M3C Academy
Transposition of the great arteries

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Neurodevelopmental outcomes in TGA

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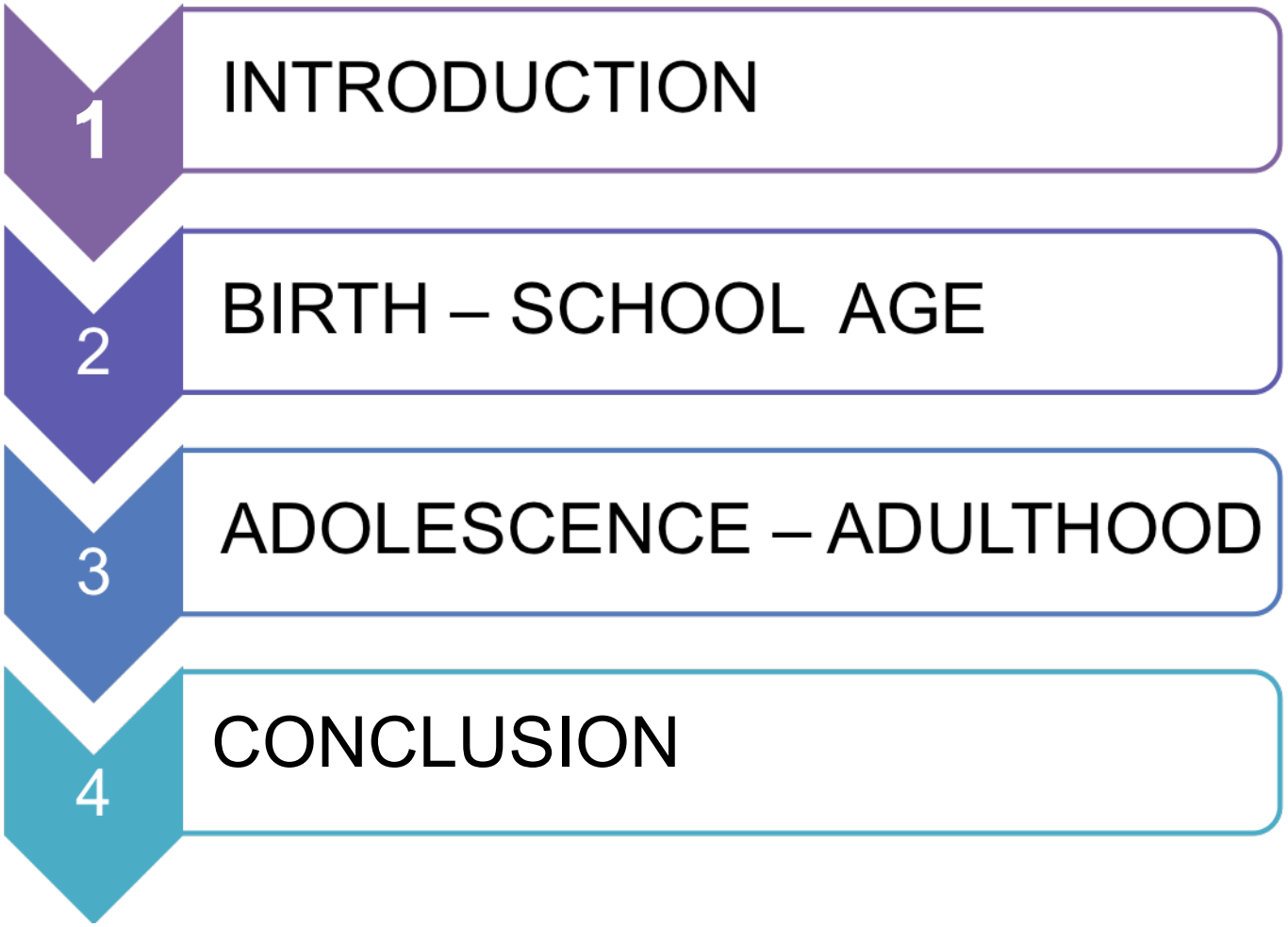
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BIRTH – SCHOOL AGE
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ADOLESCENCE – ADULTHOOD
4
CONCLUSION

Cyanotic congenital heart disease (C-CHD)

Dramatic improvement in medical and surgical care

SURVIVAL

PRONOSTIC

1985-2018

BIRTH

Acidosis and hypoxia

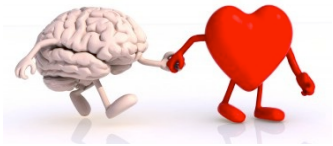
OPEN-HEART SURGERY

- ***Prolonged anesthesia***
- ***Deep hypothermic circulatory arrest***
- ***Cardiopulmonary bypass***

