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Youth with elevated psychopathic traits exhibit structural integrity deficits in the uncinate fasciculus

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ABSTRACT

Youth with elevated psychopathic traits represent a particularly severe subgroup of adolescents characterized by extreme behavioral problems and exhibit comparable neurocognitive deficits as adult offenders with psychopathic traits. A consistent finding among adults with elevated psychopathic traits is reduced white matter structural integrity of the right uncinate fasciculus (UF). The UF is a major white matter tract that connects regions of the anterior temporal lobe (i.e., the amygdala) to higher-order executive control regions, including the ventromedial prefrontal cortex. However, the relationship between youth psychopathic traits and structural integrity of the UF has been mixed, with some studies identifying a negative relationship between adolescent psychopathy scores and FA in the UF, and others identifying a positive relationship. Here, we investigated structural integrity of the left and right UF using fractional anisotropy (FA) in a large sample of $n = 254$ male adolescent offenders recruited from maximum-security juvenile correctional facilities. Psychopathic traits were assessed using the Hare Psychopathy Checklist: Youth Version (PCL:YV). Consistent with hypotheses, interpersonal and affective traits (i.e., PCL:YV Factor 1 and Facet 1 scores) were associated with reduced FA in the right UF. Additionally, lifestyle traits (i.e., PCL:YV Facet 3 scores) were associated with increased FA in the left UF. Results are consistent with previously published studies reporting reduced FA in the right UF in adult psychopathic offenders and increased left UF FA in youth meeting criteria for certain externalizing disorders.

Psychopathy is a serious personality disorder associated with interpersonal, affective, and behavioral dysfunction (Hare, 2003). Psychopaths are habitually described by their overall absence of moral emotions and a lifestyle characterized by heightened impulsivity and irresponsible behavior. This antisocial lifestyle severely increases the likelihood of a number of poor outcomes for psychopaths, including an increased risk of future recidivism (Hemphill et al., 1998). Indeed, psychopaths are four times more likely to recidivate in the twelve months following institutional release compared to non-psychopathic offenders (Rice and Harris, 1997). While only 0.5 –1% of the general population meets the established diagnostic criteria for psychopathy, the base rate increases tremendously in incarcerated settings, whereby 15 –25% of incarcerated offenders meet the criteria for psychopathy (Hare, 2003). Though comprising a minority of the general population, psychopaths are responsible for a disproportionate amount of total criminal offenses, yielding an estimated financial burden of $450 billion annually in the United States (Kiehl and Hoffman, 2011). Due to the aforementioned toll that psychopaths place on society, researchers have attempted to delineate the adolescent manifestation of this condition, as personality traits are still in nascent stages of development. In addition, intervention efforts targeted towards youth may have a better chance of altering life-course persistent antisocial behavior if started early in development (M. F. Caldwell, 2011; M. F. Caldwell et al., 2007).

Many functional magnetic resonance imaging (fMRI) studies have been performed associating affective and emotional dysfunction in youth with elevated psychopathic traits, primarily focusing on the amygdala. For example, youth with elevated psychopathic traits have exhibited reduced hemodynamic activity in the amygdala during the processing of fearful face stimuli (Jones et al., 2009; Lozier et al., 2014; Marsh and Blair, 2008; Viding et al., 2012; White et al., 2012), unpleasant pictures (Harenski et al., 2014), when viewing others in pain (Marsh et al., 2013), and during affective theory of mind processing (Sebastian et al., 2012). In addition, youth with elevated psychopathic traits have exhibited reduced gray matter volume and concentration in the amygdala (Aghajani et al., 2016; Caldwell et al., 2019; Cohn et al.,

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2016; Walters and Kiehl, 2015). The amygdala is a structure within the anterior temporal lobe that is involved in coding the affective significance of stimuli, with information processed by the amygdala typically fed forward to the ventromedial prefrontal cortex (vmPFC) to help guide decision-making (Cardinal et al., 2002). Supporting the notion of altered connectivity between the amygdala and vmPFC, youth with elevated psychopathic traits exhibit reduced seed-based functional connectivity between the amygdala and vmPFC (Aghajani et al., 2016; Marsh et al., 2008).

Seed-based functional connectivity studies suggest that white matter (WM) tracts that connect anterior temporal regions to prefrontal regions may be implicated in youth with elevated psychopathic traits, including the uncinate fasciculus (UF). The UF is the direct axonal pathway that connects the amygdala to the vmPFC (Johansen-Berg et al., 2008; Petrides and Pandya, 2007). Reduced fractional anisotropy (FA), a measure of WM structural integrity, in the UF has shown to play a critical role in emotional empathy deficits (Oishi et al., 2015). In addition, a consistent finding among adults with elevated psychopathic traits is reduced FA in the right UF (Craig et al., 2009; Hoppenbrouwers et al., 2013; Lindner et al., 2017; Motzkin et al., 2011; Sobhani et al., 2015; Sundram et al., 2012; Vermeij et al., 2018; Wolf et al., 2015). The relationship between psychopathic traits and structural integrity of the left UF is mixed, with some studies observing reduced FA of the left UF in adults scoring high on measures of psychopathy (Craig et al., 2009; Hoppenbrouwers et al., 2013; Lindner et al., 2017), whereas other studies have not found significant relationships between psychopathic traits and left UF FA (Sobhani et al., 2015; Sundram et al., 2012; Vermeij et al., 2018; Wolf et al., 2015).

