Differences in neurodevelopmental status at two years of age depending on prenatal congenital heart disease diagnosis

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Objective
To assess whether severe congenital heart disease (CHD) diagnosed prenatally affects later neurodevelopment and behaviour differently depending on their type. Also, to correlate Bayley-III test results at 2 years of age with brain magnetic resonance images acquired at 35-37 weeks of pregnancy.

Methods
This is a prospective study including 76 pregnant women carrying single pregnancies affected with major congenital heart defects diagnosed prenatally. Foetuses with extracardiac malformations and genetical alterations were excluded from the study. Foetal brain magnetic resonance was performed in all pregnant patients from 35 to 37 weeks. Brain fissure measurements from MR images were taken by a single investigator following a previously described methodology, corrected by BPD and adjusted by gender and gestational age at delivery. Bayley-III test for development and behavioural evaluation was performed by a trained psychologist at 24 months of age, including cognitive, language, motor, adaptational and social composite scales. Patients were classified into three groups depending on their CHD: septal defects (n=16), conotruncal anomalies (including Tetralogy of Fallot and Transposition of Great Arteries, n=50) and finally, left ventricular flow obstruction (LVOTO, including aortic coaptation and hypoplastic heart syndrome, n=20).

Results
All three groups obtained an average result higher than 100 points in the medium Bayley score, considered to be the expected result for healthy children (valvular group, 100.9 points; conotruncal 101.9; LVOTO 105.43 points). No statistical differences were found between groups. Lower scores were found in language and social adaptation scales. There were no differences among groups in either of the composite scales when studied separately. Our study did not find significant differences in Bayley-III test results comparing CHD children with general population at 24 months of age. Once classified into three CHD groups, there were no differences in Bayley-III average score in either composite scale compared with healthy population. Composite scales scores from Bayley test were compared separately to fissure depth measurements obtained by MRI in each of the three CHD groups using Pearson test. We found a positive correlation between BPD and social composite score (p=0.015), as well as with Silvian fissure depth and motor composite score results (p=0.041). Even though without statistical significance, a positive correlation was also found between cingulate fissure and adaptative composite score (p=0.062).

Conclusion
This trial is the first to analyse neurodevelopment in children from a heterogenous cohort of moderate and severe CHD and one of the largest published so far. At the same time, it is to our knowledge, the first attempt to correlate brain alterations found in CHD affected foetuses with neurodevelopmental evaluation results after birth. Our results show postnatal evolution to be favourable in our cohort of CHD new-borns. Following our results, neurodevelopment at 2 years of age is similar to general population in CHD patients. Literature regarding developmental evaluation in CHD mostly focus on HLHS and other severe CHD with a generally worse prognosis. In this study, we wanted to include a wider spectrum of moderate to severe CHD such as aortic coaptation and septal defects; this decision might explain why our cohort results are better than the previously described, especially in the LVOTO group. Moreover, according to data from previously published trials, differences in developmental prognosis seem to begin at two to five years of age for CHD patients therefore, it might be too soon for our cohort to show significant differences in their neurodevelopment compared to controls. We plan on continue to follow up our patients in order to evaluate neurodevelopmental prognosis in CHD children and therefore, improve prenatal parental counselling. Studies with a higher cohort and including postnatal factors such as surgery complications or breast feeding are necessary to continue to understand the impact of CHD in brain development.