POST-OPERATIVE PERIOD

Hemodynamic instability

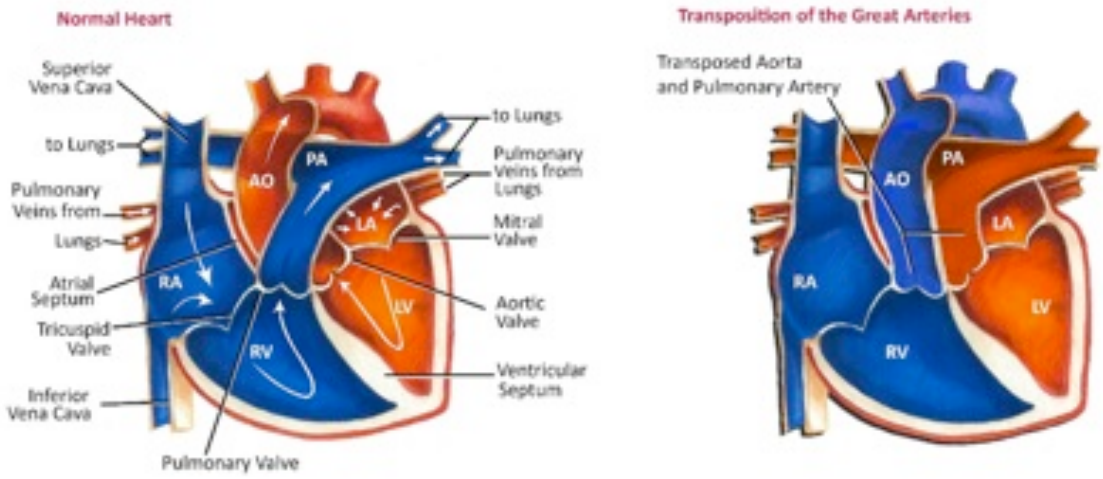
NEUROLOGICAL RISKS



Neurodevelopmental outcomes in C-CHD ?

The transposition of the great arteries (TGA) : an exemple of C-CHD

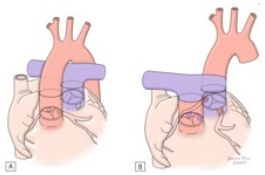
From : www.pediatricheartspecialists.com



✓ Incidence → One of the most frequent

✓ Homogeneity → Cardiac anatomy
→ Surgical intervention :
Arterial switch operation

From Martins & Castela, 2008



✓ – confounding factors → 1 open-heart surgery
→ Infrequently associated with genetic abnormalities

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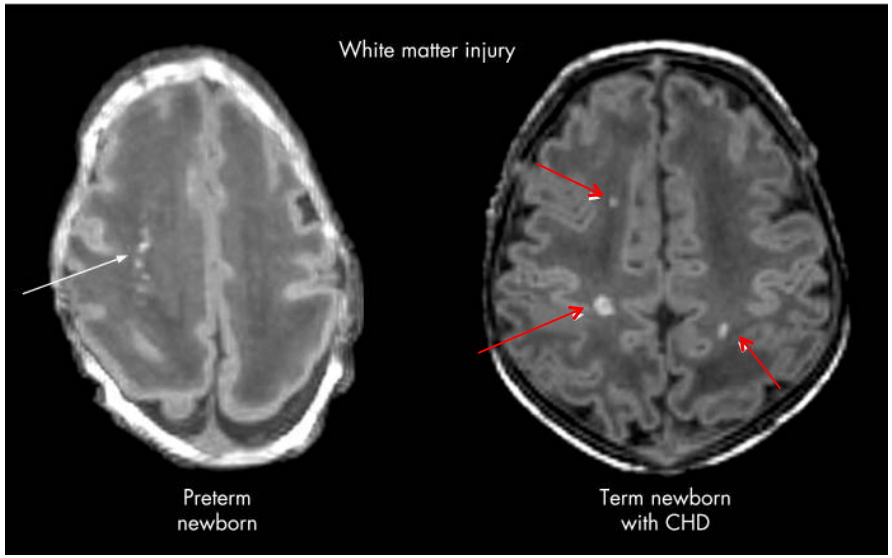
Neurological abnormalities in neonates with TGA

- ❖ Delayed brain maturation in full term newborns with TGA (Licht et al., 2009; Miller et al., 2007; Park et al., 2006; Shedeed & Elfaytouri, 2011; von Rhein et al., 2015)
- ➢ Delay in brain development may foster susceptibility to brain injury in the pre-, intra-, and post-operative periods

- ○ Brain injury in 30-60% of neonates <u>before</u> the surgery (for review : Owen et al., 2011)
  - ➢ mainly periventricular leukomalacia (ischemic white matter injury localized near the lateral ventricles)

From Miller & McQuillen, 2007 (ADC Fetal Neonatal Ed.)



