Comprehensive Psychoneuroendocrinology 7 (2021) 100070

Contents lists available at ScienceDirect

Comprehensive Psychoneuroendocrinology

journal homepage: www.sciencedirect.com/journal/comprehensive-psychoneuroendocrinology

Emerging self-regulatory skills in childhood predict cardiometabolic risk in adolescence

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ARTICLE INFO

Keywords:
Cardiometabolic risk
Self-regulation
Childhood
Adolescence

ABSTRACT

Cardiometabolic risk (CMR) has increased among adolescents. A growing literature shows that childhood self-regulatory skills are associated with obesity and CMR. However, the developmental nature of self-regulation has not been considered in existing studies. Therefore, it is unclear how specific types of self-regulation (i.e., attentional, emotional, behavioral, cognitive) at different points in development, may differentially predict CMR. Using a multi-method longitudinal design, we assessed a sample of 117 children repeatedly between ages 2 and 16. At ages 2, 4, and 7 years, self-regulation (emotional, attentional, behavioral, and cognitive) skills that were hypothesized to have emerged were assessed. Adolescent CMR indicators were assessed at age 16. Latent profile analyses identified three profiles of adolescent CMR: Low Risk (41%), Dyslipidemia Risk (49.6%), and High Risk (9.4%). Distinct self-regulation skills at each childhood age predicted CMR during adolescence. Specifically, emotional regulation skills at ages 2 and 4, food-related behavioral regulation and attentional regulation at age 4, and attentional and cognitive regulation skills at age 7 predicted adolescent CMR. Self-regulation skills are modifiable, and thus, childhood interventions aimed at improving self-regulation could reduce CMR for decades to come. However, these results suggest that the multifaceted, developmental nature of self-regulation must be considered to most effectively inform preventive interventions aimed at lowering CMR. Additionally, our study highlights the need for additional research on adolescents who show elevations of CMR without meeting criteria for obesity.

1. Emerging self-regulatory skills in childhood predict cardiometabolic risk in adolescence

Youth obesity has reached an all-time high [1]. In parallel, cardiometabolic risk (CMR), the presence of risk factors that increase the likelihood of cardiovascular events or diabetes [2], has increased among adolescents [3]. Because elevated CMR by adolescence likely puts youth on a negative trajectory toward harmful lifelong consequences, identifying early factors that predict adolescent health risk is essential. CMR may stem, at least in part, from a failure to develop early self-regulation (SR) skills [4–8]. Such skills are essential for managing some of the most universal demands placed on children, including focusing/redirecting attention, modulating emotional reactions, controlling one's impulses, and managing cognitive processes. Over time, individuals with more adaptive SR skills are better at identifying and meeting goals, which likely extends to health-related goals (i.e., maintaining a healthy weight, eating healthy foods, meeting exercise goals), and inhibiting engagement in unhealthy behaviors (i.e., eating unhealthy foods, smoking, being sedentary).

Existing work linking SR and CMR typically does not consider the developmental nature of SR, such as how different domains of SR (i.e., attentional, emotional, behavioral, cognitive) unfold across early

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https://doi.org/10.1016/j.cpnec.2021.100070
Received 20 May 2021; Received in revised form 25 June 2021; Accepted 25 June 2021
Available online 27 June 2021

development and how each domain may differentially predict CMR. A developmentally informed theory of health risk must consider the multifaceted nature of SR in order to most effectively inform CMR interventions. This study's goals were to: 1) identify person-centered profiles of adolescent CMR, and 2) identify which types of SR at different points in early development predict adolescent CMR.

1.1. Adolescent profiles of CMR

Adolescence has emerged as a key period for CMR increases. CMR is linked to increased morbidity and mortality in adulthood [9], and a high lifetime risk of cardiovascular disease (CVD) and Type 2 Diabetes [3]. CMR is more prevalent in individuals with metabolic syndrome (MetS), defined as systematic elevations of waist circumference (WC), lipids, hypertension, and fasting glucose [10]. Defining CMR/MetS in youth is challenging because there are over 40 definitions of MetS in child and adolescent populations [11]. Failure to meet criteria for any one of these definitions, nor the cutoff for any individual marker, does not necessarily denote the absence of CMR.

Given these measurement issues, the American Academy of Pediatrics (AAP) emphasized that it is the clustering of CMR factors within the adolescent that is crucial for the identification of disease risk and its prevention [11]. This clustering of factors allows early identification of youth metabolic derangement patterns that may be indicative of later CVD. This identification allows for the design of targeted interventions, whereas the use of MetS cut points likely misses identification of those who show subclinical levels of risk. Following the AAP guidance, we utilized a comprehensive lens for defining CMR by focusing on the *clustering of CMR factors within the adolescent* [11].

A hallmark feature of CMR is being overweight/obese with insulin resistance and ensuing inflammation [12]. However, CMR factors also have been observed in youth within the normal weight range [13], highlighting the need for a comprehensive approach. In adult samples, there is a group of individuals known as "*normal weight obesity*" (*NWO*) who have normal BMI values but increased CMR (i.e., WC, leptin). Few studies have identified this group in adolescence (see Hamer [14] for exception). To better identify adolescent risk profiles, we considered traditional (e.g., lipids, glucose, blood pressure, abdominal obesity) and non-traditional (e.g., C-reactive protein [CRP], leptin) CMR indicators.

CMR research has almost exclusively employed a variable-centered approach, which involves examining individual dimensions of CMR. However, CMR factors co-exist and create distinct patterns of CMR factors within individuals. Person-centered approaches (i.e., latent profile analysis [LPA]) identify specific constellations of factors that describe subgroups of individuals [15]. This approach provides insight into intraindividual patterns of CMR, as suggested by the AAP. The first aim was to identify person-centered profiles of adolescent CMR.

1.2. SR and CMR

Children's SR skills are defined as a child's ability to control their inner states or behavioral responses in order to cope effectively with environmental demands [16,17]. SR is associated with better mental health [18], fewer behavior problems [19], better social skills [20], academic adjustment [21], and lower obesity/CMR [4–8,22,23]. There are multiple ways in which children's lack of SR is associated with later CMR. SR is associated with greater engagement in healthy behaviors and fewer unhealthy behaviors [24] and lowered SR can precipitate metabolic dysfunction and low-level inflammation that may result in prefrontal cortex structure and function changes [25,26].

