Flushing out the mechanism of hot flashes

Hot flashes plague many women undergoing menopause, sometimes striking as often as once an hour and leaving the women soaked in sweat. Though scientists know very little about what causes these unpleasant internal heat waves, a new study strengthens the case implicating certain neurons within the brain's temperature-regulating center.

Researchers have suspected that the body thermostat of women who suffer from hot flashes somehow goes awry once the ovaries cease making the female sex hormone estrogen. They reason that a loss of estrogen might somehow cause certain neurons in the temperature-regulating hypothalamus to fire abnormally, releasing norepinephrine – a neurotransmitter believed to affect the body's temperature sensor.

Data indicate that norepinephrine elevations may create the illusion that the body had overheated, and trigger a variety of heat-loss strategies. Despite a normal body temperature, affected women might undergo a temporary flush and rush of heat as blood vessels near the skin surface dilated.

Robert R. Freedman at Wayne State University School of Medicine in Detroit and his colleagues decided to test that theory using certain drugs that manipulate the suspect neurons. They recruited 15 postmenopausal women, aged 43 to 63; six had never experienced a hot flash, nine others reported a mean of 10 a day.

To objectively measure hot flashes, the researchers wired their volunteers with electrodes hooked up to a computer system that recorded an electrical measure of sweating. Then the volunteers received a slow-drip intravenous infusion of saline from a hidden bottle. Varying doses of yohimbine, an experimental drug that boosts norepinephrine levels in the rat hypothalamus, were added to some of these infusions, but participants did not know when.

The computer recorded six flushes among the hot-flash-prone women during their yohimbine infusions. These same women developed no attacks during saline-only infusion, the researchers report in the October Obstetrics and Gynecology. Previously asymptomatic women remained flush free after both the yohimbine and saline-only treatments.

Next, Freedman's team followed the lead of other researchers who had shown that clonidine, a common high-blood-pressure drug, reduced hot flashes in some women. Here, the researchers infused the same nine hot-flash-prone volunteers with either saline or a saline-and-clonidine drip infusion. After an hour, the team placed hot water pads on each subject's upper body, a procedure that reliably induces hot flashes.

The Michigan researchers found clonidine indeed decreased the number of hot flashes experienced among these women – from eight during the saline-only infusion to just two among women receiving clonidine treatment.

These findings suggest yohimbine triggers hot flashes among susceptible women by spurring neurons in the hypothalamus to release norepinephrine, Freedman says. He now suspects clonidine may block those hot flashes by reducing norepinephrine overloads.

However, evidence on clonidine's therapeutic potential appears far from conclusive, according to Peter Lomax at the University of California, Los Angeles. Other teams using clonidine have failed to reduce hot flashes among postmenopausal women, he notes. Moreover, he points out that clonidine's blood-pressure-lowering side effect would preclude its use in many women.

Freedman and Lomax do agree, however, on both the value of research into the mechanisms underlying hot flashes, and the need for new and better hot-flash blockers. Hot flashes are not trivial, but "a real problem," Lomax says. In severe cases, he notes, 10-minute-long, heart-pounding, sweat-drenching episodes can not only embarrass professional women and homemakers alike, but also interfere with their ability to perform certain critical tasks – from driving to surgery.

– K.A. Fackelmann

Cry-babies demonstrate 'sweet' dispositions

A spoonful of sugar helps the medicine go down, but only a few drops of sugar-sweetened water quell the crying of newborn babies longer and more effectively than a pacifier does, a new study reports. Its authors found a small dose of sugar water also reduces crying and apparently eases pain among newborns undergoing medical procedures, such as blood collection and circumcision.

"You can't help but be struck by the power of the babies' reactions to such a small amount of sugar," says psychologist and study director Elliott M. Blass of Cornell University in Ithaca, N.Y.

Blass and colleagues Barbara A. Smith and Thomas J. Fillion, both of Johns Hopkins University in Baltimore, studied healthy 1- to 3-day-old infants in a quiet hospital-nursery room. Crying – encompassing the spectrum from full-throated cries to whimpers – first was monitored for 5 minutes among 16 babies. The infants cried for an average of 2 minutes. Then the researchers orally administered 0.1 milliliters (about the size of a teardrop) of either a 14 percent sucrose solution or sterilized water to the babies through the tip of a syringe, once a minute for 5 minutes.

The sucrose solution virtually eliminated crying while it was administered and for 5 minutes afterward, the researchers report in the September Developmental Psychology. Water failed to reduce crying.

In a second study, groups of eight infants received the same dose of 14 percent sucrose solution, once a minute, for 2, 6, or 10 minutes. Additional groups received a pacifier gently held in their mouths for 2, 6, 10, or 14 minutes.

Again, the sugar solution nearly eliminated crying, even in the 2-minute group, and its effect lasted for 5 minutes after the test ended. Pacifiers reduced crying to a lesser degree, and crying resumed within 1 or 2 minutes of pacifier removal.

A third study found that infants who ingested a sucrose solution through a pacifier cried far less than those who sucked a pacifier that delivered water.

And in a report that will soon appear in Pediatrics, Blass and a co-worker report substantial reductions in crying during and following a standard blood-collection technique (which involves pricking the heel) and circumcision. The 2- to 3-day-olds in this study received 2 milliliters of 14 percent sucrose solution orally just before the procedures.

"Babies given sucrose still cried, but they cried about half as much as those given unsweetened water," Blass notes.

Sucrose's sweet taste, independent of the introduction of a chewable plastic syringe or pacifier, calms newborns, he asserts. Combined with previous animal studies, the data suggest that sucrose-induced calming reflects activation of natural opioids in the brain, Blass maintains. For example, both morphine and sucrose infusions increase pain thresholds and reduce distress cries in 10-day-old rats; naltrexone, a substance that blocks opioid receptors and thus interferes with morphine's effects, similarly suppresses sucrose's ability to soothe.

To further explore the opioid theory, Blass and his associates plan to conduct sucrose experiments with newborn babies of heroin-addicted mothers. If the theory holds up, these opioid-tolerant infants should prove less susceptible to sucrose-induced calming than non-addicted infants.

However, while the physiological mechanisms behind a pacifier's calming effect remain unclear, Blass expects pacifiers should work just as well with addicted and non-addicted newborns.

These findings are still too preliminary to suggest whether a few drops of sugar water might help frazzled parents calm a squalling baby, Blass says. However, he and Cornell colleagues plan to study the reactions of irritable babies given a few drops of sucrose solution. *– B. Bower*