

Preterm babies do not habituate to repeated pain, shows study

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Preterm infants do not get used to repeated pain in the way that full-term infants, children and adults do habituate to pain, finds a study led by UCL (University College London) researchers.

The authors of the new *Current Biology* paper say that if [preterm](#) infants have not yet developed the mechanism that enables people to get used to moderate pain, [medical procedures](#) in their first few weeks of life could potentially impact their development.

Lead author Dr. Lorenzo Fabrizi (UCL Neuroscience, Physiology & Pharmacology) said, "The way that we can get used to things can be seen as the simplest example of behavioral and [brain plasticity](#), and it is a basic part of memory and learning. Pain habituation is important because it enables us to preserve physical, emotional, and cognitive resources by not overreacting to pain that is unavoidable or not life-threatening.

"Our findings suggest that the ability to get used to repeated pain might develop during the third trimester of pregnancy, so that babies born prematurely have not yet developed this ability that [full-term](#) babies have right from birth."

The study involved 20 infants at University College London Hospitals (UCLH). Half of them were preterm (and tested while still younger than 35 weeks gestational age), while the other half were either born at full term (seven infants) or preterm but tested at term age (three infants). The two groups were comparable in terms of their actual postnatal age, as the preterm babies had a median age of 14 days, compared to 10 days among the full-term (or term age) group.

The researchers were measuring the infants' responses to a painful but clinically required heel lance ([blood test](#)), which was conducted twice (three to 18 minutes apart) for each infant (two lances are sometimes required to collect enough blood; this is not needed for most infants so only those that needed a second lance were included in the study).

Heel lances can elicit substantial pain responses in infants, but it was not previously known whether this decreases on repeated lances. To

understand this, the researchers recorded the infants' brain activity with EEG (electroencephalography) electrodes placed on the scalp, and their heart rates using ECG (electrocardiography), while also monitoring their [facial expressions](#) and reflexes in withdrawing the leg.

The researchers found that the [brain activity](#) was not as strong immediately after the second heel lance, compared to the first, suggesting a habituation response, but this was only the case for full-term infants. They found a similar pattern for [heart rate](#) and facial expressions, as [preterm infants](#) reacted just as strongly to both heel lances, while the full-term infants appeared to habituate to the pain.

The team says this habituation response might be due to the full-term infants anticipating the imminent pain when they receive a second heel lance, so their reaction is less pronounced, or it may instead or additionally be due to their brains modulating their reflexive survival responses.

They add that habituation to pain might protect the full-term infants, but not those who were pre-term, from potential consequences to their development.

First author Dr. Mohammed Rupawala (UCL Neuroscience, Physiology & Pharmacology) said, "While unpleasant and painful clinical procedures are necessary for many young infants, there is the potential to impact their development, such as by altered pain perception, or potentially reduced gray matter or disrupted white matter in the brain."

Co-author Dr. Judith Meek, consultant neonatologist at UCLH, said, "This work raises awareness of the extra vulnerability of premature babies to [pain](#). Clinicians need to do their best to protect them from repeated painful experiences. This should be regarded as an essential component of brain oriented newborn care."

Note: Gestational age refers to the weeks elapsed since the start of the mother's last menstrual cycle. The 10 infants classified as preterm in this study had a median [gestational age](#) of 31 weeks, so they were still in developmental stages normally undergone while still in the womb.

More information: Lorenzo Fabrizi, A developmental shift in habituation to pain in human neonates, *Current Biology* (2023). [DOI: 10.1016/j.cub.2023.02.071](#). [www.cell.com/current-biology/f...0960-9822\(23\)00244-0](#)

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