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Independent Contributions of Callous-Unemotional Behaviors and Quantitative Autistic Traits to Aggression in Early Childhood

Kristen Lineback, BS, Holly C. Baer, BA Candidate, Yi Zhang, MS, David Hartenbach, BA Candidate, W. Roger Mills-Koonce, PhD, Michael T. Willoughby, PhD, Anne L. Glowinski, MD, MPE, John N. Constantino, MD, Natasha Marrus, MD, PhD

Drs. Constantino and Marrus are senior authors who contributed equally to the development of this manuscript.

Objective: Callous-unemotional (CU) behaviors and quantitative autistic traits (QATs), heritable domains implicated in social development, are both associated with reduced prosocial behavior and increased aggression at their clinical extremes. However, they are hypothesized to contribute to aggression through separate mechanisms. This study tested whether CU behaviors and QATs exhibited distinct profiles of heritable influences as well as independent contributions to early childhood aggression in a general population sample with enhanced sensitivity to clarify these relationships.

Method: Parents of 3- to 4-year-old epidemiologically representative twins ascertained from birth records (N = 113 pairs) completed questionnaires measuring CU behaviors, QATs, and aggression. Correlation coefficients indexed overlap across behaviors. Intraclass correlations were compared between monozygotic and dizygotic twins to characterize relative genetic and environmental influences. Generalized estimating equations tested contributions of CU subdomains, verified via factor analysis, and QATs to aggression.

Results: Total CU scores strongly correlated with QATs ($r = 0.54$) and aggression ($r = 0.55$), while QATs correlated moderately with aggression ($r = 0.38$). Among 3 identified CU factors, the uncaring factor strongly correlated with QATs ($r = 0.52$), while unemotional and callous factors showed small correlations ($r = 0.25$ and $r = 0.16$, respectively). QATs, aggression, and all CU factors except the callous factor showed heritable influences. Uncaring and callous factors as well as QATs demonstrated unique and shared contributions to aggression, with the callous factor being moderated by sex.

Conclusion: Partially overlapping relations support distinct mechanisms whereby CU behaviors, in particular the callous factor, and QATs contribute to early aggression. In-depth social developmental assessment may enhance personalized intervention for aggression in early childhood.

Plain language summary: In this cross-sectional dimensional approach, authors evaluated the extent to which callous unemotional behaviors and quantitative autistic traits showed independent contributions to aggression at age 3 to 4 years based on heritable and environmental influences that set the stage for future outcomes. In 224 preschool-aged twins, callous-unemotional behaviors and quantitative autistic traits were independently associated with reduced prosocial behavior and increased aggression, accounting for almost 30% of the variance in aggression and evidence of some shared genetic influences. Callous-unemotional behaviors accounted for a greater unique contribution to variation in aggression than autistic traits. Callous behavior is also strongly influenced by environmental factors and showed a stronger relationship with aggression in boys than in girls. These results suggest that in early childhood, quantitative autistic traits and callous-unemotional behaviors may represent distinct pathways to aggression.

Diversity & Inclusion Statement: We worked to ensure sex and gender balance in the recruitment of human participants. We worked to ensure sex balance in the selection of non-human subjects. One or more of the authors of this paper self-identifies as a member of one or more historically underrepresented racial and/or ethnic groups in science.

Key words: aggression; autistic traits; callous unemotional; early childhood; twin study

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Aggression, defined as any action intended to harm another individual or damage property, is a common source of significant impairment across multiple child psychiatric conditions. These behaviors are aimed at causing direct physical or verbal harm, as well as indirect relational harm, and can be classified as reactive and impulsive or premeditated and purposeful.[1] Aggression is linked to poor psychosocial outcomes, including educational underachievement, delinquency, and long-term violence,[2,3] and clinical management benefits from a comprehensive, individualized approach that accounts for distinct profiles and causes.[4] Heritability of aggression (broadly defined) is approximately 50% to 70%,[1,5] and several forms of environmental adversity are associated with elevated aggression, including maltreatment, lack of parental monitoring, and poverty.[1] Population-level stability of aggression is observable by early childhood and is also subject to heritable influences,[6] although half of children

with problematic aggression show resolution of these behaviors as adults.[7] Clarifying this heterogeneity in early childhood is thus important for determining mechanisms of aggression, contextualizing risk factors and trajectories, and identifying opportunities to improve long-term outcomes. Growing evidence for partially overlapping genetic factors across psychiatric conditions[8] suggests that characterizing independent contributions of heritable, co-occurring symptom dimensions to early childhood aggression could resolve this heterogeneity and ultimately advance individualized clinical care. Social symptom dimensions are especially relevant to parsing heterogeneity in aggression, given that several social behavioral domains are heritable[9] and disruptions in socioemotional development are strongly implicated in childhood aggression.[10]

Callous-unemotional (CU) behaviors comprise a heritable socioemotional trait domain associated with the development and persistence of aggression.[11,12] CU behaviors are characterized by low prosocial behavior, disregard for others' feelings and personal performance, and limited emotional responsiveness. These features have been quantified as a single, continuous construct as well as discrete underlying factors describing uncaring, callous, and unemotional behaviors.[13] CU behaviors, measurable by age 2 years,[14] are theorized to stem from disrupted socioemotional development of empathy and guilt as well as elevated temperamental fearlessness.[15] Family studies support moderate to high heritability of CU behaviors by early childhood,[11,16] a period of strong stability for CU behaviors, followed by increased variability in the level of stability later in childhood.[11] Heritable factors have been shown to influence stability in childhood and adolescence, with one school-age twin study discerning a greater role for shared environment in female participants with high CU behaviors.[17] Genetic influences on CU behaviors have also been shown to overlap with aggressive behaviors[18] and, similar to aggression, can be exacerbated with environmental stressors, including harsh parenting, peer exposure, and trauma.[19] Clinically, CU behaviors predict future oppositional defiant disorder and conduct disorder by age 3 years[20] and moderate the expression of aggression in the context of attention-deficit/hyperactivity disorder and oppositional defiant disorder.[21] The limited prosocial emotions specifier for conduct disorder in *DSM-5*[22] recognizes the increased severity of conduct problems in children with elevated CU behaviors, underscoring the impact of this social dimension on aggression.