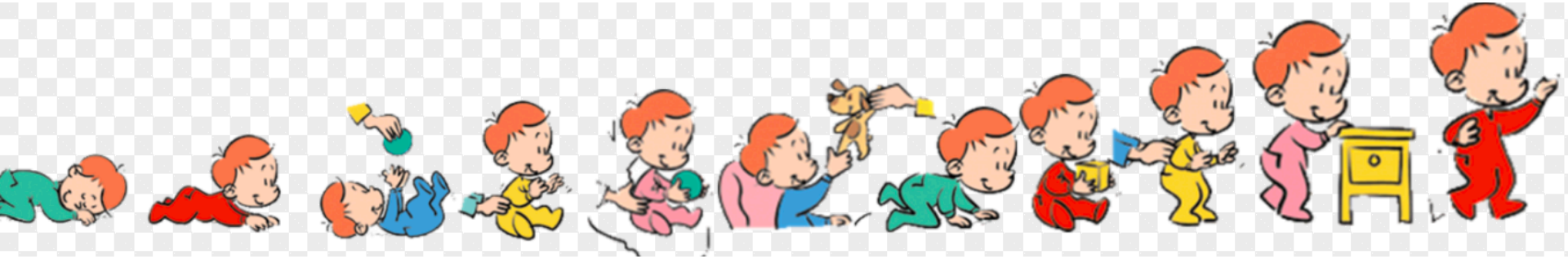
Neurological abnormalities in neonates with TGA

- New lesions or worsening of preoperative lesions occur in 67% of C-CHD patients postoperatively (Mahle et al., 2002)

- Neurologic impairments in 20-30% of children with TGA (Bellinger et al., 1999; Hövels-Gürich et al., 1997; 2001)
  - Motor dysfunction (tone alteration, ataxia or dysmetria...)
  - Speech impairment
  - Seizures
  - Cerebral palsy (5%)

Psychomotor and cognitive development in children with TGA

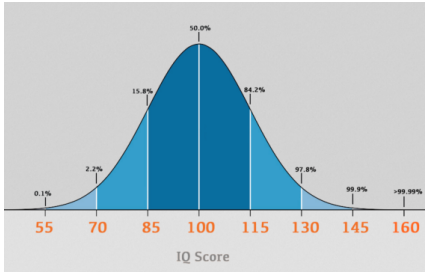
- 20-40% of children with TGA show delayed psychomotor development and 10% show delayed cognitive / language function development (Bellinger et al.,1995; 1997; 1999; McGrath et al., 2004)



- Although the disorders are usually mild to moderate,
  - ➢ continue to exhibit at school entry (Majnemer et al., 2009)
  - ➢ correlate with academic achievement and IQ at 8 years old (McGrath et al., 2004)

Neuropsychological outcomes at school age (6-12 years old)

- INTELLIGENCE QUOTIENT (IQ)



- In CHD patients, intelligence abilities (as measured by IQ scores) are generally within the normal range (for review : Bellinger & Newburger, 2010)

- However, results regarding children with TGA are more controversial (for review : Kasmi et al., 2014)

- It has become clear that IQ scores are not highly informative with regard to the cognitive outcomes of children with CHD (risk of false negative)

Neuropsychological outcomes at school age (6-12 years old)

❑ ACADEMIC SKILLS

$$\frac{2+9}{4+9}$$

A B C

- ❖ 20-30% of children with TGA experience learning disability (reading, spelling and mathematics) and 40% receive remedial services in school (Bellinger et al., 2003a; Shillingford et al., 2008)

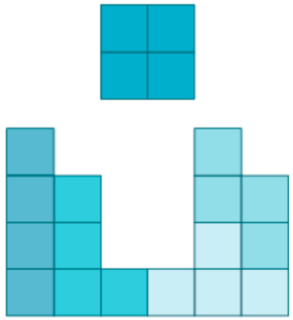
❑ LONG TERM MEMORY

- ❖ Memory performance is usually within the normal range (for review , Miatton et al., 2006)

- ➢ However, 2 studies in C-CHD population show difficulties in verbal and visual memory tasks (Bellinger et al., 2003a; Miatton et al., 2007b)

Neuropsychological outcomes at school age (6-12 years old)

- VISUO-SPATIAL SKILLS



- Ability to represent, analyze, and mentally manipulate objects

Involves many sub-skills :

