Published in final edited form as:

Clin Neuropsychol. 2019 May ; 33(4): 760–778. doi:10.1080/13854046.2018.1503333.

Visual-spatial processing style is associated with psychopathology in adolescents with critical congenital heart disease

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Abstract

Objective: To determine whether visual-spatial processing style is associated with psychopathology in a large sample of adolescents with critical congenital heart disease (CHD). Local (part-oriented) style was hypothesized to increase risk for internalizing (but not externalizing) forms of psychopathology.

Method: Participants included 278 adolescents with critical CHD (dextro-transposition of the great arteries = 134, tetralogy of Fallot = 58, single-ventricle cardiac anatomy requiring the Fontan procedure = 86). Visual-spatial processing style was indexed using Copy Style Ratings from the Rey-Osterrieth Complex Figure-Developmental Scoring System. The Schedule for Affective Disorders and Schizophrenia for School-Aged Children–Present & Lifetime Version was used to determine presence/absence of diagnosable DSM-IV psychiatric disorder(s). Processing style and psychopathology were assessed concurrently.

Results: Thirty-three percent of the sample had a part-oriented processing style. In multivariable binary logistic regression models, part-orientation was associated with more than twice the odds of having an anxiety disorder (lifetime: OR = 2.2, $p = .02$, 95% CI = 1.1–4.1; current: OR = 2.7, $p = .03$, 95% CI = 1.1–6.5) but was not associated with an increased risk for ADHD, disruptive behavior, or mood disorders (p s > .05).

Conclusions: Adolescents with critical CHD who approach complex visual-spatial materials in a local, part-oriented fashion are more likely to meet criteria for an anxiety disorder than those

who approach complexity more holistically. Part-orientation may make it more difficult for individuals to judge the relative importance of isolated details and engage in more adaptive perspective-taking.

Keywords

ADHD; anxiety; cardiac; cognitive style; pediatric

Due in large part to advances in detection and medical/surgical management over the past two to three decades, survivors of congenital heart disease (CHD) now number in the millions worldwide, including over one million children in the United States alone (Hoffman & Kaplan, 2002; Marelli, Miller, Marino, Jefferson, & Newburger, 2016; Reller, Strickland, Riehle-Colarusso, Mahle, & Correa, 2008). Approximately 40,000 children are born with some form of CHD each year; and, of these, around 25% are born with a critical form of CHD that will require intensive surgical intervention(s) to support life (Hoffman & Kaplan, 2002; Marelli et al., 2016; Reller et al., 2008). With burgeoning evidence of brain dysmaturity – including lower N-acetylaspartate:choline ratios, increased lactate, delayed gyrification and cortical folding, reduced grey and white matter volumes, and increased rates of ischemic white matter injury (e.g., Beca et al., 2013; Clouchoux et al., 2013; Licht et al., 2009; Limperopoulos et al., 2010; Rivkin et al., 2013) – as well as wide-ranging neurobehavioral and psychosocial challenges (Cassidy et al., 2017), it has become increasingly clear that critical CHD poses a serious threat to development across the lifespan.

Among the many risks associated with critical CHD are high rates of psychopathology, including both externalizing and internalizing problems (Kovacs et al., 2009; Luyckx et al., 2016; Spijkerboer, Utens, Bogers, Verhulst, & Helbing, 2008). Recognizing the limitations of informant rating scales for determining the prevalence of diagnosable psychiatric disorder(s), our group employed semi-structured clinical interviews to evaluate psychiatric outcomes in adolescents with three types of critical CHD: dextro-transposition of the great arteries (d-TGA; DeMaso et al., 2014), tetralogy of Fallot (TOF; Holland et al., 2017), and single-ventricle cardiac conditions requiring the Fontan procedure (Fontan; DeMaso et al., 2017). All three of these conditions are complex and life-threatening. In d-TGA, the aorta and pulmonary artery are transposed and must be corrected shortly after birth, typically using the arterial switch operation. TOF is characterized by the presence of four co-occurring anomalies (ventricular septal defect, pulmonary stenosis, an overriding aorta, and right ventricular hypertrophy) and one or more surgical procedures are required over the first year of life, with subsequent catheterizations or operations in a subgroup. Single-ventricle cardiac conditions, such as hypoplastic left heart syndrome, for example, are among the most severe forms of critical CHD, requiring a series of palliative surgeries, carried out over the first several years of life and ultimately culminating in the Fontan procedure. With 19–34% of adolescents in our studies meeting criteria for attention-deficit/hyperactivity disorder (ADHD) and as many as 35% meeting criteria for an anxiety disorder (DeMaso et al., 2014, 2017; Holland et al., 2017), a better understanding of the causes and correlates of this elevated risk for psychopathology represents both a clinical and research priority – especially now that more than 90% of individuals with CHD are reaching adulthood (Khairy

et al., 2010) and greater efforts are being directed toward neurodevelopmental and psychosocial treatment and prevention (Calderon & Bellinger, 2015).

