Review Article

Executive function deficits in congenital heart disease: why is intervention important?

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Abstract It is widely recognised that children with congenital heart disease (CHD) are at high risk for neurodevelopmental impairments including attention deficit hyperactivity disorder and autism spectrum disorder symptoms. Executive function impairments are one of the most prominent neurodevelopmental features associated with CHD. These deficits can have widespread debilitating repercussions in children’s neurocognitive, behavioural, and psycho-social development. There is a crucial gap in research regarding the efficacy of preventive or treatment strategies for these important cognitive morbidities. Executive functions are complex neurocognitive skills highly amenable to improvement. Evidence-based interventions have shown promising results in other paediatric populations, strongly suggesting that they might also benefit the growing population of children with CHD. In this review, we summarise the available data on executive function impairments in children and adolescents with CHD. We underline the important co-morbidity of executive dysfunction with other cognitive and psychiatric issues in CHD, which raises awareness of the crucial need to prevent or at least mitigate these deficits. Finally, we summarise future avenues for research in terms of interventions that may help reduce executive function impairments in youth with CHD.

Keywords: Executive function; CHD; cognitive interventions; working memory; neurodevelopment

Received: 18 May 2015; Accepted: 18 May 2015; First published online: 17 June 2015

Neurodevelopmental impairments are now recognised as one of the major morbidities associated with CHD. Behavioural difficulties – internalising and externalising problems – and psycho-social impairments are frequent. There is also a growing recognition that the prevalence of attention deficit hyperactivity disorder or attention deficit hyperactivity disorder-related symptoms is elevated in children with CHD, with some studies suggesting that the risk of meeting the diagnostic criteria is three to four times higher than that expected in the general population. As a group, survivors of complex CHD display a distinct neurocognitive phenotype. Lower-level skills are generally relatively intact, but the children have major difficulties integrating or coordinating these skills to achieve higher-order goals. Among the most prominent elements of the phenotype are deficits in non-verbal skills – for example, visuo-spatial skills and motor skills – social cognition, and executive functioning. The executive function deficits are of particular importance with respect to the children’s well-being as they place a child at increased risk of poorer academic achievement, including increased use of early educational and neurodevelopmental remedial services, impaired...
social adaptation,\textsuperscript{10,11} and reduced quality of life.\textsuperscript{19} Given this, we hypothesise that interventions to enhance executive functioning in children with CHD might produce benefits that, ultimately, extend beyond this domain; however, evidence-based interventions to accomplish this goal have not yet been evaluated in this population. In this review, we first summarise the data on executive function in youth with CHD, including the major co-morbidities. Second, based on these data, we describe interventions that might be beneficial.

What are executive functions and why are they important in childhood?

Executive functions refer to a set of higher-order neurocognitive abilities that serve to coordinate and organise actions towards a goal, allowing the individual to adapt to new or complex situations.\textsuperscript{20} These control processes are essential when we need to concentrate on a task, memorise and manipulate information, and generally when routines are no longer sufficient to achieve our goals. The use of executive functions is, per definition, effortful, and implies the ability to “resist temptation”, to go off “automatic-pilot” in order to anticipate, control, and plan ahead.\textsuperscript{20,21} Executive functions can be sub-divided into three major core skills\textsuperscript{20–22}: inhibitory control, which includes behavioural regulation and control of attention; working memory, the ability to keep information in mind and manipulate it; and cognitive flexibility, the ability to switch efficiently from one activity/behaviour to another or to consider information from a different perspective. As children grow older, they learn to coordinate these core components to engage in more complex goal-directed behaviour involving step-by-step planning and hypothesis-generation. Executive functions are among the neurocognitive skills with the most protracted developmental trajectory.\textsuperscript{20} They emerge early in infancy,\textsuperscript{23} undergo rapid progressions during the pre-school and school years,\textsuperscript{24,25} and continue to develop through adolescence.\textsuperscript{26,27} These higher-order skills are mediated by the maturation of neuroanatomical networks, including frontal and prefrontal structures, as well as fronto-parietal and sub-cortical networks.\textsuperscript{28,29} They are strongly dependent on the integrity of white matter brain connectivity between anterior and sub-cortical regions in childhood.\textsuperscript{29,30}