A growing literature suggests that early-developing CMR likely results, at least in part, from a lack of SR skills. A few notable limitations of existing work need to be considered, however. First, most developmental work has considered obesity as the sole indicator of CMR. Yet, CMR encompasses many commonly used (i.e., obesity) and novel (i.e., CRP) indicators. A few studies have begun to address this gap, indicating that childhood SR is associated with adult health problems [7], higher adult CVD risk [22], and adolescent general health [4]. However, research is needed to confirm a relation between childhood SR and person-centered patterns of CMR.

Another limitation of existing research is that children's delay of gratification abilities [7] and/or a composite SR score [4] is often the SR measure, which fails to consider how types of SR (attentional, emotional, behavioral, cognitive regulation) may differentially predict CMR (for exceptions see Miller [6] and Graziano [8]). Moreover, an appreciation of the developmental nature of SR is missing [7]. Most conceptualizations of SR acknowledge that self-control cuts across multiple domains of functioning that unfolds across early development [16,17]. The development of SR processes build upon one another such that rudimentary SR skills serve as building blocks for subsequent SR [27] and later developing SR skills promote refinement of earlier occurring skills.

Attentional regulation, including a child's ability to modulate the (re)direction of attention and keep a task in memory, is one of the first types of SR to emerge, albeit in a rudimentary form [28]. The development and integration of attentional systems provide the neural mechanisms needed for later emerging emotional, behavioral, and cognitive regulation skills [29,30]. Emotional regulation processes serve to maintain, inhibit, or enhance the intensity and valence of emotional experiences to accomplish an individual's goals [31] and significantly improves across early childhood [31,32]. Children who have difficulty regulating emotions likely have difficulty acquiring more complex behavioral and cognitive regulation skills. Behavioral regulation, including a child's ability to withhold a response that is not appropriate for the situation [33], is needed to adhere to rules and expectations and influences the development of more sophisticated cognitive regulation skills. Cognitive regulation, including executive function (EF) abilities, includes skills that assist in the control and coordination of information in order to achieve goal-directed action and shows substantial improvement across early to middle childhood [34].

Although these skills can be measured as distinct constructs, SR processes are also dynamically linked with one another both "in the moment" and across development [35,36]. For instance, cognitive regulation measures, such as EF, often include both behavioral regulation (i.e., inhibitory control) and cognitive switching/flexibility [37]. Thus, as more advanced skills emerge, some SR constructs may be more dynamically linked with others.

Understanding the relation between SR and CMR as predictors of disease course requires considering specific types of SR at specific points in development as predictors of CMR. We hypothesize that the *emergence* of different forms of SR is most important to consider because the most potent influence of an SR skill may be when it is first emerging; this is when there is the greatest variability across children, with individual differences largely preserved over time [38]. The second aim was to examine if specific SR processes at different ages are associated with adolescent CMR profiles, while accounting for the interdependencies among SR skills.

A multi-method, longitudinal design was employed to identify person-centered profiles of adolescent CMR and to examine which types of SR at specific points in early development predict adolescent CMR. During puberty, especially linear growth, many CMR markers are dysregulated [39–41], but revert to prepubertal levels after puberty is complete [39]. Therefore, we examined adolescent CMR profiles in order to limit the variability attributable to these transient growth-related factors. We hypothesized that three adolescent CMR profiles would emerge: a low risk group, a group that mimics the NWO group, and a high risk group. Second, we hypothesized that different forms of SR would differentiate among the risk profiles across early development [42]. Specifically, we hypothesized that early attentional and emotional regulation would predict adolescent CMR, whereas by middle childhood, more sophisticated attentional and cognitive regulation, not emotional regulation, would be better predictors of

adolescent CMR.

2. Material and methods

2.1. Participants

Participants were part of a longitudinal study from a U.S. small southeastern city. The study was approved by the Institutional Review Board at The University of North Carolina at Greensboro (IRB protocol number 07–0194; 11–0360). Details about the sample recruitment and health assessments may be found elsewhere [43–45]. The original study began when the participants were 2 years old (N = 447). Although not significantly elevated by early childhood, the original sample was over-sampled for externalizing problems resulting in 37% of children being identified as being at risk for future externalizing problems at age 2. Child race and sex were reported by mothers. Sixty percent of the sample was White, 33% African American, and 7% biracial or other. Families were economically diverse based on Hollingshead [46] scores (*range* = 14–64, $M = 39.83$, $SD = 10.66$).

Due to the timing of the health assessments in adolescence, two of the three original cohorts participated in these visits. There were no significant differences between participants who did and did not participate in the 16-year assessment in terms of race, χ^2 (3, N = 447) = 1.98, $p = .58$; 2-year SES, t (423) = 0.02, $p = .17$; or 2-year externalizing T score, t (441) = −3.84, $p = .55$. Males were slightly less likely to participate in the 16-year assessment χ^2 (1, N = 447) = 4.19, $p = .04$. One hundred ninety-six adolescents participated in the 16-year visit and 117 of these participants provided blood samples. Due to the heavy use of biomarkers in the current study, we chose to limit the study sample to the 117 (60% female) participants who provided blood samples. There were no significant differences in race/ethnicity, SES, or sex between those who provided biomarker data and those who did not.

2.2. Procedures

Upon arrival at the research laboratory, participants were greeted by a research assistant who explained the study procedures and obtained signed consent from the primary caregiver. At ages 2, 4, and 7, children were videotaped while participating in SR tasks (partially derived from the Laboratory Temperament Assessment Battery) [47] and mothers completed questionnaires. Video recordings were used for behavioral coding. At age 16, adolescents completed a blood draw, anthropometrics, and blood pressure measurements. Participants were asked to fast from food (water *ad libitum*) for 10–12 h and to refrain from vigorous exercise and alcohol consumption for 24 h prior to the blood draw. Participants were also asked to refrain from smoking/vaping in the morning prior to the blood draw. To limit the influence of acute inflammation on biomarkers, adolescents were asked to reschedule their health visit if they reported: 1) any illness or injury in the past week or surgery in the past month, 2) immunizations with the past 2 weeks, or 3) use of antibiotics, corticosteroids, or other prescription anti-inflammatories within the past 10 days.