Psychopathology has been linked to differences in style of information processing. *Processing or cognitive style* – as discussed historically by Gestalt psychologists (Navon, 1977) and, more recently, in relation to models of attentional selection (Bundesen, Habekost, & Kyllingsbæk, 2011) and central coherence (CC; Frith, 1989) – is posited to exist along a spectrum ranging from *global* (i.e., configurational, holistic, big picture, having strong CC) to *local* (i.e., part-oriented, detail-focused, analytical, having weak CC; Happe, 1999). Research into processing/cognitive style has a long and tortuous history (see Kozhevnikov, 2007 for review), having been approached by numerous investigators using a wide range of perceptual (e.g., judgment of visual illusions), visual-spatial/constructional (e.g., Rey-Osterrieth Complex Figure, Block Design), and verbal-semantic paradigms (e.g., sentence vs. word-string memory, homographs; Happe, 1999).

Whereas healthy adults tend to be biased toward initial global processing followed subsequently by attention to more local features (Poirel et al., 2014), typically-developing children seem to undergo a fairly protracted developmental transition from preferentially local to relatively more global processing beginning at around six years of age and continuing through adolescence, coincident with patterns of normative grey matter loss (Poirel et al., 2011; Scherf, Behrmann, Kimchi, & Luna, 2009). In contrast, children with autism spectrum disorders (ASD) differ from typically-developing children in that predominantly local, part-oriented cognitive/processing styles are common (Happe, 1999). A bias toward local processing has also been documented in females with anorexia nervosa, as well as in their unaffected relatives (Lang et al., 2016). In addition, healthy college-age males who exhibit local processing report more symptoms of depression and anxiety than those with global styles, who conversely endorse greater optimism and more positive mood states (Basso, Schefft, Ris, & Dember, 1996). In experimental paradigms, negative mood induction decreases holistic processing of faces (Curby, Johnson, & Tyson, 2011) and, among individuals high in trait anxiety, enhances processing of local targets on an attentional focusing task (Derryberry & Reed, 1998).

In adolescents with critical CHD, a local, part-oriented style when dealing with complex visual-spatial materials is also common. Bean Jaworski and colleagues (2017) analyzed the performance of 352 adolescents with critical CHD on the Rey-Osterrieth Complex Figure (ROCF). The ROCF is a widely-used psychological measure, clinically and in central coherence studies (Lang et al., 2016), that requires individuals first to copy and then to draw from memory a complex geometric design. In this study, drawings were scored using the Developmental Scoring System (ROCF-DSS; Bernstein & Waber, 1996) which provides an index of organizational goodness and precision of drawings (i.e., Organization), as well as the style and degree of integration demonstrated in one's approach to the task (i.e., Style). Stylistic approaches to copying the complex figure range from part-oriented, with a preference for finer details over larger perspectives (e.g., drawing each figure element in a part-by-part fashion, with little integration across elements), to more configurational, big-picture strategies. The DSS is able to differentiate *organization* and *style* insofar as drawings may be approached in a part-by-part style yet still be precise and very well organized, or

vice versa. Rate of part-orientation, which among typically-developing children tends to decrease over the course of childhood and into adolescence (Waber & Bernstein, 1995), was 32% among healthy adolescents and ranged from 25–47% across CHD types (the highest rates being seen in the Fontan group; Bean Jaworski et al., 2017). Interestingly, part-orientation (but not organization) was independently associated with higher-order academic competencies such as reading comprehension and applied math problem solving (Bean Jaworski et al., 2017), suggesting that a better understanding of *how* adolescents with critical CHD approach complexity may yield insight into other potential risks and highlight new avenues for individualized intervention.

Taken together, the foregoing suggests that a tendency toward local processing (indexed by a part-oriented approach to complex visual-spatial materials) may be characteristic of some adolescents with critical CHD, and that this style of processing may be associated with increased rates of certain forms of psychopathology. We examined these possibilities in the current study. Specifically, we hypothesized that, among adolescents with critical CHD, part-orientation would be associated with increased rates of diagnosable anxiety and mood disorders (but not disruptive behavior disorders or ADHD).

Method

Participants

Data were drawn from three well-described single-center CHD neurodevelopmental outcome studies conducted at Boston Children's Hospital (see Bellinger, Rivkin, et al., 2015; Bellinger, Watson, et al., 2015; Bellinger et al., 2011 for detailed information regarding study design and recruitment). Studies were conducted in compliance with APA ethical standards and approval was obtained from the Institutional Review Board of Boston Children's Hospital. Parents provided informed consent; adolescents provided assent.

The *d-TGA Group* included 14 to 16-year olds with d-TGA who underwent the arterial switch operation (ASO) as infants as part of the Boston Circulatory Arrest Study (Bellinger et al., 1999; Bellinger et al., 1995; Bellinger et al., 2003, 2011; Newburger et al., 1993). Exclusion criteria included low birth weight (<2.5 kg), a recognizable syndrome or associated extracardiac anomalies of more than minor severity, heart surgery prior to the ASO, or associated cardiovascular anomalies requiring surgery on the aortic arch or surgical procedures other than the ASO. The *TOF Group* included 13 to 16-year olds with surgically-palliated TOF (with or without pulmonary atresia) and most recent cardiac operation at least 3 months before neurocognitive testing. Participants with identified genetic/phenotypic syndromes (except for trisomy 21) were included. Adolescents unable to undergo MRI were excluded. The *Fontan Group* included 10 to 19-year olds with single-ventricle cardiac anatomy who underwent the Fontan procedure. Adolescents with a history of heart transplant, any cardiac surgery within 6 months of testing, or contraindications to performing an MRI were excluded.