Similar to CU behaviors, quantitative autistic traits (QATs), constitute another heritable,[23,24] early emerging aspect of social relatedness associated with aggression.[25–27] QATs represent a continuous range of deficits in reciprocal social behavior, the ability to engage in appropriate, socially and emotionally contingent interactions, which can be reliably measured in toddlers with and without autism spectrum disorder (ASD) by 18 months.[28] Extremes of these deficits align with core symptoms of ASD and entail social communication impairment (SCI) and restricted, repetitive behaviors and interests (RRBs).[29] QATs correlate with subsequent functional outcomes, including social competency in early childhood[27] and adaptive function from later childhood to adulthood.[30] Both ASD and population-level QATs are highly heritable[23,24,31] and stable from early childhood through adulthood.[32–34] ASD and QATs additionally share genetic influences[35,36] and demonstrate a male bias wherein the presence of higher average QATs in the male population[23] parallels the 4:1 male-to-female ratio in ASD.[37] Family studies testing sex differences in heritability of ASD and QATs have yielded mixed findings,[35] with some evidence of higher shared environmental influences in the female vs male population.[23] From early childhood onward, aggression is a frequent focus of clinical management in ASD, which can occur in 50% of clinically referred youth with ASD[38] and incurs negative impacts, including reduced access to schooling and services, increased risk of maltreatment, and the need for more restrictive environments.[39] Shared heritable influences may contribute to both aggression and QATs, as toddlers with an older biological sibling with ASD display increased aggressive behaviors compared with toddlers without a family history of ASD,[40] and a recent genome-wide association meta-analysis of childhood aggression revealed moderate genetic correlations with ASD.[41] Elevated QATs are also associated with increased aggressive behavior in several populations, including children with attention-deficit/hyperactivity disorder [26] and the general population.[27]

When elevated, both CU behaviors and QATs entail disturbances in social relatedness and prosocial behavior, yet their foundations and the mechanisms by which they promote aggression are hypothesized to differ. The CU domain exemplifies antisocial behaviors via a disregard for others' feelings, whereas QATs can manifest as asocial behavior due to diminished social awareness and capacity for reciprocal engagement.[42] Relatively few studies have evaluated dissociations between CU behaviors and QATs in relation to other behavioral domains. Growing literature on empathy has found that disturbances in emotional empathy, the ability to connect with others' feelings, occurs primarily with high CU behaviors, but not ASD, for which cognitive empathy, the ability to reason about others' feelings, is more affected.[43,44] Studies of children ranging from preschool age through school age, including a community sample[43] and a group with conduct problems,[44] have demonstrated that CU behaviors and QATs not only independently contribute to empathy, but also interact relative to empathy, whereby

stronger negative relations with emotional empathy occur at higher levels of CU behaviors and QATs. Relatedly, twin studies to date have additionally found predominantly independent genetic influences on CU behaviors and QATs.[45,46] These findings[42–46] collectively suggest that CU behaviors and QATs reflect distinct underpinnings and contribute independently to aspects of social engagement. In the case of aggression, unique contributions by these domains have not been explored. Novel work to characterize shared and unique influences on CU behaviors and QATs as well as their independent relations to aggression in early childhood could confer insight into the heterogeneity of aggression,[47] particularly considering the stability of these early-emerging domains[16,17,32,34] and their associations with later functional outcomes.[12,18,27,30]

To quantify unique vs shared contributions of CU behaviors and QATs to aggression, including as related to heritable influences, we applied a cross-sectional general population twin design in 3- to 4-year-olds and examined relations between underlying CU factors, QATs, and aggression. This young age range was selected due to expected growth in socioemotional abilities[15] and consolidation of ASD features,[24] along with availability of reliable, developmentally appropriate measures.[20,48,49] Via this dimensional approach, behavioral variation spanned the full developmental continuum, affording enhanced sensitivity to disaggregate behavioral contributions without being confounded by relations secondary to clinical diagnosis and impairment. As primary hypotheses, we predicted differing magnitudes of association between underlying CU factors, QATs, and aggression as well as unique contributions of CU factors and QATs to aggression. We secondarily anticipated that CU factors would show less shared heritable influence with aggression than highly heritable QATs. Lastly, we hypothesized that sex and CU factors would moderate relations between aggression and QATs, given some evidence for sex differences in etiologic influences on CU behaviors[17] and QATs,[23,35] and reported interactions of CU behaviors with QATs relative to empathy,[43,44] which similar to aggression impacts interpersonal behavior. By parsing overlapping and nonoverlapping contributions of these dimensions to aggression, we aimed to clarify the relative impact of these social domains and their heritable and environmental underpinnings on aggression, with implications for advancing assessment and individualized intervention.

METHOD

Participants

Participants consisted of twins and their parents enrolled at the Missouri site of the Early Reciprocal Social Behavior Study.[28] This longitudinal study investigated the development of social competency and QATs between ages 18 months and 4 years. Twins were epidemiologically ascertained from the Missouri general population through the Missouri Family Register, a database of birth records, between 2012 and 2015. Families were invited to participate via a mailing followed by a phone call. The consenting primary caregiver, a parent or legal guardian, was required to speak fluent English. Of 619 identified families, 204 were contacted, and 162 were enrolled. Cross-sectional data were included from 113 twin pairs with concurrent measures of CU behaviors, QATs, and aggression obtained at either 36-month or 48-month study time points. All procedures were approved by the Washington University School of Medicine Human Research Protection Office and the State of Missouri Department of Health and Senior Services Institutional Review Board.

