In Utero SARS-COV-2 Exposure and Infant Neurodevelopment

Key findings from the PROUDEST Study on the impact of maternal COVID-19 on early childhood neuropsychomotor outcomes.

Source: Motta F, Canellas-de-Castro ME, Fernandes GM, Sasaki LMP, de Araújo Júnior DA, Zaconeta AM, et al. Neuropsychomotor Development of Children Exposed to SARS-CoV-2 in Utero During COVID-19 Pandemic. Biomedicines 2025, 13, 2256.

Study Overview & Methodology

A prospective cohort investigation evaluating the impact of maternal SARS-CoV-2 on fetal neurological development.

The Cohort

- **Exposed**: 254 infants exposed to SARS-CoV-2 in utero.
- **Controls**: 15 healthy unexposed infants.
- **Focus**: Term and late-preterm infants monitored for developmental milestones.

The Diagnostic Tool

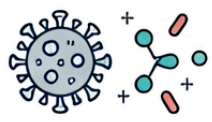
- **Scale:** Bayley-III (Gold standard for infant neurodevelopment).
- **Domains**: Cognitive, Language, and Motor skills.
- **Threshold**: Scores <85 indicate altered neurodevelopmental delay.

The Timeline

- **Milestones**: Outpatient evaluations conducted precisely at 6 months and 12 months of age to track continuous neurocognitive acquisition.

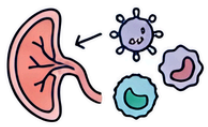
The Pathophysiological Pathway

How maternal respiratory infection translates to structural and developmental fetal impairment.



Maternal Infection

Acute SARS-CoV-2 induces an intense systemic inflammatory cytokine response.



Placental Activation

Fetal exposure to maternal inflammation triggers placental immune activation.

Brain Parenchyma Alteration

Inflammatory processes induce mild myelin edema and increase water content in the brain.

Structural Evidence

Pediatric ultrasound elastography reveals a reduction in elasticity coefficients in the deep white matter of exposed infants.

Clinical Outcome

Disruption of connectivity within language-related brain networks leads to observable developmental delays.

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Primary Clinical Outcomes: Bayley-III Evaluation

Exposed infants demonstrated significantly altered neurodevelopmental patterns compared to healthy controls.

~26%

General Developmental Delay

(Frequency of altered Bayley-III scores <85 in exposed infants across test periods)

6 Months Postpartum

Widespread Impact: Significant delays observed across all three major domains: Cognitive, Language, and Motor.

12 Months Postpartum

Targeted Language Impairment: While cognitive and motor domains showed some normalization, the **Language Domain** exhibited persistent and profound impairment.

- *Up to 28.2% of highly exposed subgroups showed altered language scores.*

Modifying Risk Factors: Exacerbating the Outcomes

The severity of neurodevelopmental delay—particularly in language—is heavily influenced by three specific maternal variables.

Timing of Infection

Highest Risk: Acute infection during the 3rd trimester or directly at delivery.

Impact: Multinomial regression shows a profound negative relationship between acute infection at delivery and cognitive/language scores scores at 12 months.

Disease Severity

Highest Risk: Mothers experiencing severe COVID-19 symptoms.

Impact: A higher maternal inflammatory burden directly correlates with increased rates of altered Bayley-III domains in the infant.

Caregiver Education Level

Highest Risk: Caregivers without a university degree.

Impact: Highlights socioeconomic disparities. Lower maternal education levels were strongly associated with higher rates of infant language developmental delays.

The Path Forward: Clinical Relevance & Action

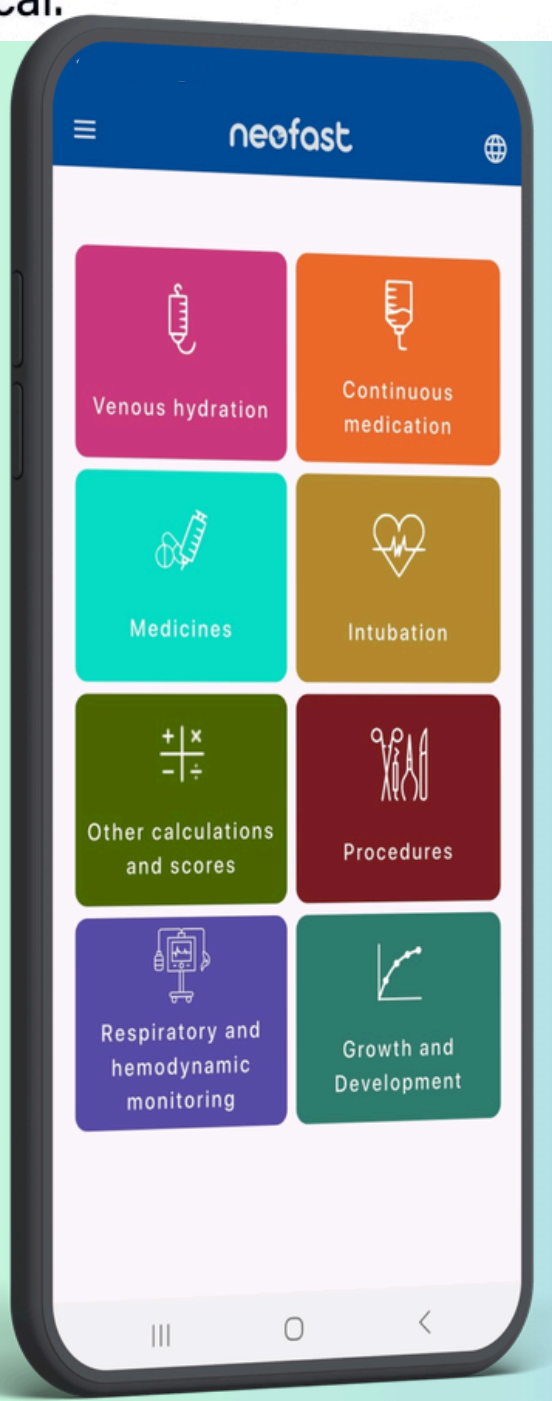
Because language acts as a driver for all subsequent cognitive skills, immediate and sustained pediatric intervention is required.

