NEUROSCIENCE

The Impact of Ultrasound on Developing Brain Neurons

A review of a recent study testing the effects of exposure of pregnant mothers to ultrasound waves on developing brain architecture.

Why was the study done? Many environmental factors can strengthen or weaken a child's developing brain architecture. A lot of attention has been paid to the weakening effects of chemical exposures, such as toxins, or even high levels of pre- or post-birth stressful conditions. Until this study, ultrasound waves have not been studied at all for their impact on brain development, even though their use has increased dramatically, particularly for medically non-indicated or commercial prenatal videos. The present study is the first to examine the potential impact of ultrasound waves, using an animal model, the mouse, which typically is used by neuroscientists to investigate the genetic and environmental influences that control the formation of brain architecture. The study was done to examine how ultrasound waves may impact the necessary contact that occurs between migrating neurons and their guide wires. This physical interaction allows the neurons to reach their final destination from their place of origin. The authors hypothesized that the ultrasound waves could distort the physical contact, thus causing the neurons to 'fall off' their guide wire tracks and stop their movement towards their final destination.

What did the study find? Exposure of pregnant mice to ultrasound waves similar to those used in humans resulted in a small but significant disruption of the movement of developing neurons from their place of origin to their final destination in the cerebral cortex. The cerebral cortex is a six-layered structure (where layer 6 is deep in the tissue and layer 1 is located along the brain surface) that is formed in an orderly fashion in mice and humans alike. Neurons destined for the deeper layers are produced and reach their final position before those located in layers closer to the surface. In this way, the neurons for the layers closer to the surface actually move over longer distances, past their older counterparts in the deep layers, to reach their final destination. It is important to emphasize that the layer in which the neurons end up in the cerebral cortex determines the types of connections they make with other neurons. These connections of the cerebral cortex are responsible for performing very complex functions, such as learning and memory, control of precise movement, speech and language, emotional regulation, and interpreting all the sensory information that comes from our surroundings. In this study, using the mouse model,

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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.**

the ultrasound exposure caused some of the neurons destined for layers closer to the surface to stop in the deeper layers, before reaching their final position. These misplaced neurons survive and may develop atypical connections because of their errant location. In the study, the longer the total amount of exposure to ultrasound waves, the greater the effect on dispersing the migrating neurons.

How was the study conducted? A special apparatus was designed and built that allowed the investigators to expose pregnant mice to ultrasound waves that were equivalent in energy intensity to the machines used in humans. There were differences, however, including a shorter distance between the source of the ultrasound waves and the fetuses in the pregnant mice, and the use of a restraint tube to hold the pregnant mouse during ultrasound wave exposure. The mice had full access to food and water during the exposure, and experiments were done to show that the restraint itself had no impact on the movement of neurons, other than for the most extreme time period. Exposures were done for six different durations: five minutes only (considered a very short, single exposure), or one, two, four, 14 or 28 individual sessions of 15 minutes each, with rest in between the sessions of multiple exposures. The impact of the ultrasound waves was tested on the movement of neurons in the cerebral cortex at the time that they were migrating along their guide wires toward the layers closest to the brain surface. The movement of the neurons was monitored by marking them with a special method at the time that they started on their journey, and then mapping the position of the neurons among the six layers of the cerebral cortex, well after they should have reached their final destination. The marking is permanent, so the mapping was done weeks after the animals were born. Some of the neurons marked before the ultrasound wave exposure ended up stopping in deeper layers (layers 5-6), rather than layers 2-3, where they should have ended their migration.

What do the findings mean? The map created in the study was used to calculate a 'dispersion index', meaning what fraction of neurons destined for the higher layers ended up lost in the deeper layers of the cortex. Normally, without ultrasound wave exposure, the index is about 2 percent, so there is very little error normally. At the extreme times of exposure, the dispersion was approximately 19 percent. Exposure times that were more like human conditions resulted in 9 percent dispersion. The error in terms of overall brain architecture does seem relatively small. However, the findings show that ultrasound waves can disrupt physical interactions between migrating neurons and their fiber guides. Human neurons migrate for much longer distances in the fetal brain compared to the mouse model used here. This means that the neurons take much longer (days to weeks) to get to their final destination, perhaps leaving them more vulnerable to possible disturbances by extreme, multiple exposures to ultrasound waves. Legitimate and well-controlled ultrasound can be a benefit for diagnosing potentially important medical conditions that may be amenable to interventions. However, the FDA in 2004 warned against excessive or medically non-relevant ultrasound wave exposures during pregnancy. While we do not know the functional implications of small amounts of neuron dispersions to the wrong layers of the cerebral cortex, the findings from this mouse model provide the first neuroscience-based justification for the FDA recommendations.

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