NIH Public Access
Author Manuscript
J Pediatr. Author manuscript; available in PMC 2015 October 01.

Published in final edited form as:
J Pediatr. 2014 October ; 165(4): 760–766. doi:10.1016/j.jpeds.2014.06.029.

Psychiatric Disorders and Function in Adolescents with d-TGA

David R DeMaso, MD[1,2,4], **Madelyn Labella, BA**[1], **George Alexander Taylor, BA**[1], **Peter W Forbes, MA**[1], **Christian Stopp, MS**[2], **David C Bellinger, PhD, MSc**[1,2,4,5], **Michael J Rivkin, MD**[1,3,4], **David Wypij, PhD**[2,4,5], and **Jane W Newburger, MD, MPH**[2,4]

[1]Department of Psychiatry, Boston Children's Hospital, Boston, MA

[2]Department of Cardiology, Boston Children's Hospital, Boston, MA

[3]Department of Neurology, Boston Children's Hospital, Boston, MA

[4]Harvard Medical School, Boston, MA

[5]Department of Biostatistics, Harvard School of Public Health, Boston, MA

Abstract

Objective—To compared adolescents with with d-transposition of the great arteries (d-TGA) with healthy adolescents with respect to prevalence of psychiatric disorders and global psychosocial functioning.

Study design—Subjects, consisting of 139 adolescents with d-TGA (16.1±0.5 years) and 61 healthy adolescents (15.3±1.1 years) without known risk factors for brain disorders, underwent a battery of assessments, including semi-structured psychiatric interviews; self-report measures of depressive, anxiety, and disruptive behavior symptoms; and brain magnetic resonance imaging. Previous cognitive functioning and parental stress assessments at age eight as well as parental post-traumatic stress at age 16 years were explored as potential risk factors predictive of overall psychiatric functioning.

Results—Compared with healthy adolescents, adolescents with d-TGA had higher lifetime prevalence of structured interview-derived ADHD (19% versus 7%, P=0.03), along with reduced global psychosocial functioning (80.6±11.2 versus 87.2±7.1, P<0.001) as well as significant increases in self-reported depressive (P=0.01), anxiety (P=0.02), and disruptive behavior symptoms (parent P<0.001 and adolescent P=0.03). Nevertheless, these youth scored in the non-clinical range on all self-report measures. Level of global psychosocial functioning was positively related to cognitive functioning (P<0.001) and negatively related to parental stress (P=0.008).

© 2014 Mosby, Inc. All rights reserved.

Corresponding Author: David R DeMaso, MD, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA; tel 617-355-6724, fax 617-730-0428, david.demaso@childrens.harvard.edu,.

The authors declare no conflicts of interest.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Conclusions—Although adolescents with d-TGA demonstrate significant resilience to known neuropsychological and academic deficits, they show increased rates of ADHD and reduced psychosocial functioning. Impaired cognitive functioning and parental stress at younger age emerged as significant risk factors for psychiatric impairment.

Keywords

brain; adolescents; transposition of great vessels; psychiatric disorder; ADHD

Since 1988, the Boston Circulatory Arrest Study (BCAS) has followed a cohort of children with d-transposition of the great arteries (d-TGA).[1] The impact of this cardiac defect and associated treatment on the neuropsychological status of these patients has been prospectively evaluated in the perioperative period and at ages one, four, eight, and 16 years. Adolescents with d-TGA were more likely than healthy referent subjects to have focal and multifocal brain abnormalities and to require multiple remedial services, including tutoring, grade retention, early intervention, occupational therapy, and special education.[2] Deficits were identified in multiple functional domains, including attention, executive functioning, memory, motor, and visual-spatial function.[2-5]

These neuropsychological deficits would appear to put affected youth at risk for disabling psychiatric disorders. However, the literature has only focused on patient and parent symptom self-reports as opposed to clinician diagnosis of disorder. The American Heart Association has noted that parents of children with complex congenital heart disease (CHD) report the presence of internalizing (e.g., anxiety, somatic complaints, depressive symptoms) and externalizing (eg, inattention and hyperactivity) problems in 15-25% of their children, and nearly 20% of adolescents with CHD report self-perceived impaired psychosocial functioning.[6] A meta-analysis of 11 studies reported that significant emotional problems generally only surface in adolescence and only in those with the most severe heart disease.[7] Self-reported lower health-related quality of life deficits have also been reported in several studies of pediatric heart disease.[8,9] The only study to date specifically assessing diagnostic outcomes with structured interviews found that nearly 22% of a mixed heart lesion severity cohort in Portugal had a psychiatric disorder (predominantly depression and anxiety).[10]

We describe the presence of psychiatric disorders, as well as the level of psychosocial functioning, in the BCAS cohort at age 16 years. Adolescents with d-TGA were compared with healthy adolescents with respect to the prevalence of structured interview-derived psychiatric disorders and clinician-rated global psychosocial functioning.