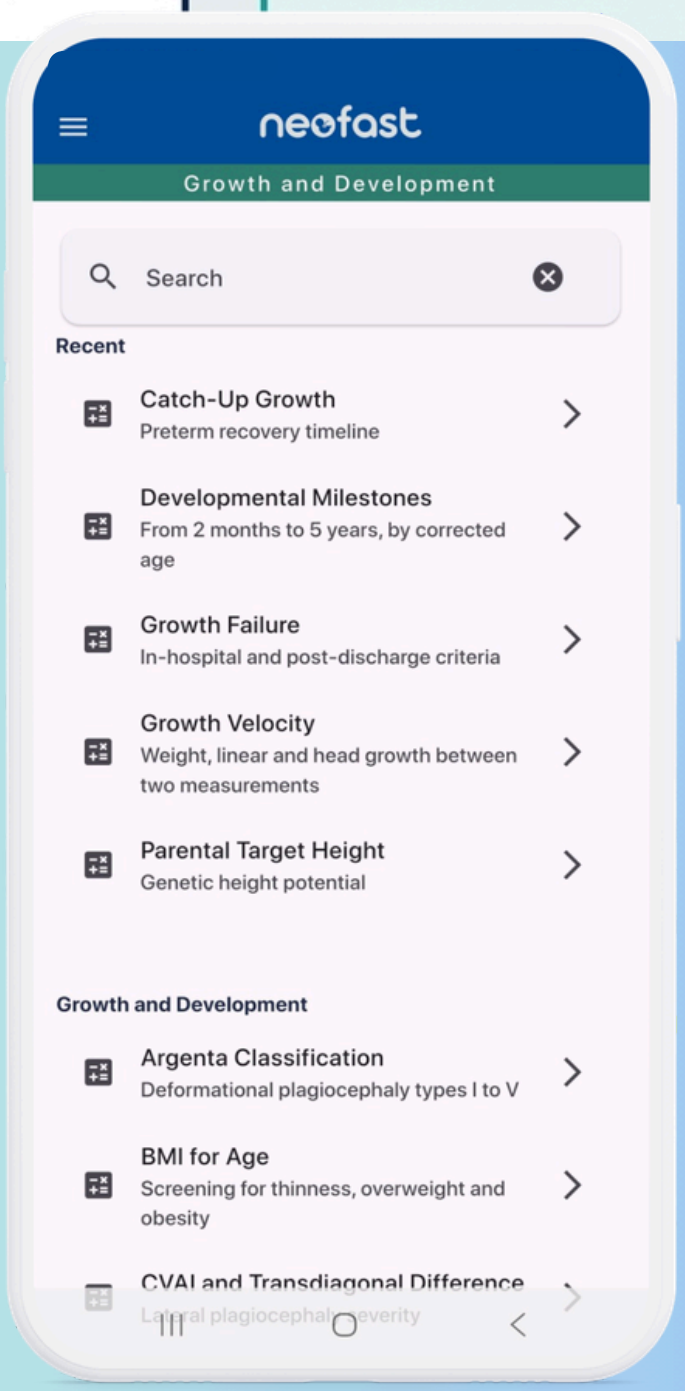
The Clinical Mandate

- **Targeted Screening:** Universal screening for maternal infections and detailed post-natal developmental assessment are vital for exposed cohorts.
- **Serial Childcare Follow-up:** Constant, systematic monitoring of neurodevelopment is essential during the first two years of life, when neurocognitive acquisitions are most critical.

The Role of Early Stimulation

- **Harnessing Neural Plasticity:** Despite structural deep white matter changes, the infant brain is highly adaptable.
- **Targeted Intervention:** Directed early stimulation and pediatric therapy can rewire neural pathways, actively mitigating long-term deficits in language acquisition, socialization, and academic achievement.





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