



Neurocognitive and Psychological Outcomes in Adults With Dextro-Transposition of the Great Arteries Corrected by the Arterial Switch Operation

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Background. Neurodevelopmental impairments have frequently been described in children and adolescents with dextro-transposition of the great arteries (d-TGA). The arterial switch operation (ASO) to correct d-TGA has been used for more than 30 years, and more than 90% of these patients now reach adulthood. However, very little is known about their long-term functional outcomes. The present study investigated neurocognitive outcomes and the prevalence of psychiatric disorders in adults with d-TGA corrected by ASO.

Methods. Neurocognitive functioning was comprehensively assessed (general intellectual functioning, language, attention, visual-spatial skills, executive functions, memory) in 67 adults (59.7% men) with d-TGA (aged 22.9 ± 3.4 years) and in 43 healthy individuals. The prevalence of psychiatric disorders, including depression and anxiety, was evaluated using a structured diagnostic interview. We also analyzed patient- and operative-related risk factors associated with outcomes.

Results. Compared with the general population and the control group, adults with d-TGA displayed reduced performance in tasks assessing attention, visual-spatial skills, executive functions, and memory (all $p < 0.05$). Compared with controls, patients had also a higher lifetime prevalence of depression (43% vs 19%, $p = 0.008$) and anxiety disorders (54% vs 33%, $p = 0.025$). Predictors of long-term outcomes included gender and parental socioeconomic and educational status (all $p < 0.05$).

Conclusions. Adults who have undergone a neonatal ASO to correct d-TGA have an increased risk of cognitive deficits and psychiatric disorders. Evaluation of long-term neuropsychological and psychosocial outcomes in early adulthood is a crucial step to anticipate for adapted treatment strategies in adults with congenital heart disease.

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Children and adolescents with critical congenital heart disease (CHD) are at risk of neurodevelopmental dysfunction [1]. More specifically, youth with dextro-transposition of the great arteries (d-TGA) display an alarmingly high prevalence of neuropsychological and psychiatric morbidities [2, 3]. Although the arterial switch operation (ASO) to correct d-TGA has been the method of choice for more than 25 years and more than 90% of

patients now reach adulthood [4], the long-term neurocognitive and psychological trajectory of this population remains scarcely known. Very few studies have explored neuropsychological outcomes in adults with mixed types of CHD [5, 6], and to date, none has focused on the adult neuropsychological and psychiatric outcomes of the specific population with d-TGA corrected with the ASO [7].

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Abbreviations and Acronyms

ASO	= arterial switch operation
CHD	= congenital heart disease
CI	= confidence interval
CVLT	= California Verbal Learning Test
DHCA	= deep hypothermic circulatory arrest
d-TGA	= dextro-transposition of the great arteries
MINI	= Mini International Neuropsychiatric Interview
OR	= odds ratio
SEES	= socioeconomic and educational status
WAIS-III	= Wechsler Adult Intelligence Scale, Third Edition
WCST	= Wisconsin Card Sorting Test

The primary aim of this study was to evaluate the neuropsychological and psychiatric outcomes of adults with d-TGA who underwent the neonatal ASO. Our secondary aim was to identify medical, operative, and sociodemographic factors associated with neurocognitive outcomes as well as with anxiety and depression disorders in the group with d-TGA.

Patients and Methods

The Paris-Sud University Medical Center Ethics Committee approved this multicenter study. Written informed consent of all participants was obtained.

Patients

Eligible patients (aged ≥ 18 years) born with d-TGA between 1984 and 1995 were identified by reviewing medical records in 2 major hospitals: Necker Children's Hospital and Marie Lannelongue Hospital (Ile-de-France, France). Inclusion criteria were diagnosis of d-TGA (with intact ventricular septum or with ventricular septal defect) corrected by ASO during the first 2 months of life and French as a primary language. We excluded patients who had (1) birth weights below 2.5 kg, (2) any known genetic anomalies, (3) associated extracardiac or cardiovascular anomalies requiring aortic arch reconstruction, or (4) reported severe sensory deficits (vision, hearing) or severe neurologic comorbidities (eg, traumatic brain injury, brain tumors).

A control group of healthy adults, enrolled from the same geographic area, was matched with the d-TGA group by age, gender, and educational level. These control participants were recruited from diverse environments (universities, training centers, hospital employees, and patients' friends) through public study flyers and by asking patients to invite random friends to participate.

Assessments

Assessments were performed by an experienced clinical neuropsychologist (L.K.) and lasted approximately 3 hours. **NEUROPSYCHOLOGICAL ASSESSMENT.** We used standardized tests to evaluate neurocognitive functioning in different

domains. The Wechsler Adult Intelligence Scale, Third Version (WAIS-III) [8] evaluates global intellectual functioning. It provides four indexes: Verbal Comprehension (general knowledge, language), Working Memory (short-term and working memory), Perceptual Organization (visual-spatial skills), and Processing Speed (attention and processing speed). All WAIS-III scores have a mean of 100 and a SD of 15.

The Wisconsin Card Sorting Test [9] measures executive functions, and more precisely, the ability to infer rules (abstraction abilities) and to shift cognitive strategies in response to environmental changes (cognitive flexibility). We present Wisconsin Card Sorting Test scores of perseverative errors and conceptual answers (mean, 50; SD, 10).

Finally, the California Verbal Learning Test [10] is an episodic memory test (ie, long-term memory for specific events/experiences). Scores from long-delay free recall, long-delay cued recall, and correct recognition tasks are presented. The California Verbal Learning Test norms are based on subjects' sex, age, and educational level. Two types of calibration were established: one with reduced deviations (for variables with normal distribution), the other with percentiles (in case of nonnormal distribution).

For all neurocognitive tests, higher scores indicate better performances. The proportion of patients with impaired scores on neurocognitive tasks was also investigated, using the -1 SD and -2 SD cutoff criteria. A score -1 SD or lower from the expected mean (or ≤ 16 th percentile) indicates at least mild cognitive difficulties, whereas a score -2 SD or lower (or ≤ 2 nd percentile) translates moderate to severe cognitive deficits.

PSYCHIATRIC ASSESSMENT. The Mini-International Neuropsychiatric Interview (MINI) [11], a structured diagnostic interview, was used to screen for current and lifetime psychiatric disorders using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Version [12] criteria. This instrument allows the diagnosis of several psychiatric disorders, such as mood disorders (eg, major depressive disorder, hypomania), anxiety disorders (eg, generalized anxiety disorder, obsessive-compulsive disorder), drug dependence, and eating and psychotic disorders.

Statistical Analysis

Results are given as mean \pm SD or percentage. We used the independent sample *t* test to compare the d-TGA and control groups on numeric variables. The χ^2 test was used for comparisons of categoric variables between groups. Binomial tests were used for comparisons of frequencies observed in the d-TGA group vs those expected in the general population (ie, proportions with scores ≤ -1 SD and ≤ -2 SD).

Linear and logistic stepwise regressions were used to identify risk factors for all neurocognitive outcomes and selected psychiatric outcomes (ie, lifetime anxiety and depression disorders) among the potential predictors listed in Table 1. Predictors associated with outcomes at *p* of less than 0.20 in univariate analyses were included in multivariate adjusted stepwise regression analysis with a retention criterion of *p* below 0.05. Variables for linear

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