Executive function deficits are implicated in various neurological disorders, including attention deficit hyperactivity disorder,\textsuperscript{31} and can result from factors that perturb early brain development, such as preterm birth.\textsuperscript{32} Executive dysfunctions can adversely impact many aspects of children’s development. They are more strongly associated with school readiness than is IQ, and they predict both mathematics and reading competence throughout the school years.\textsuperscript{33} Research on typical and atypical paediatric populations has demonstrated that executive functions are necessary to decode other people’s mental and emotional states and to respond to rapid-paced social interactions\textsuperscript{34,35} and can interfere with children’s ability to identify their own emotional states. They are also associated with the risk of psychiatric disorders including anxiety and depression.\textsuperscript{36} Non-treated childhood executive dysfunction may also predispose the individual to later addiction,\textsuperscript{37} eating disorders and obesity,\textsuperscript{38} lower employability, and risk-taking behaviours, which not only pose a problem for the individual child but also for the society.\textsuperscript{39}

Executive function impairments in children with CHD

As it became clearer that global intellectual delay — that is, IQ score — was not the major concern in children with isolated CHD — that is, CHD not associated with a genetic syndrome — recent studies have focussed on more specific neuropsychological deficits including executive dysfunction. These studies have reported impairments in various aspects of executive functioning, including control of attention, self-regulation, working memory, cognitive flexibility, and planning and organisational skills.\textsuperscript{8–10,12–17}

Executive function deficits in children with CHD were first reported by the Boston Circulatory Arrest Study in 8-year-old children with d-TGA that had been repaired in infancy.\textsuperscript{12} Metacognitive aspects of behaviour, such as organisation and planning, were particularly impaired. On standardised tests commonly used in patients with frontal lobe damage — for example, Trail Making Test and Wisconsin Card Sorting Test — the children had substantial difficulty alternating between tasks and committed more perseverative errors, suggesting impairments in cognitive flexibility. Sustained attention was also impaired, as omission and commission errors were twice as frequent in patients with d-TGA compared with normative values. Qualitative observations of executive functions were obtained using the Rey–Osterrieth Complex Figure. The proportion of children whose copy of the design was scored at the lowest level of organisation was more than twice the percentage observed in the standardisation sample.\textsuperscript{7} The children with d-TGA focussed on details at the expense of the figure’s global organisation elements, resulting in very poor performances. More recent findings also reported specific deficits in executive functions in school-aged children with corrected isolated d-TGA.\textsuperscript{9} At age 7, patients had significant
difficulties elaborating a strategy to achieve a goal – for example, anticipating the right number of actions in order to correctly reproduce a visual model. Even when they succeeded, they needed more time to complete the tasks, suggesting problems with planning skills. Other executive functions were also altered. The children committed more errors on the Animal Stroop naming task, on which they were required to ignore visual distractors. Cartoon farm animals with non-matching head–body pairs were shown – for example a cow’s body with the head of duck – and children had to control the automatic tendency to focus on the animal’s head and instead give a response based on the identification of the animal’s body. The d-TGA group also performed significantly worse than the control group on a test measuring behavioural control – that is, Statue subtest from the NEPSY. Overall, a significant proportion of patients failed, at age 7, tasks typically passed by 5-year-old children. Verbal and visuo-spatial working memory skills were also significantly different in the group with d-TGA. These data suggest that, by school-age, many aspects of executive functions are impaired in children with CHD.

Other studies are consistent with these findings.

Hovels-Gurich et al.\textsuperscript{15,16} found attentional and executive control impairments in 7-year-old children with tetralogy of Fallot who underwent open-heart surgery before 12 months of age. Compared with a control group of healthy children as well as with a group of children who underwent reparative open-heart surgery for ventricular septal defect, children with tetralogy of Fallot had difficulty inhibiting responses to visual distractors. Their deficits were specific to the executive control of attention, as other lower-level attentional skills such as alerting and orientation did not differ from those of the comparison groups. The authors hypothesised that the deficits in executive control that they observed suggested anomalies in anterior brain networks, including cingulate and lateral prefrontal cortex.\textsuperscript{16} Although this study did not evaluate the neuroanatomical correlates of the executive control dysfunctions, it raised questions regarding the impact of complex cyanotic CHD on the development of higher-order cortical networks that involve the prefrontal cortex.