METHODS

The Boston Circulatory Arrest Study (BCAS) has followed a cohort with d-transposition of the great arteries (d-TGA) who underwent an arterial switch operation (ASO) as infants between 1988 and 1992. This longitudinal study has examined this cohort at critical developmental time periods – infancy (1 year), pre-school (4 years), school-age (8 years), and adolescence (16 years). The eligibility criteria, trial methods, and outcomes have been previously described.[1-5] At 16 years, the cohort received assessments of their

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

neuropsychological status, their brain structure, and their psychiatric status. The latter assessments are the main focus of this manuscript.

A referent comparison group of healthy adolescents was recruited using criteria adapted from the National Institutes of Health MRI Study of Normal Brain Development,[11] which excluded subjects with disorders recognized to affect brain structure and function. This study was approved by the Hospital's Committee on Clinical Investigation and conducted in accordance with institutional guidelines. Parents provided informed consent and adolescents provided assent.

The Schedule for Affective Disorders and Schizophrenia for School-Aged Children - Present and Lifetime Version (K-SADS-PL) is a structured psychiatric interview that was administered to each adolescent and one or both parent(s) to assess current and lifetime history of DSM-IV mood, anxiety, and disruptive behavior disorders.[12] The interviews were performed by bachelor degree-level assessors who underwent extensive training on the use of the instrument. All interviews were reviewed with a board certified child and adolescent psychiatrist to determine final diagnoses, if any. Data from the parent and adolescent interviews were combined using standard procedures to obtain a set of psychiatric diagnoses. The main endpoints were binary: whether or not the adolescent met criteria for a current or lifetime target psychiatric diagnosis.

The *Children's Global Assessment Scale* (CGAS) was completed by study clinicians based on information obtained from the K-SADS-PL.[13] The CGAS condenses knowledge about an adolescent's psychosocial functioning from the previous 30 days into a single score on a 100 point scale (where >70 indicates normal functioning, and ≤70 indicates pathological functioning).

The *Brief Psychiatric Rating Scale for Children* (BPRS-C) is a 21-item clinician-rated scale that yields a concise descriptive profile applicable to a range of adolescent psychopathology through scores on seven scales of pathology (behavioral problems, depression, thinking disturbance, psychomotor excitation, withdrawal retardation, anxiety, and organicity), as well as a summary total severity score, which served as the main endpoint.[14]

The *Children's Depression Inventory* (CDI) is a 27-item questionnaire given to both parents and adolescents that assesses the frequency and severity of depressive symptoms over the previous two weeks.[15] The CDI provides scores in five domains (negative mood, ineffectiveness, negative self-esteem, interpersonal problems, and anhedonia) as well as a total summary score, which served as the main endpoint.

The *Revised Children's Manifest Anxiety Scale* (RCMAS) is a 37-item self-report measure completed by the adolescent that yields scores on four subscales (social desirability, social concerns/concentration, physiological anxiety, and worry/oversensitivity) as well as a summary total score, which served as the main endpoint.[16]

The *Child Stress Disorders Checklist* (CSDC) is a 36-item measure that assesses acute stress and post-traumatic symptoms in children.[17] Parents in the d-TGA group completed the CSDC using their child's cardiac illness as a traumatic event, and parents in the referent

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

group completed the measure if they could identify at least one past traumatic event experienced by their child. The CSDC yields scores in five subscales (re-experiencing, avoidance, numbing and dissociation, increased arousal, and impairment in functioning) as well as a CSDC total posttraumatic symptom score, which served as the main endpoint.

The *Conners' ADHD Rating Scales* (CADS, parent and adolescent versions*)* consists of 18 items linked to specific DSM-IV criteria, as well as 12 general items yielding an overall ADHD index.[18] ADHD index scores on parent and adolescent versions of CADS were converted into T-scores which served as the main endpoints.