Inconsistent results have similarly been obtained between studies investigating the relationship between UF FA and youth with elevated psychopathic traits. For example, one study found that youth with elevated psychopathic traits exhibited reduced FA in the right UF (Breeden et al., 2015); however, two other studies have associated higher youth psychopathy scores with increased FA in the right UF (Pape et al., 2015; Passamonti et al., 2012). Similarly, mixed results have been obtained regarding the relationship between youth psychopathy scores and FA in the left UF. Specifically, while one study has observed a negative relationship between youth psychopathy scores and left UF FA (Breeden et al., 2015), other studies have observed a positive relationship between youth psychopathy scores and left UF FA (Pape et al., 2015; Passamonti et al., 2012; Sarkar et al., 2013). Increased FA within the left and right UF in youth with elevated psychopathic traits is consistent with previous studies performed with youth meeting criteria for certain externalizing disorders, including Conduct Disorder (CD) (Passamonti et al., 2012; Sarkar et al., 2013; Zhang et al., 2014). However, it should be noted that other externalizing disorders, including attention-deficit/hyperactivity disorder (ADHD), have been associated with reduced FA in the UF (Konrad and Eickhoff, 2010; Shaw et al., 2014).

Here, we sought to expand upon previous research by investigating the relationship between youth psychopathic traits assessed via the Hare Psychopathy Checklist: Youth Version (PCL:YV) (Forth et al., 2003) and the structural integrity of both the left and right UF via FA in a high-risk sample of $n = 254$ incarcerated male adolescent offenders. We specifically hypothesized that a significant negative relationship would emerge between PCL:YV scores and FA in the right UF, consistent with previously published studies in both youth (Breeden et al., 2015) and adults scoring high on psychopathic traits (Craig et al., 2009; Hoppenbrouwers et al., 2013; Lindner et al., 2017; Motzkin et al., 2011; Sobhani et al., 2015; Sundram et al., 2012; Vermeij et al., 2018; Wolf et al., 2015). Furthermore, we hypothesized that FA in the left UF would be significantly positively related to youth psychopathic traits reflecting general externalizing psychopathology, including impulsivity and stimulation seeking, consistent with previously published reports associating increased FA in the left UF with youth meeting criteria for certain externalizing disorders, including CD (Passamonti et al., 2012; Sarkar et al., 2013; Zhang et al., 2014).

1. Method

1.1. Participants

Participants included $n = 296$ incarcerated male adolescent offenders recruited from juvenile correctional facilities in the states of New Mexico and Wisconsin. Participants were excluded from analyses for meeting the following criteria: occurrence of a traumatic brain injury (TBI) accompanied with a significant loss of consciousness ($n = 17$), as TBIs play a significant role in WM structural integrity (Yuan et al., 2007), or an estimated IQ score less than 70 ($n = 11$). Additionally, participants were excluded for meeting diagnostic criteria for psychosis ($n = 5$) and significant outliers regarding FA values ($n = 9$). This resulted in a final sample of $n = 254$ incarcerated male adolescent offenders, ranging from 14 to 18 years of age ($M = 17.04$ years, $SD = 1.08$ years) at the time of MRI data collection. The sample was predominantly right-handed, with 10% reporting left-hand dominance. Participants largely self-identified as Hispanic/Latino (48%), with the remaining identifying as Black or African American (29%), White (16%), American Indian or Alaskan Native (5%) or Native Hawaiian or other Pacific Islander (1%). One percent of the sample chose not to disclose their race or ethnicity.

Initial contact was made by research staff with potential study participants and informed consent was obtained. Individuals provided written informed assent in conjunction with parent/guardian consent. Participants were informed of their right to terminate participation at any point, the lack of institutional benefits, and that their participation would not affect their facility or parole status. Participants received remuneration at the hourly labor wage of the facility. All research protocols were approved by the Ethical and Independent Review Services (E&I), the Office for Human Research Protections (OHRP), and the juvenile correctional facilities where data collection occurred.

1.2. Assessments

Psychopathic traits were assessed using the Hare PCL:YV (Forth et al., 2003), an interview-based assessment measuring interpersonal, affective, lifestyle, and developmental/antisocial traits related to the adolescent manifestation of psychopathy. Each of the twenty items on the PCL:YV is scored based on the following criteria: a score of *zero* reflects the item does not apply to the individual, a score of *one* implies the item applies somewhat to the individual, and a score of *two* means that the item definitely applies to the individual. PCL:YV total scores can range from 0 to 40. The mean PCL:YV total score in the current sample was 24.71 ($SD = 6.20$), with total scores ranging from 2 to 38. The Cronbach's alpha for the PCL:YV (all items) was 0.80, reflecting good internal consistency. In addition to PCL:YV total scores, we incorporated the use of a two-factor model of psychopathic traits, with Factor 1 comprising interpersonal and affective traits and Factor 2 consisting of lifestyle and antisocial/developmental traits (Neumann et al., 2006). The mean PCL:YV Factor 1 score was 8.01 ($SD = 3.32$) and the mean Factor 2 score was 15.13 ($SD = 2.81$) in the current report. PCL:YV Factor 1 and 2 scores were significantly positively correlated ($r = 0.52$, $p < .001$), consistent with previous reports (Mailloux et al., 1997). We also examined a four-facet model of psychopathic traits, with four latent facets representing the underlying dimensions of the adolescent expression of psychopathy: interpersonal (Facet 1), affective (Facet 2), lifestyle (Facet 3), and antisocial/developmental (Facet 4), respectively (Neumann et al., 2006). We investigated both factor and facet scores of the PCL:YV to reveal more specific directional and stable effects than those with PCL:YV total scores alone. For example, factor and facet scores of the PCL-R are associated with dimensional traits that have often revealed discrete

