NEUROSCIENCE

Prenatal and Infant Exposure to an Environmental Pollutant Damages Brain Architecture and Plasticity

A review of a recent study examining the subtle, yet serious long-term effects of prenatal exposure to PCBs.

Why was the study done? The architecture of the developing brain is shaped over time by the interactions of a child with the environment. Normal experiences, like seeing or hearing, stimulate patterns of nerve cell activity that determine which interconnections -- called synapses -- are formed in the brain. The developing brain is thus highly sensitive to both positive and negative environmental influences that can strengthen or weaken the final architecture of brain circuits. The exposure of children to industrial chemicals and heavy metals, such as lead, threatens the formation of healthy brain architecture. To date, most research studies in animals have examined the most severe impact of pre- and postnatal exposure to chemicals on brain architecture that may result in gross behavioral disruption. Typically, the absence of gross changes in either architecture or behavior is interpreted as a lack of impact on brain development. However, this interpretation does not recognize the full extent of the damage that is occurring. We know that many toxic chemicals can interfere with the naturally occurring brain chemicals that mediate learning from experiences. Neuronal communication at developing synapses is essential for the formation of precise brain architecture that controls such functions as vision, hearing, and touch. Abnormal sensory map formation can lead to significant learning problems, potentially affecting reading and other cognitive skills that are essential for success in school. With this in mind, these investigators performed studies on rats to determine whether exposing animals to a common chemical pollutant during pregnancy and nursing causes fundamental disruptions in brain architecture or function in developing rats.

What did the study find? We begin to hear sounds even in the womb, and the infant auditory system continues to require normal hearing experiences to form a precise architecture of nerve connections. The connections are imprecise early in development, but become more finely tuned with hearing experience. The ability to distinguish sounds at different frequencies, and to identify subtle differences in sounds that are essential for learning language and for developing reading skills, resides in the architecture of connections

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Suggested citation: National Scientific Council on the Developing Child, Science Briefs: *Prenatal and Infant Exposure to an Environmental Pollutant Damages Brain Architecture and Plasticity* (2007). Retrieved [date of retrieval] from http://www.developingchild.net.

SCIENCE BRIEFS summarize the findings and implications of a recent study in basic science or clinical resesarch. Studies are selected for review based on their scientific merit and contributions to understanding early development. No single study is definitive, of course. Understanding of early development is based on many studies that, taken together, permit broad conclusions and human applications. Generalizing to human children the results of studies with animals, for example, must be done cautiously and confirmed by research with children and their families. The National Scientific Council rests its work on a rigorous discussion of the validity of many studies like these conducted over many years and using different methodologies and samples.

in the auditory region of the cerebral cortex, where the final processing of complex sound information occurs. The final architecture of adult connections emerges over postnatal development in the rat much as it occurs in children. First, the authors showed that animals exposed to an environmental pollutant—non-coplanar bichlorinated biphenyls (PCBs)— during development exhibited normal sensitivities to different levels of sounds, from soft to loud. Second, the authors showed that PCB exposure resulted in grossly abnormal patterns of brain activity when stimulated by different, highly specific sound frequencies. There was little predictability to the disturbances, with some animals having synapses in the cerebral cortex that were responsive to only a few frequencies, some animals in which there were clusters of synapses that were completely unresponsive to sound, and some that were responsive but the organization of information was severely disrupted. The authors went on to show that the deleterious effects reside in the PCBs disrupting the normal balance between synapse excitation and inhibition in the auditory circuits. This balance is essential for activating the most powerful synapses when a specific sound frequency is applied, and at the same time, silencing those synapses that should not respond to that particular tone frequency. This balance controls how finely tuned and accurate the sensory map becomes over time. Finally, the synapses in animals exposed to PCBs were impaired in their ability to change their responses when exposed to new sound patterns. In contrast, synapses in normal animals can adapt to different patterns of sounds, a characteristic known as developmental plasticity that is related to learning. Thus, information was getting from the environment to the auditory cortex, but failed to produce a brain architecture that was able to handle the diversity of sounds that are normal for the animal.

How was the study conducted? Female laboratory rats were fed PCB-coated corn flakes during pregnancy and throughout the period of nursing, 21 days after birth. Control animals were fed corn flakes without the chemical toxin. The young adult offspring were placed in a sound-attenuation chamber in which tones at different frequencies and intensities were provided through speakers located on either side of the ears of each animal. Animals were deeply anesthetized and the physiological activity of synapses was recorded with an electrode placed in the auditory cortex. The responses to sounds at different intensities were noted at different places across the auditory cortex, essentially defining an architectural blueprint of connections. By moving the electrode systematically to different locations in the auditory cortex, the locations at which synapses were activated by tones of different frequencies were identified. The location of the best responses to a particular tone was noted on the blueprint of the auditory cortex. In this way, by the end of the experiment, the investigators were able to determine the details of the architecture of the auditory blueprint.

What do the findings mean? The authors found that PCB exposure does not cause gross changes to the developing brain, nor even impede the ability of the auditory system to hear sounds at different intensities. However, they show clearly that the ability to recognize sounds of different frequencies—an essential skill for making both gross and subtle distinctions between kinds of sounds (like 'pa' and 'ca')—is impaired. Moreover, they demonstrate that the ability of the developing auditory circuits to change is impaired, consistent with the idea that brain plasticity during sensitive periods of development is disrupted. The authors note that this is the key mechanism that the brain uses for learning new skills in all animal species and humans. Thus, the lack of gross changes in brain architecture should not be interpreted to mean that all is normal. More refined measurements are necessary to detect impairments in brain architecture and function that elude the current level of testing.

Title and Authors: Perinatal exposure to a noncoplanar bichlorinated biphenol alters tonotopy, receptive fields and plasticity in the auditory cortex. Proceedings of the National Academy of Science, USA 104:7646-7651. Kenet, T., Froemke, R.C., Schreiner, C.E., Pessah, I.N. and Merzenich, M.M.