The *Conduct Disorder Scale* (CDS) is a 40-item behavioral checklist linked to the DSM-IV conduct disorder criteria that yields scores in four subscales (aggressive conduct, hostility, deceitfulness/theft, and rule violations).[19] The conduct disorder quotient, a cumulative figure derived from these subscales, served as the main endpoint.

A description of comparisons between the d-TGA and referent groups in structural MRI outcomes has been provided previously.[2] MRI abnormalities were significantly more prevalent in the d-TGA group than in the referents (33% versus 4%; $P<0.001$) and most commonly consisted of focal/multifocal abnormalities (23% versus 0%; $P<0.001$) and brain mineralization/deposits (21% versus 0%; $P<0.001$).[2]

Given the unique long-term perspective of the BCAS, we explored the relationship of psychiatric disorder and global psychosocial functioning to physical illness severity, neuropsychological functioning, and parental stress at age eight, as well as parental post-traumatic stress at age 16, in order to identify potential risk factors predictive of psychiatric dysfunction.

The *WISC-III Full Scale IQ score*, assessed at age eight for the d-TGA group and age 16 for the referent group, was used to characterize overall cognitive functioning.[20] The WISC-III was not re-administered to the d-TGA group at age 16, as IQ scores measured at ages 8 and 16 correlate at higher than 0.85[21], suggesting that little new information would be gained.

The *Parenting Stress Index* (PSI) was administered to the parent at the BCAS 8-year assessment. It is a 120-item measure that assesses the parental perception of the parent-child system.[22] The PSI total stress score is derived from two scales: child domain (measuring parent-child system stress caused by the child's functioning) and parent domain (measuring parent-child system stress caused by the parent's functioning). The total stress score provides a global measure of parenting stress.

The *Posttraumatic Stress Diagnostic Scale* (PDS) examined possible medical trauma from raising a child with d-TGA.[23] The PDS is a 49-item parent self-report measure that assesses the DSM-IV PTSD diagnostic criteria in the parent, and yields an ordinal severity score (mild, moderate, moderate-severe, or severe). The parents in the d-TGA group at age 16 years completed the PDS using their child's cardiac illness as a traumatic event, and referent group parents completed the measure if they had experienced at least one past traumatic event.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Data Analyses

The presence of psychiatric disorders and global psychosocial functioning (CGAS scores) were our primary outcome variables. The d-TGA group was compared with the referent group using two-sample *t*-tests with equal variance for continuous variables and Fisher's exact tests or Cochran-Armitage exact trend tests for categorical variables on demographic and medical history, neuropsychological functioning, and parental stress. Fisher's exact tests were used to compare the groups based on lifetime and current K-SADS-PL psychiatric disorder classification. Psychosocial functioning measures were compared using two-sample *t*-tests with unequal variance for group means and Fisher's exact tests for meeting clinical thresholds.

Stepwise regression techniques were used in the d-TGA group to evaluate global psychosocial functioning (CGAS scores) and psychiatric disorder in relation to physical illness severity (presence of a ventricular septal defect, randomized treatment assignment to deep hypothermic circulatory arrest or low-flow bypass, illness severity as measured by history of hospital seizures, highest tertile of length of hospitalization, any operations since the arterial switch operation, and high catheterization exposure), cognitive functioning (IQ), and parental stress measures (PSI and PDS). The key analytic questions were whether physical illness severity in infancy, cognitive functioning at age eight, parental stress at child's age of eight, and parental post-traumatic stress at age 16 years were associated with CGAS score via linear regression or ADHD diagnosis via logistic regression. Other covariates considered included age, sex, family social status, and MRI findings. All *P* values are two-sided and $P<0.05$ was used as the threshold for statistical significance.

RESULTS

Of 159 infants enrolled in the BCAS alive and living in the US at age 16, 139 (87%) returned for follow-up assessment (mean age of 16.1±0.5 years).[2] The referent group consisted of 61 healthy adolescents (15.3±1.1 years) without known risk factors for brain disorders. At 16-year follow-up, the d-TGA group had a greater percentage of males than the referent group (75% versus 49%, $p<0.001$), reflecting expected male predominance found with this lesion. The d-TGA group also had more Caucasians (93% versus 79%, $P=0.02$) and were of lower family social status (mean Hollingshead Index, 45.6 versus 52.7, $P<0.001$). The two groups did not differ in birth weight or gestational age.