Medical and Demographic Data

Medical/surgical and socio-demographic data were collected via medical record review, family interviews, and questionnaires. Socioeconomic status (SES) was estimated using the Hollingshead (1975) four-factor index of social status.

Neurobehavioral and Psychiatric Assessment

All three studies included neuropsychological and psychiatric evaluations (see Bellinger, Rivkin, et al., 2015; Bellinger, Watson, et al., 2015; Bellinger et al., 2011; DeMaso et al., 2014, 2017; Holland et al., 2017 for primary outcomes). The following variables were included in the current study.

Processing Style.—Style of processing was indexed using Copy Style Ratings from the ROCF-DSS. The ROCF-DSS (Bernstein & Waber, 1996) is a developmentally-informed scoring method that quantifies (1) the organizational goodness of the drawings and (2) the process or style by which participants approach the task. By accounting systematically for the continuity/discontinuity of individual line production, the DSS is able to capture the style demonstrated when managing complex visual-spatial materials. The DSS has been shown to have acceptable psychometric properties as evidenced by high interrater reliability for both organization (.95) and style ratings (.88), and good discriminant validity across a range of clinical and neurodevelopmental populations (Bernstein & Waber, 1996). The ROCF was administered by either a licensed psychologist (D.C.B.) or a supervised research assistant. Figure drawings were scored by two research assistants who were trained and monitored in using the DSS by one of the DSS authors (J.H.B.). The scoring procedure included systematic double-scoring of the drawings by J.H.B. (1 in 5 out of the first 100 protocols to establish interrater reliability; 1 in 10 protocols subsequently to maintain reliability), regular double-scoring by the research assistants, and consultation (with J.H.B.) to reconcile differences on challenging protocols. For this study, we were particularly interested in adolescents demonstrating a strong bias toward local/part-oriented processing; therefore, participants were classified as either “part-oriented” or “other”. See Bean Jaworski et al. (2017) for a detailed examination of ROCF-DSS performance among this combined cohort of adolescents with critical CHD.

Psychiatric Disorders.—The Schedule for Affective Disorders and Schizophrenia for School-Aged Children – Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) was administered to determine presence/absence of diagnosable Anxiety, Mood, Disruptive Behavior, and Attention Deficit/Hyperactivity disorder(s), as per Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria. The K-SADS-PL is a clinician-administered, semi-structured interview. Adolescents and their parent(s) were each interviewed separately and the information obtained was combined according to standard procedures as provided by the K-SADS-PL. Core psychiatric findings from the CHD groups included in the current study have been presented previously (DeMaso et al., 2014, 2017; Holland et al., 2017).

Intellectual Functioning.—The Wechsler Intelligence Scales were used to evaluate intellectual functioning (Full Scale IQ), as well as perceptual reasoning (Perceptual

Reasoning Index/Performance IQ), which served as covariates in our multivariable models. TOF and Fontan groups were evaluated as adolescents: <16 years: WISC-IV; 16 years: WAIS-III. Intellectual functioning was measured in the d-TGA group at approximately 8 years using the WISC-III (Bellinger et al., 2003).

Statistical Analysis

Demographic characteristics were compared across CHD groups using Analysis of Variance (ANOVA) with Bonferroni correction for *post hoc* tests, for continuous variables; Pearson's chi-square or Fisher's exact tests, for binary variables. Rates of part-orientation (vs. not) and psychiatric diagnoses were compared across groups using the Pearson's chi-square test. Univariable and multivariable binary logistic regression models were constructed to examine predictors of risk for diagnosable psychiatric disorders. Covariates of interest included part-orientation, CHD group, family socioeconomic status (SES), sex, age at assessment, and IQ. In addition to part-orientation, which was included as an independent variable in all multivariable models, covariates associated with psychiatric outcomes at $p < .20$ in univariable models were also included in multivariable (forward selection) binary logistic regression models. Multinomial logistic regression was used to examine associations between part-orientation and psychiatric comorbidity.

Statistical analyses were conducted using SPSS Statistics Version 23 (IBM, Armonk, NY).

Results

Participant Characteristics

Participants were 382 adolescents with critical CHD who participated in the three larger outcome studies. Of these, data were excluded from participants with a possible/definite genetic/phenotypic condition [$n = 88$ (23.0%)], Full Scale IQ scores below 70 [$n = 37$ (9.7%)], and/or missing IQ data [$n = 4$ (1.0%)]. The final sample consisted of 278 adolescents (d-TGA, $n = 134$; TOF, $n = 58$; Fontan, $n = 86$). Sample characteristics are presented in Table 1.

Processing Style

Copy Style Ratings could not be located for 2 participants (0.01%). Analyses were conducted using pairwise exclusion. The ROCF-DSS classified 92 participants (33.3%) as having a part-oriented style, including 25.4% of the d-TGA group, 35.1% of the TOF group, and 44.7% of the Fontan group. Prevalence of part-orientation was higher in the Fontan group than in the d-TGA group, $\chi^2(1) = 8.81$, $p = .003$, but did not differ significantly between d-TGA and TOF, $\chi^2(1) = 1.86$, $p = .17$, or Fontan and TOF, $\chi^2(1) = 1.31$, $p = .25$, groups.

