



WUNDER Lab Newsletter

Letter from Investigators

Thank you to all families for participating in our research about understanding early brain development of infants and its effects on a child's development. We wanted to send you some updates about the Washington University Neonatal and Developmental Research (WUNDER) Lab. At the time of our last newsletter, we were in the process of seeing our oldest NICU graduates at their 5 and 6 year follow-up visits. The lab has been busy! We're almost finished with our first wave of follow-up visits of 5 and 6 year olds and we're seeing several cohorts of children return for their 2 year visits! We have made some wonderful additions to the research team, and papers are being published about the children's time in the NICU and early childhood.

The WUNDER lab continues to follow several groups of preterm children who have participated in research studies since they were in the NICU. Last year, we also began studying term-born children at early school age, which has allowed us to further explore the impact of prematurity on children.

As always, it has been a joy to see your children back for follow-up visits and watch them learn and grow. For those who have not yet returned, we look forward to seeing you soon! We are incredibly grateful to each of you for your continued participation in our research studies that allow us to better understand early brain development.

Best,

Drs. Cynthia Rogers and Chris Smyser

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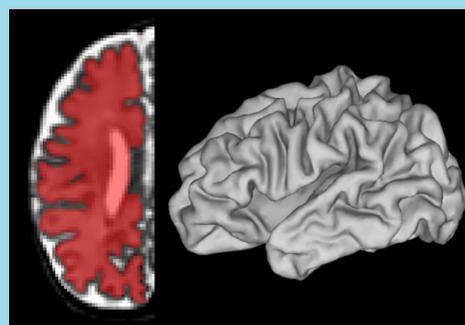
How the Brain Folds in Preterm Infants

A recent paper published by the WUNDER Team investigated the impact of preterm birth and other factors on how the brain folds during the babies' time in the NICU.

Few studies have directly tested for abnormalities of the brain's folding in relation to neurodevelopmental challenges in preemies. During the last trimester of pregnancy, the brain's surface goes through a period of rapid growth and folding, which may be disrupted by preterm birth and the challenges associated with living in the NICU environment.

We studied the effects of preterm birth on the brain's folding by mapping the surface of the brain in 52 of our preemies who were all born at 30 weeks or less and had no brain injury. We compared the preemies to 12 term-born infants. We used the MRI scan that occurred around 40 weeks for the preemies and the term-born infants, right before most of the preemies went home from the NICU.

The study found that preterm birth disrupts the brain's overall folding and also focuses on specific areas of the brain. This disruption is influenced by both the growth the baby undergoes in utero and their growth once they are born.



Engelhardt *et al.* (2015) Regional Impairment of Cortical Folding in Premature Infants. *Annals of Neurology*

These publications were made possible thanks to the contribution of your children and your family! Thank you so much for your continued support.

Vesoulis *et al.* (2014). Early electrographic seizures, brain injury and neurodevelopmental risk in the very preterm infant. *Pediatric Research*

Reynolds *et al.* (2014). Factors that Influence Cerebral Maturation on aEEG within the NICU in the Preterm Infant. *Acta Paediatrica*

McPherson *et al.* (2014) Neonatal Pain control and Neurologic Effects of Anesthetics and Sedative in Preterm Infants. *Clinics in Perinatology*

Reynolds *et al.* (2014) Maternal Obesity and Risk for Autism and Developmental Delay among Very Preterm Infants. *Journal of Perinatology*

Estep *et al.* (2014) Diffusion Tractography and Neuromotor Outcome in Children with Early White Matter Injury. *Pediatric Research*

Paul *et al.* (2014) An Allometric Scaling Relationship in the Brain of Preterm Infants. *Annals of Clinical and Translational Neurology*

Smyser *et al.* (2015) Cortical Gray and Adjacent White Matter Demonstrate Synchronous Maturation in Very Preterm Infants. *Cerebral Cortex*

Rogers *et al.* (2015) Regional White Matter Development in Very Preterm Infants: Perinatal Predictors and Early Developmental Outcomes. *Pediatric Research*

Ferradal *et al.* (2015) Functional Imaging of the Developing Brain at the Bedside Using Diffuse Optical Tomography. *Cerebral Cortex*

How Infection Impacts Early Childhood Development

A recent paper published by the WUNDER Team studied the link between infection around the time of delivery and neurodevelopment in preterm infants. Premies can often score lower on scales of motor functioning, language, memory, and general intelligence. With high rates of perinatal and neonatal infections in premies, infection may be one of the factors contributing to poorer developmental outcomes.

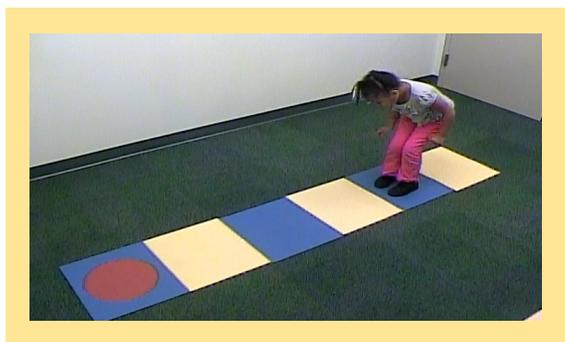
The infants had MRIs of their brain which were analyzed for brain injury, size, and damage to a particular tissue: the white matter. Two-year follow-up included motor, cognitive and language testing.

The study found that neonatal sepsis was related to changes in brain structure, but did not affect two-year developmental scores. Instead, those scores were worse in children exposed to maternal infection in the reproductive system or infection in the amniotic fluid.

These findings suggest that infection is associated with neurodevelopmental outcomes in preterm infants; however, additional research is needed to further clarify some of these findings. Although neonatal sepsis was not associated with changes in two-year developmental outcomes, there may be more subtle changes that can only be detected as these children enter school age.

Lee *et al.* (2014) The impact of prenatal and neonatal infection on neurodevelopmental outcomes in very preterm infants. *Journal of Perinatology*

What the WUNDER Lab Does at Follow-Up



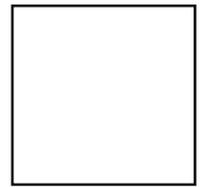
The Movement Assessment Battery for Children is used to assess children's motor skills. Tasks include hopping on mats and catching bean bags.

The Clinical Evaluation of Language Fundamentals measures a broad range of expressive and receptive language skills in young children.



At age 2 and age 5, during the Parent Child Interaction, parents and children play together with toys such as puzzles and books.





How Preterm Brains Function

The WUNDER Team recently published a paper reporting the effects of prematurity on development of brain function (as opposed to brain structure) in infants during the period of time around their original due date.

A new MRI technique, resting-state functional magnetic resonance imaging (rs-fMRI), was used to study functional brain development in both term and prematurely-born infants. rs-fMRI studies show how different areas of the brain work together by measuring similarities and differences in blood flow in the brain. It is a good technique to use in infants because its only requirement is that the infant lay still in the MRI scanner while the pictures are being taken.

Twenty-five prematurely-born and twenty-five term-born infants had MRI scans performed. Maps of brain function showed small differences between the preterm and term infants in the areas of the brain that were studied. However, when more advanced testing was performed, there were differences between the two groups, with premature infants showing smaller values. These findings tell us that while typical patterns of brain function are seen in premature infants, the amount of activity is reduced in comparison to infants born at term. Additional studies are being conducted now to determine whether these tests of brain function help to predict outcomes in premature infants.

Smyser *et al.* (2015) Resting-State Network Complexity and Magnitude Are Reduced in Prematurely Born Infants. *Cerebral Cortex*