2.3. Measures

2.3.1. SR

SR skills that were hypothesized to have emerged were assessed with developmentally appropriate tasks at each laboratory visit. Behavioral regulation was not assessed as a separate measure at age 7; however, it was considered within the cognitive regulation measure, which includes inhibitory control and cognitive switching/flexibility. Two trained coders blind to the study hypotheses scored the videotaped tasks.

Age 2 Emotional Regulation was indexed by a global regulation measure during the High Chair task [48], defined as the use of skills (e.g., distraction, sucking) that were used to decrease distress. In this task, the child was placed in a high chair without any toys or snacks for 5 min. The mother was seated nearby and was instructed to respond to her child as she deemed necessary. Emotional regulation was coded from 0 (*no control of distress*) to 4 (*regulation of distress during most of the task*). Two trained coders worked together on 15% of the videotaped sessions and independently scored another 15% for reliability, resulting in a Cohen's Kappa of .96.

Age 4 Emotional Regulation was coded based on children's regulation during the Perfect Circles task [49]. Children were asked to draw perfect circles and told that the circle was not right after each attempt and asked to draw another one for 3.5 min. Emotional regulation was coded from 0 (*no control of distress*) to 4 (*regulation of distress during most of the task*). Two trained coders worked together on 15% of the videotaped sessions and independently scored another 15% for reliability, resulting in a Cohen's Kappa of .72.

Age 7 Emotional Regulation was coded during the Puzzle Box task [50]. A puzzle box was placed in front of the child that contained a draping cloth with sleeves at the front of the box. The child placed their arms through the sleeves and put together a puzzle in the box without looking. Emotional regulation was coded from 0 (*no control of distress*) to 3 (*regulation of distress during most of the task*). Two trained coders worked together on 15% of the videotaped sessions and independently scored another 15% for reliability, resulting in a Cohen's Kappa of .82.

Age 2 and 4 Behavioral Regulation was measured using the Gift Delay task [33]. The experimenter placed a gift in front of the child and then left the room and the child was told not to touch the gift until their return. Behavioral regulation was coded as the proportion of time that the child spent not touching the gift. The reliability was excellent at age 2 ($r = 0.99$) and age 4 ($r = 0.99$).

At the age 4 assessment, children were asked to wait before taking an M&M from under a cup (four trials, delays of 10, 20, 30, and 15 s) [33]. There were two parts to each trial: 1) the time from the start of each trial until the time that the tester lifted the bell to indicate the halfway point, 2) the time from the tester lifting the bell until the bell is rung to indicate the end of the wait. Coding for each trial ranged from 1 (*child eats the snack during part I*) to 7 (*child waits until the bell is rung*) (ICC = 0.92). Children received 1-2 additional points if they kept their hands on the mat during one or both parts of the trial (ICC = 0.90). The maximum number of points a child could receive (higher number indicating greater behavioral regulation) was 36 points.

Age 2 Attentional Regulation was measured during a task in which children watched a 5-min segment of the videotape 'Spot', a story about a puppy exploring a neighborhood. The overall duration, the proportion of time the child spent looking at the video, was coded. The reliability was excellent ($r = 0.98$).

Age 4 and 7 Attentional Regulation was assessed using maternal reports on the attentional focusing subscale of the Children's Behavior Questionnaire-Short Form (CBQ-SF) [51]. Six items measured children's tendency to maintain focus on a task and were averaged ($\alpha = 0.68$ and 0.70 for the age 4 and 7 measures, respectively).

Age 7 Cognitive Regulation was indexed through an EF measure on the Delis-Kaplan Executive Function System Color-Word Interference Test [52]. The inhibition/switching score, the completion time on the trial which was converted to a standardized score based on the normative data in the D-KEFS scoring manual, was used as a measure of cognitive regulation. This measure included an inhibitory control (i.e., reading the word that is presented in a dissonant colored ink) and a cognitive switching/flexibility component (i.e., switching between naming the dissonant ink colors and reading the conflicting words).

2.3.2. CMR

Traditional (i.e., glucose, blood pressure, lipids, abdominal obesity) and non-traditional (i.e., CRP, leptin) CMR indicators were used to provide a comprehensive CMR measure. Mean arterial pressure (MAP), defined as a time-weighted average of blood pressure during the cardiac cycle, was calculated from resting systolic (SBP) and diastolic (DBP) blood pressure. WC (cm) was measured at the natural waist (smallest

point) between the iliac crest and the rib cage. WC, not BMI, was included as the measure of obesity in the current study because BMI is a body shape marker that strongly correlates with percent body fat at the population level [53]. However, abdominal obesity (i.e., WC) increases risk of chronic disease irrespective of BMI [54–56]. CRP, a systemic inflammatory marker, is used for adult risk stratification [12], while leptin is an adipokine that is associated with increased body fat, appetite control, energy expenditure, and other physiological processes associated with CMR.

Blood was collected into serum separator tubes and frozen. Small aliquots of frozen serum were later thawed to reach room temperature and assayed for blood lipids (e.g., high-density lipoprotein; HDL and non-HDL; Wako Chemical, Richmond VA) and fasting blood glucose (Cayman Chemical, Ann Arbor MI) using standard procedures outlined by the company and with an EPOCH plate reader (BioTek, Winooski VT). Leptin and CRP were analyzed with multiplex assays (RND Systems, Minneapolis MN) using the Luminex SD (Luminex, Austin TX).

3. Results

3.1. Analytic strategy and preliminary analyses

LPA was used to identify subgroups of adolescents with similar patterns of CMR (leptin, glucose, HDL, non-HDL, WC, MAP, and CRP) in MPlus version 7.4 (Muthen & Muthen, Los Angeles CA). LPA offers many advantages over traditional cluster techniques (i.e., cluster analysis). For example, LPA uses a formal statistical model based on probabilities to classify cases [57] and more appropriately handles missing data than traditional cluster techniques by assuming the data are Missing Completely at Random (MCAR), thereby allowing the model parameters to be informed by all cases [58]. Multiple sets of starting values were specified to assess model identification. A model with 2–5 profiles were fit. Determination of best model fit was evaluated with AIC, BIC, sample size adjusted BIC, the adjusted Lo-Mendell-Rubin Likelihood Ratio Test (LMR-LRT), and Entropy.