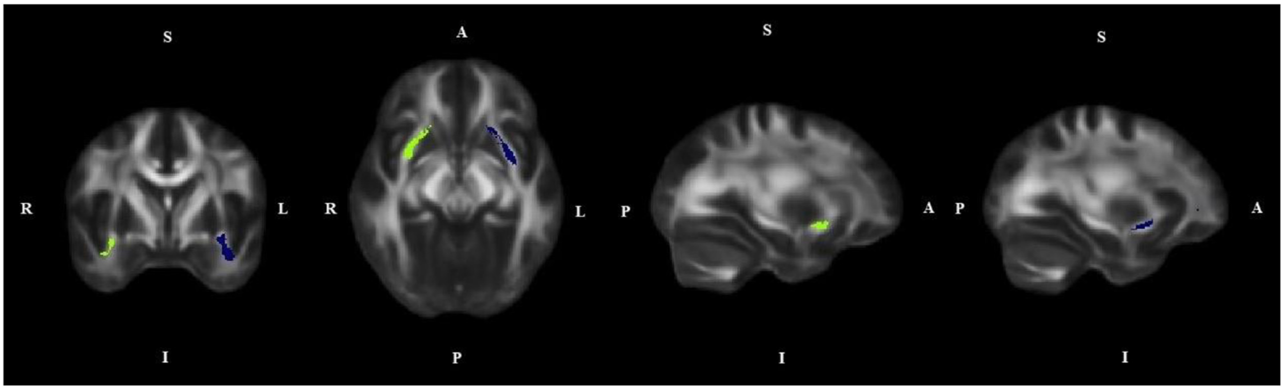

Fig. 1. Anatomical location of the left and right uncinate fasciculus, defined as per the JHU atlas, is displayed on the JHU template. The left uncinate fasciculus is outlined in the color blue and the right uncinate fasciculus is outlined in the color green. R = right; L = left; A = anterior; S = superior; I = inferior; P = posterior.

(sometimes opposing) relationships with neurobiological measures (Anderson et al., 2015; Juárez et al., 2013; Maurer et al., 2016; Philippi et al., 2015; Steele et al., 2016). In addition, a negative relationship between PCL-R Factor 1 and Facet 1 scores and FA in the right UF has been observed in previously published reports in adult psychopathic offenders (Lindner et al., 2017; Vermeij et al., 2018; Wolf et al., 2015).

1.3. Additional assessments

In addition to investigating psychopathic traits, additional assessments were administered to assess IQ, substance dependence, psychopathology, and TBI. Full-scale IQ was estimated using the Wechsler Adult Intelligence Scale – 3rd Edition (WAIS-III) (Wechsler, 1997) for participants sixteen years of age or older and from the Wechsler Intelligence Scale for Children – 4th Edition (WISC-IV) (Wechsler, 2003) for participants younger than sixteen years of age (M = 90.78, SD = 10.83). Psychopathology, including measures of CD, Oppositional Defiant Disorder (ODD), ADHD, and substance dependence were assessed using the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (Kaufman et al., 1997). Number of substance dependencies were calculated by summing the total number of substances (both alcohol and drug, including cannabis, stimulants, sedatives/hypnotics/anxiolytics, cocaine, opioids, phencyclidine [PCP], hallucinogens, solvent/inhalants, and other substances) for which participants met lifetime dependence diagnoses (M = 1.68, SD = 1.60). Additionally, history of TBI was evaluated using a post-head injury symptoms questionnaire (King et al., 1995).

1.4. MRI data acquisition

Diffusion-weighted echo-planar MRI was acquired at the juvenile correctional facilities where data collection occurred using the Mind Research Network's Siemens 1.5T Avanto Mobile MRI System equipped with a 12-element head coil. Diffusion sensitizing gradients were applied along 30 non-collinear directions ($b$value = 800 s/mm^2). Five interleaved non-diffusion weighted (b value = 0 s/mm^2) volumes were collected during each run to enable corrections for motion and eddy current distortions. Images were collected with the following parameters: repetition time (TR) = 9200 ms, echo time (TE) = 84 ms, field of view = 256 × 256 mm, matrix size = 128 × 128, slice thickness = 2 mm, no gap, voxel size = 2 × 2 × 2 mm^3, 70 slices. The sequence was repeated twice, and the data were combined to improve the signal-to-noise ratio. Head motion was limited using padding and restraint.

