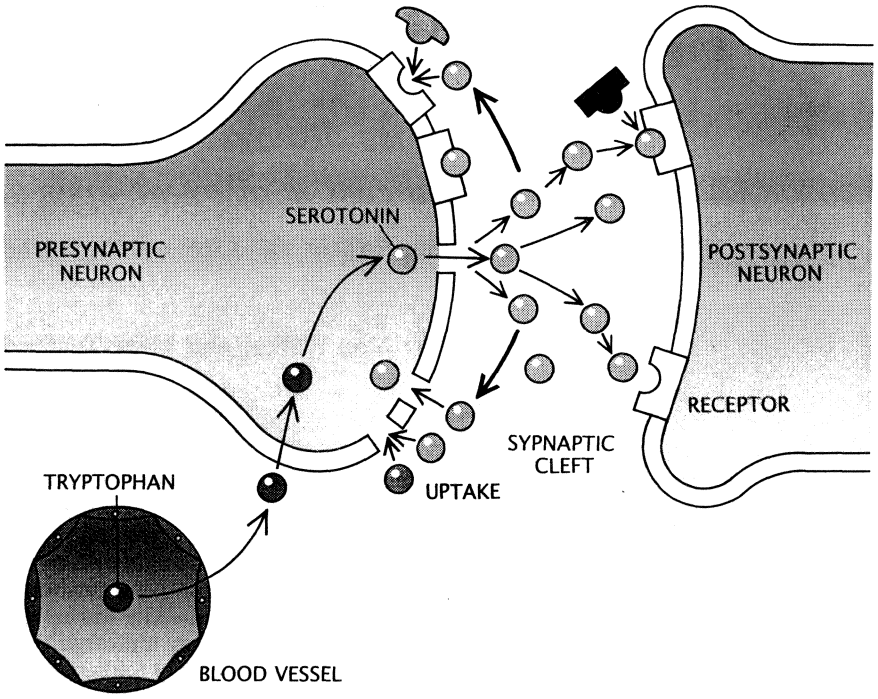
In general we have found that drugs that selectively facilitate serotonin-mediated neurotransmission (such as *d*-fenfluramine, femoxetine, fluoxetine, zymelidine and fluvoxamine) tend to cause weight loss, whereas drugs that block serotonin-mediated transmission or antidepressants that interact with neurotransmitters other than serotonin have the opposite effect: they often induce carbohydrate craving and subsequent weight gain.

No one could reasonably claim that the symptoms of SAD, CCO or PMS are inconsequential. Prolonged periods of deep depression and irritability can sorely compromise a person's ability to sustain essential human relations. But surely it is not abnormal to feel one's spirits flagging in the fall, to sometimes crave chocolate or pasta, to put on a few pounds every winter or to feel grumpy when beset by menstrual cramps.

Indeed, seasonal changes in behavior afflict normal people as well as those with SAD. Among 200 subjects

chosen at random from the New York City telephone directory and surveyed by Terman and his associates, half said they are less energetic in the fall and winter. Forty-seven percent said they gained weight during those months, 31 percent said they slept more and 31 percent said they were not as interested in social activities. Among respondents who reported a decline in energy at some time during the year, about 50 percent said their slump occurs in the fall and winter; only 12 percent said it occurs in summer. Terman concluded that a significant percentage of New York's population suffers from a mild form of SAD; we suspect that the inhabitants of other northern cities, such as Boston or Minneapolis, are similarly affected.

In Tromsø, Norway, which at a latitude of 69 degrees does not see the sun rise above the horizon between November 20 and January 20, midwinter insomnia is thought to affect 24 percent of the population. Charles S. Mullin, Jr., of the U.S. Naval Academy has described widespread sleeplessness, depression, irritability, impaired cognition and the gain of as much as from 20 to 30 pounds among scientists and military personnel who overwinter in Antarctica. The fact that SAD reaches its peak incidence in the Southern Hemisphere in June and July, incidentally, indicates that it is not simply a form of holiday blues or the result of melancholy reflections occasioned by the ending of another year.



SEROTONIN regulates carbohydrate consumption. The process begins with the amino acid tryptophan (*orange*), which circulates through the blood to the brain, where it enters the raphe nuclei. After entering a presynaptic neuron, tryptophan is converted by way of a two-step process into serotonin (*yellow*). Serotonin is then released into the synaptic cleft separating the presynaptic neuron from the postsynaptic neuron. Serotonin that reaches the postsynaptic neuron binds to special receptors. Serotonin levels rise in response to carbohydrate consumption. As more serotonin is released, more information is thus transferred to the postsynaptic neuron, where it activates a feedback mechanism. When its concentration is high, serotonin binds to presynaptic receptors, thereby suppressing the release of additional serotonin from the presynaptic neuron. It can also be rapidly removed from the synapse by uptake into the presynaptic neuron. Drugs that enhance serotonin's release (*green*) or that block its reuptake (*blue*) increase information transfer across the synapse and diminish carbohydrate snacking; drugs that block postsynaptic serotonin receptors (*red*) increase appetite, particularly for carbohydrates.

Is SAD, then, merely an exaggeration of the normal human response to diminishing light levels in fall and winter? Is it perhaps analogous to hibernation? Probably not. Hibernating animals characteristically lower their body temperature, cease reproductive activity and spend the winter in deep sleep. People with SAD do none of those things; if anything, the time they spend in deep sleep (measured by electroencephalogram) is reduced.

Perhaps contemporary lifestyles increase vulnerability to seasonal depression by diminishing the amount of time we expose ourselves to light: Daniel Kripke and his fellow workers measured the amount of time per day that healthy elderly subjects in San Diego—a region of particularly favorable climate—were exposed to sunlight. Surprisingly, the men were in sunlight for only 75 minutes out of each 24-hour period, the women for only 20 minutes. We need not all live in California, but perhaps most of us need to be exposed to more light, as our ancestors were. Perhaps much as office workers join health clubs to compensate for the lack of exercise, people with indoor jobs need to arrange for adequate exposure to light.

Much remains to be learned about mood and appetite disorders and about the link between serotonin and melatonin. Why does a SAD patient, for example, respond equally well to supplemental lighting, which presumably acts by affecting melatonin, and to drugs that stimulate the release of serotonin? And where might those treatments act in the sequence of pathophysiologic processes leading to SAD? Before we can answer those two questions, it would help to know whether or not light or melatonin has a direct effect on serotonin-releasing neurons. Until we have better answers, we can at least be grateful for the fact that these disorders respond to novel and effective therapies—even if the mechanisms by which the therapies work remain a mystery.

FURTHER READING

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