✓localization

✓analysis of spatial relations

✓mental imagery, navigation and rotation

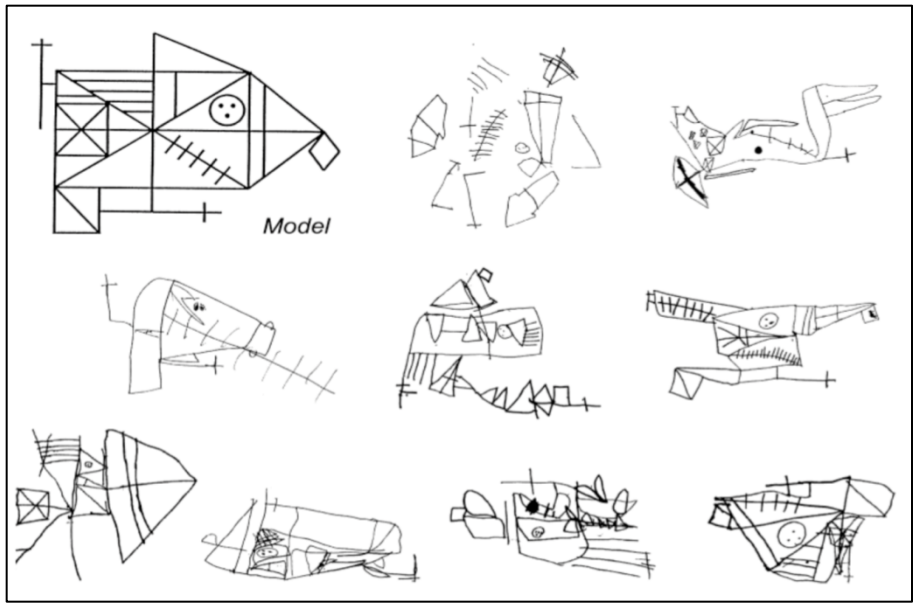
✓capacity to copy or rebuild a model (drawing, 3D construction)

Neuropsychological outcomes at school age (6-12 years old)

VISUO-SPATIAL SKILLS

- Visuo-spatial skills are areas of cognitive function that seem to be particularly vulnerable in children with C-CHD (Bellinger et al., 2003a; 2003b; Mahle et al., 2006; Miatton et al., 2007b; Wright & Nolan, 1994)

- 52% of children with TGA present visuo-spatial deficits (Bellinger et al., 2003b)



Examples of Rey–Osterrieth complex figure copies of 8 years-old children with TGA who present visuo-spatial deficits.

The model that was available to the child is also presented.

(*from* Bellinger et al., 2003b, JDBP)

Neuropsychological outcomes at school age (6-12 years old)

❑ EXECUTIVE FUNCTIONS

- Set of cognitive processes that are necessary for the cognitive control of behavior : selecting and successfully monitoring behaviors that facilitate the attainment of chosen goals

  - ✓ attentional control
  - ✓ working memory (short-term storage and manipulation of stored information)
  - ✓ cognitive flexibility (flexibly adapting to changed circumstances, task switching)
  - ✓ inhibition (self-control and interference control)
  - ✓ planning
  - ✓ problem solving

Neuropsychological outcomes at school age (6-12 years old)

EXECUTIVE FUNCTIONS

- Children with TGA demonstrate deficits in tasks involving different executive processes (attentional control, working memory, inhibition, cognitive flexibility, planning...) (Bellinger et al., 2003a; Calderon et al., 2010, 2012; Cassidy et al., 2015)

- Executive impairments observed at 5 years old remain apparent at age 7 (Calderon et al., 2014)

- Executive deficits were associated with higher prevalence of behavior disorders (Bellinger et al., 2003a) and remedial service use (speech and language therapy, psychotherapy, occupational therapy...) (Calderon et al., 2013)

Neuropsychological outcomes at school age (6-12 years old)

❑ SOCIAL COGNITION

- Set of cognitive and emotional processes involved in social interactions

(allows to interact appropriately with others)

✓Knowledge of social rules and conventions

✓Interpret non-verbal signals of emotion (tone of voice, facial emotional expressions, gaze, body posture...)

✓Identify the emotional and cognitive states of others (thoughts, beliefs, feelings, intentions and desires) = “theory of mind”

Neuropsychological outcomes at school age (6-12 years old)

- SOCIAL COGNITION

- Facial expression recognition seems to be generally preserved in children with TGA (Calderon et al., 2014)

Sample of test : « The Child Affective Facial Expression »

(From LoBue & Thrasher, 2015)

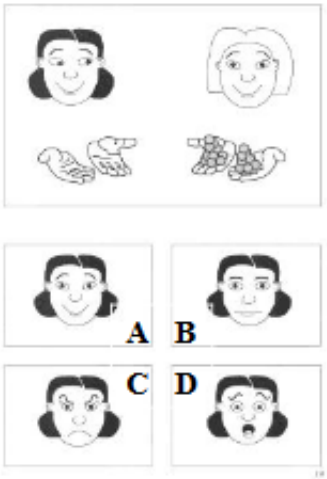
Neuropsychological outcomes at school age (6-12 years old)

SOCIAL COGNITION

- Children with TGA demonstrate difficulties in identifying the emotional and cognitive states of others (Theory of Mind deficits) (Calderon et al., 2010; 2012; 2014)