Individuals were classified into profiles based on their highest probability of profile membership. The groups were saved and used as the dependent variable in multinomial logistic regression models in SPSS version 18 (SPSS, Chicago IL), with the high-risk profile serving as the reference group. Sex and SES were included as covariates. By including each type of SR at each age in the same model, their shared variance was accounted for. Missing data for the predictor variables were imputed using multiple imputation (EM algorithm) [59]. Full information maximum likelihood (FIML) was used to handle missing data in the LPA analyses. All data was examined for normality. CRP and leptin were skewed and therefore transformed using natural log. Two participants had CRP values slightly greater than 10 mg/L. There is some guidance to eliminate data from individuals with CRP values above 10 mg/L [61], yet growing evidence indicates that eliminating individuals with high CRP values underestimates chronic disease risk [e.g., 62]. Thus, we chose to include all participants in study analyses in accordance with this guidance and in consideration of our stringent screening procedures. Descriptive statistics and correlations are provided in Table 1.

3.2. Identifying latent profiles of CMR

There were no significant differences by race/ethnicity across the CMR variables [$F(3, 113) = 0.18–1.73$, p = ns], and therefore we did not include race/ethnicity in the LPA analyses. LPA fit indices for a 2-class model [AIC = 6582.05, BIC = 6642.82, E = 0.94, *Adj. p* LMR-LRT ($p < .05$)], 3 class model [AIC = 6514.25, BIC = 6597.12, E = 0.92, *Adj. p* LMR-LRT ($p < .05$)], and 4 class model (AIC = 6557.35, BIC = 6599.31, E = 0.89, *Adj. p* LMR-LRT ($p > .05$)], were compared. The 4-class model's LMR-LRT test became non-significant. The 3-class model was selected as the best-fitting model (Fig. 1) [60].

Table 1
Correlations and descriptive statistics.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. 2yr Emotional Reg (Obs)	–																
2. 2yr Behavioral Reg (Obs)	.39***	–															
3. 2yr Attentional Reg (Obs)	.38***	.28**	–														
4. 4yr Emotional Reg (Obs)	.01	.19*	.18	–													
5. 4yr Behavioral Reg (Obs)	.33***	.92***	.23*	.22*	–												
6. 4yr Behavioral Reg-Food (Obs)	.05	.11	.14	.28**	.17	–											
7. 4yr Attentional Reg (Rep)	.18	.16	.29**	.15	.11	.01	–										
8. 7yr Emotional Reg (Obs)	-.09	.15	-.10	.00	.15	.19	-.05	–									
9. 7yr Attentional Reg (Rep)	.14	.09	.19	.19*	.02	.03	.53***	-.12	–								
10. 7 yr Cognitive Reg (Obs)	-.15	-.03	-.12	.12	-.10	.17	.03	.04	.09	–							
11. 16 yr HDL	.05	.03	.08	.17	.03	.08	.12	-.10	.19	.09	–						
12. 16 yr Leptin	-.31***	-.21*	-.23*	-.13	-.19*	-.06	-.09	-.03	-.20*	-.20*	-.07	–					
13. 16 yr Glucose	.05	-.01	-.08	-.15	-.03	-.10	-.10	.09	-.05	-.12	-.52***	.20*	–				
14. 16 yr WC	-.34***	-.25**	-.18	-.27**	-.31***	-.29**	-.14	-.14	-.20*	-.21*	-.04	.62***	.08	–			
15. 16 yr MAP	-.14	-.24*	-.19*	-.14	-.28**	.06	-.22*	-.12	0.09	-.02	-.06	.17	.16	.42***	–		
16. 16 yr Non-HDL	.07	.09	-.02	-.03	.11	.00	.11	-.12	.08	.11	-.43***	.03	.32***	-.15	.01	–	
17. 16 yr CRP	-.19	-.04	-.13	-.16	-.06	-.13	-.12	.06	-.13	-.07	-.13	.36***	-.03	.40***	.14	-.06	–
Mean	3.17	0.16	.40	3.32	0.10	31.23	4.50	2.60	4.82	9.11	61.67	13.84	86.14	79.00	83.74	146.88	1.20
Standard Deviation	1.07	0.28	.20	0.59	0.18	7.85	0.69	0.70	0.92	3.32	23.66	17.24	26.01	14.53	8.85	52.58	2.09
Minimum	.00	.00	.04	2.00	.00	4.00	2.89	.00	2.17	2.00	6.49	0.21	47.00	59.80	61.00	53.17	.00
Maximum	4.00	1.00	.90	4.00	0.76	36.00	6.00	3.00	6.50	15.00	129.49	95.18	189.00	148.50	104.00	315.04	10.91

Note: ***p < .001; **p < .01; *p < .05; Obs = Observed; Rep = Parent Reported; Values reported prior to standardizingCRP = C-reactive protein, HDL = high-density lipoprotein, MAP = mean arterial pressure, WC = waist circumference.