1.5. DTI analyses

DTI data was collected across two experimental runs and concatenated into one 4D NIFTI file. Concatenated tables of b-values and gradient directions from two runs were created using the dcm2nii program (https://people.cas.sc.edu/rorden/mricron/dcm2nii.html). The quality of diffusion-weighted images were checked for 1) striated artifacts caused by subject motion related to signal dropout, 2) external radio-frequency leakage in the MRI room or subject motion related to excessive background noise in the phase-encoding direction, and 3) large motion in the absence of signal dropout (Caprihan et al., 2011, 2015). If any slice had a problem for a given gradient direction, we excluded the entire volume, instead of the specific slice. We excluded less than 10% of gradient directions using the above-mentioned pruning procedure. Eddy current and motion-induced distortions of diffusion-weighted images were performed. The b = 800 s/mm^2 images were registered to b = 0 s/mm^2 images with a mutual information cost function. The rotated part of the transformation was then extracted and each gradient direction vector was rotated (Leemans and Jones, 2009). Using the FMRIB's Diffusion Toolbox (FDT) in FMRIB Software Library (FSL) version 4.1 (www.fmrib.ox.ac.uk/fsl/), we performed brain extraction from the b0 image to remove non-brain tissue, correction of eddy current-induced possible distortions of diffusion-weighted images, and construction of FA maps. Tract Based Spatial Statistics (TBSS) workflow (Smith et al., 2006) of FSL was used to non-linearly warp the individual FA maps to the 1.0 × 1.0 × 1.0 mm^3 FA template in the MNI space. To minimize the partial volume effect, non-linearly warped FA images were averaged to construct the WM skeleton image. Subsequently, ROI averaged values were extracted from each participant from the intersection of the skeleton image and the Johns Hopkins University (JHU) WM atlas ROIs (Mori et al., 2005). The ROIs investigated from the JHU atlas in the current report included the left and right UF (see Fig. 1). Exploratory analyses investigated the relationship between PCL:YV facet scores and FA in the other remaining ROIs obtained from the JHU atlas, including the anterior thalamic radiation, corticospinal tract, cingulum, forceps major, forceps minor, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, and superior longitudinal fasciculus. At the request of reviewers, exploratory analyses were conducted on the relationship between PCL:YV Facet scores and additional measures of white matter structural integrity, including mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) (see supplementary material for full statistics).

2. Results

2.1. Correlational results

Number of substance dependencies were significantly positively

Table 1
Correlations between PCL:YV scores and Covariate measures.

	PCL:YV Total	PCL:YV F1	PCL:YV F2	PCL:YV Facet 1	PCL:YV Facet 2	PCL:YV Facet 3	PCL:YV Facet 4	Sub Use	IQ	Avg. FA
PCL:YV Total	___									
PCL:YV F1	.881**	___								
PCL:YV F2	.833**	.516**	___							
PCL:YV Facet 1	.722**	.858**	.377**	___						
PCL:YV Facet 2	.766**	.828**	.498**	.421**	___					
PCL:YV Facet 3	.726**	.459**	.861**	.375**	.401**	___				
PCL:YV Facet 4	.638**	.384**	.777**	.233**	.423**	.349**	___			
Num. Sub. Dep.	.040	−.074	.140*	.000	−.130*	.117	.115	___		
IQ	−.095	−.063	−.129*	.024	−.136*	−.137*	−.068	.297**	___	
Avg. FA	.040	.091	−.020	.115	.034	.004	−.042	−.005	.086	__

Note. Assessments: PCL:YV F1 and F2 are the factor scores derived from the PCL:YV (Forth et al., 2003); Num. Sub. Dep. refers to the number of substance dependencies obtained from the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (Kaufman et al., 1997); Avg. FA refers to the TBSS-skeleton average FA value.

** $p < .001$,.

* $p < .05$.

correlated with PCL:YV Factor 2 scores ($r = 0.14$, $p = .026$) and significantly negatively correlated with PCL:YV Facet 2 scores ($r = -0.13$, $p = .039$). IQ scores were significantly negatively correlated with PCL:YV Factor 2 scores ($r = -0.13$, $p = .040$), Facet 2 scores ($r = -0.14$, $p = .030$), and Facet 3 scores ($r = -0.14$, $p = .029$). IQ scores were significantly positively correlated with number of substance dependencies ($r = 0.30$, $p < .001$). PCL:YV scores and covariate measures were not significantly correlated with TBSS-skeleton average FA values (see Table 1 for the remainder of correlations between PCL:YV scores and covariate measures).

2.2. Multiple regression analyses

2.2.1. Right UF multiple regression analyses

A first set of multiple regression analyses were performed to test the hypothesis that reduced FA of the right UF would be predicted by PCL:YV total, factor, and facet scores using our entire sample of $n = 254$ incarcerated male adolescent offenders. Each of the multiple regression analyses performed had FA values from the right UF as the dependent measure, and either PCL:YV total, factor, or facet scores and three covariate measures (i.e., IQ scores, number of substance dependencies, and TBSS-skeleton average FA) as simultaneous predictor variables in separate analyses performed. IQ scores were included as a covariate measure, as higher FA in the right UF has been associated with higher intelligence (Yu et al., 2008). We investigated substance use severity as a covariate, to ensure that results were strictly driven by adolescent psychopathic traits, and not comorbid substance use. Finally, we investigated TBSS-skeleton average FA as a covariate to ensure that results were specifically related to structural integrity of the right UF, controlling for FA maturation throughout the entire brain. The UF is one of the last WM tracts to reach its maturational peak (Giorgio et al., 2010; Lebel et al., 2008), and individual participants might have prototypical maturation associated with other WM tracts beyond the right UF, as FA in these regions peaks earlier in life (Beaulieu, 2002).