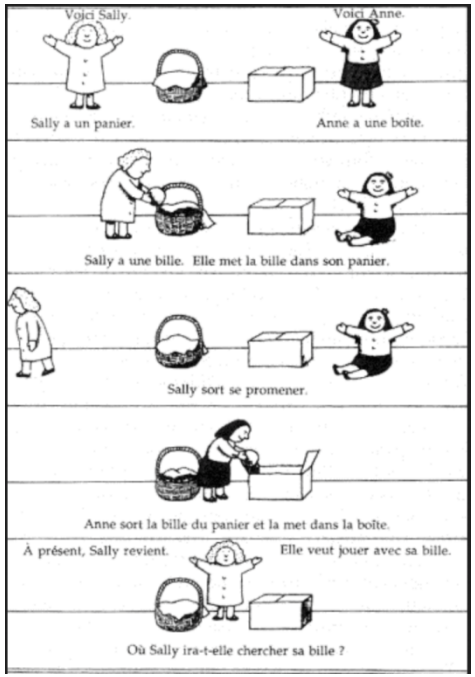
➢ To attribute an emotion to a character (basic emotions, desires, concealed emotion, ambivalence, guilt…)

This girl [right] is teasing this girl [left] because she has a lot of marbles whereas this girl [left] doesn't have any.
This girl [left] is smiling because she doesn't want to show this girl [right] how she is feeling inside.
• How is this girl [left] feeling inside? Is she happy, alright, angry or scared?



« Test of Emotion Comprehension »
Pons, Harris & de Rosnay, 2004

➢ To attribute cognitive mental states to a character (false-belief tasks)



Sample of False beliefs task « Sally & Anne Test »
Wimmer & Perner, 1983

Neuropsychological outcomes at school age (6-12 years old)

- Higher prevalence of behavioral disorders and Attention Deficit Hyperactivity Disorder (ADHD) in TGA population (Bellinger et al., 2009; Hövels-Gürich et al., 2002b)

  - 20-49% of externalizing and/or internalizing disorders (depression, anxiety, oppositional defiant disorder)

  - Risk of ADHD : 2-4 times higher

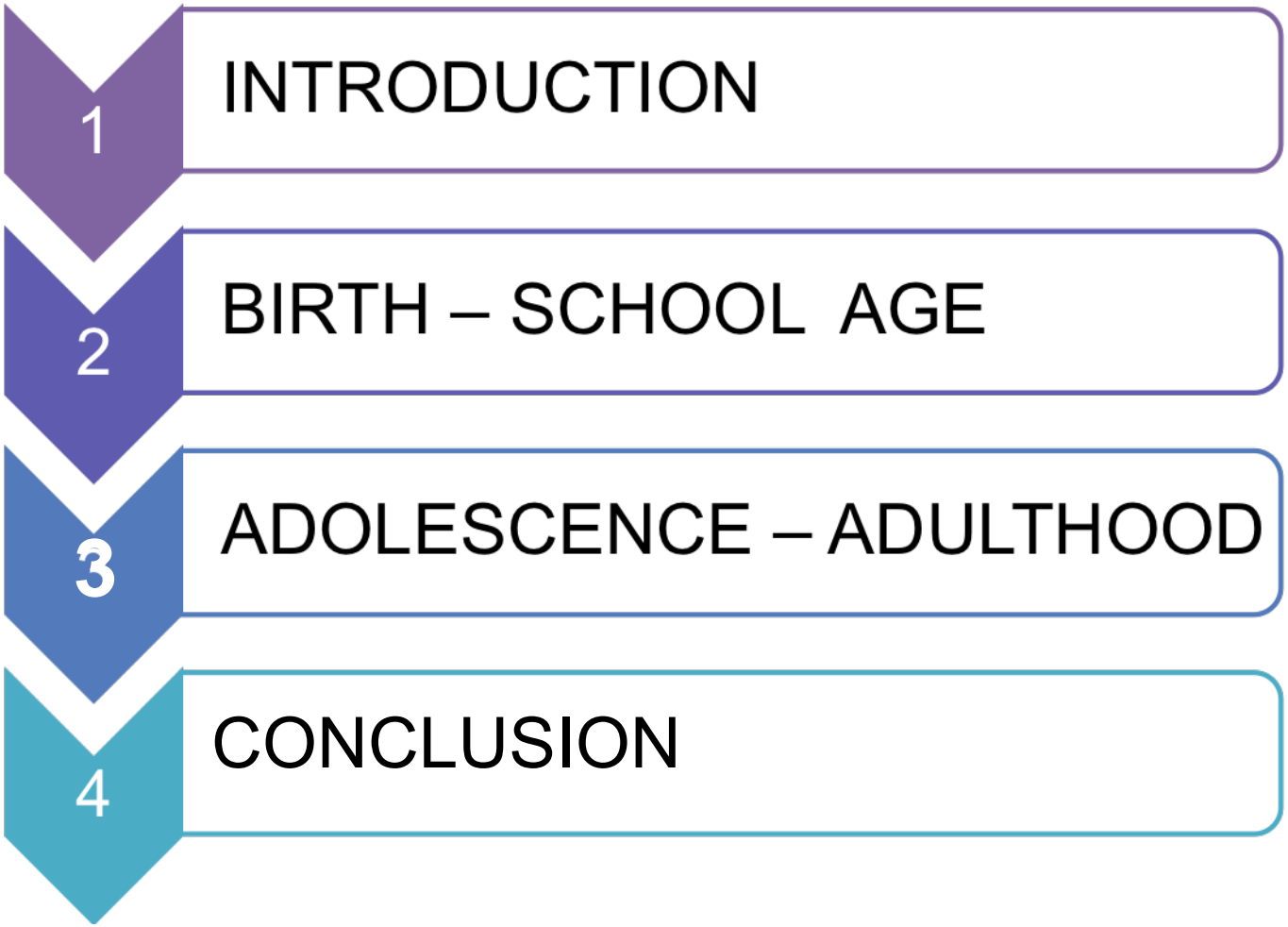
Neuropsychological outcomes at school age (6-12 years old)