Adolescents with d-TGA were more likely than the referent group to meet the K-SADS-PL criteria of a lifetime psychiatric diagnosis ($P=0.04$; Table I). This difference was primarily driven by the greater proportion of d-TGA patients diagnosed with lifetime attention-deficit/hyperactivity disorder (ADHD), 19% as compared with 7% of the referent group ($P=0.03$). Current diagnoses of ADHD were more common in the d-TGA group (16%) than the referent group (3%, $P=0.01$). However, the groups were similar in prevalence of mood or anxiety disorders.

Both groups demonstrated global psychosocial functioning well above the threshold of clinical risk for psychopathology.[13] However, adolescents with d-TGA scored significantly lower on the CGAS than the referent group ($P<0.001$; Table II) and a greater proportion of

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

the d-TGA group scored in the pathological functioning range on the CGAS (15% versus 3%, *P*=0.02).

Performance of the groups differed significantly on the psychiatric symptom measures (Table II). Although mean BPRS-C total severity scores were low for both groups, indicating little clinical difficulty, BPRS-C scores of the d-TGA group were significantly higher (i.e., worse) than those of the referent group (*P*=0.01).

The CDI total T scores of both groups fell within the normal range, though the mean score in the d-TGA group was significantly higher than in the referent group (*P*=0.01). Although mean RCMAS total anxiety scores did not indicate clinical anxiety in either group,[16] the d-TGA group reported significantly more anxiety than the referent group (*P*=0.02). A comparison of CSDC total post-traumatic symptom scores showed d-TGA patients had more symptoms than their referent counterparts whose parents endorsed a past trauma (*P*=0.001).

After arterial switch procedure in infancy, the average durations of intubation after surgery, intensive care unit stay, and days in the hospital were 4.2±5.7 days, 6.7±6.6 days, and 11.1±8.2 days, respectively. Twenty-two infants (of 108 measured) experienced EEG activity consistent with seizures in the 48 hours after undergoing surgery and 9 (of 139) experienced definite clinical seizures. Subsequent cardiac operations after the ASO occurred in 11% of the group, and 7% had high catheterization exposure, defined as ≥3 diagnostic catheterizations or ≥2 interventional catheterizations with any number of diagnostic catheterizations. The d-TGA group received ADHD treatment medication (9%) and other psychotropic medications (6%).

The mean full-scale IQ score for the d-TGA group at age 8 years was signigicantly lower than the full-scale IQ score for the referent group at 16 years (*P*<0.001; Table III).

The mean total PSI score for the d-TGA group was within the range of normal family function (Table III). The mean PDS symptom severity score for d-TGA parents was 3.0±4.9, which falls in the mild range of symptom severity. Twenty-five parents in the referent group endorsed having experienced at least one past traumatic event and subsequently completed the PDS. They received a mean score of 3.6±6.1, which was within the mild range of symptom severity and not significantly different from the d-TGA group.

Using linear regression, higher PSI scores were significantly associated with lower global psychosocial functioning (CGAS scores) (*P*=0.008), even after adjusting for neuropsychological functioning (IQ) and PDS severity (Table IV). Similarly, PDS severity was associated with lower CGAS scores, such that children of parents with moderate/severe PDS symptoms earned CGAS scores that were on average 8.6 points lower than children of parents with no symptoms (*P*=0.02). Higher IQ scores at age eight years were associated with higher CGAS scores at age 16 years after adjusting for the two parental stress measures: a 1 SD increase in IQ was associated with an estimated 2.9 point increase in CGAS (*P*<0.001). Age, sex, family social status, ventricular septal defect, assignment to deep hypothermic circulatory arrest, history of hospital seizures, longer length of hospitalization, any operations since ASO, and high catheterization exposure were not

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

significantly related to global psychosocial functioning as measured by the CGAS when adjusting for IQ and parental stress.

Logistic regression was used to identify predictors of a K-SADS-PL diagnosis of ADHD, the psychiatric diagnosis primarily accounting for the significant differences between the d-TGA and healthy referent groups. Higher parental stress scores as measured by PSI at age eight were significantly associated with a higher risk of lifetime diagnosis of ADHD (P=0.04; Table IV). Other factors including intellectual functioning at age 8 and physical illness severity were not significantly associated with an ADHD diagnosis.

Secondary analyses were conducted using the 111 d-TGA subjects with associated MRI data. The presence of a structural brain abnormality did not significantly predict global psychosocial functioning (CGAS scores) or ADHD diagnosis either in univariate analyses or when added to the regressions outlined above.