Additional exploratory multiple regression analyses were performed, in which we added group membership for CD/ODD or ADHD as predictor variables, to investigate whether these conditions were significant predictors of increased or reduced FA in the left and right UF in the current report, consistent with previously published studies identifying increased FA in the UF in CD (Passamonti et al., 2012; Sarkar et al., 2013; Zhang et al., 2014) and reduced FA in the UF in ADHD (Konrad and Eickhoff, 2010; Shaw et al., 2014) (see supplementary materials for full statistics).

In sum, three separate multiple regression analyses were performed testing our *a priori* hypotheses, with right UF FA entered as the dependent measure. We implemented a Simes–Hochberg multiple comparison correction procedure to all multiple regression analyses performed (Hochberg, 1988; Simes, 1986) to maintain the family wise error rate at an acceptable level. This correction is in the class of sequential Bonferroni correction methods, which consists of arranging the obtained *p*-values within a family of tests from largest to smallest and excluding tests on a sequential basis on whether they are associated with a *p*-value that is less than a previously adjusted alpha level. All significant results reflect this correction.

In the first multiple regression analysis performed, PCL:YV Facet scores (i.e., PCL:YV Facet 1, 2, 3, and 4 scores) were entered along with covariate measures (i.e., IQ scores, number of substance dependencies, and TBSS-skeleton average FA) to see if any variables entered into analyses were significant predictors of FA within the right UF. The second multiple regression analysis was identical to Regression 1, but PCL:YV Facet scores were replaced with PCL:YV Factor 1 and 2 scores. Finally, in the third multiple regression analysis performed, PCL:YV Factor 1 and 2 scores were replaced by PCL:YV total score.

In Regression 1, PCL:YV Facet 1 scores emerged as a significant predictor of reduced FA in the right UF ($\beta = -0.10$, $p = .040$). In addition, two variables emerged as significant predictors of increased FA in the right UF: number of substance dependencies ($\beta = 0.11$, $p = .020$) and TBSS-skeleton average FA ($\beta = 0.71$, $p < .001$) (Simes-Hochberg corrected *p*-value of 0.05) (see Table 2).

In Regression 2, PCL:YV Factor 1 scores emerged as a significant predictor of reduced FA within the right UF ($\beta = -0.13$, $p = .012$). In addition, two variables emerged as significant predictors of increased FA in the right UF: number of substance dependencies ($\beta = 0.11$, $p = .022$) and TBSS-skeleton average FA ($\beta = 0.71$, $p < .001$) (Simes–Hochberg corrected *p*-value of 0.025) (see Table 2).

In Regression 3, PCL:YV total scores were not a significant predictor of reduced FA within the right UF ($\beta = -0.05$, $p = .287$). In Regression 3, two variables emerged as significant predictors of increased FA in the right UF: number of substance dependencies ($\beta = 0.14$, $p = .003$) and TBSS-skeleton average FA ($\beta = 0.90$, $p < .001$) (Simes-Hochberg corrected *p*-value of 0.0125) (see Table 2).

2.3. Left UF multiple regression analyses

A second set of multiple regression analyses were performed, nearly identical to those reported above, with the dependent variable changed to FA values in the left UF instead of the right UF to test additional *a priori* hypotheses. In Regression 1, PCL:YV Facet 3 scores were a significant predictor of increased FA within the left UF ($\beta = \; = 0.09$, $p = \; = .034$). Additionally, TBSS-skeleton average FA was a significant predictor of increased FA within the left FA ($\beta = 0.82$, $p < .001$) (Simes–Hochberg corrected *p*-value of 0.05).

In Regression 2, PCL:YV Facet scores were replaced with PCL:YV Factor scores. Here, PCL:YV Factor 1 and 2 scores were not significant

Table 2
Multiple Regression Analyses with PCL:YV scores entered with Covariates Predicting FA in the Right UF.

Regression 1 Predictors	B	SE B	t	β	Sig.
PCL:YV Facet 1	−0.001	.000	−2.062	−.104	.040
PCL:YV Facet 2	−0.001	.001	−0.917	−.050	.360
PCL:YV Facet 3	0.001	.001	1.894	.097	.059
PCL:YV Facet 4	−0.000	.001	−0.025	−.001	.980
Num. Sub. Dep.	0.001	.001	2.345	.112	.020
IQ	0.000	.000	1.414	.066	.159
Avg. FA	0.891	.055	16.130	.711	< .001

Regression 2 Predictors	B	SE B	t	β	Sig.
PCL:YV Factor 1	−0.001	.000	−2.537	−.132	.012
PCL:YV Factor 2	0.001	.000	1.649	.087	.100
Num. Sub. Dep.	0.001	.001	2.310	.109	.022
IQ	0.000	.000	1.311	.061	.191
Avg. FA	0.892	.055	16.208	.712	< .001