RISK FACTORS OF NEURODEVELOPMENTAL OUTCOMES

Complex interaction between different risk factors

(for reviews, Latal et al., 2009; Miatton et al., 2006)

- **Pre-operative factors** (patient-related factors) : gestational age, birth weight, genetic abnormalities and polymorphisms…
- **Intra-operative factors** : use and duration of deep hypothermic circulatory arrest, duration of cardiopulmonary bypass, level of hematocrit…
- **Post-operative factors** : postoperative oxygen saturation level, length of stay in intensive care unit...
- **Socio-environmental factors** : parental educational level, socioeconomic status and psychological well-being…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Neuropsychological outcomes of adolescents with TGA

- **2 longitudinal studies** : follow-up from pre-school age to adolescence

➢ « the Boston Circulatory Arrest study » (Bellinger et al., 1995, 1999, 2003a, 2011)

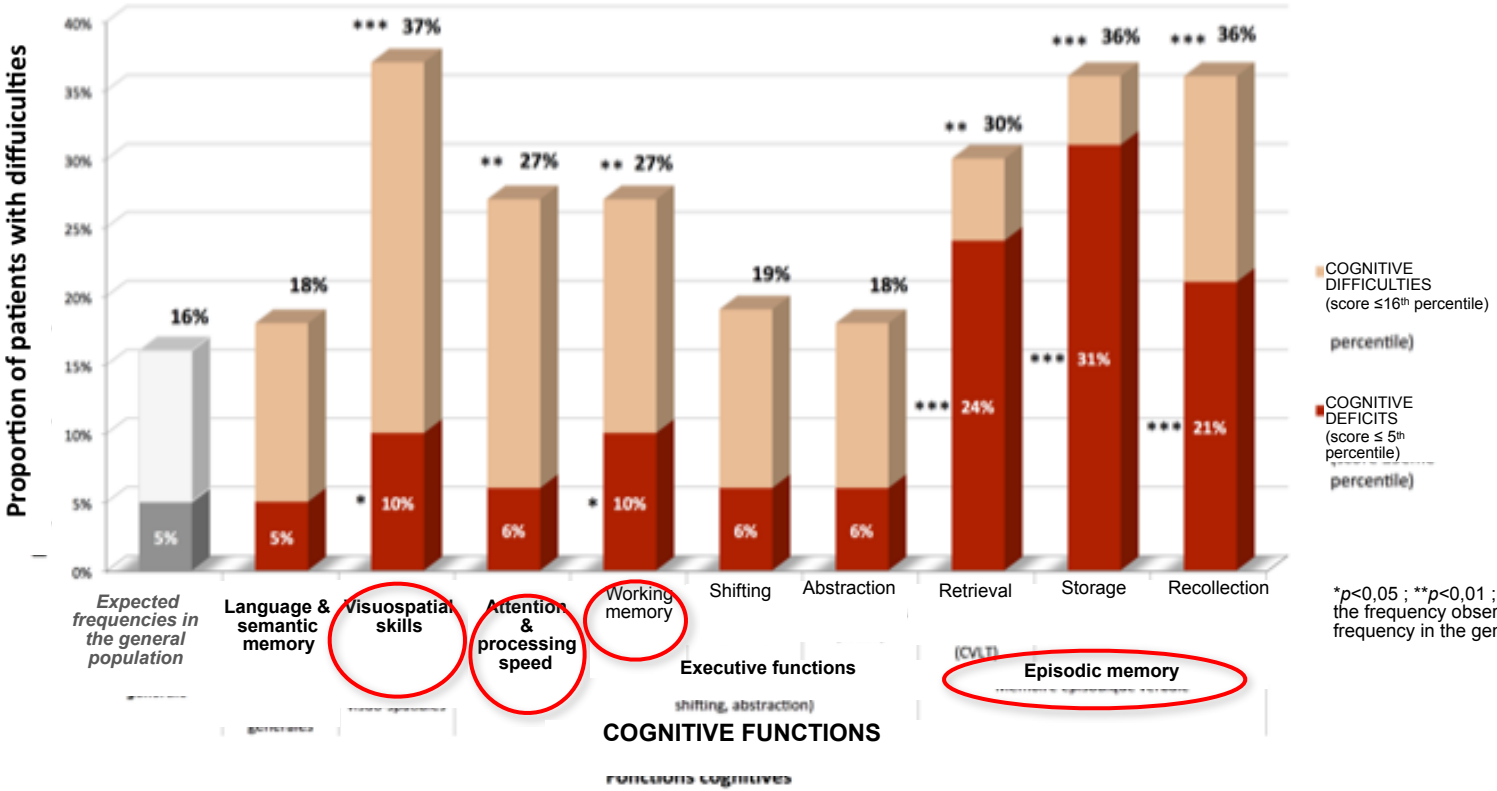
➢ « the Aachen TGA study » (Heinrichs et al., 2014; Hövels-Gürich et al., 1997; 2002a)