DISCUSSION

The most common psychiatric diagnosis in our d-TGA group was ADHD, present in 16% of subjects. Our findings are concordant with previous publications demonstrating a high lifetime prevalence of ADHD, with inattention and hyperactivity, in children with congenital heart disease.[24-26] Given the high rates of ADHD associated with d-TGA,[27-29] the effectiveness of stimulants in ADHD,[30,31] and the reported tolerability of these medications in youth with complex heart disease,[28] primary care clinicians and cardiologists should consider psychotropic medication as a treatment option.

In the current study, impaired cognitive functioning and parental stress at age eight years emerged as significant risk factors for adolescent psychiatric dysfunction. This finding is consistent with previous reports in which problematic cognitive and family functioning were associated with poorer individual emotional adjustment.[32,33] Parental stress was more closely related to the child's psychosocial functioning than physical illness severity. However, the causal direction is unclear: higher parental stress in childhood may have contributed to self-regulatory dysfunction in adolescence, or early symptoms of ADHD may have increased parental stress in childhood.

We found no relationship of abnormalities on anatomic structural MRI with psychiatric functioning, similar to the reported absence of such MRI abnormalities with neuropsychological deficits in the d-TGA cohort.[2] We previously reported that this group demonstrates differences of white matter microstructure, as reflected by diminished fractional anisoptropy, in cerebral deep white matter, brainstem, and cerebellum as compared with the referent group.[34] It is likely that routine anatomic structural MRI has insufficient sensitivity to detect correlations between brain structure and psychiatric functioning.

These findings should be interpreted in light of several limitations. Generalizability might be limited as the trial was conducted at a single center on a sample consisting largely of white male subjects, as well as by use of older methods of operative/perioperative strategies that have changed over the 20 years since enrollment. Comparing IQ scores at age 8 for the d-

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

TGA group to referent group IQ scores at age 16 years is another limitation; however intellectual scores between age 8 and 16 are highly correlated, suggesting similar results would be found with contemporaneous assessment.[21] We compared adolescents with d-TGA to healthy patients without known disorders that could affect brain structure and function; it is likely that differences between our cohort and the general population including patients with such disorders would have been smaller. The use of academic and behavioral services might have been inflated in our group compared with similar patients receiving routine care, as recommendations made for these "clinically indicated" services were made at earlier cohort evaluations. If subjects did benefit from any services that they received, they might have had better outcomes than would otherwise be expected among adolescents with d-TGA.

Adolescents with d-TGA appear to be at an increased risk for ADHD and reduced psychiatric functioning compared with healthy adolescents. These difficulties appear to be most pronounced in the context of impaired cognitive functioning and parenting stress. Primary care clinicians and cardiologists should be alert to the early identification of psychiatric problems in adolescents with complex heart disorders, particularly in the context of struggles with learning and family adjustment.

Acknowledgments

Supported by National Heart, Lung and Blood Institute (HL77681), Farb Family Fund, National Center for Research Resources (RR02172), and National Institute of Child Health and Human Development (HD18655).

References

1. Newburger JW, Jonas RA, Wernovsky G, Wypij D, Hickey PR, Kuban KC, et al. A comparison of the perioperative neurologic effects of hypothermic circulatory arrest versus low-flow cardiopulmonary bypass in infant heart surgery. N Engl J Med. 1993; 329:1057–1064. [PubMed: 8371727]
2. Bellinger DC, Wypij D, Rivkin MJ, DeMaso DR, Robertson RL, Dunbar-Masterson C, et al. Adolescents with d-transposition of the great arteries corrected with the arterial switch procedure: neuropsychological assessment and structural brain imaging. Circulation. 2011; 124:1361–1369. [PubMed: 21875911]
3. Bellinger DC, Jonas RA, Rappaport LA, Wypij D, Wernovksy G, Kuban KC, et al. Developmental and neurologic status of children after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass. N Engl J Med. 1995; 332:549–555. [PubMed: 7838188]
4. Bellinger DC, Wypij D, Kuban KC, Rappaport LA, Hickey PR, Wernovsky G, et al. Developmental and neurological status of children at 4 years of age after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass. Circulation. 1999; 100:526–532. [PubMed: 10430767]
5. Bellinger DC, Wypij D, duPlessis AJ, Rappaport LA, Jonas RA, Wernovksy G, et al. Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: the Boston Circulatory Arrest Trial. J Thorac Cardiovasc Surg. 2003; 126:1385–1396. [PubMed: 14666010]
6. Marino BC, Lipkin PH, Newburger JW, Peacock G, Gerdes M, Gaynor JW, et al. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management. A scientific statement of the American Heart Association. Circulation. 2012; 126:1143–1172. [PubMed: 22851541]
7. Karsdorp PA, Everaerd W, Kindt M, Mulder BJ. Psychological and cognitive functioning in children and adolescents with congenital heart disease: a meta-analysis. J Pediatr Psychol. 2007; 32:527–541. [PubMed: 17182669]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