Measures

Preschool Inventory of Callous-Unemotional Traits. The Preschool Inventory of Callous-Unemotional Traits (ICU), a parent-report questionnaire adapted from versions for older ages,[20] assesses features of CU traits, including low guilt and empathy, a lack of concern about performance, and deficient affect.[48] ICU items comprise subscales corresponding to uncaring, callous, and unemotional behaviors. These subscales have also been identified as latent factors in full-length and shortened ICU versions (Table S1, available online), both of which have shown good reliability, validity, and discriminatory properties.[13,20] In consultation with experts on child CU behaviors (MTW and WRM-K), 10 of 24 ICU items (Table 2) were selected across all subscales to capture sufficient variation for indexing individual differences and behavioral correlations while reducing participant burden. A new developmentally accessible item, "Child appears shameless," was included to enhance sensitivity by indexing the CU feature of lack of interpersonal regard apart from attributes of self-centeredness or low remorse, as covered in preexisting items. Items were rated on a scale of 0 to 3, representing responses ranging from "not true" to "definitely true." Higher scores indicated more CU behaviors and items querying prosocial behaviors were reverse-scored. Items displayed good internal consistency in our sample (Cronbach $\alpha = .77$).

Social Responsiveness Scale, Second Edition. The Social Responsiveness Scale, Second Edition (SRS-2) is a well-validated 65-item QAT scale that exhibits high internal consistency, test-retest reliability, temporal stability, and interrater reliability.[49] QATs on the SRS encompass both *DSM-5* core symptom domains of ASD, namely, social

communication deficits, indexed by the SCI subscale, and restricted repetitive interests and behaviors, indexed by the RRB subscale. Higher scores correspond to greater ASD traits. The SRS quantifies QATs in individuals with and without ASD across the general population and distinguishes individuals with ASD at a level 3 SDs above the general population mean. Age-appropriate parent-report versions[49] included the preschool SRS (used for ages 30-48 months) and school-age SRS (used ages $\geq$48 months). QAT scores displayed excellent internal consistency in the sample (Cronbach $\alpha = .93$), comparable to that obtained for the normative sample ($\alpha = .95$).[49]

Child Behavior Checklist. The Child Behavior Checklist (CBCL) is an established parent-report measure of behavior problems.[50] Preschool forms (ages 1.5-5 years) exhibit high test-retest reliability, interrater reliability, and temporal stability and differentiate between clinically referred children and controls with 84.2% accuracy. Items in the Aggressive Behavior subscale, the primary outcome measure, probe a range of aggressive behaviors, including physical, verbal, and relational aggression. CBCL aggression scores in the sample displayed excellent internal consistency ($\alpha = .90$), comparable to values from the normative sample ($\alpha = .92$).[50]

Goldsmith Child Zygosity Questionnaire. The Goldsmith Child Zygosity Questionnaire is a parent-report measure[51] that consists of 27 questions addressing the similarity of physical characteristics between twins. Its classification of monozygotic (MZ) vs dizygotic (DZ) twin pairs has shown greater than 93% agreement with DNA markers and blood type.[51] Genetic testing via DNA acquired by buccal swab in 24 randomly selected twin pairs from our study confirmed zygosity determination in all cases.

Analysis

Analyses were cross-sectional and used concurrent, most recently acquired data for either the 36- or 48-month time points. Data visualizations used raw scores for the ICU and CBCL aggression subscale and normed T scores for the SRS-2. Correlation coefficients were obtained as standardized β coefficients from generalized estimating equations (IBM SPSS version 28; IBM Corp., Armonk, New York). These linear models evaluated bivariate relations while accounting for nonindependence of twin data through a robust estimator of standard error based on an exchangeable correlation matrix. Criteria for small, medium, and large correlation coefficients were $r = 0.1$, $r = 0.3$, and $r = 0.5$, respectively. Intraclass correlations (ICCs) were compared between MZ twins, who share 100% of their DNA, and DZ twins, who share 50% of their DNA on average, where higher ICCs for MZ vs DZ twins are consistent with heritable influences. For within-twin within-trait correlations, ICCs were inputted into Falconer's formula [heritability = $2 (r_{MZ} - r_{DZ})$], where r denotes the correlation coefficient, to calculate heritability. For cross-twin cross-trait correlations, higher MZ vs DZ ICCs (ratio >1) are consistent with shared heritable influences.[45]

Exploratory factor analysis (EFA) (IBM SPSS version 28) was performed on the 11 CU items, as latent CU factors have frequently been identified in the literature.[13] An α factor analysis with quartimax rotation was applied to facilitate identification of minimally correlated and interpretable factors. Factor selection relied on the Kaiser criterion of eigenvalues >1 and interpretability. Factor loadings $\geq$0.3 were considered for factor membership. To confirm model fit, EFA was followed by a confirmatory factor analysis conducted in R Studio using lavaan.[52,53] To account for nonindependence of twin data, the confirmatory factor analysis incorporated multilevel structural equation modeling of the EFA-identified structure within twin pairs as level 1 and between twin pairs as level 2. Four conventional fit indices were implemented to evaluate convergence of model fit across multiple approaches. Per common guidelines, thresholds for acceptable fit were comparative fit index and Tucker-Lewis index $\geq$0.90 and for good fit were comparative fit index and Tucker-Lewis index $\geq$0.95, root mean square error of approximation $\leq$0.05, and standardized root mean square residual $\leq$0.08. For further details and references regarding fit indices and programs used for analysis, see methods section of Supplement 1, available online.