- High rate of cognitive deficits concerning various domains (expressive language, memory), in particular, visuo-spatial skills and executive functions

- Difficulties tend to increase with age

Neuropsychological outcomes of adults with TGA

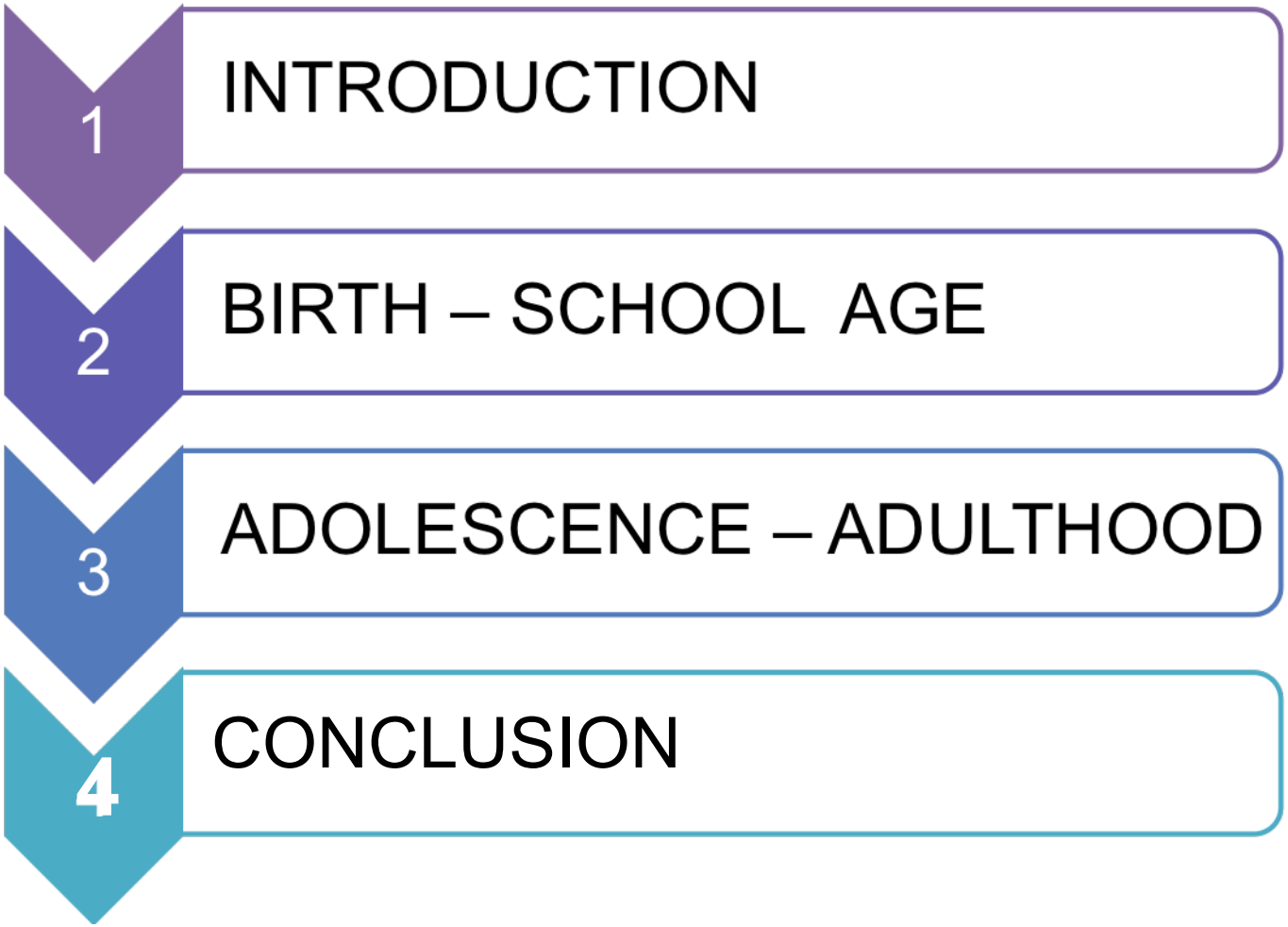
Proportion of patients with cognitive difficulties or deficits



*p<0,05 ; **p<0,01 ; ***p<0,001 : significant difference between the frequency observed in d-TGA group and the expected frequency in the general population

