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Fruits of Their Labour

Mothers who consume more fruit while pregnant may give their babies a brain boost

If a woman you know announces she's expecting, skip the cards and flowers—send her a fruit basket instead. If she eats enough apples, berries and bananas, she just may give her baby a head start in early brain development.

It may sound unlikely, but AllerGen researcher Dr. Piush Mandhane, an associate professor of pediatrics at the University of Alberta, has uncovered a link between a mother's fruit consumption during pregnancy and her baby's developmental test scores at one year of age.

Dr. Piush Mandhane, Associate Professor
University of Alberta

Dr. Mandhane made the discovery after analyzing data from AllerGen's CHILD Study (CHILD). CHILD is a national birth cohort study, with sites in Edmonton, Vancouver, Toronto and Manitoba, that is following 3,500 Canadian infants and their families to understand how early life experiences shape health and well-being in childhood. Dr. Mandhane leads the Edmonton study site.

For his research, Dr. Mandhane focused on a subset of nearly 700 mothers and children involved in CHILD, and analyzed the data after the children underwent a cognitive test at one year of age.

What he found took him by surprise: babies born to mothers who consumed six or more servings of fruit per day during pregnancy scored six or seven points higher on an infant development scale at age one compared to babies whose mothers ate less than one serving of fruit. "I wasn't looking for it, I wasn't expecting it, but I couldn't ignore it," Dr. Mandhane says. "The difference was significant."

Pregnant women are typically told what *not* to consume during pregnancy, with alcohol, caffeine and junk food topping the list. They're also advised to eat a balanced diet and ensure that they get enough of the nutrients (such as folic acid, iron and iodine) to support normal brain development.

Dr. Mandhane's research puts a new spin on nutrition during pregnancy. His results suggest that it's not just the nutrients that count, but their source. "Fruit juice did not have the same beneficial effect on infant development," he says, "nor did prenatal consumption of vegetables."

A sleepy start

When Dr. Mandhane designed his study, he didn't intend to look at fruit. "We wanted to learn how early childhood sleep duration and disruption affect an infant's cognitive development. Initially, I thought a mom's sleep pattern might have a bearing on her child's brain development and intellectual performance."

That's why he turned to CHILD: the study's database houses extensive information on each mother's prenatal habits and personal environment—her diet, medications, stress levels, and even the quantity and quality of her sleep.

The study children also complete the Bayley Scales of Infant Development (BSID III test), a standardized test of mental and motor development at age one. While not a true IQ test—one-year-olds are too young for that—the Bayley test takes inventory of things a young toddler can do, such as stacking blocks or finding hidden objects, says Dr. Mandhane.

A careful analysis of the data did not support Dr. Mandhane's hypothesis that a mother's sleep disruption affects her baby's brain development. But his research had also taken into account the mothers' eating habits—and that's when he uncovered the fruit effect.

"Each extra serving of fruit boosted the child's cognitive development, right up to six or seven servings a day," Dr. Mandhane says. Such a dose-response effect—the higher the dose, the greater the effect—is one of the hallmarks of a good study. "What surprised me most was the size of the effect —more than half a standard deviation, which is significant.

The gestational age of the child at birth also highlighted the effect: the earlier a child was born, the more obvious the fruit effect. In women who gave birth to preterm children, "having one extra serving of fruit per day gave the baby the same benefit as being born a whole week later," says Dr. Mandhane.

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When my data analyst showed me the figures, I couldn't believe it. I asked her to run the numbers again."

Digging deeper, Dr. Mandhane's team also looked into the specific nutrients the mothers had consumed. Two "stars" emerged: lycopene, a natural pigment that gives fruits and vegetables—such as tomatoes, grapefruit and watermelon—a red color, and fructose, the natural sugar found in most fruit and vegetables. The gestational age of the child at birth also highlighted the effect: the earlier a child was born, the more obvious the fruit effect. In women who gave birth to preterm children, "having one extra serving of fruit per day gave the baby the same benefit as being born a whole week later," says Dr. Mandhane. "That's a meaningful advantage."