Psychopathology

Prevalence of K-SADS-PL-derived psychiatric disorders was: anxiety disorders (25.0% lifetime, 12.5% current), mood disorders (9.0% lifetime, 2.1% current), disruptive behavior disorders (27.8% lifetime, 25.7% current), and ADHD (27.1% lifetime, 25.7% current). For reference, prevalence rates for these disorders in the United States population are

approximately 2–20% for anxiety disorders, 7% for major depressive disorder, 3–4% for disruptive behavior disorders (e.g., oppositional defiant disorder, conduct disorder), and 5% for ADHD (Canino, Polanczyk, Bauermeister, Rohde, & Frick, 2010; Costello, Egger, & Angold, 2005; Kessler, Patukhova, Sampson, Zaslavsky, & Wittchen, 2012; Polanczyk, De Lima, Horta, Biederman, & Rohde, 2007).

With respect to *lifetime* comorbidity rates, 15 adolescents (5.4%) met criteria for both an anxiety disorder and ADHD; 6 (2.2%) met criteria for both an anxiety disorder and a mood disorder; 10 (3.6%) met criteria for both ADHD and a mood disorder; and, 3 (1.1%) met criteria for an anxiety disorder, a mood disorder, and ADHD. With respect to *current* comorbidity rates, 10 adolescents (3.6%) met criteria for both an anxiety disorder and ADHD; 1 (0.4%) met criteria for both an anxiety disorder and a mood disorder; 5 (1.8%) met criteria for both ADHD and a mood disorder; and, 1 (0.4%) met criteria for an anxiety disorder, a mood disorder, and ADHD. Of note: ADHD is nested within the supra-ordinate disruptive behavior disorder category; and, in the current sample, these two diagnoses are nearly collinear ($r_{pb} = .98$ and $.94$ for lifetime and current, respectively), resulting in similar inference patterns when one is substituted for the other in statistical analyses.

Prevalence of anxiety disorder (lifetime: $\chi^2(1) = 13.92, p < .001$; current: $\chi^2(1) = 12.83, p < .001$), ADHD (lifetime: $\chi^2(1) = 6.23, p = .01$; current: $\chi^2(1) = 8.46, p = .004$), and disruptive behavior disorders (lifetime: $\chi^2(1) = 6.42, p = .01$; current: $\chi^2(1) = 8.46, p = .004$) was significantly higher in the Fontan than in the d-TGA group. The Fontan group also had higher rates of anxiety disorders (lifetime: $\chi^2(1) = 6.51, p = .01$; current: $\chi^2(1) = 13.87, p < .001$) than the TOF group, but did not differ from the TOF group in rates of ADHD or disruptive behavior disorders ($ps > .05$). Disorder rates did not differ significantly between d-TGA and TOF groups ($ps > .07$); therefore, d-TGA and TOF groups were combined to form a “biventricular CHD” (i.e., 2V) group for subsequent analyses.

Processing Style and Psychopathology

Rates of part-orientation among adolescents with critical CHD and a diagnosable psychiatric disorder are presented in Table 2. In univariable analysis, part-orientation was associated with 2.5 times the odds of having a lifetime anxiety disorder ($OR = 2.5, p = .004, 95\%CI = 1.3–4.7$), and more than 3 times the odds of having a current anxiety disorder ($OR = 3.4, p = .005, 95\%CI = 1.5–7.9$), but was not associated significantly with ADHD (lifetime: $OR = 1.3, p = .36, 95\%CI = 0.7–2.4$; current: $OR = 1.3, p = .35, 95\%CI = 0.7–2.4$), disruptive behavior disorders (lifetime: $OR = 1.3, p = .32, 95\%CI = 0.8–2.4$; current: $OR = 1.3, p = .35, 95\%CI = 0.7–2.4$), or mood disorders (lifetime: $OR = 1.3, p = .54, 95\%CI = 0.5–3.2$; current: $OR = 1.6, p = .48, 95\%CI = 0.4–6.2$).

In multivariable analysis, part-orientation remained a significant independent predictor of both lifetime ($OR = 2.2, p = .02, 95\%CI = 1.1–4.1$) and current anxiety disorders ($OR = 2.7, p = .03, 95\%CI = 1.1–6.5$) but was not associated significantly with ADHD, disruptive behavior disorders, or mood disorders (Table 3). Adolescents in the Fontan group had significantly higher rates of anxiety disorders, ADHD, and disruptive behavior disorders than adolescents in the biventricular CHD group. In subsequent sensitivity analyses, which we conducted to examine the impact of substituting visual-spatial reasoning (PRI/PIQ) for

FSIQ as a covariate in our models, the pattern of findings and inferences remained highly consistent. Indeed, the only substantive difference was that sex (male vs. female) did not remain a significant factor in the models examining ADHD (current) and disruptive behavior disorder (current) diagnoses.

Finally, we examined part-orientation in relation to psychiatric comorbidity. Twelve of 13 (92%) adolescents with more than 1 lifetime psychiatric disorder – and 6 of 8 (75%) with more than 1 current psychiatric disorder – were classified as part-oriented by the ROCF-DSS. Nonetheless, results from two multinomial logistic regression models showed that for both lifetime and current diagnoses, adolescents meeting criteria for more than 1 psychiatric disorder did not exhibit significantly higher rates of part-orientation than those meeting criteria for 1 (lifetime: OR = 1.5, $p=.38$; current: OR = 0.9, $p=.88$) or 0 psychiatric disorders (lifetime: OR = 2.3, $p=.06$; current: OR = 1.8, $p=.28$).

