A mixed bag: Differential influences of oxygenation and perfusion on brain development in congenital heart disease

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Central Message

Clarifying the specific hemodynamic influences on brain development across the diverse spectrum of congenital heart disease will inform rational strategies for neuroprotection.

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It is now established that neonates with congenital heart disease (CHD) have impaired brain growth and maturation before surgery. Smaller brain volumes and less-mature patterns of macro- and microstructural brain development are seen before and after birth.¹⁻³ Multiple factors have been implicated in this pathway, including innate genetic abnormalities, disturbed placental health, and direct trophic influences of reduced cerebral oxygenation and perfusion.⁴⁻⁶

Lim and colleagues⁷ investigated the latter, using cine phase-contrast imaging to measure cerebral blood flow and calculate oxygen delivery in neonates with various forms of CHD preoperatively. Compared with healthy neonates, those with CHD had similar cerebral blood flow but reduced oxygen delivery. These differences were most apparent in the neonates with single-ventricle physiology and transposition of the great arteries. Further, reduced oxygen delivery was associated with a smaller and less-mature brain. Previous work from this group similarly suggested relatively preserved cerebral blood flow in the late prenatal period.⁶ Their findings differ from other studies using near-infrared spectroscopy and pulsed arterial spin-label perfusion imaging that show reduced cerebral blood flow in cohorts more heavily weighted with obstructive left-sided lesions such as hypoplastic left heart syndrome.^{8,9}

Although technical differences may in part account for the discrepancy, the contrasting results likely also reflect that the relative contributions of abnormal cerebral blood flow and oxygenation differ among forms of CHD. In transposition of the great arteries, one would expect preserved cerebral blood flow with reduced oxygenation as the authors found. On the other hand, in severe left outflow tract obstructions such as hypoplastic left heart syndrome with aortic atresia, one might expect reduced cerebral flow with less marked oxygenation differences. Doppler investigations similarly

indicate variable cerebrovascular compensatory responses depending on the type of heart disease evaluated.¹⁰ Although single-center studies often necessarily include various forms of CHD due to sample size limitations, CHD is heterogeneous, and different hemodynamic factors may dominate in different lesions. Further investigations using standardized techniques across large multicenter cohorts to allow subgroup analyses are critical to integrate cerebral findings with cardiac anatomy and establish the pathophysiologic processes operating in different disease forms.

Efforts that enhance technical capabilities of measuring cerebral blood flow and oxygenation in CHD are central to improving cardiac brain care. They may suggest practice modifications to improve neurologic outcome, such as earlier surgery for patients with low cerebral oxygen delivery. More broadly, coupling these measures with detailed structural neuroimaging data and performing longitudinal measurements will clarify the timing of onset and causal pathways of brain disease in CHD and illuminate potential preventive strategies. As the field moves toward neuroprotection trials, direct measures of cerebral perfusion and oxygen delivery are important early outcomes, because neurodevelopment takes years to establish.

In CHD, we have a unique opportunity to identify patients at risk for brain injury before and/or during the ischemic insult. Clarifying the specific physiologic derangements that affect brain development across the

diverse spectrum of CHD will promote rational strategies to mitigate these deleterious influences on the brain.

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