Regression 3 Predictors	B	SE B	t	β	Sig.
PCL:YV Total	0.000	.000	−1.068	−.047	.287
Num. Sub. Dep.	0.002	.001	2.975	.137	.003
IQ	0.000	.000	0.993	.046	.322
Avg. FA	0.879	.055	15.916	.702	< 0.001

Note. Regression 1: $R^2 = 0.534$, $R = 0.731$, $F(253) = 40.261$, $p < .001$; *Regression 2:* $R^2 = 0.531$, $R = 0.729$, $F(253) = 56.248$, $p < .001$; *Regression 3:* $R^2 = 0.521$, $R = 0.722$, $F(253) = 67.766$, $p < .001$. Significant results are those that survive a Simes-Hochberg multiple comparison correction.

Table 3
Multiple Regression Analyses with PCL:YV scores entered with Covariates Predicting FA in the Left UF.

Regression 1 Predictors	B	SE B	t	β	Sig.
PCL:YV Facet 1	−0.001	.000	−1.473	−.061	.142
PCL:YV Facet 2	0.000	.000	−0.548	−.024	.584
PCL:YV Facet 3	0.001	.000	2.138	.090	.034
PCL:YV Facet 4	−0.001	.001	−0.976	−.040	.330
Num. Sub. Dep.	0.001	.001	1.142	.045	.254
IQ	0.000	.000	1.105	.043	.270
Avg. FA	1.088	.048	22.600	.821	< .001

Regression 2 Predictors	B	SE B	t	β	Sig.
PCL:YV Factor 1	0.000	.000	−1.698	−.073	.091
PCL:YV Factor 2	0.000	.000	1.131	.050	.259
Num. Sub. Dep.	0.001	.001	1.110	.043	.268
IQ	0.000	.000	0.958	.037	.339
Avg. FA	1.091	.048	22.631	.823	< .001

Regression 3 Predictors	B	SE B	t	β	Sig.
PCL:YV Total	−0.000	.000	−0.652	−.024	.515
Num. Sub. Dep.	0.001	.000	1.555	.059	.121
IQ	0.000	.000	0.752	.029	.453
Avg. FA	1.083	.048	22.519	.817	< .001

Note. Regression 1: $R^2 = 0.684$, $R = 0.827$, $F(253) = 75.997$, $p < .001$; *Regression 2:* $R^2 = 0.679$, $R = 0.824$, $F(253) = 104.898$, $p < .001$; *Regression 3:* $R^2 = 0.676$, $R = 0.822$, $F(253) = 129.697$, $p < .001$. Significant results are those that survive a Simes–Hochberg multiple comparison correction.

predictors of FA within the left UF. Instead, TBSS-skeleton average FA emerged as a significant predictor of increased FA within the left UF ($\beta = 0.83$, $p < .001$) (Simes-Hochberg corrected *p*-value of 0.025).

In Regression 3, PCL:YV Factor scores were replaced with PCL:YV total scores. Here, PCL:YV total scores were not a significant predictor of FA within the left UF. Instead, TBSS-skeleton average FA was a significant predictor of increased FA within the left UF ($\beta = 0.82$, $p < .001$) (Simes-Hochberg corrected *p*-value of 0.0125) (see Table 3 for multiple regression analyses with left UF FA entered as the dependent measure).

2.4. *Supplementary multiple regression analyses*

In supplementary multiple regression analyses performed, PCL:YV Facet 2 scores emerged as a predictor of reduced FA within other WM tracts, including the left cingulum, left and right inferior fronto-occipital fasciculus, right inferior longitudinal fasciculus, and the left temporal portion of the superior longitudinal fasciculus. Additionally, group membership of CD/ODD or ADHD did not emerge as significant predictors of either the left or right UF in multiple regression analyses performed. Furthermore, PCL:YV Facet scores emerged as predictors of other measures of WM structural integrity, including MD, AD, and RD, in several of the twenty ROIs investigated (see supplementary materials for full statistics). Important to note, none of the aforementioned PCL:YV-related findings obtained in the supplementary analyses would survive stringent multiple comparisons correction.