8. Uzark K, Jones K, Slusher J, Limbers CA, Burwinkle TM, Varni JW. Quality of life in children with heart disease as perceived by children and parents. Pediatrics. 2008; 121:e1060–e1067. [PubMed: 18450848]
9. Marino BS, Tomlinson RS, Wernovsky G, Drotar D, Newburger JW, Mahony L, et al. Validation of the pediatric cardiac quality of life inventory. Pediatrics. 2010; 126:498–508. [PubMed: 20805147]
10. Freitas IR, Castro M, Sarmento SL, Moura C, Vianna V, Areias JC, et al. A cohort study on psychosocial adjustment and psychopathology in adolescents and young adults with congenital heart disease. BMJ Open. Jan 28.2013 3(1):e001138. doi: 10.1136/bmjopen-2012-001138.
11. Evans AC. The NIH MRI study of normal brain development. Neuroimage. 2006; 30:184–202. [PubMed: 16376577]
12. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry. 1997; 36:980–988. [PubMed: 9204677]
13. Shaffer D, Gould MS, Brasic J, Amborsini P, Fisher P, Bird H, et al. A Children's Global Assessment Scale (CGAS). Arch Gen Psychiatry. 1983; 40:1228–1231. [PubMed: 6639293]
14. Hughes CW, Rintelmann J, Graham JE, Lopez M, MacCabe N. A revised anchored version of the BPRS-C for childhood psychiatric disorders. J Child Adolesc Psychopharmacol. 2001; 11:77–93. [PubMed: 11322749]
15. Kovacs, M. Children's Depression Inventory: Technical Manual. Multi-Health Systems; North Tonawanda (NY): 1992.
16. Reynolds, CR.; Richmond, BO. Revised Children's Manifest Anxiety Scale: Manual. Western Psychological Services; Los Angeles: 1985.
17. Saxe G, Chawla N, Stoddard F, Kassam-Adams N, Courtney D, Cunningham K, et al. Child Stress Disorders Checklist: a measure of ASD and PTSD in children. J Am Acad Child Adolesc Psychiatry. 2003; 42:972–978. [PubMed: 12874500]
18. Conners, CK. Conners' Rating Scales-Revised: User's Manual. Multi-Health Systems; North Tonawanda (NY): 1997.
19. Gilliam, JE. Conduct Disorder Scale: Examiner's Manual. PRO-ED; Austin: 1997.
20. Wechsler, D. Wechsler Intelligence Scale for Children. 3rd ed. The Psychological Corporation; San Antonio: 1991.
21. Mortensen EL, Andresen J, Kruuse E, Sanders SA, Reinisch JM. IQ stability: The relation between child and young adult intelligence test scores in low birth weight samples. Scandinavian Journal of Psychology. 2003; 44:395–398. [PubMed: 12887561]
22. Abidin, RR. Parenting Stress Index: Professional Manual. 3rd ed. PAR; Lutz (FL): 1995.
23. Foa, EB. Posttraumatic Stress Diagnostic Scale: Manual. NCS Pearson; Minneapolis: 1995.
24. Karl TR, Hall S, Ford G, Kelly EA, Brizard CP, Mee RB, et al. Arterial switch with full-flow cardiopulmonary bypass and limited circulatory arrest: neurodevelopmental outcome. J Thorac Cardiovasc Surg. 2004; 127:213–222. [PubMed: 14752433]
25. Neufeld RE, Clark BG, Robertson CM, Moddemann DM, Dinu IA, Joffe AR, et al. Five-year neurocognitive and health outcomes after the neonatal arterial switch operation. J Thorac Cardiovasc Surg. 2008; 136:1413–1421. [PubMed: 19114183]
26. Hovels-Gurich HH, Seghaye MC, Dabritz S, Messmer BJ, von Bernuth G. Cognitive and motor development in preschool and school-aged children after neonatal arterial switch operation. J Thorac Cardiovasc Surg. 1997; 114:578–585. [PubMed: 9338643]
27. Hansen E, Poole TA, Nguyen V, Lerner M, Wigal T, Shannon K, Wigal SB, Batra AS. Prevalence of ADHD symptoms in patients with congenital heart disease. Pediatr Int. 2012; 54:838–843. [PubMed: 22882233]
28. Batra AS, Alexander ME, Silka MJ. Attention-deficit/hyperactivity disorder, stimulant therapy, and the patient with congenital heart disease: evidence and reason. Pediatr Cardiol. 2012; 33:394–401. [PubMed: 22298228]
29. Shillingford AJ, Glanzman MM, Ittenbach RF, Clancy RR, Gaynor JW, Wernovsky G. Inattention, hyperactivity, and school performance in a population of school-age children with complex