To evaluate unique contributions of QATs and CU factors (independent variables) to aggression (dependent variable), generalized estimating equations served as linear models accounting for nonindependence of twin data, as noted above. Scores for CU factors were generated from summed item composites. A hierarchical approach with incremental additions of independent variables allowed comparisons of unique contributions of variables across models. Potential sociodemographic covariates of maternal education level (coded as a categorical variable of yes/no bachelor's degree or above) and annual income categorically coded as terciles (low income: <$60,000; middle income: $\geq$$60,000 and <$120,000; high income: $\geq$$120,000) were tested for significant relations with aggression before inclusion in models. Sex was a categorical variable in all models, which also tested for moderation by sex and CU factors. Incremental fit indices included the quasi-likelihood under independence model criterion and corrected quasi-likelihood under independence model criterion, whose values were

TABLE 1 Participant Characteristics

Characteristic	Study population (N = 224)		
	n		
Twin pair zygosity			
MZ female	24		
MZ male	19		
DZ female	19		
DZ male	21		
DZ opposite sex	30		
	n	(%)	
Sex			
Female	115	(51.3)	
Male	109	(48.7)	
	Mean	(SD)	
Age, y	3.51	(0.46)	
	n	(%)	
Race			
American Indian or Alaska Native	0	(0.0)	
Asian	4	(1.8)	
Black or African American	27	(12.1)	
More than one race	16	(7.1)	
Other Pacific Islander	0	(0.0)	
White	177	(79.0)	
Ethnicity, Hispanic			
Yes	18	(8.0)	
No	206	(2.0)	
Maternal education			
High school graduate	12	(10.6)	
Some college education	11	(9.7)	
College degree (associate or bachelor)	62	(54.9)	
Graduate degree	22	(19.5)	
Not reported	6	(5.3)	
Annual income			
<$29,999	8	(7.1)	
$30,000-$59,999	23	(20.4)	
$60,000-$89,999	23	(20.4)	
$90,000-$119,999	24	(21.2)	
$120,000-$179,999	17	(15.0)	
>$180,000	12	(10.6)	
Not reported	6	(5.3)	
	Mean	(SD)	[range]
Behavioral scores			
Total CU behaviors	5.47	(3.92)	[0-19]
Social Responsiveness Scale-2 T scores	46.13	(7.46)	[35-92]
CBCL Aggression scores	5.99	(0.38)	[0-26]

Note: Scores on Social Responsiveness Scale index quantitative autistic traits. CBCL = Child Behavior Checklist; CU = callous-unemotional; DZ = dizygous; MZ = monozygous.

compared across interrelated models. Smaller values denoted greater fit.

RESULTS

Participant Characteristics

Using general population birth records in Missouri, 44 MZ and 67 DZ twin pairs were identified (Table 1). Similar proportions of same-sex male and female twin pairs and overall percentages of male and female participants were observed. Twins were 79.5% White, resembling the 81.2% White population in Missouri overall at the time of enrollment.[54] Median income of the sample, $60,000 to $90,000/year, was higher than the average $47,000/year for Missouri at that time.[54] Four children (1.8%) had a parent-reported community diagnosis of ASD, in line with the estimated ASD prevalence in the United States of 1.9% at the time of the study.[36]

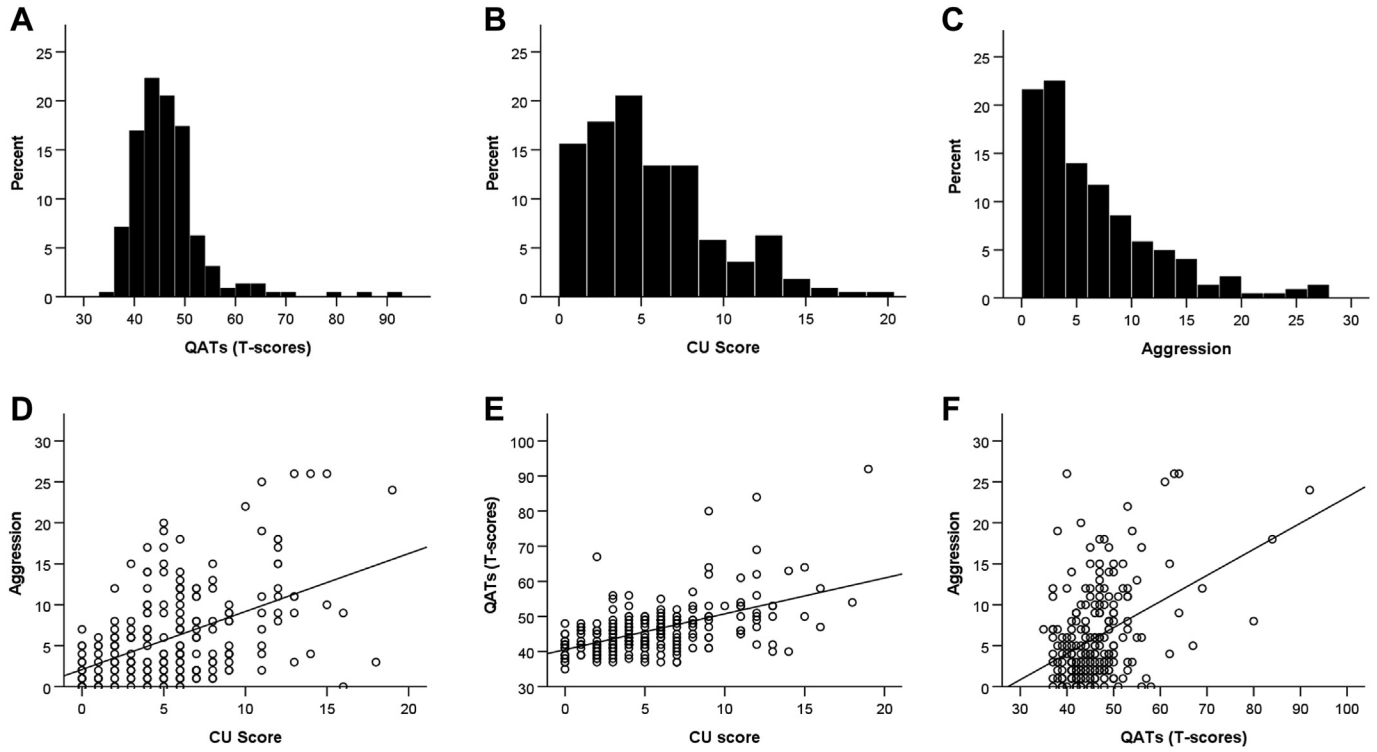
Correlations Between CU Behaviors, QATs, and Aggression