Discussion

In this study, adolescents with critical CHD who approached visual-spatial complexity in a part-oriented fashion were at 2–3 times the risk for diagnosable anxiety disorders than those who approached complexity more holistically. In contrast, part-orientation was not associated with increased rates of disorders of mood regulation (e.g., depression) or behavior regulation (i.e., disruptive behavior disorders or ADHD).

Rates of part-orientation and psychopathology, particularly anxiety disorders, ADHD, and disruptive behavior disorders, were both statistically significantly higher among adolescents with single-ventricle cardiac conditions who underwent the Fontan procedure than adolescents with biventricular CHD (i.e., d-TGA and TOF). Single-ventricle cardiac conditions are among the most severe forms of CHD and are associated with more adverse outcomes than biventricular CHD across a range of neurobehavioral domains (e.g., Bean Jaworski et al., 2017; Cassidy, White, DeMaso, Newburger, & Bellinger, 2015). The etiology of this elevated risk is almost certainly multifactorial and not easily disentangled, potentially related to genetic factors, lower oxygen delivery to the brain in utero, and greater perioperative and longer-term morbidities after birth, such as multiple operations with exposure to anesthesia and ischemia/reperfusion injury (Diaz et al., 2016), periods of malnutrition, prolonged hypoxemia, slower rates of postnatal brain growth (Peyvandi et al., 2017), increased rates of new white matter injury after surgery (Beca et al., 2013), and 11 times higher frequency of abnormality on magnetic resonance imaging, as reported in this cohort of adolescents who underwent the Fontan (Bellinger, Watson, et al., 2015) – all of which may be conspiring to increase risk for children and adolescents with single-ventricle CHD.

Why Anxiety Disorders?

Despite an elevated risk for both anxiety disorders and ADHD in our sample of adolescents with critical CHD (DeMaso et al., 2014, 2017; Holland et al., 2017), part-orientation was exclusively associated with anxiety disorders. The literature examining information processing in individuals with anxiety is extensive, providing robust evidence of both interpretational and attentional biases among anxious children and adolescents. On average,

anxious children tend to interpret ambiguous situations negatively and are biased toward the perception of threat cues in their environment, picking up on fearful stimuli faster and at lower levels than non-anxious children (Hadwin, Garner, & Perez-Olivas, 2006). The focus of these studies has been the emotional valence of social information and how it is perceived, attended to, and acted upon. Little attention has been devoted to understanding how one's style of processing and approach to managing complexity may be related to increased risk for anxiety.

One possibility is that strong part-orientation may limit one's ability to appreciate the so-called "bigger picture". Lacking a broader frame of reference, one may have difficulty assigning appropriate value to individual details, making it difficult to appreciate how they fit together coherently, which for some may be disorienting, confusing, frustrating, or even frightening. An individual with this part-oriented bias may be at risk for being overwhelmed by the constant experience of being unable to adequately integrate and organize stimuli coming in from the environment – leading to a sustained high state of arousal that is manifest as anxiety. Conversely, it may be that heightened arousal/anxiety may increase one's propensity toward focusing on individual details, at the expense of seeing the bigger picture. Further research is necessary to examine the directionality of this association.

But why was part-orientation *not* also associated with mood disorders, as we had hypothesized on the basis of prior research? This may be an issue of timing. Considering the developmental psychopathology of depressive disorders – which tend to increase in later adolescence/early adulthood (Cole et al., 2002) – our sample of CHD adolescents may simply be too young for the period of highest risk for depression. Moreover, to the extent that anxiety may also increase risk for depression (Cummings, Caporino, & Kendall, 2014), it is possible that the adolescents meeting criteria for an anxiety disorder in our study may be among those at highest risk for developing depression in the future. Should this be the case, it will be important to examine whether the combination of an anxiety disorder and a part-oriented processing style further amplifies this risk.

Implications for Treatment

Evaluation of an adolescent's style of processing and psychosocial adjustment status has the potential to provide clinical neuropsychologists with useful information and tools to support subsequent treatment. In therapeutic settings, the generalization of skills and strategies is a primary goal. This is true of all forms of psychotherapy. Indeed, the ultimate measure of therapeutic progress is real-world progress, that is, the development and implementation of practical strategies that enable someone to manage symptoms at home, school, and within the community. It is one thing to learn an effective symptom-management strategy within a highly controlled clinic setting; it is another to carry that strategy into the real world and deploy it appropriately, as called for by the situation. The latter requires the appreciation of parallels between the clinic and the real world, and the integration of those distinct experiences into a single, coherent personal narrative that can then facilitate the transfer of knowledge and skills from one setting to the next. In the case of anxiety management, this can be expected to be less intuitive and, as such, more challenging for highly part-oriented adolescents who may not readily generalize across contexts. For such individuals,

connections will instead need to be made explicit, deliberately linking one experience or setting to the next and role-playing the application of strategies in a highly concrete fashion.

