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Low production of serotonin in the brainstem a likely cause for SIDS

Doctors closing in on mysterious cause of death in infants

Boston, Mass. – Taking the next step in more than 20 years of research, researchers at Children's Hospital Boston have linked sudden infant death syndrome (SIDS) with low production of serotonin in the brainstem, based on a comparison of brainstem samples from infants dying of SIDS compared to brainstems of infants dying from other, known causes.

The findings, published in the Feb. 3 issue of *The Journal of the American Medical Association*, may give a concrete approach to identifying babies at risk for SIDS, the leading cause of death for infants between 1 and 12 months old in the United States.

In the brainstem, serotonin helps regulate some of the body's involuntary actions, such as breathing, heart rate and blood pressure during sleep. The researchers, led by Children's neuropathologist Hannah Kinney, MD, believe that a low serotonin level impairs the function of the brainstem circuits that regulate these activities, putting a baby at risk for sudden death from stresses such as rebreathing carbon dioxide when sleeping in the face down position.

The future goal of this work is to devise a test to identify infants with a serotonin brainstem defect early, and to develop preventive treatments that would correct the serotonin deficiency.

In 2006, Kinney and colleagues showed that SIDS is associated with abnormalities in the number of cells and receptors related to serotonin in the brainstem, but it wasn't clear whether SIDS may be caused by overproduction or underproduction of the chemical.

In the new study, the team measured the levels of serotonin and tryptophan hydroxylase, the enzyme that helps make serotonin, in 36 infants dying from SIDS and two control groups (5 infants dying acutely from other causes, and 5 hospitalized infants with chronic hypoxia-ischemia (insufficient oxygen supply to tissues)). Tissue samples from the brainstem were obtained from autopsies and provided by research partners at the San Diego County Medical Examiner's Office in California.

Compared with controls, the serotonin levels in the lower brainstem were 26 percent lower in the SIDS cases compared to controls, while the tryptophan hydroxylase levels

were 22 percent lower. Levels of binding to serotonin receptors were also lower by more than 50 percent. The consistency and correlation of these findings with each other reinforce the idea that SIDS in the majority of cases is a disorder of serotonin in the brainstem, the researchers say.

“The baby looks normal during the day; there’s nothing that would tell you that baby is going to die of SIDS that night,” says Kinney, who has studied SIDS for more than 20 years. “There’s something about sleep that unmasks the defect, which we believe is in serotonin circuits: the baby experiences some kind of stress during sleep, such as rebreathing carbon dioxide in the face-down position or increased temperature from over-bundling, that cannot be compensated for by the defective brainstem circuits, and the baby then goes on to die.”

In a normal baby rebreathing carbon dioxide, serotonin pathways in the brainstem would stir the baby awake long enough to turn its head, allowing it to breathe fresh air, Kinney adds. A baby with low serotonin levels in the brainstem may never stir.

SIDS has puzzled doctors and families for decades, but once the medical community recognized that a baby’s position while sleeping affects the risk for SIDS, national awareness campaigns sprouted to persuade parents to place babies to sleep on their backs. However, such campaigns haven’t completely solved the problem, prompting ongoing research to find a biological component to SIDS.

While this study provides strong evidence for a biological cause of SIDS, it also shows that other risk factors, such as sleeping on one’s stomach, can aggravate the risk. Of the SIDS infants in the current study, 95 percent died with at least one risk factor, and 88 percent died with at least two.

The next step in this research is to find out what causes abnormally low serotonin levels in the first place. Genetic variations may be partly responsible, says neuroscientist David Paterson, PhD, in Kinney’s lab, a contributing author of the paper. Kinney’s lab is searching for such variations.

In the meantime, parents should remove unnecessary SIDS risk factors, Kinney says. During pregnancy, there is no safe level of alcohol a mother can drink and no safe level of smoking, both firsthand and secondhand. Until 12 months of age, babies should sleep on their backs in a crib with a firm mattress, and without toys, soft pillows, excessive blanketing or excessive clothing.

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MD, Elisabeth A. Haas, BA, Christina Stanley, MD, Eugene E. Nattie, MD, Felicia L. Trachtenberg, PhD, Hannah C. Kinney, MD. Brainstem serotonergic deficiency in Sudden Infant Death Syndrome. *JAMA* Feb. 3, 2010, Vol. 303, No. 5.

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