Score distributions for CU, QAT, and aggression scores all were unimodal and continuous (Figure 1A-C). There were no sex differences in CU behaviors ($p = .95$), QATs scored as sex-normed SRS-2 T scores ($p = .79$), or aggression ($p = .53$). All 3 domains were significantly correlated as well (Figure 1D-F). CU behaviors exhibited similarly high correlations with aggression ($r = 0.55$, 95% CI [0.39, 0.71], $p < .001$) and QATs ($r = 0.54$, 95% CI [0.34, 0.74], $p < .001$), whereas QATs moderately correlated with aggression ($r = 0.38$, 95% CI [0.26, 0.50], $p < .001$). Based on r^2, CU behaviors shared 29% variance with QATs and 30% variance with aggression, which shared nominally less variance, 13%, with QATs. Correlations across the 3 behaviors did not significantly differ in magnitude, however, as indicated by overlapping CIs.

Factor Analysis of CU Behaviors

To investigate whether CU subdomains vs total CU behaviors showed more differentiated relations with QATs and aggression, EFA was performed to characterize latent CU dimensions. Three factors with eigenvalues greater than 1 (range 1.1-3.5) were identified (Table 2), and Kaiser-Meyer-Olkin = 0.83, indicating good sample adequacy. Factor 1 accounted for 25.0% variance, factor 2 accounted for 7.6% variance, and factor 3 accounted for 5.1% variance, totaling 37.6% variance explained. A confirmatory factor analysis of the identified factor structure confirmed fit indices within the acceptable to good range (comparative fit index = 0.95, Tucker-Lewis index = 0.91, root mean

FIGURE 1 Histograms and Relationships for Behavioral Scores



Note: Distribution of (A) QATs T scores, (B) raw total CU scores, and (C) raw aggression scores in general population of 3- to 4-year-olds (N = 224 twins from 113 pairs). Scatter plot representations of the relations between (D) CU score and aggression, (E) CU scores and QATs, and (F) QATs scores and aggression for all available twins. Fit line is included for illustrative purposes and does not account for non-independence of twin data. CU = callous-unemotional behavior; QATs = quantitative autistic traits.

square error of approximation = 0.046, standardized root mean square error = 0.076).

Factor 1 items related to concern for others' feelings, concern about performance, and guilt, consistent with the uncaring factor identified in prior literature (Table S1, available online). Factor 2 items, which related to disregard for others' feelings, have previously been observed in a callous factor, while factor 3 items describing constraints on emotional expression corresponded to a previously described unemotional factor. Based on the interpretability of these factors and their convergence with the literature, they are referred to as uncaring (factor 1), callous (factor 2), and unemotional (factor 3) in the remainder of the article.

TABLE 2 Exploratory Factor Analysis of Items From Inventory of Callous-Unemotional Traits

	Loadings		
Selected items	**Factor 1: uncaring**	**Factor 2: callous**	**Factor 3: unemotional**
Tries not to hurt others' feelings	0.76	—	—
Concerned about others' feelings	0.72	—	—
Always tries his/her best	0.66	—	—
Does things to make others feel good	0.65	—	—
Feels bad/guilty when doing something wrong	0.60	—	—
Apologizes (says sorry to persons he/she have hurt)	0.58	—	—
Does not care whom he/she hurt to get wants	—	0.51	—
Seems shameless	—	0.43	—
No remorse after doing something wrong	—	0.42	—
Does not show emotions	—	—	0.53
Hides his/her feelings from others	—	—	0.31

TABLE 3 Twin Intraclass Correlations and Estimated Heritable Influences

		MZ values		DZ values		
Twin-twin correlations	**No. pairs (MZ, DZ)**	**ICC**	**95% CI**	**ICC**	**95% CI**	**H^2**
CU behaviors	111 (44, 67)	0.77	0.58, 0.88	0.70	0.52, 0.82	0.14
Uncaring	111 (44, 67)	0.81	0.65, 0.89	0.62	0.39, 0.77	0.38
Callous	111 (44, 67)	0.26	−0.36, 0.59	0.57	0.30, 0.74	N/A
Unemotional	111 (44, 67)	0.69	0.44, 0.83	0.25	−0.22, 0.54	0.69
QATs	111 (44, 67)	0.85	0.72, 0.92	0.31	−0.12, 0.58	0.85
Aggression	110 (44, 66)	0.85	0.72, 0.92	0.46	0.12, 0.67	0.79
		MZ values		**DZ values**		
Cross-twin cross-trait correlations	**No. pairs (MZ, DZ)**	**ICC**	**95% CI**	**ICC**	**95% CI**	**ICC MZ/DZ ratio**
CU behaviors–QATs	111 (44, 67)	0.63	0.44, 0.76	0.38	0.13, 0.56	1.7
Uncaring–QATs	111 (44, 67)	0.53	0.28, 0.69	0.34	0.08, 0.53	1.6
Unemotional–QATs	111 (44, 67)	0.60	0.38, 0.74	0.30	0.01, 0.50	2
CU behaviors–aggression	110 (44, 66)	0.36	0.02, 0.58	0.33	0.06, 0.52	1.1
Uncaring–aggression	110 (44, 66)	0.28	−0.10, 0.53	0.31	0.03, 0.51	0.9
Unemotional–aggression	110 (44, 66)	0.06	−0.11, 0.23	0.06	−0.15, 0.26	1
QATs–aggression	110 (44, 66)	0.56	0.33, 0.71	0.23	−0.08, 0.45	2.4