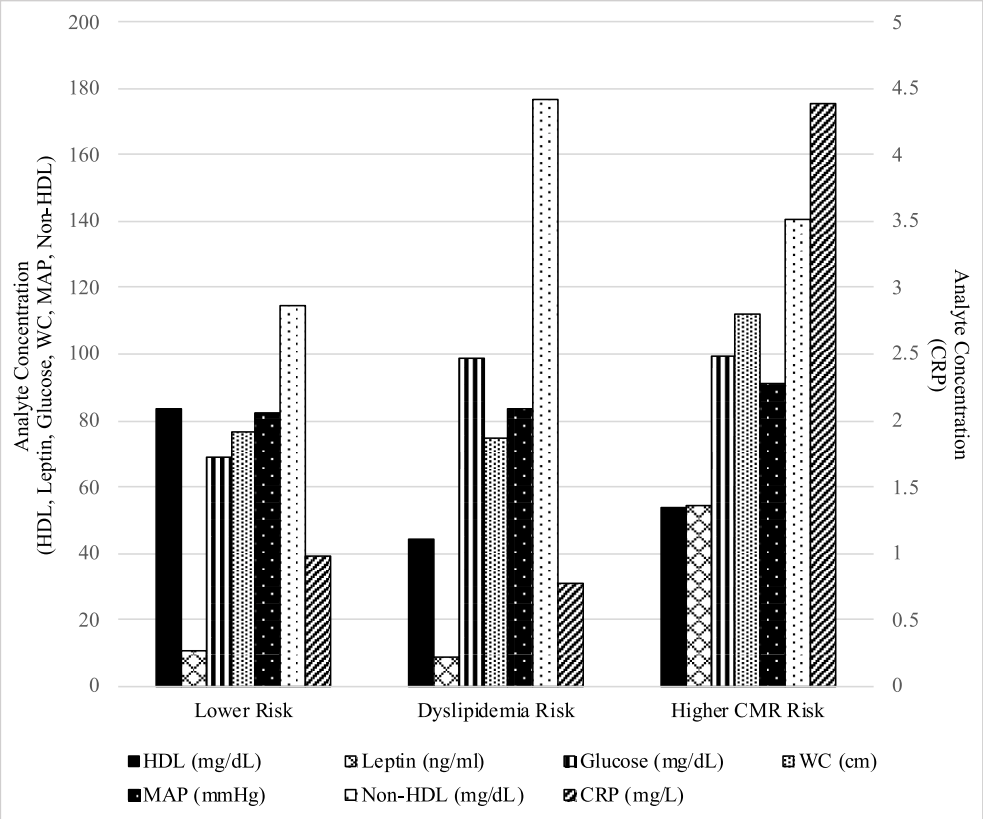

Fig. 1. Adolescent profiles of CMR

The *Low Risk* group ($N = 48$, 41%) had low leptin, glucose, and non-HDL, with high HDL. The *Dyslipidemia Risk* group ($N = 58$, 49.6%) had high glucose and non-HDL, but low HDL, leptin, WC, MAP, and CRP. The *High Risk* group ($N = 11$, 9.4%) included adolescents who had high leptin, glucose, WC, MAP, CRP, and moderate non-HDL. Table 2 contains descriptive statistics for the demographic and CMR variables by profile. Because there is mixed guidance regarding the inclusion of individuals with high CRP values [61,62], we lowered the values of the participants with CRP values above 10 mg/L to 9.99 mg/L and reran the models to ensure that high values were not skewing the results. The model fit statistics indicated that the 3-profile solution still was the best fit and participant profile membership was unchanged. Therefore, we included these participants in the final model.

Table 2
Means and standard deviations for continuous variables and N and prevalence of categorical variables for demographic and individual CMR variables across the three profiles of CMR.

	Low Risk (n = 48; 41%)	Dyslipidemia Risk (n = 58; 50%)	High CMR (n = 11; 9%)
	Mean (SD) or N (%)	Mean (SD) or N (%)	Mean (SD) or N (%)
White	34 (71%)	32 (55%)	4 (36%)
Female	29 (60%)	34 (59%)	7 (64%)
SES	46.24 (10.91)	44.73 (12.90)	42.78 (15.73)
BMI percentile	64.15 (25.62)	60.13 (27.84)	98.40 (1.82)
HDL (mg/dL)	84.46 (15.23)	44.37 (10.96)	53.47 (20.44)
Leptin (ng/ml)	10.34 (8.86)	8.97 (10.29)	54.79 (20.93)
Glucose (mg/dL)	67.78 (11.01)	98.94 (23.60)	100.03 (36.41)
WC (cm)	76.74 (9.12)	74.61 (9.03)	112.06 (15.98)
MAP (mm Hg)	82.51 (9.06)	83.52 (8.58)	90.90 (6.27)
Non-HDL (mg/dL)	113.30 (32.53)	175.91 (52.16)	140.42 (35.25)
CRP (mg/L)	.97 (1.99)	.79 (1.18)	4.40 (3.42)

3.3. SR predictors associated with CMR profiles

Average posterior probabilities were 0.98 for *Low Risk*, 0.95 for *Dyslipidemia Risk*, and 0.99 for *High Risk,* suggesting low classification error. Differences among SR variables by sex, race/ethnicity, and SES were examined. There were significant sex differences in children's age 4 behavioral regulation in response to food ($t = -3.21$, $p < .01$) and SES differences in children's age 7 cognitive regulation ($r = 0.31$, $p < .01$). There were no significant race/ethnicity differences in SR variables, and therefore race was not included in the logistic regression analyses. Sex or SES did not predict profile membership. Different types of SR abilities at different ages uniquely predicted membership in the CMR profiles (Table 3; Fig. 2).

3.3.1. Age 2 SR

Age 2 emotional regulation predicted membership in the *Low Risk* as compared to the *High CMR* group at $OR = 2.48$ (95% $CI = 1.05, 5.85$). With a 1 *SD* increase in emotional regulation, children were almost 3 times as likely to be in the *Low Risk group*. For each *SD* increase in emotional regulation at age 2, the odds of being in the *Dyslipidemia Risk* group increased by 2.28 (95% $CI = 1.03, 5.02$) as compared to the *High CMR* group. Behavioral and attentional regulation at age 2 were not uniquely associated with profile membership.

3.3.2. Age 4 SR

Age 4 emotional regulation predicted membership in the *Low Risk* as compared to the *High Risk* group at $OR = 4.60$ ($CI = 1.34, 15.79$). Thus, with a 1 *SD* increase in emotional regulation, the odds of being in the *Low Risk* group increased by 4.6. Stronger behavioral regulation in response to food was associated with greater odds of being in the *Low Risk* as compared to the *High Risk* group at $OR = 2.02$ (95% $CI = 1.01, 4.01$). With a 1 *SD* increase in behavioral regulation in response to food, children were about 2 times more likely to be in the *Low Risk* profile.

Table 3
Multinomial logistic regressions.