This potential constraint to generalization is likely to be particularly salient in the case of cognitive behavioral therapy (CBT) – arguably the most popular and most highly effective modality for treating anxiety (Weisz et al., 2017). Adolescents with a strong part-orientation bias may not be able to take full advantage of such approaches without considerable adaptations. A meaningful goal in CBT for anxiety is to be able to focus on understanding and managing the core elements of anxiety itself, rather than on the specific instances of anxiety that present from day-to-day or week-to-week. As a practical matter for the therapist, this is the difference between the identification of tools to help the adolescent manage the frustration or emotional dysregulation associated with anxiety, on the one hand, and the introduction of more complex cognitive modification techniques that challenge negative thoughts, reframe perceptions/interpretations, and prompt consideration of alternatives, on the other. Although subtle in some respects, this shift in focus marks a profoundly important transition point in treatment: from treating symptoms to treating cause. It hinges on the ability to transcend individual examples and avoid getting so mired down in the details that one is unable to maintain a broader view of the treatment and progress to date. The ability to flexibly engage a global, bigger picture perspective would likely be quite useful (and perhaps even necessary) for making this kind of conceptual leap. By extension, adolescents more prone to (over-)focusing on details and individual experiences may well have a harder time keeping those larger-scale treatment goals in mind, with consequent impact on their treatment progress.

An important addition to the CBT toolkit – for maximal effectiveness with a broad range of patients – will then be strategies that explicitly cue global processing, encouraging patients to actively look for the “big picture.” Such cognitive tools exist – typically in the literature on metacognition and metacognitive therapy (Fisher, McNicol, Young, Smith, & Salmon, 2015). These promote a systematic, stepwise approach to problem-solving through the application of brainstorming strategies, for example. These tools should be introduced and modeled, both for adolescents and for their caregivers, who will then be equipped to help adolescents in applying these strategies appropriately outside the clinic.

Reflections on the Style Construct

In this study we have taken a narrow view of processing/cognitive style. Different interpretations should also be explored [see Kozhevnikov (2007) for review]. There are two distinctions of note. First, is style a *preference* or a *constraint*? When faced with complex materials is one *more likely to lead* from a detail-focused position or from a “big picture” stance – even though one has the flexibility to approach the task in more than one way (i.e., a *preference*)? Or, as in the case of individuals with known neurodevelopmental disorder, do variables associated with the disorder limit the way in which one can approach complex materials (i.e., a *constraint*)? This seems particularly pertinent when examining the performance of the adolescents in this study whose development, by virtue of having CHD, is proceeding along alternate trajectories than their typically-developing peers. We note, however, that what looks like, and is frequently labeled as, “part orientation” in this type of

scenario may have little to do with cognitive or processing style per se, but may be the outcome of more fundamental neuropsychological or cognitive deficits that limit the degrees of freedom one has available when working with complex materials. We attempted to mitigate this by restricting our sample to normally-intelligent adolescents and examining Full Scale IQ as a covariate in our regression models. Future studies into the neurobehavioral implications of part-orientation among children and adolescents with CHD will need to explore interactions with other known domains of vulnerability for this population such as executive function – particularly flexibility/shifting – (Cassidy et al., 2015) and social cognition (Bellinger, 2008).

The second consideration invokes the role of contextual variables. It is well known that behavioral responses of all types can be primed. Such effects can be subconscious or subliminal and deliberately introduced in formal paradigms (Dasgupta & Greenwald, 2001; Maier, Berner, & Pekrun, 2003; Ramscar, 2016). They can also result from specific demand characteristics in a given situation (D'Souza, Booth, Connolly, Happé, & Karmiloff-Smith, 2015), from an individual's interpretation of what she or he has perceived (Misener & Libben, 2017), or from language used in the context of a query about a remembered event (Loftus, 2005). Given this, style of processing may not be a unidirectional process – in the sense of a skill or talent one *has* and *consciously applies* to some external problem or task in the world – but rather one that is elicited dynamically from interaction with the environment. This would then suggest that, just as negative mood induction has been shown to enhance local processing (Curby et al., 2011; Derryberry & Reed, 1998), it may be possible, in specified situations, to apply active cues that prime more global, holistic processing. More research is needed to investigate this possibility. It will be particularly valuable to determine how, and to what extent, holistic priming may be harnessed therapeutically, particularly in the treatment of anxiety.

Strengths and Limitations

The major strengths of this study are two-fold. The first is the use of semi-structured clinical interviews to derive psychiatric diagnoses. This is particularly notable considering that almost all prior studies of psychosocial adjustment in individuals with CHD (e.g., Luyckx et al., 2016; Spijkerboer et al., 2008) have relied on questionnaires and rating scales that tend to be more vulnerable to a range of informant and response biases (Pedregon, Farley, Davis, Wood, & Clark, 2012). The second is the emphasis on the *process* by which adolescents with critical CHD approached complex visual-spatial materials, rather than the more typical emphasis on the finished product itself (Bellinger, Rivkin, et al., 2015; Bellinger, Watson, et al., 2015; Bellinger et al., 2011). As noted by Werner (1937), “the solution to a given problem (achievement) is neither an adequate index of the developmental stage of the organism doing the problem-solving nor uniquely indicative of a specific underlying mechanism but...an analysis of the process by which a solution is achieved may have such explanatory power” (Bernstein, 2013, p. 300). Understanding and analyzing *process* in this way yields new insight into risk for psychopathology among adolescents with critical CHD, and sheds light on potential interventions (and roadblocks) that should be the focus of future studies.

