

## Long-Term Impact of Preterm Birth and Neonatal Stress on Chronic Pain in Adulthood

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### Abstract

Preterm Birth (PTB) and neonatal stress exposure have been linked to various long-term health complications. However, their potential associations with chronic pain in adulthood remain underexplored. This study aims to evaluate the relationships between PTB, neonatal stress exposure, and the development of chronic pain later in life. Data from a cohort of individuals born preterm and full-term were analysed, assessing factors such as early-life stress, the onset of chronic pain, and its persistence into adulthood. Results suggest that preterm birth and neonatal stress exposure significantly increase the likelihood of chronic pain, with implications for early interventions to prevent long-term pain-related outcomes.

**Keywords:** Preterm birth; Neonatal stress; Chronic pain; Adulthood; Early-life stress; Pain management; Long-term Health effects; Preterm infants

### Introduction

Preterm birth (PTB) refers to the birth of an infant before 37 weeks of gestation, a condition affecting approximately 10% of live births globally. Neonatal stress, including exposure to medical procedures, intensive care environments, and prolonged hospitalization, is common in preterm infants. These early-life adversities have been associated with a variety of long-term health challenges, including developmental delays, behavioral disorders, and an increased risk for chronic diseases. Emerging evidence suggests that individuals born prematurely may be at a higher risk for experiencing chronic pain in adulthood. The mechanisms underlying this association are not fully understood but may involve altered neurodevelopment, heightened sensitivity to pain, and long-term effects of neonatal stress exposure. This study aims to investigate the association between PTB, neonatal stress exposure, and the onset of chronic pain in adulthood, providing insights into the potential long-term consequences of early-life adversity [1,2].

### Preterm birth and its prevalence

Preterm birth (PTB) is defined as a birth occurring before 37 weeks of gestation and affects approximately 10% of live births worldwide. PTB can result from various factors, including maternal health issues, infections, and complications during pregnancy. The incidence of PTB has been rising in many regions due to improved medical technologies, but it still presents significant risks to infant health. Preterm infants often face a range of immediate health concerns, such as respiratory difficulties and feeding problems, and are frequently placed in neonatal intensive care units (NICUs) for specialized care and monitoring [3].

### Neonatal stress and long-term health impacts

Neonatal stress, defined as the physical and psychological strain experienced by newborns, particularly in the NICU setting, is a common challenge for preterm infants. Stressors such as medical interventions, prolonged hospital stays, and sensory overload during neonatal care can have lasting effects on brain development and overall health. Research has shown that neonatal stress can lead to developmental delays, behavioral issues, and even chronic health conditions in adulthood. Understanding the role of neonatal stress in shaping long-term outcomes, such as chronic pain, is crucial to addressing the needs

of preterm infants in both the short and long term [4].

### Description

A cohort of individuals born preterm (before 37 weeks) and full-term ( $\geq 37$  weeks) was analyzed. Participants were followed from birth through adulthood, with assessments of neonatal stress exposure, pain perception, and chronic pain occurrence in adulthood. Neonatal stress exposure was measured through clinical records of medical interventions, including intubation, surgeries, and duration of neonatal intensive care unit (NICU) stays. Chronic pain was defined as persistent pain lasting for more than three months in adulthood, as reported by participants during interviews [5].

### Results

Among the preterm cohort, 47% reported experiencing chronic pain in adulthood, significantly higher than the 28% observed in the full-term group. This finding underscores the heightened vulnerability of individuals born prematurely to long-term pain-related issues. Further analysis revealed that the risk of chronic pain was substantially elevated in those who had undergone severe neonatal stress, such as prolonged stays in the neonatal intensive care unit (NICU) and invasive medical procedures like intubation or surgery. These stressors, which are common in preterm infants, may disrupt early neurodevelopment, increasing the likelihood of pain sensitivity later in life [6].

In addition to the higher overall prevalence of chronic pain, a larger proportion of preterm individuals reported persistent pain at multiple sites, including the back, joints, and headaches such as migraines. These pain sites suggest a broad impact on the musculoskeletal and neurological systems. Regression analysis demonstrated that preterm

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birth, combined with neonatal stress exposure, was a significant predictor of chronic pain, even after accounting for other factors like age, gender, and lifestyle. This indicates that the combination of preterm birth and early-life stress can have lasting consequences on pain perception, pointing to the need for early interventions to mitigate these long-term effects [7,8].

## Discussion

The findings suggest a strong association between preterm birth, neonatal stress exposure, and chronic pain in adulthood. The neonatal period, particularly in preterm infants, is a critical window of vulnerability for the development of pain processing mechanisms. Neonatal stress could alter neural pathways involved in pain perception, leading to an increased sensitivity to pain in later life. Additionally, the prolonged hospitalizations and medical interventions common among preterm infants may contribute to the heightened pain response observed in adulthood. These results are consistent with previous studies that have shown altered pain thresholds and pain-related disorders in individuals with early-life adversity, including preterm birth. However, the exact biological mechanisms remain to be elucidated, and further research is needed to explore how early-life factors contribute to the chronic pain trajectory [9,10].

## Conclusion

This study highlights the significant impact of preterm birth and neonatal stress exposure on the development of chronic pain in adulthood. Given the growing prevalence of preterm births worldwide, it is crucial to recognize the long-term implications of early-life stress on pain outcomes. Early interventions, including pain management strategies and stress reduction during the neonatal period, may help mitigate the risk of chronic pain in later life. Future research should focus on identifying the specific neurobiological mechanisms involved

and the potential for therapeutic interventions to reduce the long-term impact of neonatal stress on pain perception.

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