But what if the women who consumed more fruit took better overall care of themselves than the fruit avoiders, and that's why their babies did better? Fortunately, Dr. Mandhane's study accounted for such differences. He also teased out other variables that could have skewed the results, such as family income and education. The fruit effect persisted. Still, Dr. Mandhane wasn't fully satisfied. "I kept wondering if we had missed a confounding factor that could explain the effect."

Fly guy adds to the buzz

In search of answers, Dr. Mandhane teamed up with pediatric neurologist Dr. François Bolduc, also an associate professor at the University of Alberta. A specialist in how genes affect the memory and mental ability of both humans and fruit flies, Dr. Bolduc has been dubbed the "fly guy" because of the more than 300,000 fruit flies he keeps in his university lab.

Familiar to most of us as household pests circling over bruised bananas, fruit flies have a surprising capacity to learn. More than that, says Dr. Bolduc, "they have 85% of the genes involved in human brain function, which makes them a great model for studying our own learning and memory."

Would Dr. Mandhane's fruit effect hold up in fruit flies as well? To find out, Dr. Bolduc enhanced the diet of a group of pregnant fruit flies with a combination of orange and tomato juices. He then exposed their offspring to two different odours, one of them accompanied by a mild electric shock.

Two minutes later, he presented the young flies with the same odours and counted the proportion of those that steered clear of the scent associated with a shock—a measure of their ability to learn from experience. To test the flies' longer-term memory, he repeated the exercise a day later—a rather long stretch in the month-long life of a fruit fly.

The results echoed Dr. Mandhane's observations in humans: offspring of the flies who consumed a fruit-enhanced diet scored 30% higher on learning and more than twice as high on long-term memory tests than offspring of those fed a standard diet.

Dr. Bolduc repeated the experiment several times, each time with similar results. He also experimented with feeding fruit

juice directly to young flies after birth rather than to their pregnant mothers, "but this didn't improve their learning," he says. "It looks like the juice is doing something prenatally to enhance brain development."

What happens next

EBioMedicine published the Mandhane/Bolduc study in May 2016. The news circled the globe and propelled Dr. Mandhane into the media spotlight, an outcome he credits largely to AllerGen. "Without AllerGen, CHILD wouldn't exist, and without CHILD, my own study would not have been possible," he says simply. CHILD has expanded its research scope well beyond its original thrusts of asthma and allergy, and "the data can be used to explore many other questions, as my study has shown."

At the same time, Dr. Mandhane cautions against "over-interpreting" his findings. First, he must address a burning question: Does the fruit effect persist as the children get older? To find out, he plans to re-run his analysis using the children's cognitive test scores at ages two, three and beyond.

"At age three, we can test higher cognitive functions like planning and multitasking," he says. If prenatal fruit boosts these functions, "there may be a real benefit to promoting greater fruit intake during pregnancy, particularly if we can improve outcomes for premature babies, who are at higher risk of intellectual delays," he explains. "Going from an IQ of 100 to 105 may not make a significant difference in a child's life, but moving from 85 to 90 certainly can."

He and Dr. Bolduc aren't finished working with fruit flies, either. They would like to understand, at the biochemical level, how and why prenatal fruit gives such an advantage to offspring. Perhaps something in the fruit boosts the growth of the brain's neurons? Or perhaps the fruit switches on key developmental genes through an epigenetic effect? Identifying the stages of pregnancy when fruit intake has the most influence is also on the researchers' to-do list. "When we know more, we may be able to develop targeted therapies that turn on the same pathways that the fruit is turning on," Dr. Mandhane says.

In the meantime, he cautions pregnant women against going overboard on fruit—especially if it leads them to gain excess weight, which could increase the risk of gestational diabetes. Instead, Dr. Mandhane suggests they turn to Canada's Food Guide, choosing whole foods over processed ones whenever possible. "Whole foods provide an array of important nutrients, some of which we may not even know about," he says. "It may take a little more time to peel an orange, but it's definitely worth it."