3. Discussion

This study investigated the relationship between youth psychopathy scores assessed via the PCL:YV and structural integrity of both the left and right UF in a high-risk sample of incarcerated male adolescent offenders. Consistent with our hypotheses, higher PCL:YV scores were significantly negatively related to FA within the right UF. Specifically, higher PCL:YV Factor 1 and Facet 1 scores, reflecting interpersonal dysfunction, including impression management, a grandiose sense of self-worth, pathological lying, and manipulation for personal gain, were associated with reduced FA in the right UF. The results obtained in the current report are consistent with studies performed with both youth (Breeden et al., 2015) and adults (Craig et al., 2009; Hoppenbrouwers et al., 2013; Lindner et al., 2017; Motzkin et al., 2011; Sobhani et al., 2015; Sundram et al., 2012; Vermeij et al., 2018; Wolf et al., 2015) scoring high on psychopathic traits. In addition, our results are consistent with previously published studies associating reduced FA in the right UF specifically with higher Factor 1 and Facet 1 scores of the PCL-R (Lindner et al., 2017; Vermeij et al., 2018; Wolf et al., 2015). However, our results are also inconsistent with other studies, which have identified significant negative relationships between right UF FA and PCL-R Factor 2 scores (Hoppenbrouwers et al., 2013; Sundram et al., 2012) and Facet 2 scores (Vermeij et al., 2018). These disparate results may arise due to the smaller sample sizes recruited in other published reports (i.e., all under 30 total participants) (Hoppenbrouwers et al., 2013; Sundram et al., 2012; Vermeij et al., 2018), which may result in spurious results between psychopathic traits and FA in the UF. The larger sample size reported in the current report affords us the opportunity to detect statistically significant effects with greater precision. Furthermore, our current results may deviate from previously published reports due to differences in sample composition, especially regarding differing operational definitions of psychopathy used between studies. For example, previous reports have considered participants to be ‘psychopathic’ if they scored above a 23 (Hoppenbrouwers et al., 2013) or 25 (Sundram et al., 2012; Vermeij et al., 2018) on the PCL-R total score, which is considerably lower than the traditional cut-off score of 30 typically used. These reports also recruited participants from community samples; participants recruited from community samples tend to score significantly lower on measures of psychopathy (Neumann and Hare, 2008). As such, differing results may be due to the higher overall range of PCL:YV total scores in the current report (i.e., 8–38) compared to previously published reports using the PCL-R with a lower overall range of scores

(Hoppenbrouwers et al., 2013; Sundram et al., 2012; Vermeij et al., 2018).

The results in the current report support the notion that psychopathic personality is neurodevelopmental in nature, as youth with elevated psychopathic traits exhibit a number of structural abnormalities consistent with adult psychopathic offenders as young as fourteen years of age, including reduced gray matter volume and concentration in the amygdala (Aghajani et al., 2016; B. M. Caldwell et al., 2019; Cohn et al., 2016; Walters and Kiehl, 2015), anterior cingulate (B. M. Caldwell et al., 2019; Sebastian et al., 2012), hippocampus (Cope et al., 2014; Wallace et al., 2014), insula (B. M. Caldwell et al., 2019; Cohn et al., 2016; Raschle et al., 2018), parahippocampal gyrus (Cope et al., 2014; Ermer et al., 2013), posterior cingulate (B. M. Caldwell et al., 2019; Ermer et al., 2013), orbitofrontal cortex (B. M. Caldwell et al., 2019; Cope et al., 2014; Ermer et al., 2013), and temporal pole (B. M. Caldwell et al., 2019; Cope et al., 2014; Ermer et al., 2013; Steele et al., 2017; Wallace et al., 2014), and reduced FA within the right UF (Craig et al., 2009; Hoppenbrouwers et al., 2013; Lindner et al., 2017; Motzkin et al., 2011; Sobhani et al., 2015; Sundram et al., 2012; Vermeij et al., 2018; Wolf et al., 2015).

Reduced FA in the UF has been previously associated with deficits in emotional empathy (Oishi et al., 2015) and may relate to reduced functional connectivity previously observed between the amygdala and vmPFC in youth with elevated psychopathic traits in fMRI studies (Aghajani et al., 2016; Marsh et al., 2008). Specifically, Marsh et al. (2008) found that youth with elevated psychopathic traits exhibited reduced functional connectivity between the amygdala and vmPFC when processing fearful facial expressions (Marsh et al., 2008). Youth with elevated psychopathic traits have typically exhibited reduced hemodynamic activity in the amygdala when processing fearful facial expressions (Jones et al., 2009; Lozier et al., 2014; Marsh and Blair, 2008; Viding et al., 2012; White et al., 2012) and exhibit deficits in processing fearful facial stimuli in general (Blair and Coles, 2000; Blair et al., 2001). Blair's *Violence Inhibition Mechanism* model (Blair, 1995) suggests that certain emotions, including fear, serve as potential distress cues to help stop the continuation of aggressive behavior (Blair, 1995). As the amygdala codes the affective significance of stimuli and feeds this information forward to the vmPFC to guide decision-making (Cardinal et al., 2002), combined with studies observing reduced functional (Aghajani et al., 2016; Marsh et al., 2008) and structural (Breeden et al., 2015) connectivity between the amygdala and vmPFC, youth with elevated psychopathic traits may not view fearful facial expressions as affectively significant and exhibit decreased sensitivity to such distress cues.

The results obtained in the current report are also inconsistent with two other studies performed associating increased youth psychopathy scores with higher FA in the right UF (Pape et al., 2015; Passamonti et al., 2012). Important to note, these latter reports assessed psychopathic traits using self-report measures. Studies have shown that the expert-rated PCL:YV and self-report measures do not provide a compatible assessment of psychopathic traits (Fink et al., 2012; Lee et al., 2009; Skeem and Cauffman, 2003). Additionally, studies have shown dissimilar executive functioning (Baskin-Sommers et al., 2015), functional neuroimaging (Harenski et al., 2014), and error-related processing (Maurer et al., 2018) deficits when comparing expert-rater based and self-report measures of adolescent psychopathic traits within the same sample. Thus, inconsistent results between our study and previously published studies may relate to differing instruments used to assess psychopathic traits.