With respect to intervention, it is important to note that deficits in executive functions have an early onset in children with complex CHD, starting in the pre-school years.\textsuperscript{14,17} Moreover, 4-year-olds with hypoplastic left heart syndrome and d-TGA\textsuperscript{17} showed lower performances on a test of behavioural control that required them to inhibit a motor response – “move, open their eyes, etc.” – potentially triggered by external stimuli or distractors. These findings were more extensively confirmed in pre-school children with d-TGA at the mean age of 5.\textsuperscript{10,14} Calderon et al.\textsuperscript{10,14} compared the performances of a group of 5-year-old children with isolated d-TGA with those of an aged-matched control group on a comprehensive battery of age-appropriate executive function measures. Although both groups had normal IQ scores and no apparent comprehensive language deficit, children with d-TGA obtained lower scores than their typically developing peers on most tests. They committed more errors on the Animal Stroop task and on tests measuring behavioural control, displaying impulsivity, and struggling to focus on the tasks. Finally, these studies reported that the children had substantial difficulties switching flexibly from one task to another – for example, name a picture based on its colour, then name it based on its shape, and alternate between these rules.\textsuperscript{10,14}

It is also important, with regard to risk factors, that children with a d-TGA that was diagnosed postnatally obtained worse scores on executive function tests than children with d-TGA that was diagnosed prenatally, suggesting a potential link between the severity and duration of cyanosis and/or the risk of neonatal hypoxic-ischaemic injury and the degree of later executive dysfunction.\textsuperscript{10} Furthermore, deficits in different aspects of executive function follow different natural histories over time. Calderon et al.\textsuperscript{14} showed that deficits in inhibitory control improved over the period from 5 to 7 years of age, whereas deficits in cognitive flexibility tended to worsen. This potential for change in the severity of some aspects of executive dysfunction suggests that a developmental catch-up to age-expected milestone is possible. This, in turn, creates hope that early intervention would be effective in enhancing the recovery process.

**Long-term deficits in adolescents with CHD**

Executive function impairments persist to adolescence in children with various types of CHD.\textsuperscript{8,13,40} In the Boston Circulatory Arrest Study, formal neuropsychological testing, as well as parent and teacher reports, indicated that 16-year-old children with d-TGA continued to struggle with several aspects of executive functioning.\textsuperscript{8} They scored lower than expected on several sub-tests of the Delis–Kaplan Executive Function System battery. As was observed in assessments conducted at 8 years of age, lower-level skills such as number and alphabetic sequencing were intact, but the adolescents had difficulty switching back and forth between these well-learned sequences, suggesting cognitive inflexibility.\textsuperscript{6} Their difficulties were also apparent on a task assessing inhibitory control (Stroop Test), on which they were required to ignore salient cues and name the colour of the ink in which a word was printed when that colour conflicted.
with the word — for example the word “blue” was printed in red ink. They had particular difficulty with the Sorting sub-test of the Delis–Kaplan battery, on which they had to identify the principle used by the examiner to sort a series of cards. This might reflect difficulties in abstract thinking and cognitive flexibility — that is, trouble thinking about the same material in different ways. Parent and teacher reports using the Behavior Rating Inventory of Executive Function provided evaluations of multiple dimensions of executive functioning in daily life. Compared with the scores of the standardisation sample, scores of patients were elevated by 1 SD or more — indicating greater difficulty — on the shift scale, which assesses cognitive flexibility, and three of five scales contributing to the Meta-Cognition Index (Initiate, Working Memory, Plan/Organise). Executive function scores of adolescents with cyanotic CHD – d-TGA, tetralogy of Fallot, and single ventricle cardiac anatomy who underwent the Fontan operation were also reported in adolescents with single ventricle malformations. Overall, children with three forms of major cyanotic CHD – d-TGA, tetralogy of Fallot, and single ventricle – performed significantly worse than comparison groups on most tests of executive functions. Verbally mediated executive skills were altered to a similar degree in adolescents with all three forms of CHD; however, adolescents with d-TGA had better outcomes in visuo-spatially mediated executive function abilities than adolescents with tetralogy of Fallot or hypoplastic left heart syndrome, suggesting that the type of CHD affects the specific manner in which executive dysfunction is expressed.

Importantly, general problems in executive functions have also been reported in European cohorts of adolescents with CHD undergoing infant heart surgery, including cyanotic and acyanotic cardiac malformations. Altogether, these findings indicate that CHD poses a serious threat to the development of these higher-order neurocognitive functions, and that the identification of strategies to prevent or limit the impact of these deficits constitutes an urgent need in the care of patients with CHD.