	CMR Group Contrasts											
	Low Risk vs. High Risk				Dislipidemia Risk vs. High Risk				Dislipidemia Risk vs. Low Risk			
	(n = 48; 41%) (n = 11; 9%)				(n = 58; 50%) (n = 11; 9%)				(n = 58; 50%) (n = 48; 41%)			
	B (SE)	OR	p	95% CI	B (SE)	OR	p	95% CI	B (SE)	OR	p	95% CI
2-year Self-Regulation												
Sex	.43 (.85)	1.50	.61	(.29, 8.14)	.01 (.81)	1.00	.99	(.20, 4.89)	-.44 (.46)	.65	.34	(.26, 1.58)
SES	.07 (.04)	1.07	.08	(1.00, 1.15)	.05 (.04)	1.05	.19	(.98, 1.13)	-.02 (.02)	.98	.34	(.94, 1.02)
Emotional Regulation (Obs)	.91 (.44)	2.48	.03	(1.05, 5.85)	.82 (.40)	2.28	.04	(1.03, 5.02)	-.09 (.32)	.92	.78	(.49, 1.71)
Behavioral Regulation (Obs)	-.04 (.39)	.97	.93	(.44, 2.10)	-.14 (.37)	.87	.71	(.42, 1.80)	-.11 (.28)	.90	.71	(.52, 1.56)
Attentional Regulation (Obs)	.38 (.35)	1.46	.29	(.73, 2.90)	.19 (.32)	1.21	.57	(.64, 2.27)	-.19 (.24)	.83	.43	(.52, 1.32)
4-year Self-Regulation												
Sex	−1.04 (1.14)	.35	.36	(.04, 3,31)	-.77 (1.09)	.46	.48	(.06, 3.90)	.27 (.51)	1.31	.60	(.48, 3.55)
SES	.08 (.05)	1.09	.06	(1.00, 1.19)	.07 (.04)	1.07	.10	(.99, 1.16)	-.02 (.02)	.99	.50	(.94, 1.03)
Emotional Regulation (Obs)	1.52 (.63)	4.60	.02	(1.34, 15.79)	1.10 (.60)	2.99	.06	(.93, 9.63)	-.43 (.28)	.65	.13	(.38, 1.13)
Behavioral Regulation (Obs)	-.33 (.39)	.72	.40	(.33, 1.56)	-.44 (.35)	.64	.21	(.32, 1.28)	-.11 (.29)	.89	.69	(.51, 1.56)
Behavioral Regulation-Food (Obs)	.70 (.35)	2.02	.04	(1.01, 4.01)	.43 (.29)	1.54	.13	(.88, 2.71)	-.27 (.25)	.77	.28	(.47, 1.25)
Attentional Regulation (Rep)	1.00 (.67)	2.70	.04	(1.02, 10.11)	.60 (.64)	1.82	.35	(.52, 6.43)	-.40 (.30)	.67	.18	(.38, 1.20)
7-year Self-Regulation												
Sex	-.73 (1.03)	.48	.48	(.06, 3.61)	−1.12 (1.03)	.33	.27	(.04, 2.44)	-.39 (.47)	.68	.41	(.27, 1.70)
SES	.05 (.05)	1.06	.28	(.96, 1.16)	.06 (.05)	1.06	.25	(.96, 1.17)	.00 (.02)	1.00	.86	(.96, 1.05)
Emotional Regulation (Obs)	.60 (.53)	1.84	.23	(.60, 5.45)	.63 (.55)	1.87	.25	(.64, 5.50)	.38 (.29)	1.46	.19	(.83, 2.56)
Attentional Regulation (Rep)	1.04 (.48)	2.87	.03	(1.10, 7.41)	1.06 (.48)	2.89	.03	(1.12, 7.43)	.04 (.24)	1.04	.86	(.66, 1.66)
Cognitive Regulation (Obs)	.98 (.49)	2.66	.04	(1.01, 7.00)	.96 (.49)	2.61	.04	(1.01, 6.88)	-.02 (.23)	.98	.94	(.63, 1.54)

Note: Obs = Observed; Rep = Parent Reported; All variables are standardized for interpretability.

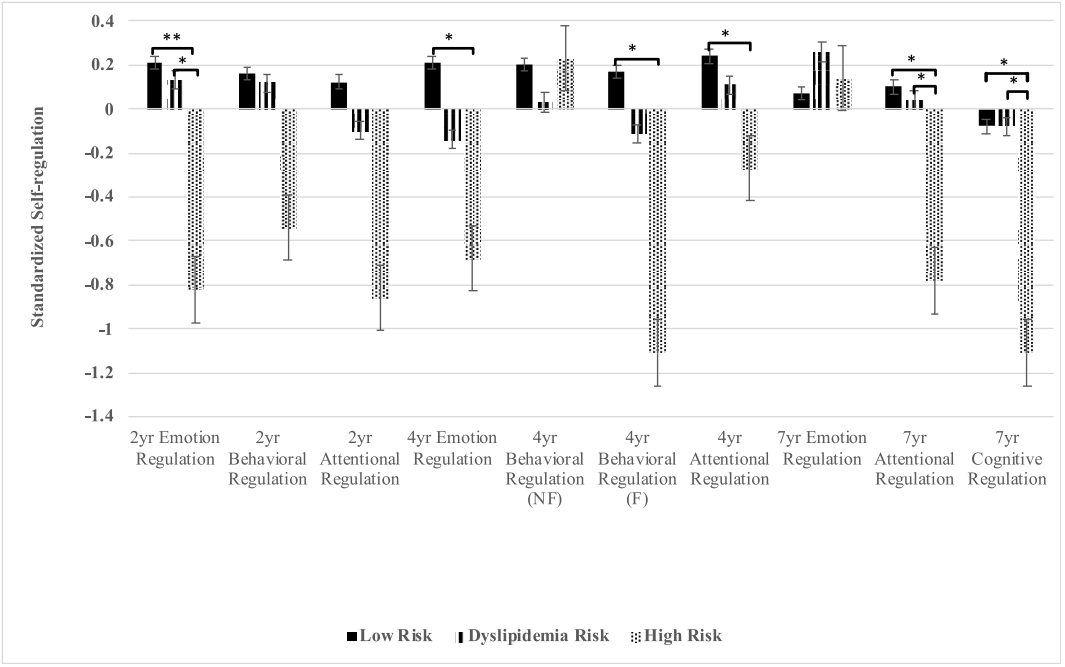

Fig. 2. Self-regulation differences by CMR profiles.
*$p < .05$, **$p < .01$; NF=Non-food-related/Gift Delay, F=Food-related/Snack Delay.