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

congenital heart disease. Pediatrics. 2008; 121:e759–67. doi: 10.1542/peds.2007-1066. [PubMed: 18381503]

30. The MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder (ADHD). Arch Gen Psychiatry. 1999; 56:1073–1086. [PubMed: 10591283]
31. Wolraich M, Brown L, Brown RT, DuPaul G, Earls M, Feldman HM, et al. Sub-committee on Attention-Deficit/Hyperactivity Disorder; Steering Committee on Quality Improvement and Management. ADHD: Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. Pediatrics. 2011; 128:1007–1022. [PubMed: 22003063]
32. DeMaso DR, Campis LK, Wypij D, Bertram S, Lipshitz M, Freed M. The impact of maternal perceptions and medical severity on the adjustment of children with congenital heart disease. J Pediatr Psychol. 1991; 16:137–149. [PubMed: 2061786]
33. Campis LB, DeMaso DR, Twente AW. The role of maternal factors in the adaptation of children with craniofacial disfigurement. Cleft Palate Craniofac J. 1995; 32:55–61. [PubMed: 7727488]
34. Rivkin MJ, Watson CG, Scoppettuolo LA, Wypij D, Vajapeyam S, Bellinger D, et al. Adolescents with d-transposition of the great arteries repaired in early infancy demonstrate reduced white matter microstructure associated with clinical risk factors. J Thorac Cardiovasc Surg. 2013; 146:543–549. [PubMed: 23375991]

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

TABLE 1

K-SADS-PL Psychiatric diagnoses of adolescents with d-transposition of the great arteries (d-TGA) and referent group of healthy adolescents without known risk factors for brain disorders

	d-TGA (n=139)		Referent (n=61)		*P* value[a]	
	Lifetime	**Current**	**Lifetime**	**Current**	**Lifetime**	**Current**
	Number of subjects (%)					
Any Psychiatric Disorder[a]	48 (35)	32 (23)	12 (20)	7 (11)	0.04	0.08
Mood Disorders	10 (7)	6 (4)	4 (7)	0	1.0	0.18
Major Depressive Disorder	8 (6)	5 (4)	3 (5)	0	1.0	0.33
Psychotic Features	1 (1)	1 (1)	0	0	1.0	1.0
Depressive Disorder NOS	1 (1)	0	1 (2)	0	0.52	-
Bipolar I Disorder	1 (1)	1 (1)	0	0	1.0	1.0
Anxiety Disorders	16 (12)	7 (5)	5 (8)	4 (7)	0.62	0.74
Panic Disorder	2 (1)	1 (1)	1 (2)	1 (2)	1.0	0.52
Separation Anxiety Disorder	4 (3)	2 (1)	0	0	0.32	1.0
Simple Phobia	5 (4)	3 (2)	4 (7)	3 (5)	0.46	0.37
Social Phobia/Avoidant Disorder	3 (2)	1 (1)	0	0	0.55	1.0
Generalized Anxiety Disorder	2 (1)	1 (1)	1 (2)	1 (2)	1.0	0.52
Obsessive-Compulsive Disorder	1 (1)	0	0	0	1.0	-
Posttraumatic Stress Disorder	0	0	1 (2)	1 (2)	0.31	0.31
Disruptive Behavior Disorders	27 (19)	22 (16)	5 (8)	3 (5)	0.06	0.04
Attention-deficit/hyperactivity Disorder	26 (19)	22 (16)	4 (7)	2 (3)	0.03	0.01
Oppositional Defiant Disorder	2 (1)	1 (1)	1 (2)	1 (2)	1.0	0.52
Other Disorders						
Chronic Motor or Vocal Tic Disorder	5 (4)	2 (1)	1 (2)	0	0.67	1.0
Transient Tic Disorder	2 (1)	1 (1)	0	0	1.0	1.0
Anorexia Nervosa	0	0	1 (2)	0	0.31	-

K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School-Aged Children - Present and Lifetime Version; NOS = not otherwise specified

Subjects may have had more than one psychiatric disorder at the time of evaluation.