Note: *For H^2 estimates over 1, estimates were capped at MZ correlations. CU = callous-unemotional behaviors; DZ = dizygotic; H^2 = heritability; ICC = intraclass correlation coefficient; MZ = monozygotic; N/A = not applicable; QATs = quantitative autistic traits.*

Correlations for CU factors were not significant between uncaring and unemotional factors ($r = -0.03$, 95% CI [−0.15, 0.08], $p = .59$) or callous and unemotional factors ($r = 0.13$, 95% CI [−0.05, 0.32], $p = .16$). The uncaring and callous factors exhibited a moderate correlation ($r = 0.25$, 95% CI [0.12, 0.38], $p < .001$) commensurate with 6.3% shared variance (r^2). Overall, CU factors were largely independent, demonstrating distinct CU subdomains.

Heritable Influences for CU Factors, QATs, and Aggression

To determine whether differences in the relative contributions of heritable influences were present across behaviors, ICCs for all behaviors were compared between MZ and DZ twin pairs (Table 3), followed by an estimate of heritability. Total CU scores exhibited slightly higher correlations for MZ vs DZ twin pairs, resulting in an estimated heritability of 14%. Among CU factors, the unemotional factor displayed the highest heritability, 69%, followed by the uncaring factor, 38%. The callous factor showed higher DZ vs MZ correlations, suggesting no detectable heritable influences and predominantly environmental influences. This contrasted with the high heritability observed for QATs, 85%, and aggression, 79%.

Cross-twin cross-trait ICCs (Table 3) compared for MZ vs DZ twin pairs qualitatively supported shared heritable influences across behaviors when MZ correlations exceeded DZ correlations. These were evaluated for all behaviors except the callous factor, which was not heritable. CU behaviors showed strong evidence for overlapping genetic factors with QATs, especially the unemotional factor (MZ/DZ ratio = 2), which similar to QATs showed substantial heritability. Strong support was also observed for shared genetic factors of QATs and aggression (MZ/DZ ratio = 2.4).

Relations Between CU Factors, QATs, and Aggression

Correlations between individual CU factors, QATs, and aggression were next examined. CU factors showed significant correlations with QATs across a wide range, with a low correlation for the callous factor ($r = 0.16$, 95% CI [0.04, 0.27], $p = .008$), a moderate correlation for the unemotional factor ($r = 0.25$, 95% CI [0.06, 0.43], $p = .008$), and a high correlation for the uncaring factor ($r = 0.52$, 95% CI [0.29, 0.75], $p < .001$). The correlation between the callous factor and QAT was significantly lower than that for the uncaring factor, as illustrated by nonoverlapping CIs. QATs displayed low shared variance (r^2) with the callous factor, 2.6%, and the unemotional factor, 6.3%, but more substantial shared variance with the uncaring factor, 27%.

CU factors also showed varying relations with aggression. Correlations for the uncaring and callous factors were similarly moderate ($r = 0.45$, 95% CI [0.29, 0.60], $p < .001$, and $r = 0.40$, 95% CI [0.23, 0.57], $p < .001$), which corresponded to shared variance with aggression of 20.3% and 16%, respectively. The correlation for the unemotional factor was not significant ($r = 0.15$, 95% CI [−0.004, 0.30], $p = .06$).

Contributions of CU Factors and QATs to Aggression

Generalized estimating equation models next tested whether CU factors and QATs independently contributed to aggression (Table 4; Table S2, available online). Models including sex examined associations for CU factors and QATs separately and in combination. The unemotional factor and sociodemographic factors of income level and maternal education were not included in models, as these did not show significant relationships to aggression (income level: $ps \geq .12$; maternal education: $p = .75$; unemotional factor: $p = .06$). Incremental changes in variance (adjusted R^2) were compared across models to quantify unique contributions of CU factors and QATs to aggression.

Models 1a through 1c (Table 4) tested the uncaring and callous factors and QATs separately. These behaviors showed similar contributions to aggression: uncaring $R^2 =$ 16.6%; callous $R^2 = 17.3\%$; QATs $R^2 = 15.5\%$. Sex was not significant in these or any subsequent models.

Model 2 (Table 4) evaluated the uncaring and callous factors with QATs simultaneously. All 3 showed significant relations with aggression, accounting for 29.7% of the variance. Comparisons of the variance in this model with that for models featuring paired subsets of behaviors, eg, uncaring and callous factors together (Table S2, available online), indicated the uncaring factor accounted for 0.9% unique variance, the callous factor accounted for 8.5% unique variance, and QATs accounted for 5.1% unique variance (Figure S1, available online). By extension, 15.2% of the contribution to variance in aggression was shared between CU factors and/or QATs.

Model 3 tested for the presence of moderating influences by sex. Sex specifically moderated the callous factor and accounted for a 2.6% increase in variance for aggression. A stronger relation was observed between the callous factor and aggression in male participants (standardized $B =$ 0.55, 95% CI [0.35, 0.74], $p < .001$) compared with female participants (standardized $B = 0.24$, 95% CI [0.004, 0.47], $p = .047$), indicating that the same increase in callous behavior exhibited a greater impact on aggression in male than female participants. In contrast, CU factors did not significantly moderate effects of QATs (model 4). Model 3, which accounted for the greatest variance in aggression, 32.3%, also exhibited the lowest quasi-likelihood under independence model criterion and corrected quasi-likelihood under independence model criterion values, corresponding to best fit.