Behavioral regulation in a non-food context was not associated with CMR profile membership. Attentional regulation predicted the odds of being in the *Low Risk* as compared to the *High Risk* group by 2.70 (*OR* = 2.70, *CI* = 1.02, 10.11), indicating that with a 1 *SD* increase in attentional regulation abilities children were almost 3 times more likely to be in the *Low Risk* profile.

3.3.3. Age 7 SR

Greater attentional and cognitive regulation at age 7 were significantly associated with a greater likelihood of being in the *Low Risk* and *Dyslipidemia Risk* groups when compared to the *High Risk* group. Greater attentional regulation at age 7 predicted the odds of being in the *Low Risk* or *Dyslipidemia Risk* groups, as compared to the *High Risk* group (*OR* = 2.89, 95% *CI* = 1.12, 7.43 and *OR* = 2.89, *CI* = 1.12, 7.43, respectively). These results suggest that as attentional regulatory abilities increase, children were almost 3 times more likely to fall into the *Low Risk* or *Dyslipidemia Risk* profiles. Greater cognitive regulation predicted being in the *Low Risk* or *Dyslipidemia Risk* groups, as compared to the *High Risk* group at *OR* = 2.66 (95% *CI* = 1.01, 7.00) and *OR* = 2.61 (95% *CI* = 1.01, 6.88), respectively. With each 1 *SD* increase in cognitive regulation, children were about 2.5 times more likely to be in the *Low Risk* or *Dyslipidemia Risk* profiles. Emotional regulation at age 7 was not uniquely associated with profile membership.

4. Discussion

This is the first known study to establish that distinct domains of SR at different points during childhood differentially discern among profiles of adolescent CMR. Our study had several major findings. First, we identified three distinct profiles of CMR during adolescence. Forty-one percent of adolescents in our sample were in the *Low Risk* group and 9% were in the *High Risk* group. Arguably, the most notable finding regarding the CMR profiles was that half (50%) of the adolescents were classified into the *Dyslipidemia Risk* profile, a group characterized by a clustering of high glucose and adverse lipids—in the absence of obesity or elevated inflammation. Of considerable importance is the fact that this profile parallels some of the dysfunction noted in the "normal-weight metabolically unhealthy" phenotype or "NWO" observed in adults.

In *NWO*, the individual's obesity level is within the normal range (using BMI), but there is increased presence of CMR, including increased WC and leptin. NWO occurs in children and adolescents and its presence in childhood predicts lower insulin sensitivity in youth [14]. The *Dyslipidemia Risk* profile identified in the current study is intriguing since, unlike most NWO adults, our adolescents did not have increased WC or leptin levels but displayed elevations in biomarkers implicit in metabolic dysfunction, such as glucose and non-HDL cholesterol. It is unclear whether this difference is specifically related to the developmental stage of adolescence or whether it represents the initial stage of NWO that becomes fully established in adulthood. Additional research is needed to replicate these findings in other samples, as well as establish whether this profile holds from adolescence into adulthood.

The *High Risk* CMR group included adolescents who had the typical clustering of CMR associated with obesity and inflammation [14]. The prevalence of this group was similar to MetS prevalence in studies of similar-aged adolescents [63]. Supplemental analyses indicated this group was at high risk using traditional definitions of MetS, suggesting that these adolescents have significant risk for multiple health complications in adulthood. Notably, this group had significantly elevated CRP ($M = 4.4$ mg/L), well above the 3.0 mg/L cut-point used for increased risk of CVD in adults [14]. Given the significant differences in CRP levels between the *High Risk* CMR group and the other groups, simply utilizing CRP levels >3 mg/L would have distinguished this group. It is unclear if this would generalize to other adolescent samples and should be considered further.

The second goal was to examine SR skill development across childhood as predictors of adolescent CMR. Existing work addressing the association between SR and CMR has not been informative about which types of SR (i.e., emotional, behavioral, attentional, cognitive), or what points in development, are most predictive of CMR. Two studies examined specific types of SR independently as predictors of obesity [6,8]; however, no known studies have examined specific forms of SR as predictors of CMR longitudinally. When examining probabilities of CMR group membership, four domains of SR predicted adolescent CMR, although the type of predictive SR skill varied by age following a theoretically expected pattern. At age 2, emotional regulation—one of the earlier-emerging SR abilities—distinguished among patterns of adolescent CMR, whereas by age 7, more sophisticated attention and cognitive skills, not emotional regulation, differentiated patterns of CMR. Specifically, we found that children with better emotional regulation skills at ages 2 and 4, greater behavioral regulation skills in response to food and attentional regulation skills at age 4, and better attentional and cognitive regulation skills at age 7 were more likely to be in the *Low Risk* group as compared to the *High Risk* group. Importantly, this provides the first known evidence that the ability to predict adolescent CMR using childhood SR followed a developmental pattern.

The ability to appropriately regulate emotional arousal is a central developmental skill associated with a range of adjustment outcomes [32], including obesity/CMR [6,8]. This study extends this work by showing this association across a 14-year period and employing a more comprehensive measure of CMR. By preschool, however, CMR profiles were no longer differentiated solely by emotional regulation, and instead also by attentional and behavioral regulation. Similar to other work [6], we found that behavioral regulation in the context of food, but not in the context of other potentially rewarding experiences (i.e., unwrapping a gift) at age 4 predicted later CMR. Together these studies suggest that behavioral regulation around food, as early as preschool, needs to be addressed in CMR prevention. It is important to note, however, that in this study the design of the behavioral regulation tasks differed in more ways than just the presentation of food (M&Ms) or a wrapped gift. The experimenter left the room in the wrapped gift task, whereas in the food-related behavioral regulation task the experimenter was present (creating a social context to the task) and presented the child with a series of trials increasing in length. Moreover, the study design did not include behavioral regulation tasks in response to food at ages 2 and 7 and thus, unlike other studies [6] these data do not provide insight into the importance of this skill in response to food across early development. Future studies should replicate these findings in tasks that mirror one another more similarly in design from toddlerhood through middle childhood.

