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UFRGS researchers find new way to treat event responsible for baby suffocation

Findings show a 50% reduction in injuries caused by neonatal hypoxia-ischemia, an event that causes damage to babies' nervous system cells. In the study, a residue produced by the body after physical activities known as lactate was used on the treatment. The research was chosen to be the cover of the Neuroscience journal

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A UFRGS research has shown that it is possible to reduce as per 50% the lesions caused by neonatal hypoxia-ischemia, an event characterized by baby suffocation usually caused by complications in pregnancy or childbirth. Neonatal hypoxia-ischemia causes damage to the cells of the baby's nervous system, which can provoke motor problems, cerebral palsy and even lead to death. Knowing how deadly such event can be, the researchers decided to test lactate as a treatment strategy for this perinatal accident. Lactate is also known as lactic acid, a residue produced in the muscles after physical activities and that usually causes discomfort. This substance, which used to be considered a mere metabolic residue that should be expelled by the human body, but new research tracks have pointed out to positive effects of it on the nervous system, which led to the idea of testing it in the case of neonatal hypoxia-ischemia. The study was published in [Neuroscience magazine, on the cover](#). The journal, maintained by International Brain Research Organization (IBRO), is a world reference of the Neurosciences area.

The hypoxic-ischemic phenomenon can be hard to diagnose, and its consequences can appear up to the age of 2 years old. Professor [Luciano Stürmer de Fraga](#), head UFRGS Physiology Department explains that hypoxia-ischemia does not necessarily have a main cause: there is a lack of gas exchange - and therefore oxygen - in the lungs, causing problems for the baby. "A common cause is nuchal cord, which is the wrapping of the umbilical cord around the baby's neck," he exemplifies. [Isadora Tassinari](#), researcher of the same research program, adds that these are events that can happen not only during childbirth, but also before and after it.

How the study was conducted

Isadora explains that, during the hypoxic-ischemic event, a reduction of oxygen and glucose reaching the nervous system is observed, shortening which puts the whole body at risk. These hypoxic-ischemic events kill nerve cells which will never regenerate again - hence the seriousness of the damage caused. In the research, scientists used lactate to reduce the extent of damage, simulating hypoxia-ischemia in an animal model, in seven-day-old mice. These rodents were chosen because they have a similar nervous system to the newborn baby human.

In order to submit the animals to the hypoxic-ischemic event, they had their right carotid artery (a blood vessel in the neck region that supplies the nervous system) obstructed. Then, they were exposed to an atmosphere with only 8% oxygen for an hour. Our goal was to actually cause an injury to the rodents' nervous system much alike the one caused in those babies. "We caused this injury in rats and then tested possible neuroprotective agents, so that they could reduce this injury," Luciano points out. Thirty minutes later, the rats were divided into two groups: one of them received an injection of lactate as a treatment; and the other was given nothing. The researchers then tested the behavior and reflex of the animals, since episodes of hypoxia-ischemia often cause motor damage - they checked, for example, whether the mice could move correctly, or stand in case they were turned upside down. After we calculated the amount of brain lesions, it was found that the group to which lactate was given had a lesion-reduction of almost 50% in the size when compared to the other group. Besides, the mice that received the injection showed less motor damage than the others. The researcher explains that although the functioning of lactate is clear, this model of study cannot describe how and with what mechanisms this substance acts. "The result was empirical: it is possible to observe motor improvements and the reduction of the lesion, but we do not know yet the limits of dosages or time to perform the injection other than the parameters adopted for this study," he says. Luciano adds that another similar research carried out in France has achieved similar results, even using different lactate dosages and different times, what seems to indicate safety in the use of the substance.