Because QATs have been found to represent both a singular dimension and underlying SCI and RRBs subdomains,[29] analogous hierarchical models separately explored contributions of SCI and RRBs to aggression (Table S3, available online). Similar to total QATs, both

TABLE 4 Models for Contributions of Callous-Unemotional Behavior (CU) Factors and Quantitative Autistic Traits (QATs) to Aggression

	Model 1a: uncaring		Model 1b: callous		Model 1c: QATs		Model 2: CU factors and QATs		Model 3: moderation by sex		Model 4: moderation by sex and CU factors	
Intercept	0.04	(−0.16, 0.24)	0.04	(−0.13, 0.22)	0.04	(−0.16, 0.24)	0.05	(−0.12, 0.22)	0.04	(−0.12, 0.21)	0.02	(−0.16, 0.19)
Sex	−0.08	(−0.30, 0.15)	−0.09	(−0.33, 0.15)	−0.08	(−0.32, 0.15)	−0.10	(−0.31, 0.11)	−0.09	(−0.30, 0.11)	−0.12	(−0.32, 0.09)
Uncaring	0.45	(0.29, 0.60)***	–		–		0.24	(0.06, 0.41)**	0.14	(−0.05, 0.34)	0.12	(−0.07, 0.32)
Callous	—		0.40	(0.23, 0.57)***	–		0.24	(0.16, 0.47)***	0.48	(0.31, 0.65)***	0.44	(0.26, 0.61)***
QATs	—		—		0.38	(0.26, 0.50)***	0.23	(0.09, 0.37)**	0.27	(0.12, 0.42)***	0.26	(0.11, 0.42)***
Sex × uncaring	—		—		—		—		0.12	(−0.18, 0.42)	0.16	(−0.13, 0.45)
Sex × callous	—		—		—		—		−0.33	(−0.56, −0.11)**	−0.28	(−0.51, −0.05)*
Sex × QATs	—		—		—		—		−0.03	(−0.31, 0.26)	−0.14	(−0.45, 0.17)
Uncaring × QATs	—		—		—		—		—		0.05	(−0.01, 0.10)
Callous × QATs	—		—		—		—		—		0.08	(−0.03, 0.19)
QIC	193.45		190.13		189.59		166.84		165.63		165.79	
QICC	191.13		187.14		188.72		162.54		160.79		162.38	
R^2	0.162		0.180		0.173		0.310		0.345		0.310	
Adjusted R^2	0.155		0.173		0.166		0.297		0.323		0.297	

Note: *Standardized β coefficients are reported. Values for parameters are displayed with 95% CIs in parentheses. QIC = quasi-likelihood under independence model criterion; QICC = corrected quasi-likelihood under independence model criterion.*
*p < .05; **p < .01; ***p < .001.

SCI and RRBs uniquely contributed to aggression relative to CU factors. RRBs accounted for greater unique variance, 11.7%, compared with SCI, 3.2% (Table S3, available online). There were no significant effects for moderation by sex or CU factors for either SCI or RRBs.

DISCUSSION

Using a cross-sectional dimensional approach, we evaluated the extent to which CU behaviors and QATs show independent contributions to aggression at age 3 to 4 years, a foundational stage for later outcomes. To our knowledge, this study is the first to evaluate independence of CU behaviors and QATs, including their heritable and environmental influences, in early childhood. Together, the identified CU factors and QATs accounted for 29.7% of the variance in aggression, nearly evenly divided between unique and shared variance (Figure S1, available online). In early childhood, CU behaviors and QATs thus comprise distinct aspects of social relatedness that each substantially contribute to aggression. The stability of aggression and these trait domains as well as long-term risks of sustained aggression reinforce the importance of evaluating and managing both CU behaviors and ASD traits in young children with impairing aggressive behavior.

As hypothesized, extracted CU factors, which corresponded to prior literature[13] (Table S1, available online), displayed distinct associations with QATs and aggression. The callous factor, the largest contributor of unique variance to aggression (8.5%), exhibited no genetic influences. Its minimal correlation with QATs aligned with our hypothesis that CU behaviors, compared with QATs, would share lower genetic influences and, conversely, more environmental influences with aggression. Of note, this absence of heritable influence for the callous factor contrasts with heritability of the uncaring and unemotional factors in the sample and CU behaviors in the literature.[16,19,55] While such variance may be partly attributable to different ages or methodological issues, it nonetheless supports that robust characterization of the genetic architecture of CU behaviors warrants incorporation of individual CU factors. The callous factor was also the only factor moderated by sex in relation to aggression. This novel finding contrasts with moderation by sex of only the uncaring factor in a recent study of aggression in Nigerian adolescents.[56] Although incipient work in this area has not converged on consistent findings, these observations support a role for clarifying sex moderation of CU factors to inform relations to outcomes.

Uncaring and unemotional factors, similar to aggression, displayed genetic influences, but their associations with aggression were minimal compared with the callous factor. Only 0.9% variance was uniquely explained by the uncaring factor, and none was explained by the unemotional factor. The descending order of associations with aggression—callous > uncaring > unemotional—accords with a meta-analysis[57] delineating the same profile of CU factor relations with externalizing behavior. This profile also dovetails with divergence of the unemotional factor, which also showed the lowest correlations with other CU factors and much higher heritability. Similar dissociations have previously been observed at older ages[55,57]; thus, results here substantiate the distinction of this factor by early childhood and the possibility that variation in the unemotional factor represents more separate etiological influences compared with other CU factors.

QATs, which appear to share genetic factors with aggression,[40,41] displayed substantial overlapping heritable influences with aggression and contributed 5.1% unique variance. Contrary to prior studies of empathy,[43,44] there was no evidence of interactions between CU factors and QATs, implying that moderating effects may occur in specific developmental and functional contexts. Overall, disparate associations for CU factors and QATs are in keeping with the recognized multifactorial etiology of aggression and potential mechanisms of heterogeneity.[47] Further, they confirm that by early childhood, CU behaviors, anchored by fundamental disregard for others, show measurable distinctions from the impaired social awareness that is a hallmark of QATs.