We found that PCL:YV Facet 3 scores, reflecting general externalizing psychopathology, including stimulation seeking, a parasitic lifestyle, lacking goals, impulsivity, and irresponsibility, were associated with increased FA in the left UF. These traits are commonly shared across various externalizing disorders, including CD, which have been previously associated with increased FA in the left UF (Passamonti et al., 2012; Sarkar et al., 2013; Zhang et al., 2014). In supplementary analyses performed, group membership of CD/ODD was not significantly associated with increased FA in the left UF, likely due to the lack of variation in scoring, whereby only $n = 15$ participants did not meet criteria for CD/ODD. Thus, we may have observed significant effects with PCL:YV Facet 3 scores, but not CD/ODD group membership, due to the higher variance observed with Facet 3 scores (i.e., 1–10) in the current sample. Increased FA may reflect an increase in myelination (i.e., pruning failure) (Beaulieu, 2002) and has been previously associated with risk-taking (Berns et al., 2009). Thus, results in the current report reveal interesting lateralization effects in a sample of high-risk incarcerated male adolescent offenders, whereby youth interpersonal psychopathic traits were associated with reduced FA in the right UF, whereas youth psychopathic traits reflective of general externalizing psychopathology were associated with increased FA in the left UF.

4. Limitations

Limitations in the current study should be noted, which may reduce the generalizability of our findings. First, the best evidence of the continuity of psychopathic traits from adolescence to adulthood comes from longitudinal evidence showing moderate stability of psychopathic traits from age 13 to 23 (Lynam et al., 2007). As such, there exists the possibility that youth in the current study may not eventually meet the established criteria for psychopathy as adults. Longitudinal research is desperately needed to measure whether WM structural abnormalities in youth samples can serve as a potential biomarker for the development of adult psychopathy, especially since reduced FA in the right UF is more consistently reported in adults with elevated psychopathic traits (Craig et al., 2009; Hoppenbrouwers et al., 2013; Lindner et al., 2017; Motzkin et al., 2011; Sobhani et al., 2015; Sundram et al., 2012; Vermeij et al., 2018; Wolf et al., 2015). Second, the current sample is limited to incarcerated adolescent male offenders. Thus, it is not known whether our results extrapolate to incarcerated adolescent female offenders. A previous report in adult females scoring high on psychopathic traits observed a significant negative relationship between psychopathy scores and FA in the right UF (Lindner et al., 2017); however, it is not currently known whether adolescent females scoring high on psychopathic traits exhibit similar structural integrity deficits. Finally, while we observed that youth psychopathic traits reflecting general externalizing psychopathology (i.e., PCL:YV Facet 3 scores) were associated with increased FA in the left UF, exploratory analyses included in our supplementary material did not associate group membership of conditions including CD/ODD or ADHD with increased or reduced FA in the left or right FA. The lack of variance in scoring for these conditions is likely responsible for the lack of statistically significant effects in the current report. Additionally, while some studies have associated increased FA in the UF in individuals meeting criteria for CD (Passamonti et al., 2012; Sarkar et al., 2013; Zhang et al., 2014), and reduced FA in the UF in individuals meeting criteria for ADHD (Konrad and Eickhoff, 2010; Shaw et al., 2014), contradictory effects have been reported (Finger et al., 2012; Haney-Caron et al., 2014; Silk et al., 2009). Thus, not only should future studies be performed to assess the true association between externalizing disorders and UF FA, additional studies should explore the relationship between psychopathic traits, externalizing disorders, and UF FA within the same sample, to see if similar lateralization effects obtained in the current study extend to other samples.

5. Conclusions

Higher PCL:YV Factor 1 and Facet 1 scores were associated with reduced FA in the right UF, consistent with studies performed with both youth (Breeden et al., 2015) and adults (Craig et al., 2009; Hoppenbrouwers et al., 2013; Lindner et al., 2017; Motzkin et al., 2011; Sobhani et al., 2015; Sundram et al., 2012; Vermeij et al., 2018;

Wolf et al., 2015) with elevated psychopathic traits. These results support the hypothesis that psychopathic personality is neurodevelopmental in nature and may relate to some of the characteristics inherent to youth with elevated psychopathic traits, including empathy-related deficits and dysfunctional processing of negative emotions, including fear. Additionally, we found that PCL:YV Facet 3 scores were associated with increased FA in the left UF, consistent with previously published studies where conditions characterized by general externalizing psychopathology, including CD, were associated with increased FA in the left UF (Passamonti et al., 2012; Sarkar et al., 2013; Zhang et al., 2014). Results obtained in the current report suggest unique lateralization effects, whereby youth interpersonal psychopathic traits may be associated with reduced FA in the right UF, whereas traits reflective of general externalizing psychopathology, may be associated with increased FA in the left UF.

Credit author statement

J. Michael Maurer, Subhadip Paul, & Prashanth K. Nyalakanti implemented the analytical approach andperformed the data analysis. J. Michael Maurer and Nathaniel E. Anderson initially drafted the manuscript. All authorsdeveloped interpretations and provided critical revisions and approved the final manuscript for submission. Kent A.Kiehl led the NICHD and NIMH projects that collected the data and conceived of the study approach.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.nicl.2020.102236.

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