Co-morbidity of executive dysfunction and other cognitive and psychiatric issues in CHD

Executive function deficits in children with CHD adversely impact other developmental domains and are associated with reduced quality of life. In the Boston Circulatory Arrest Study, 8-year-old children with d-TGA showed impaired language scores on reading comprehension and struggled to solve problems involving mathematical computation. An analysis of their difficulties revealed that the basic skills to accomplish these tasks were intact. Children scored at age-level on a test of single-word reading and had acquired basic mathematical concepts; however, they showed important difficulties integrating or coordinating these basic skills — for example, extracting the meaning from connected discourse and applying the math concepts to solve a problem — suggesting problems with working memory and organisational abilities. Executive dysfunction was also observed in children’s oral and written higher-order language skills, such as narrative and pragmatic language tasks. In general, children with d-TGA failed to organise a set of data, plan, structure, monitor, and modify output based on feedback. Whether the task involved the assembly of story elements into a coherent narrative or the correct assembly of the individual elements of a complex design, the children appeared to be lost in the details, failing to see and show how the pieces fit to make a well-formed whole.

Deficits in social cognition, including impaired Theory of Mind and complex emotion comprehension, are also part of the neurocognitive phenotype of children with complex CHD. Children and adolescents with d-TGA, tetralogy of Fallot, and univentricular hearts have reduced abilities to appreciate and make effective use of knowledge about the mental and emotional states of other people, such as identifying another’s intentions and understanding his or her perspective as different from one’s own. Importantly, social cognition deficits have been significantly associated with problems in self-regulation and inhibitory control of attention. Indeed, in the study by Calderon et al. 7-year-old children with d-TGA who failed at standard false-belief tasks assessing Theory of Mind skills also obtained lower scores on executive function tests – for example, Stroop-like tasks. When asked what a character would think/do in the false-belief stories, children tended to reflect on their own perspective and knowledge of the situation, failing to consider the character’s point of view. Children with CHD who display executive dysfunction on formal neuropsychological tests may find establishing and maintaining social relationships to be challenging, especially upon reaching adolescence. Peer interactions become more rapid in pace and information processing demands – for example, facial expression and body language and complex emotions – allegiances shift and need to be updated frequently, and much of the language used involves complex forms such as irony and sarcasm, where the surface form does not match the underlying meaning.
Early executive dysfunction may, therefore, derail normal cognitive and adaptive functioning processes and potentially increase the risk of psychiatric disorders in children with CHD.

Indeed, several studies have identified internalising problems, particularly social withdrawal, anxiety, and depressive symptoms, in children and adolescents with CHD who have undergone open-heart surgery.\(^4^4\) Externalising problems have also been reported, including disruptive behaviour, impaired self-regulation and control abilities, and attention deficit hyperactivity disorder – for example, 22% in adolescents with d-TGA compared with around 7% in the general population.\(^4^4\) Although some children and adolescents with CHD do not display the hyperactivity component of attention deficit hyperactivity disorder, we hypothesise that, in some cases, these patients present a “sluggish cognitive tempo”.\(^3^1\) These patients have slow processing speed of information, weak attentional skills, and poor working memory abilities that resemble the cognitive and behavioural profile of children diagnosed with attention deficit disorder.\(^2^0\) Recent data in adolescents with d-TGA indicated that worse psycho-social health status and quality of life was more strongly associated with concurrent executive dysfunction and attention deficit hyperactivity disorder symptoms than with other deficits identified by a neuropsychological evaluation,\(^1^9\) suggesting a link between executive impairments and reduced functioning and self-perception in everyday life.

Finally, as many patients with CHD require lifelong medical follow-up and some may have chronic heart conditions, sufficient cognitive abilities for self-management are required to guarantee an optimal prognosis. In that context, as observed in patients with other chronic diseases, executive dysfunction may strongly affect patients’ ability to adhere to medical recommendations and follow-up.\(^4^6\) Indeed, a great number of CHD patients are lost to follow-up during the transition to adult healthcare,\(^4^7\) and we hypothesise that difficulties in self-organisation and other executive issues may be among the factors contributing to this problem. Furthermore, as has been observed in patients with other developmental disorders such as attention deficit hyperactivity disorder,\(^4^8\) executive dysfunction in children with CHD might lead to inappropriate risk-taking – for example alcohol or other substance abuse – and poor decision-making skills.