[a] Fisher exact test.

[b] Includes DSM-IV Axis I mood, anxiety, disruptive behavior and other disorders referenced in table but excludes elimination disorders and intellectual ability.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

TABLE 2

Dimensional measures of psychosocial functioning in adolescents with d-transposition of the great arteries (d-TGA) and referent group of healthy adolescents without known risk factors for brain disorders

	Type of report	d-TGA (*n* = 139)	Referent (*n* = 61)	*P* value[a]
		Mean ± SD		
Global Psychosocial Functioning				
Children's Global Assessment Scale	Clinician	80.6 ± 11.2	87.2 ± 7.1	<0.001
Psychiatric Symptoms				
Overall Symptom Scale				
Brief Psychiatric Rating Scale for Children: Total Severity Score	Clinician	2.5 ± 5.2	1.1 ± 2.3	0.01
Depressive Symptoms				
Children's Depression Inventory: Total T-Score	Self	43.5 ± 8.2	41.0 ± 5.8	0.01
Anxiety Symptoms				
Revised Children's Manifest Anxiety Scale: Total Anxiety T-Score	Self	43.1 ± 11.8	39.1 ± 10.2	0.02
Child Stress Disorders Checklist: Total Posttraumatic Symptom Score	Self	4.2 ± 5.5	1.9 ± 2.3[b]	0.001
Disruptive Behavior Symptoms				
Conners' ADHD/DSM-IV Scales: ADHD Index T Score	Parent	53.6 ± 13.0	46.3 ± 6.0	<0.001
Conners' ADHD/DSM-IV Scales: ADHD Index T Score	Self	48.0 ± 10.5	44.8 ± 8.9	0.03
Conduct Disorder Scale: Conduct Disorder Quotient	Parent	47.6 ± 10.1	44.6 ± 7.4	0.02

ADHD = attention-deficit/hyperactivity disorder; DSM-IV = American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, 4th edition

[a] Two-sample *t*-test with unequal variances.

[b] For adolescents in the referent group, 21 Child Stress Disorders Checklist values are available.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

TABLE 3

Measures of neuropsychology functioning and parental stress in adolescents with d-transposition of the great arteries (d-TGA) and referent group of healthy adolescents without known risk factors for brain disorders

	d-TGA (*n* = 139)	Referent (*n* = 61)	*P* value[a]
	Mean ± SD or %		
Neuropsychology functioning and parental stress			
Full-Scale IQ (d-TGA at 8 yr, referent at 16 yr)	98 ± 15	108 ± 11	<0.001
Parenting Stress Index (at 8 yr)	205 ± 41	-	-
Posttraumatic Stress Diagnostic Scale			
Symptom Severity Score	3.0 ± 4.9	3.6 ± 6.1[b]	0.55
Symptom Severity Rating			0.87
None	46	44	
Mild	46	44	
Moderate/Severe	9	12	

[a] Two-sample *t*-tests with equal variance for continuous variables and Cochran-Armitage exact trend test for the Symptom Severity Rating.

[b] For adolescents in the referent group, 25 Posttraumatic Stress Diagnostic Scale values are available.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

TABLE 4

Significant predictors of CGAS score (n = 131) and ADHD diagnosis (n=134) in adolescents with d-transposition of the great arteries

Dependent Variable	Predictor Variables	ß (95% CI)	*P* value
CGAS	Full-Scale IQ (at 8 yr)	0.19 (0.08, 0.30)	<0.001
	Parenting Stress Index (at 8 yr)	−0.05 (−0.09, −0.01)	0.008
	Posttraumatic Stress Diagnostic Scale		0.02
	Symptom Severity Rating:		
	None	---	---
	Mild	−2.21 (−5.53, 1.12)	0.19
	Moderate/Severe	−8.57 (−14.50, −2.63)	0.005
		OR (95% CI)	***P* value**
K-SADS-PL Lifetime Diagnosis of ADHD	Parenting Stress Index (at 8 yr)	1.012 (1.001, 1.023)	0.04

CGAS = Children's Global Adjustment Scale; ADHD = attention-deficit/hyperactivity disorder; CI = Confidence interval; K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School-Aged Children - Present and Lifetime Version