- Cognitive deficits associated with :
  - – educational level
  - + grade retention at school (81% *vs* 46%)
  - + unemployment (33% *vs* 6%)

From Kasmi, Calderon et al. (2017)
Neurocognitive and psychological outcomes in adults with d-TGA.
Annals of Thoracic Surgery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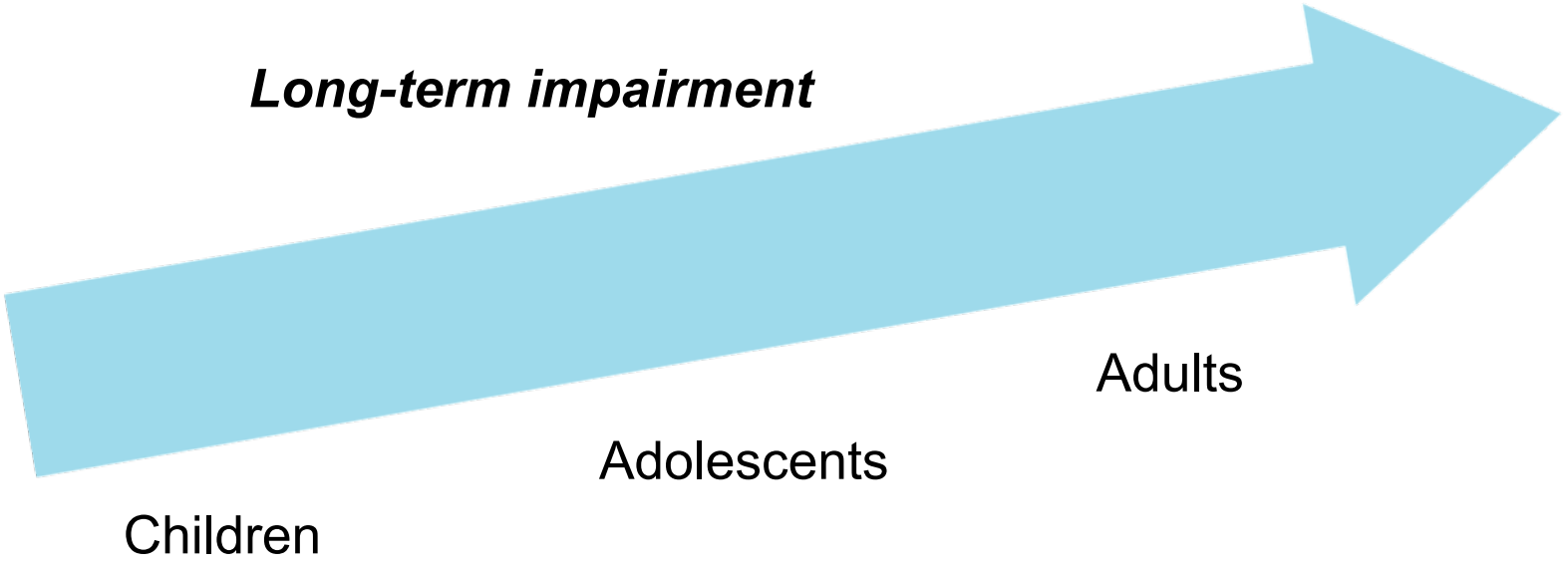
Summary

Neuropsychological trajectory of patients with TGA



« Growing into a deficit »
Bellinger & Newburger, 2010

Cascade effect : early deficits mediate the expression of new symptoms and/or the worsening of pre-existing impairments

Interventions to improve outcomes

- Neuroprotection strategies
- Formal neurodevelopmental screening / evaluation :
  "cardiac neurodevelopmental programs" = to incorporate neurodevelopmental follow-up as an integral component of cardiac care
- Structured computerized training of specific impaired cognitive abilities (e.g., working memory training programs)
- Individual Cognitive Behavioral Therapy and/or group support therapy for stress and anxio-depressive syndrome reduction (e.g., ACT & mindfulness)

Literature reviews

- Bellinger & Newburger (2010). Neuropsychological, psychosocial, and quality-of-life outcomes in children and adolescents with congenital heart disease. *Progress in Pediatric Cardiology, 29(2), 87–92.* http://doi.org/10.1016/j.ppedcard.2010.06.007

- Kasmi, Bonnet, Montreuil, Kalfa, Geronikola, Bellinger & Calderon (2017). Neuropsychological and psychiatric outcomes in d-transposition of the great arteries across the lifespan: a state-of-the-art review. *Frontiers in Pediatrics, 5, 59.* http://doi.org/10.3389/fped.2017.00059

- Miatton, Wolf, François, Thiery & Vingerhoets (2006). Neurocognitive Consequences of Surgically Corrected Congenital Heart Defects: A Review. *Neuropsychology Review, 16(2), 65–85.* http://doi.org/10.1007/s11065-006- 9005-7

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Thank you for your attention