About neonatal hypoxia-ischemia

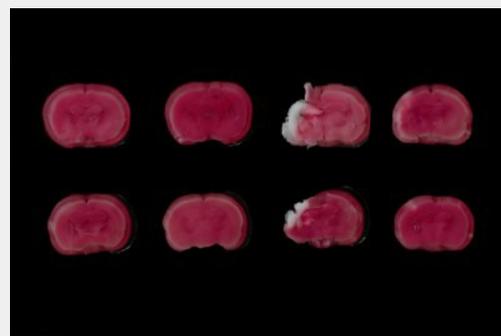
The Coordinator to the Graduate Program in Physiology states that the prevalence of hypoxia-ischemia is quite variable. Scientific articles published in the United States and in Europe indicate a number ranging from 1 to 8 cases for every thousand births, but Luciano points out that this rate can be much higher, according to the socioeconomic conditions of the country or the region analyzed. In Brazil, however, there is no centralized data on the disease. But it is a known event, although it is not easy to diagnose or obtain data on how common it is. The professor adds that, according to the World Health Organization (WHO), there is an average of 900 thousand to 1 million deaths each year due to the disease. "Hence the discussion around any therapy that reduces mortality by 1%, for example, means saving the lives of ten thousand children," Luciano points out. The study was part of Isadora's master's research, guided by Luciano and co-guided by [Ana Helena Paz](#), professor of the same program.

Scientists explain that the only treatment currently recommended by the WHO for this event is therapeutic hypothermia, which consists in cooling the child, either aided by mattresses and thermal pillows, or without equipment - with an ice bath - in order to decrease the metabolic activity of the baby and also to reduce its need for oxygen and energy. The problem is that few hospitals have the right equipment to initiate the treatment and there is a time-window of only 6 hours after the accident for intervention, after which the therapy can cause more damage than benefit. Luciano explains that there are hospitals, such as the Hospital de Clínicas de Porto Alegre (HCPA), that only submit patients to hypothermia when the hypoxia-ischemia occurred in the institution itself, during or after childbirth. Patients arriving from other hospitals by ambulance, since it is not possible to know exactly for how long they have been poorly oxygenating, cannot undergo neonatal hypothermia. Besides, the neuroscientist explains that this treatment is not highly effective.

Isadora says that the effects of lactate on the nervous system have been studied for about three decades, but under different parameters, such as in cases of head trauma, which have even reached clinical studies. "It was found that in fact it is an energy substrate and even some cells prefer lactate as 'food'," she explains. So basically, the idea is to supply the lacking-of-energy nervous system (as a result of asphyxiation and low oxygenation) with this natural metabolic residue of the human body in order to reduce the damage caused by the accident.

Scientists intend to test the substance in other ways before getting to clinical studies. They believe that one can still combine therapeutic hypothermia with lactate and test other dosages and observe other possible effects. "It was possible to notice that the animals experienced a discrete appetite loss on the days they took the injections, although we do not have statistical data for this, for example," says Isadora. "We wanted to study the effect of the substance on the brain, but we also observed general effects which can contribute to the protection of the nervous system, and which are not necessarily side effects," adds Luciano. Finally, the researcher says that she intends to follow up the study as for her PhD, seeking to explain how lactate acts precisely, in addition to observing the animals for longer periods. Furthermore, there is also the idea of working with cell cultures, studying how they react to lactate in isolation, in a cell culture of neurons and other nervous system cells.

Isadora says that, despite so many demotivating factors - research budget cuts and general devaluation of science -, the invitation to be on the front cover of this reputable magazine was a boosting factor. "This imprints even more value to the results we have so far achieved. It was something unexpected and it's a huge recognition." She explains that, generally, the covers of such magazines involve high-end techniques not yet available at UFRGS or even in Brazil. "We were looking forward to being able to publish the study. And then we were invited to compete for the cover," celebrates Luciano. For the cover of the Journal, the researchers had to prepare an image with a staining technique called triphenyltetrazolium (TTC), in which basically the lesion caused by hypoxia-ischemia in the brain is colored.



At the top line, the images show the brain of male animals belonging to four groups (from left to right): Control, Control treated with lactate, hypoxia-ischemia and hypoxia-ischemia treated with lactate. The bottom line shows female brains, in the same o

Scientific article

Tassinari, Isadora et al. *Lactate Administration Reduces Brain Injury and Ameliorates Behavioral Outcomes Following Neonatal Hypoxia-Ischemia*. *Neuroscience*, v. 448, 2020. Available at: <<https://doi.org/10.1016/j.neuroscience.2020.09.006>>

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