The findings are limited by the following. First, part-orientation was operationalized using a single modality (i.e., complex visual-spatial materials) at one point in time. It should be extended in other domains – verbal-semantic and/or perceptual processing (Happé, 1999) – to determine whether processing style patterns are observed more generally. Second, a causal direction (part-orientation $\longleftrightarrow$ anxiety) cannot be determined from these cross-sectional data. Moreover, part-orientation and anxiety may share a common etiology such as white matter injury for which individuals with CHD are particularly vulnerable (Morton, Ishibashi, Jonas, & Gallo, 2015). Longitudinal investigations are needed to determine whether the presence of a part-oriented cognitive style earlier in childhood confers greater risk for the development of psychopathology later on; we are currently analyzing additional data to speak directly to this issue. Third, we focused specifically on those adolescents with the most pronounced part-orientation biases; it may be possible, using more fine-tuned instruments, to tap into finer gradations of the processing style spectrum allowing for evaluation of a dose-response relationship between part-orientation and risk for psychopathology. Fourth, future studies should consider onset and severity of psychiatric diagnoses, rather than simply presence/absence; and, considering the high rates of autism spectrum disorders reported among children with critical CHD (Tsao et al., 2017), autism should be included among the outcomes of interest. Fifth, while we would anticipate stability in IQ across childhood and adolescence, the fact that IQ was not measured concurrently in our d-TGA group is a limitation. Finally, despite a large sample size, the three studies from which these data were pooled were single-center studies examining a restricted range of critical CHD types among mostly white/Caucasian patients; further investigations are needed to see if our results generalize across diverse settings and cardiac lesions, as well as in the context of other medical conditions associated with an increased risk for anxiety.

Conclusion

Adolescents with critical CHD who tend to approach complex visual-spatial materials in a part-oriented fashion are at greater risk for anxiety than those who approach complexity more holistically. Part-orientation may make it more difficult for individuals to judge the relative importance of isolated details and engage in more adaptive perspective-taking, which may in turn contribute to an increased risk for anxiety.

Acknowledgments

This work was supported in part by grants from the National Heart, Lung, and Blood Institute (HL77681, HL74734, and HL096825); the Farb Family Fund; and, the National Center for Research Resources (RR02172). The authors have no conflicts of interest to declare. The authors thank the adolescents and parents who participated in this study and Megan Cassidy, PhD for her insight around psychotherapeutic implications.

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Table 1

Sample characteristics

	d-TGA (<i>n</i> = 134)	TOF (<i>n</i> = 58)	Fontan (<i>n</i> = 86)	Full Sample (<i>n</i> = 278)	<i>p</i>	Pairwise Comparisons (<i>p</i> < .05)
Family SES ^a	46.17 ± 12.23	49.69 ± 11.78	50.90 ± 11.86	48.37 ± 12.17	.01	Fontan > d-TGA
Sex (male) <i>n</i> (%)	105 (78.4%)	32 (55.2%)	56 (65.1%)	193 (69.4%)	.003	d-TGA > TOF, Fontan
Race (white) <i>n</i> (%)	122 (91%)	52 (89.7%)	70 (81.4%)	244 (87.8%)	.09	--
Gestational age (weeks)	39.73 ± 1.24	39.31 ± 2.50	39.19 ± 1.68	39.47 ± 1.71	.05	None
Birthweight (kg)	3.55 ± 0.45	3.27 ± 0.63	3.38 ± 0.59	3.44 ± 0.54	.002	d-TGA > TOF
Age at assessment	16.08 ± 0.51	14.69 ± 1.21	13.85 ± 2.86	15.10 ± 1.98	<.001	d-TGA > TOF, Fontan; TOF > Fontan
FSIQ score	99.10 ± 14.25	99.33 ± 14.53	96.79 ± 12.54	98.44 ± 13.80	.41	--
PRI/PIQ score	96.78 ± 13.24	99.45 ± 14.33	97.87 ± 11.68	97.67 ± 13.02	.42	--
Current stimulant medication <i>n</i> (%)	25 (18.9%)	6 (10.3%)	13 (15.1%)	44 (16.0%)	.34	--
Current other psychotropic medication <i>n</i> (%)	7 (5.2%)	2 (3.4%)	4 (4.7%)	13 (4.7%)	.87	--
History of psychotherapy/counseling <i>n</i> (%)	33 (25%)	13 (22.8%)	39 (45.3%)	85 (30.9%)	.002	Fontan > d-TGA, TOF

Note. d-TGA = dextro transposition of the great arteries; TOF = tetralogy of Fallot; Fontan = single-ventricle cardiac conditions requiring the Fontan procedure; SES = socioeconomic status; FSIQ = Full Scale IQ; PRI = Perceptual Reasoning Index; PIQ = Performance IQ. Continuous variables were compared using Analysis of Variance. Dichotomous variables were compared using chi-square test. Data presented as Mean ± SD unless otherwise specified.

^aHollingshead, A. A. (1975). Four-factor index of social status. Unpublished manuscript, Yale University, New Haven, CT

Table 2
Frequency of part-orientation among adolescents with critical congenital heart disease and a diagnosable psychiatric disorder

	Anxiety Disorder		Mood Disorder		ADHD		DBD	
	Lifetime	Current	Lifetime	Current	Lifetime	Current	Lifetime	Current
Part-oriented	26 (51%)	15 (60%)	9 (39%)	4 (44%)	24 (38%)	22 (39%)	25 (38%)	22 (39%)
Other	25 (49%)	10 (40%)	14 (61%)	5 (56%)	39 (62%)	35 (61%)	40 (62%)	35 (61%)
TOTAL	51	25	23	9	63	57	65	57

Note. *n* (%). ADHD = Attention Deficit/Hyperactivity Disorder; DBD = Disruptive Behavior Disorder.