**Executive function interventions in CHD: avenues for future research**

As we achieve a more nuanced understanding of the neurocognitive sequelae of CHD, it becomes increasingly evident that we must identify appropriate early preventive and treatment strategies. Considerable effort has been invested in identifying foetal and neonatal neuroprotection in CHD to reduce brain injury in these patients.\(^4^9\) However, despite these successes, neurodevelopmental impairment continues to be reported even in the most recent cohorts,\(^1\) indicating the need for parallel investigation of the efficacy of evidence-based neurocognitive interventions.

To date, very few studies have evaluated interventions aiming at improving neurocognitive outcomes in CHD and none have been directed towards executive dysfunction. McCusker et al\(^5^1\) proposed the first trial of a psychological intervention to promote adjustment in young children with CHD and their families. This intervention focussed on maternal and family functioning, parent–child relationships, individualised psycho-education, and outreach to community healthcare providers. Significant effects of the intervention were observed on maternal mental health and family functioning; however, this intervention did not have any effect on parent and teacher ratings of the children’s behaviour and school achievement. Indeed, although psychological family-centred interventions may significantly reduce parental stress and, secondarily, improve children’s neurodevelopmental outcomes, a targeted neurocognitive approach is needed to address the specific executive impairments in children with CHD.

Multiple approaches could be implemented to prevent or reduce executive dysfunction in children. These approaches are not mutually exclusive, although a proof of concept should be provided in patients with CHD before such interventions are implemented. Psycho-stimulant medications, such as methylphenidate, which target the dopaminergic system involved in prefrontal cortex control processes, have been long used in children with attention deficit hyperactivity disorder to improve working memory and attentional performance. Whether its use in children with CHD diagnosed with attention deficit hyperactivity disorder can be recommended is beyond the scope of this review; however, it is noteworthy that many children with CHD display executive dysfunction without meeting the criteria for a diagnosis of attention deficit hyperactivity disorder. Thus, in most cases, cognitive and/or behavioural interventions may be more appropriate to address these issues. Interestingly, similar to the effects of psycho-stimulants, intensive computerised training targeting working memory has recently been associated with changes in dopamine receptor density, leading to subsequent improvements in working memory and overall executive functions.\(^5^2\)

Several randomised controlled studies in typically developing children\(^5^3\)–\(^5^5\) and in children with various conditions, including low working memory spans,\(^5^6\) have provided evidence of the efficacy of cognitive training interventions; however, studies in children with CHD remain sparse. The next steps towards developing evidence-based interventions in CHD should encompass the use of both developmental and neurocognitive training approaches, and include the use of a dual approach to support the development of neurocognitive abilities, self-regulation, and self-control skills.
attention deficit hyperactivity disorder,\textsuperscript{37,58} and extremely low birth weight,\textsuperscript{59,60} have demonstrated that executive functions and particularly working memory skills can be significantly improved by cost-effective interventions.\textsuperscript{61} Cogmed is one of the most widely used interventions that specifically targets executive functions through working memory training, and it has repeatedly been found to be successful.\textsuperscript{57,58} This evidenced-based computerised program can be used with pre-school children,\textsuperscript{53,55} school-aged children, and adolescents,\textsuperscript{56-58,60} providing the flexibility needed to intervene at all developmental ages. Similar to other executive function computerised programs,\textsuperscript{54} Cogmed can be applied in a hospital or laboratory setting; however, Cogmed is also frequently used as a home-administered intervention, reducing the need for repeated hospital visits. Structured computerised training programs such as Cogmed are presented in a child-friendly computer-game format and usually require between 20 and 45 minutes of daily training for 5 weeks or more, depending on the child’s age. Clinical support and close monitoring are provided by a developmental psychologist, who provides weekly telephone feedback on the child’s progress. Improved performance after the use of Cogmed and other similar computerised working memory programs has been reported not only for the executive skills on which training is provided but also for the multi-modal non-trained skills.\textsuperscript{57,58,55,56} The use of intensive computerised programs in children has also been associated with a reduction in the number of inattentive symptoms as well as with significant improvements in mathematics, reading, and language skills.\textsuperscript{56,62,60} Some studies also demonstrate that positive effects may last 3–6 months,\textsuperscript{58} although reports have not been consistent on the longer-term efficacy of such interventions. Nevertheless, there is neurobiological evidence that well-structured computerised programs strengthen higher-order cortical activations, leading to neural changes in intra-parietal/prefrontal networks in adults\textsuperscript{65} and in children.\textsuperscript{64} These findings provide cause for hope that such neural plasticity might be induced in patients with CHD who undergo training. An ongoing randomised controlled trial at Boston Children’s Hospital will hopefully provide some insights into the feasibility and efficacy of interventions such as Cogmed in children with CHD.

