What’s known:
Eight of every 1,000 children born each year have congenital heart disease (CHD). Although recent advances have greatly improved the survival of these children, up to 55 percent will be left with injury to the brain’s white matter, which is critical for aiding the brain’s various regions to connect and communicate. The resulting spectrum of neurological deficits can have significant costs for the individual, their family and society. Although studies have demonstrated that white matter injuries due to CHD have many contributing factors, including abnormal blood flow to the fetal brain, many questions remain about the mechanisms that cause these injuries and the best interventions.

What’s new:
A Children’s National Health System research team combed existing literature to develop a review article detailing the current state of knowledge on CHD and white matter injury. The scientists write that advances in neuroimaging — including magnetic resonance imaging, magnetic resonance spectroscopy, Doppler ultrasound and diffusion tensor imaging — have provided a wealth of knowledge about brain development in patients who have CHD. These techniques alone are unable to provide pivotal insights into how CHD affects cells and molecules in the brain. Thus, an array of preclinical models will be necessary to elucidate the underlying mechanisms responsible for this type of neurological injury. Postmortem tissue from patients with CHD also can complement imaging and preclinical studies, expanding understanding. Together, these findings will create a strong foundation on which to build new therapies and to determine the timing of treatment windows to improve neurological outcomes for patients with CHD.

Questions for future research:
Q: What are the cellular and molecular mechanisms that underlie white matter injury in patients with CHD?
Q: Are prenatal or postnatal insults related to CHD more damaging to white matter?
Q: Can scientists create preclinical models that can accurately recapitulate the white matter damage that occurs with different types of CHD in humans?
Q: Which therapies best mitigate white matter damage in patients who have CHD?

Cardiac abnormalities are the most common birth defects and patients who suffer from these conditions often experience a variety of neurological deficits throughout life, often resulting from white matter injuries. The study authors discuss recent clinical and preclinical studies examining the effects of cardiac abnormalities — and their treatment — on white matter and argue that further integration of these two approaches is necessary to identify novel therapeutic targets and to improve standards of care. The cover image depicts the consequential malfunction of the brain during congenital heart defects. Cover image by Katie Sokolowski, based on design by Paul Morton, Alex Son and Katie Sokolowski.