Table 3

Results of univariable and multivariable logistic regression analyses predicting lifetime and current psychiatric disorder classification

	ANXIETY DISORDER											
	Lifetime						Current					
	Univariable			Multivariable			Univariable			Multivariable		
	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p
SES	1.0	1.0–1.1	.06	-	-	-	1.0	1.0–1.1	.31			
Sex (Male vs. Female)	0.8	0.4–1.5	.48				0.8	0.3–1.8	.54			
Age at assessment (per year)	0.9	0.8–1.1	.19	-	-	-	0.7	0.6–0.9	<.001	-	-	-
FSIQ (<85 vs. 85)	0.9	0.4–2.1	.88				1.9	0.8–4.8	.18	-	-	-
CHD type (1V vs. 2V)	3.4	1.8–6.3	<.001	2.9	1.5–5.5	.001	7.0	2.8–17.5	<.001	6.2	2.4–15.7	<.001
Part-oriented (vs. other)	2.5	1.3–4.7	.004	2.2	1.1–4.1	.02	3.4	1.5–7.9	.005	2.7	1.1–6.5	.03

	MOOD DISORDER											
	Lifetime						Current					
	Univariable			Multivariable			Univariable			Multivariable		
	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p
SES	1.0	1.0–1.0	.82				1.0	0.9–1.1	.91			
Sex (Male vs. Female)	0.4	0.2–0.9	.02	0.4	0.1–0.8	.02	0.9	0.2–3.6	.86			
Age at assessment (per year)	1.3	1.0–1.7	.05	1.3	1.0–1.7	.05	1.3	0.9–1.9	.20			
FSIQ (<85 vs. 85)	0.7	0.2–2.3	.52				1.3	0.3–6.5	.74			
CHD type (1V vs. 2V)	1.5	0.6–3.6	.38				0.6	0.1–3.1	.57			
Part-oriented (vs. other)	1.3	0.6–3.2	.54				1.6	0.4–6.2	.48			

	ADHD											
	Lifetime						Current					
	Univariable			Multivariable			Univariable			Multivariable		
	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p
SES	1.0	1.0–1.0	.15	-	-	-	1.0	1.0–1.0	.23			
Sex (Male vs. Female)	2.2	1.1–4.4	.03	2.5	1.2–5.2	.01	1.9	0.9–3.7	.08	2.2	1.0–4.5	.04
Age at assessment (per year)	0.9	0.8–1.0	.10	-	-	-	0.9	0.8–1.0	.06	-	-	-
FSIQ (<85 vs. 85)	2.3	1.2–4.4	.01	2.8	1.4–5.6	.004	2.4	1.2–4.8	.01	2.9	1.4–6.0	.003
CHD type (1V vs. 2V)	2.2	1.2–3.9	.01	2.5	1.4–4.6	.003	2.5	1.4–4.5	.003	2.8	1.5–5.3	.001
Part-oriented (vs. other)	1.3	0.7–2.4	.36				1.3	0.7–2.4	.35			

	DISRUPTIVE BEHAVIOR DISORDER											
	Lifetime						Current					
	Univariable			Multivariable			Univariable			Multivariable		
	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p
SES	1.0	1.0–1.0	.13	-	-	-	1.0	1.0–1.0	.23			
Sex (Male vs. Female)	2.0	1.0–4.0	.04	2.3	1.1–4.7	.02	1.9	0.9–3.7	.08	2.2	1.0–4.5	.04
Age at assessment (per year)	0.9	0.8–1.0	.05	-	-	-	0.9	0.8–1.0	.06	-	-	-
FSIQ (<85 vs. 85)	2.2	1.1–4.2	.02	2.6	1.3–5.2	.007	2.4	1.2–4.8	.01	2.9	1.4–6.0	.003

	DISRUPTIVE BEHAVIOR DISORDER											
	Lifetime						Current					
CHD type (1V vs. 2V)	2.2	1.2–3.9	.007	2.5	1.4–4.6	.003	2.5	1.4–4.5	.003	2.8	1.5–5.3	.001
Part-oriented (vs. other)	1.3	0.8–2.4	.32				1.3	0.7–2.4	.35			

Note: $n = 278$. d-TGA and TOF groups did not differ significantly on rates of part-orientation or psychopathology and thus were combined into a biventricular CHD group (i.e., “2V”) for regression analyses. Covariates significant at $p < .20$ in univariable analysis were included in multivariable analysis. Multivariable logistic regression used forward selection criteria to retain significant covariates. Dashes denote covariates that were significant in univariable analysis but not significant in multivariable analysis. CHD = congenital heart disease; d-TGA = dextro transposition of the great arteries; TOF = tetralogy of Fallot; ADHD = Attention Deficit/Hyperactivity Disorder; 1V = single-ventricle CHD; 2V = biventricular CHD; SES = socioeconomic status; FSIQ = Full Scale IQ; OR = odds ratio, CI = confidence interval.