NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD
SCIENCE BRIEFS

NEUROSCIENCE

Maternal Hormones Prepare Fetuses for Stress of Delivery

A review of a recent study investigating the role of hormones produced by expecting mothers in protecting fetal brains from stress during delivery.

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Why was the study done? Delivery is a stressful event that can be associated with high risk to the fetal brain. With birth complications, there is increased risk to have a developmental disorder, for example. Even the risk for psychiatric disorders, which may not be diagnosed until adulthood, is dramatically increased with birth complications such as hypoxia or other accidents. There were two key issues addressed by the study. First, why are brain neurons so susceptible to the stresses of birth? The study shows that reduced oxygen levels at birth can do significant damage by causing brain neurons to become overexcited. This overactivity causes the neurons' cell membrane to become destabilized, like a wall that is stressed by an earthquake, which allows an excess of substances that had previously been kept out, like calcium, to seep or pour through the wall and poison the cell. Second, given that being overexcited is damaging to developing neurons, is there a way in which newborn brain cells are protected naturally from the stresses of birth? The scientists studied, in detail, the degree to which neurons before and just after birth were able to be excited, and whether the mother had any influence on this state of excitation.

What did the study find? The hormone oxytocin, which is normally produced at high levels by mothers to facilitate birth of the fetus, has a short but very powerful impact on the neurons in a fetus' brain just before birth, which may protect them from the stresses that can occur during delivery, such as accidental lack of oxygen (hypoxia). This study investigated how oxytocin from rat mothers can affect neuron excitability in their fetuses at birth, given that over-excitation of developing neurons makes them more susceptible to stressors. As expected, this study reproduced previous findings that the neurotransmitter known as GABA is excitatory prenatally, and during the first two postnatal weeks. Unexpectedly, however, GABA becomes inhibitory for a very brief period just before birth and through the day of birth, corresponding in time to the preparation for delivery by the mother. This switch from excitation to a brief, transient period of inhibition could be sped up in the womb by administering oxytocin to the mother and prevented by using a drug that blocks the actions of oxytocin in the fetal brain. Experiments introducing a lack of oxygen to the rat fetuses before birth caused neurons in the brain to show signs of injury, and blocking

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.

oxytocin activity caused the fetal neurons to show greater signs of injury. This is the first study to show that a maternal hormone thought only to be involved in preparation for birth by the mother also prepares the fetal brain for the potential complications and well-known stressors that arise during delivery.

How was the study conducted? Beginning a few days before birth and then every 12 hours through birth and up to four days after birth, the authors measured electrical activity in the part of the brain involved in memory and learning, the hippocampus, studying the activity of individual neurons as GABA was applied to the cell. The authors found that GABA excited, or *depolarized*, the hippocampal neurons a few days before birth and a few days after, as reported in other studies previously. By one day before delivery through the first 24 hours after delivery, GABA caused the neurons to become *hyperpolarized*. This means that the neuron is a state in which it cannot be readily excited. Remarkably, the peak of this switch from *depolarized* to *hyperpolarized* state occurs approximately one to two hours before delivery. If the neurons were removed from the fetal brain before the switch and grown in a culture dish, the cells never exhibited the switch. This suggested that some factor from the mother might be responsible for the switch. Oxytocin, a multifaceted brain hormone whose production by the mother increases dramatically around birth, is secreted into the blood, facilitating uterine contractions that are essential for the birth process. During delivery, oxytocin secreted by the mother can cross the placenta and enter into the fetus, including the fetal brain. To test the actions of oxytocin, the authors applied the hormone when the neurons are normally excited by GABA, and surprisingly, saw a dramatic switch to inhibition. Detailed studies of the physiology of the neurons showed that oxytocin changes the membrane properties of the cells to alter how much chloride and calcium flow into the cell when they are exposed to GABA. Giving the mother a drug that blocks the actions of oxytocin eliminated or significantly delayed the switch in the fetuses to GABA inhibition, which caused the fetal hippocampal neurons to show signs of damage sooner when exposed to a birth stressor, such as a lack of oxygen for a brief period of time.

What do the findings mean? These findings in rats demonstrate that the mother is involved in a previously unknown way in preparing the baby's brain for the stresses of the delivery process, which can include reduced oxygen for periods of time. The influence of the hormone oxytocin is substantial, and thus, fetal brain neurons can be more vulnerable to birth complications if the production of oxytocin by the mother is disrupted. Treatment of the mother with drugs that facilitate or block the actions of oxytocin not only will affect the birth process, but now we need to be aware that such treatments can positively or negatively impact the state

of excitability of neurons in the baby's brain. This study was done in an animal model, so we do need to determine when the actions of oxytocin are at their peak in human fetuses around birth. Given that birth complications are among the highest of risk factors for neurodevelopmental and psychiatric disorders, the study suggests that the maternal-fetal connection is an important one that can have long-term impacts on health outcomes.

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