

# Brain malformations significantly associated with preterm birth

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New research out of Wake Forest University School of Medicine provides for the first time a solid scientific answer for the long-standing question of whether there is an association between preterm birth and brain malformations.

In a study of more than 1,000 preterm infant autopsies, researchers found that there is a strong association between congenital brain defects and preterm birth, leading investigators to believe that something about the brain malformations may be causing preterm birth and providing a possible study path toward a better understanding of the problem.

The study appears in the June issue of *Pediatric Research*. It is the first to investigate the risk of being born preterm for infants who have a variety of congenital brain defects.

"The most important thing about this study is that to-date, it is still unknown why there are so many preterm births. This study suggests that one way to look for the causes of preterm birth is to look at those types of brain malformations that have very strong association with preterm birth, and see if there is some sort of difference between those babies and full-term babies - some sort of soluble factor or an increased amount of something in the preterm babies that is not found in other babies," said William R. Brown, Ph.D., a research associate professor of radiologic sciences and author/investigator for the study.

Funded by the National Institutes of Health, March of Dimes Birth

Defects Foundation and the Pratt Family Foundation, Brown's research on brain malformations and preterm birth grew out of a study of bleeds in the brains of babies, where researchers found that a large percentage of the babies being studied had small, unrecognized types of brain malformations that warranted further investigation.

Previous studies have shown that malformations of other parts of the body are associated with preterm birth. However, though there has been evidence suggesting brain malformations are also associated with preterm birth, it has been difficult to document such an association because brain defects can be hidden within the cranium and may remain undetected until autopsy, whereas malformations of other parts of the body can be determined through birth registries.

For his study, Brown looked at 1,168 autopsy files that contained congenital brain defects as well as information on the gestational age at birth of the subject. For comparison, Brown also looked at published files of over 7,000 infants with "significant birth defects of any kind" and more than 260,000 infants without brain defects. The control cases came from a large registry published by the Metropolitan Atlanta Congenital Defects Program.

In his review, Brown found that, in the autopsy cases with brain defects, the mean gestational age was 36.6 weeks, whereas the data showed a mean gestational age of 39.9 weeks for infants with no defects and a gestation of 38.1 weeks for infants with defects of any kind. "Preterm" birth is defined as 20 to 36 weeks gestation, while "term" birth is defined as 37 to 41 weeks. Only 9.3 percent of babies born without defects were preterm, compared to 21.5 percent of those with defects. In the autopsy cases with brain defects, the rate of preterm birth was even greater at 33.1 percent, showing the strongest association between the two.

Some types of brain defects have a stronger association with preterm

birth than others, the study showed. The list itself could possibly offer some clue to the association. Among the malformations studied with the highest rates of preterm birth were hydrocephaly, an abnormal buildup of cerebrospinal fluid (CSF) in the ventricles of the brain (65.2 percent); anencephaly, a defect in the closure of the neural tube during fetal development resulting in the absence of a major portion of the brain, skull, and scalp (57.7 percent); multicystic encephalomalacia, the formation of multiple cystic cavities of various sizes in the cerebral cortex (50.5 percent); and hydranencephaly, a rare condition in which the brain's cerebral hemispheres are absent and replaced by sacs filled with cerebrospinal fluid (38.5 percent).

"There are a lot of preterm births where there are no apparent causes," Brown said. "I speculate that brain defects or other defects not easily detected could be causing some of them and perhaps we should focus on studying coagulopathy (a tendency to excessive blood coagulation and formation of blood clots) to find what the association is between that and preterm birth.

"The placenta could be a key element," he added. "In placental conditions such as preeclampsia, which is strongly associated with preterm birth, there may be blood clots coming from the placenta, causing brain damage and malformations in the brain and then, perhaps, the malformed fetus induces its own preterm birth or perhaps the coagulopathy causes the preterm birth through some other mechanism. The next step is to look at the brain malformations that have the strongest association with preterm birth and see if it's possible to identify the factors associated with those malformations that may be causing [preterm birth](#). These are possible new directions to explore."

Meanwhile, Brown endorses the use of folic acid before and during pregnancy.

"It's not completely known how it works, but it could be impacting coagulopathy because folic acid is involved with the pathways that are also involved with coagulation," he said.

Source: Wake Forest University Baptist Medical Center ([news](#) : [web](#))

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