Within QATs, both SCI and RRBs domains displayed unique contributions to aggression, which were greater for RRBs than SCI (11.8% vs 3.4%). RRBs could proximally trigger aggression, for example, through reactivity in the context of interference with RRBs or indirectly as a function of cognitive or self-regulatory capacities affected in RRBs, as both aggression and RRBs have been linked to reduced executive function.[58] Additionally, rigidity, low tolerance of change, and sensory sensitivities encompassed by RRBs may prompt emotional dysregulation and subsequent aggression.[59] Given these associations as well as the relatively high unique contribution for RRBs, one future direction involves investigating whether variation in RRBs is more related to impulsive, reactive aggression than CU factors, which have been more closely linked to premeditated aggression.[12] Further, management options for RRBs in children with ASD and aggression, such as applied behavioral analysis, may ameliorate tendencies toward aggression and warrant further investigation, as this evidence base is less well developed than that for SCI.[60]

Independent contributions of CU behaviors and QATs to aggression further highlight the importance of multidimensional, trait-based assessment in early

childhood. More comprehensive clinical assessment of these behaviors at younger ages could refine diagnostic formulations and guide personalized interventions that leverage early neuroplasticity to foster cumulative socio-emotional learning and optimized trajectories. For example, patients with relative elevations of callous behaviors, a CU factor predominantly influenced by environmental variation, could be more readily directed to family-focused interventions that address psychosocial factors such as harsh parental affect or maltreatment, with monitoring of treatment responses in male and female patients given observed moderation of callous behaviors by sex. For patients with elevated QATs and aggression, social skills training could minimize situational communication breakdowns that instigate aggression.

Finally, instances of shared variance across CU factors and QATs imply potentially intersecting developmental pathways that could also inform clinical care. Moderate correlations between QATs and the unemotional factor, with evidence for shared genetic influences, align with reduced emotional responsiveness observed for high CU behaviors and ASD[42] and suggest a common treatment target to enhance overall adaptive function. Strong correlations and shared heritable influences for QATs and the uncaring factor, which encompasses diminished prosocial tendencies to help others or make others feel good, could also reflect QAT-related reductions in social interest and/or competency. Additional evaluation of QATs could therefore elicit complementary information on social deficits that may be amenable to skill-based interventions as part of comprehensive treatment for aggression.

Study strengths include the dimensional twin study design incorporating CU subdomains, rather than total CU behaviors, to enhance sensitivity for differentiating overlapping and nonoverlapping genetic influences and interrelationships across CU behaviors, QATs, and aggression. The relatively small sample size, however, precluded formal modeling of genetic, shared environmental, and nonshared environmental effects or evaluation of these effects across sex. The parent-report metrics, although clinically informative and feasible, posed greater subjectivity than direct assessment, and the application of a subset of ICU items constrained detectable variation and interpretability of CU factors. Larger, longitudinal studies with the full ICU are warranted to test for replication of CU factors and their interrelations as well as extend our cross-sectional findings to elucidate contributions of CU subdomains and QATs to the emergence and course of aggression. Nevertheless, several findings, including the CU factor structure,[13] corroborated prior literature, supporting the validity of our initial findings. Lastly, the general population sample, while reflecting the predominantly White population of Missouri, had limited representation of other racial and ethnic groups as well as a slightly elevated median income. Inclusion of diverse and underrepresented groups is needed to investigate both generalizability of findings across groups at varying risk and to identify potential high-yield environmental targets for intervention within specific populations.

In conclusion, this study demonstrates that although CU behaviors and QATs both involve restricted prosocial behavior, distinct profiles of genetic and environmental influences and contributions to aggression highlight separate roles in susceptibility to psychopathology. These findings signal important clinical opportunities for earlier, better specified risk assessment and treatment planning as well as translational opportunities to investigate genetic factors underlying these heritable behaviors, which could inform novel biological treatments. By addressing unique and shared associations of these social domains with aggression, clinicians can enhance individualized mental health care and long-term outcomes.

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Mss. Lineback, Baer, and Zhang, Mr. Hartenbach, and Drs. Glowinski, Constantino, and Marrus are with Washington University School of Medicine in St. Louis, Missouri. Dr. Mills-Koonce is with the University of North Carolina at Chapel Hill, North Carolina. Dr. Willoughby is with RTI International, Raleigh, North Carolina. Dr. Glowinski is with the University of California San Francisco, California. Dr. Constantino is with Emory University School of Medicine, Atlanta, Georgia.

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Author Contributions
Conceptualization: Lineback, Hartenbach, Mills-Koonce, Willoughby, Glowinski, Constantino, Marrus
Data curation: Zhang, Constantino, Marrus
Formal analysis: Lineback, Marrus
Funding acquisition: Constantino, Marrus
Investigation: Lineback, Baer, Constantino, Marrus
Methodology: Lineback, Baer, Zhang, Mills-Koonce, Willoughby, Constantino, Marrus
Project administration: Constantino
Resources: Constantino
Software: Zhang
Supervision: Lineback, Glowinski, Constantino, Marrus
Validation: Zhang, Willoughby, Constantino, Marrus
Visualization: Lineback, Baer, Marrus
Writing — original draft: Lineback, Baer, Hartenbach, Constantino, Marrus
Writing — review and editing: Lineback, Baer, Zhang, Hartenbach, Mills-Koonce, Willoughby, Glowinski, Constantino, Marrus

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Correspondence to Natasha Marrus, MD, PhD, Division of Child and Adolescent Psychiatry, Department of Psychiatry, Washington University School of Medicine, 660 South Euclid Avenue, Box 8504, St. Louis, MO 63110; e-mail: natasha@wustl.edu

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