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Fetal Consciousness' Impact on Equine Neonatal Health

Originally published on TheHorse.com

Somewhere between when the birthing process begins and when the long-legged foal takes his first wobbly steps, he transitions from an unconscious fetus to a conscious horse. And while owners might just be happy to see their new arrival waking up to the world, researchers now believe that the fetal consciousness transition could have a significant impact on neonatal health.

John Madigan, DVM, MS, Dipl. ACVIM, ACAW, professor in the Department of Medicine and Epidemiology at the University of California, Davis, School of Veterinary Medicine, presented a lecture entitled "Why Foals Don't Gallop *in Utero*: Studies in Transitions of Fetal Consciousness with Implications for Neonatal Health," at the 2013 American College of Veterinary Internal Medicine Forum, held June 12-15 in Seattle, Wash.

Background

For many years, Madigan said, veterinarians and researchers believed neonatal maladjustment syndrome (or NMS, also known as dummy foal syndrome) to be caused by pre-, intra-, or postnatal hypoxia (lack of oxygen). This oxygen deprivation results in neurologic deficits, behavioral abnormalities, and sometimes death.

Madigan said common clinical signs are consistent with brain hypoxia and include:

- Altered states of consciousness, ranging from mild mental deficits to coma;
- Abnormal behavior, including lack of affinity for the mare, not nursing, excessive vocalizations, and wandering;
- Blindness; and
- Paroxysmal (spasmodic or seizurelike) behaviors.

"Histopathologic (microscopic) evidence of cerebral hemorrhage and hypoxia has been detected in some severely affected foals in the mid-1970s," Madigan said. "However, many foals in recent studies do not have histological evidence of hypoxia, edema, or hemorrhage." Additionally, he noted, about 80% of foals with NMS fully recover, unlike hypoxic human infants who retain neurologic deficits.

These disparities prompted Madigan and colleagues to take a closer look at what else might cause NMS.

Recent Research

Madigan and colleagues began by looking at steroids with important neuromodulatory roles, called 5?-reduced pregnanes (such as progesterogen), which are often referred to as neurosteroids. He explained that foals are subjected to high levels of progestogens while in the dam's uterus; these steroids essentially keep the foal in a quiet state to prevent damage to the mare.

"Neonatal foals have high concentrations of pregnanes at birth, which begin to decrease rapidly within an hour of birth and continue to decline over the first 24-48 hours of life," Madigan said.

"Compared to healthy age-matched neonatal foals, NMS foals show significant ongoing elevation of plasma pregnant concentrations."

He noted that his team's research has shown that other ill neonatal foals with weakness and lethargy believed to be associated with conditions such as sepsis also have elevated plasma pregnane levels, although not has elevated as that of NMS foals.

Madigan and colleagues administered a pregnane called allopregnanolone to healthy equine neonates in the experimental setting to produce clinical signs consistent with NMS (e.g., the foals don't want to nurse, don't recognize the dam, etc.). These effects were short-lasting, and foals returned to normal after administration ceased, he said.

Madigan said that while the team administered allopregnanolone, Monica Aleman, DVM, PhD, Dipl. ACVIM, used an electroencephalogram to evaluate electrical impulses in the foals' brains. He said the readings were consistent with slow wave sleep while the foals were standing.

"These data suggest that these steroids can cross the blood-brain barrier and exert neuromodulatory effects, which at high concentrations may have a dampening effect in the central nervous system with resulting alterations in states of consciousness, altered behavior, and responsiveness to stimuli, such as observed in NMS cases," Madigan said.

Madigan hypothesized that a possible reason neurosteroids might persist and prompt NMS-like signs in some foals is that normal signaling events during the birthing process don't take place properly. For instance, he said, if a foal passes rapidly through the birth canal or is delivered via cesarean section, normal transition signals that prompt a reduction in fetal pregnane levels might not take place, leaving the foal with elevated neurosteroid levels.

"There must be a clear and reliable signal that it is safe for the foal to wake up, to transition the consciousness," Madigan said.

Another theory, he said, is that some neonates revert to fetal-like brain status in response to adverse effects after birth.

Possible Treatments

"Based on these findings, the concept of reducing post-birth circulating plasma pregnanes would seem to offer a potential new therapeutic option for NMS foals and perhaps other ill foals which appear weak and are not nursing," Madigan said. He noted future studies will evaluate this more closely.

Additionally, he said, his team is evaluating the possible use of a technique he and his colleagues developed called squeeze-induced somnolence, which is believed to mimic passage through the birth canal. Madigan said this method might signal to the foal that he is outside the uterus and that it's time for pregnane production to decrease, allowing him to stand, nurse, and run. Squeeze-induced somnolence involves applying pressure to the thoracic (chest) area in healthy foals to induce recumbency, non-rapid eye movement sleep, muscle relaxation, and increased β-endorphin levels. It does not appear to have any adverse effects.

During their studies the team noted a unique hormone surge after 20 minutes of squeezing, which is about the normal amount of time a foal is squeezed in the birth canal during a normal delivery, Madigan said. The internal signal for the foal to "wake up" involves the hypothalamic pituitary adrenal axis, which they believe down regulates the pregnane secretion so the foal can transition to birth consciousness.

Also during his presentation Madigan speculated that this new concept might have important human neonatal health implications. He said there have been several reports of premature human babies pronounced dead by doctors that begin breathing and awaken while being held and squeezed by their mothers. Madigan said this practice—termed "kangaroo care"—has been shown to arouse infants better than an incubator.

Take-Home Message

Madigan and colleagues are continuing research on the mechanisms behind NMS and possible treatments. A better understanding of this phenomenon could lead to rapid treatments in the field and less need for intensive care of the dummy or ill foal.