

The “Heart-and-Brain Interaction” in Hypoplastic Left Heart Syndrome – The Impact of Hemodynamics on Neurodevelopmental Outcome before Fontan Procedure

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Objectives: The long-term impact of altered hemodynamics after stage II in children with hypoplastic left heart syndrome (HLHS) on cerebral growth and neurodevelopmental outcome is unknown. Elevated vascular pressures before Fontan procedure may be associated with smaller brain volumes and poorer neurodevelopmental outcome.

Methods: Semi-automated segmentation of cerebral MRI scans and neurodevelopmental assessment with Bayley-ScalesIII (BS) and neurological examination were conducted in 29 children with HLHS (18 male, 25 Hybrid) before Fontan procedure at mean age of 27.4±4.1 months, and in 8 controls.

Hemodynamic measures before Fontan were assessed with cardiac catheterization.

Results: Superior caval vein (SVC) pressure and atrial pressure were median (range) 10 (5-18) and 6 (4-14) mmHg, respectively. BS were favourable with mean(±SD) Cognitive Composite Scale (CCS) 97±12, Language Composite Score (LCS) 96±14, and Motor Composite Scale (MCS) 96±16. Brain volumes were significantly reduced compared to controls, while cerebrospinal fluid (CSF) volumes were elevated. White and deep gray matter volumes were significantly lower after Norwood procedure. (Table 1). Atrial pressure correlated with reduced brain volumes (total brain volume (gray, deep grey and white matter) $r=-0.46$, $p=0.012$, white matter $r=-0.47$, $p=0.010$; gray matter $r=-0.46$, $p=0.013$), while SVC pressure did not correlate with brain volumes, but with increased CSF volume ($r=0.45$, $p=0.014$). The later finding correlated neurodevelopmental outcome for all BS with CCS $r=-0.40$ ($p=0.028$), LCS $r=-0.59$ ($p=0.003$), MCS $r=-0.51$ ($p=0.004$). SVC pressure greater than 12.5 mmHg was associated with poorer performance for all BS (CCS $p=0.025$, LCS $p=0.001$, MCS $p=0.012$).

Conclusions: Impaired hemodynamics before Fontan procedure in HLHS patients may affect the “Heart-and-Brain” interaction: On one hand, cerebral growth (total, white, gray matter) may be affected by impaired myocardial performance (determined by increased atrial pressures) resulting in an impaired somatic and cerebral perfusion. On the other hand, impaired cerebral venous downstream (determined by increased SVC pressure) results in increased CSF volume and impaired neurodevelopmental outcome. Future studies have to evaluate other potentially contributing factors such as CSF flow dynamics, altered aortic arch vascular compliance after Norwood surgery, use of systemic medication reducing systemic and pulmonary vascular resistance for a better understanding of this “Heart-and-Brain” interaction.

| | Hybrid (n=24) | Norwood (n=5) | Control (n=8) | P-value Hybrid vs. Norwood | P-value Hybrid vs. Control | P-value Norwood vs. Control |
|-------------------------------------|-------------------|-------------------|------------------|----------------------------|----------------------------|-----------------------------|
| Age at MRI [months] | 27.6 ± 4.3 | 26.4 ± 3.3 | 29.7 ± 9.5 | 0.63 | 0.45 | 0.28 |
| Total grey matter volume [ml] | 622.6 ± 60.7 | 577.6 ± 42.1 | 685.2 ± 86.2 | 0.101 | 0.051 | 0.030 |
| Subcortical grey matter volume [ml] | 44.4 ± 3.9 | 38.4 ± 4.1 | 49.6 ± 6.7 | 0.005 | 0.051 | 0.019 |
| White matter volume [ml] | 284.9 ± 30.8 | 255.2 ± 18.6 | 331.1 ± 64.3 | 0.032 | 0.041 | 0.045 |
| Cerebrospinal fluid volume [ml] | 17.6 (13.1, 22.5) | 17.9 (13.1, 23.6) | 11.9 (9.5, 13.8) | 0.933 | 0.009 | 0.045 |

Table 1. Data are given as n (%), mean and SD or median and interquartile-range (Q1, Q3) P-values by Kruskal Wallis and post hoc Mann-Whitney U test.