Although rudimentary attentional regulation skills emerge in infancy, these skills continue to develop throughout the preschool and school years and are essential building blocks for later developing cognitive regulation skills. Building on developmental work showing that childhood attentional regulation is a central predictor of adjustment, our results indicated that attentional regulation was consistently a predictor of adolescent CMR, showing significant effects both in preschool and childhood. Interestingly, we did not find that age 2 attentional regulation predicted adolescent CMR. Although against expectations, the attentional regulation measure employed at age 2 was not originally designed to be used as an attentional regulation task, but instead a task to keep children calm to assess baseline physiology. Thus, although this measure does imply children's attentional regulation, or ability to sustain attention, it is not a traditionally employed measure. Future studies are needed to confirm if attentional regulation in toddlerhood is also a significant regulatory ability that predicts adolescent CMR.

Finally, we found that children with better cognitive regulation (EF) skills at age 7 were less likely to be in the *High Risk* profile compared to the *Low Risk* group. Prior work indicates that individuals with better EF abilities are more likely to enact physical activity intentions, successfully quit smoking, and less likely to consume fatty foods or develop problems with alcohol [24,64,65]. Importantly, this is one of the only studies showing that this association exists from childhood, when these skills develop, and predicts to adolescence when risky health behaviors emerge. Thus, these results provide the first known evidence that adolescent CMR profiles can be differentiated by childhood SR and that it is important to consider when distinct SR skills emerge when considering SR skills as predictors of CMR. This is essential information to modify existing obesity/CMR preventive intervention efforts.

It is important to note that our identification of various CMR patterns, and thus different patterns of underlying metabolic derangements, allowed for greater understanding of how CMR develops across time through tracking both clinical and subclinical levels of early CMR. Not only is this identification important for preventive intervention efforts on a physiological level, but our investigation of how the development of SR distinguishes among risk profiles informs prevention efforts on a psychological level. Specifically, our results indicate that not only are there significant differences among the *Low* and *High CMR Risk* groups in terms of childhood SR, but there are also differences in SR between the *Dyslipidemia Risk* and *High Risk* groups. If the traditional CMR/MetS cut-offs, or even a continuous risk variable similar to those used in the adult literature, had been employed, this nuanced difference would not have been discovered, which hinders early prevention efforts.

An important consideration is that the association between SR and CMR is likely bidirectional. Among young children, the prevalence of

the components of CMR is still low, and it is likely that the SR skills measured here preceded the emergence of CMR factors. Once CMR factors have emerged, however, the associations between SR and CMR likely become bidirectional. Metabolic dysfunction and low-level inflammation may result in prefrontal cortex structure and function changes that lead to SR difficulties [25], which, in turn, could further increase CMR. Furthermore, a recent review on elevated inflammation suggested that chronic pro-inflammatory states are involved in biobehavioral alterations that contribute to SR failures [66]. However, this work was mostly based on cross-sectional or short-term longitudinal studies, that provide limited information about directionality across longer developmental periods. More work is needed to better understand how SR-CMR links emerge and change across development.

It is also important to note that many factors influence SR and CMR development. Growing evidence suggests that the environment [67,68] predicts adolescent and adult CMR and thus developing SR skills are only one avenue by which CMR may develop. Additionally, there are a variety of environmental factors that influence an individual's SR abilities. For instance, it is well-established that caregiver behaviors contribute significantly to the development of SR [20,69]. Moreover, empirical and theoretical work has highlighted the underlying biological components (i.e., genes, neural, cardiovascular) of individual differences in SR [e.g. Refs. [70,71]]. Thus, research is needed to consider the role of underlying factors involved in the early SR-CMR link.

A few study weaknesses must be considered. First, the current study has a relatively modest sample size. Although sample size has not been found to have a consistent effect on power in detecting the correct number of profiles [72], it is possible that having a larger sample size would produce different profile solutions that better separate youth. Future studies are needed to replicate our findings with a larger sample of participants to ensure generalizability of our findings. Second, we employed laboratory measures of each SR process except for age 4 and 7 attentional regulation, which was reported by mothers. Although a widely used maternal report of attentional regulation was used, future work should employ laboratory measures of attentional regulation to see if these associations hold. In addition, in the current study we did not employ a traditional measure of attentional regulation at age 2. Given that attentional regulation skills begin to develop in infancy, future work is needed to confirm our findings. Also, the measures of emotional regulation solely considered the regulation of anger. Future studies should consider the importance of the regulation of other emotions (i.e., fear, sadness, excitement) in predicting CMR. Finally, future work should consider including each form of SR at multiple timepoints to assess which type of SR at which time point is the most important predictor of CMR.

Moreover, this study did not address the many possible mechanisms by which there is an association between different domains of SR and adolescent CMR. For instance, SR is linked with greater engagement in healthy behaviors and fewer unhealthy behaviors [24], which could explain the SR-CMR link. Other developmental processes, including peer influences, puberty, adolescent self-regulation skills, and parental support, to name a few, could also explain these associations. In addition, a lack of SR can precipitate metabolic dysfunction and low-level inflammation that may result in prefrontal cortex structure and function changes that lead to SR difficulties [25,26]. Moreover, there is growing evidence of biological (brain derived neurotrophic factor [BDNF]) [73] and genetic [74] links between attention (i.e., ADHD) and obesity. Thus, developmental studies that address the underlying mechanisms by which SR skills in childhood are associated with later CMR are needed.

5. Conclusion

Given the increasing rates of youth CMR [1], identifying early factors that predict adolescent health risk is essential. This study's results offer a novel and nuanced view of adolescent CMR and childhood SR. We identified three distinct adolescent profiles of CMR—*Low Risk*, *Dyslipidemia Risk*, and *High Risk* groups—which can be utilized for identifying disease risk and its prevention. This study also provides insight into which types of SR at different points in early development predict adolescent CMR at the individual level. Common risk factors for CMR, such as poverty and family history are not easily modifiable, but here we provided evidence of which modifiable SR processes, and at what points in early development, are the most important predictors of adolescent CMR. Identifying these processes has significant implications for modifying existing preventive intervention programs to maximize the impact and highlights the need for interdisciplinary work to address how early developing skills can be predictive of various forms of adjustment.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This research was supported by the National Institute of Health [grant numbers MH 55625, MH 55584, MH 58144, HD 078346]. The authors also thank the families who generously gave their time to participate in the study.

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