Other non-pharmacological techniques have been tested in children with executive function deficits, including those diagnosed with attention deficit hyperactivity disorder, with promising results. Training of executive functions within the classroom setting has shown significant reduction of “off-task” behaviour in school-age children.\textsuperscript{65} This type of supportive intervention is typically monitored by a specialised educator who helps children to improve executive functions that are important for learning and classroom behaviour – for instance, a child might make use of memory-strategy cards that remind him or her of appropriate behaviours – for example, “I repeat what is said” or “I wait until it’s my turn”. Mindfulness training involving sitting meditation and activities to promote sensory awareness and attention regulation have also produced improvements in children’s self-regulation skills, pro-social behaviour,\textsuperscript{66} and emotion regulation.\textsuperscript{67} This type of approach is supported by data showing the brain-based mechanisms underlying these improvements, including enhanced activations in the anterior cingulate cortex and cortical and sub-cortical connectivity.\textsuperscript{67} Age-appropriate mindfulness training, meditation, and relaxation techniques may also benefit patients with CHD who present psychopathological co-morbidities including anxiety and depression disorders, with or without executive dysfunction. Finally, aerobic exercise may also improve children’s general cognitive functioning and executive functions.\textsuperscript{61} The only randomised controlled trial in CHD published to date showed positive effects of an exercise programme on health-related quality of life in children and adolescents with tetralogy of Fallot and with a Fontan circulation.\textsuperscript{68} Compared with the control group, children who received the intervention showed greater improvement in self-reported cognitive functioning, and their parents reported improved social functioning. Although this study did not use formal neuropsychological testing or any measure of executive functions, there is strong evidence that physical exercise robustly increases prefrontal cortex activations and executive function.\textsuperscript{69} Recent randomised controlled trials in healthy 7- to 9-year-old children demonstrated that an after-school physical activity programme involving age-appropriate exercises for aerobic fitness significantly improved brain and behavioural indices of executive control.\textsuperscript{70} Interestingly, these improvements were specific to tasks requiring inhibitory control and cognitive flexibility. No changes were observed on lower-level abilities. Changes after intervention could also be observed at a neurophysiologic level, as children assigned to the physical training intervention showed larger changes in fronto-parietal activation of attention networks.\textsuperscript{70} Physical activity and sport practice should be monitored in some children with CHD, but the cognitive and social benefits of these activities should be further investigated in our patients.

Conclusion

Executive function impairments are commonly observed in patients with CHD, even in the absence
of a formal attention deficit hyperactivity disorder diagnosis. These neurocognitive difficulties can have widespread adverse effects on children’s cognitive development, psycho-social functioning, and quality of life. There is an urgent need to develop and test the efficacy of evidence-based interventions to address these difficulties throughout childhood and adolescence. The earlier we can implement such interventions, the better the prognosis is likely to be. Computerised working memory training and other more ecological techniques may help improve the developmental trajectories of these children. Importantly, as executive functions are closely linked to other cognitive, including social, processes, the impact of interventions targeting executive functions is likely to transfer to these other, related areas. This is conjectural, however, and remains to be demonstrated. Multi-disciplinary efforts should be made to provide a proof of concept that these preventive interventions can be implemented in a clinical setting in patients with CHD. The costs and accessibility of these interventions are important considerations. A close partnership among medical caregivers, neuropsychologists, and families would facilitate the prevention and treatment of the neurodevelopmental morbidities associated with CHD. Evidence-based interventions are now available, and until we evaluate their efficacy in reducing neurodevelopmental morbidities in patients with CHD, a large gap will remain in the care that we provide to them.

Acknowledgement
None.

Financial Support
Post-doctoral fellowship from L’Oréal-UNESCO awarded to Dr J. Calderon.

Conflicts of Interest
None.

Ethical Standards
The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees (Boston Children’s Hospital).

References


