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Original article

White matter correlates of psychopathic traits in a female community sample

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Abstract

Psychopathy comprises interpersonal, affective, lifestyle and antisocial facets that vary dimensionally in the population and are associated with criminal offending and adverse psychosocial outcomes. Evidence associating these facets with white matter microstructure of the uncinate fasciculus and the cingulum tracts is inconsistent and derives principally from studies of male offenders. In a sample of 99 young women presenting a range of scores on the Psychopathy Checklist: Screening Version, we used Diffusion Tensor Imaging, tractography and Tract-Based Spatial Statistics to investigate microstructure across the brain and of the uncinate fasciculus and cingulum. Right uncinate fasciculus microstructure was negatively associated with the interpersonal facet, while cingulum integrity was not associated with any facet of psychopathy. Whole-brain analyses revealed that both affective and lifestyle facets were negatively correlated with white matter microstructure adjacent to the fusiform gyrus, and the interpersonal facet correlated negatively with the integrity of the fornix. Findings survived adjustment for the other facet scores, and age, verbal and performance IQ. A similar negative association between the interpersonal facet and uncinate fasciculus integrity was previously observed in male offenders. Thus, previous evidence showing that psychopathic traits are associated with functional and structural abnormalities within limbic networks may also apply to females.

Key words: uncinate fasciculus; tractography; fusiform gyrus; fornix; TBSS; cingulum

Introduction

Psychopathy comprises four facets of personality and behavior: an interpersonal facet indexing conning, manipulation, and deceitfulness; an affective facet indexing callousness, lack of empathy and guilt, and failure to take responsibility for one's own actions; a life-style facet indexing risk-taking, rebelliousness, and impulsivity; and one facet indexing antisocial behavior (Hare, 2003). These facets vary dimensionally in the population (Guay *et al.*, 2007), remain relatively stable from childhood through early adulthood and predict multiple adverse psychosocial and mental health outcomes, and criminal offending, over and above conduct problems (McMahon *et al.*, 2010;

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Hemphälä and Hodgins, 2014; Hemphälä *et al.*, 2015; Waller *et al.*, 2016). High scores on all four facets of the Psychopathy Checklist Revised (PCL-R) (Hare, 2003) identify the syndrome of psychopathy. Most offenders presenting the syndrome of psychopathy presented Conduct Disorder (CD) prior to age 15 and Antisocial Personality Disorder (ASPD) (American Psychiatric Association, 2013) as adults (Ogloff, 2006). These disorders index a life-long pattern of antisocial behavior but not the interpersonal and affective facets of psychopathy. Approximately half as many women as men present the syndrome of psychopathy (Vitale *et al.*, 2002) and females with psychopathy show more deceitful behavior and lack of control than males, who in turn present more antisocial behavior (Strand and Belfrage, 2005). In community samples, females obtain lower total and facet scores than males (Cale & Lilienfeld, 2002; Hemphälä and Tengström, 2010; Berkout *et al.*, 2011). Little is known about the neural correlates of psychopathy traits in females since almost all research on psychopathy has focused on males.

In male, and a few mixed-sex samples, hyper-reactivity of the amygdala in response to negative emotional stimuli has been consistently associated with the lifestyle and antisocial facets of psychopathy and diagnoses of CD/ASPD, while the interpersonal and affective facets that are unique to psychopathy have been associated with amygdala hypo-reactivity (Gordon *et al.*, 2004; Coccaro *et al.*, 2007; Herpertz *et al.*, 2008; Carré *et al.*, 2012; Sebastian *et al.*, 2012; Viding *et al.*, 2012; Harenski *et al.*, 2014; Hyde *et al.*, 2014; Lozier *et al.*, 2014). These functional neuroimaging findings combined with findings of abnormalities of grey matter limbic structures (Aoki *et al.*, 2014) led researchers to investigate the uncinate fasciculus (UF) white matter tract that connects the amygdala to the orbitofrontal cortex (OFC) (Von Der Heide *et al.*, 2013). Studies have examined the structural architecture of the UF using Diffusion Tensor Imaging (DTI) and proxy measures such as fractional anisotropy (FA), axial and radial diffusivity (AD and RD) (Alexander *et al.*, 2007). Several studies have shown that relatively reduced structural integrity of UF is associated with antisocial behavior and psychopathy. Most of these studies, however, focused on male offenders, with only a few including non-offenders and females (see Supplementary Table S1).

Early work examined small samples of male violent offenders incarcerated in a forensic psychiatric hospital. Scores for the behavioral factor of psychopathy were found to be negatively associated with reduced FA of the right UF (Craig *et al.*, 2009), and reduced FA in a cluster in the right frontal lobe that included the UF (Sundram *et al.*, 2012). In a study of incarcerated male offenders, those with the syndrome of psychopathy showed reduced integrity of the right UF and reduced OFC-amygdala functional connectivity (Motzkin *et al.*, 2011). In another study of male offenders, reduced FA in a cluster covering the left UF was negatively associated with the sum of interpersonal and affective facet scores, while the sum of the lifestyle and antisocial facets was negatively associated with integrity of a cluster covering the striato-thalamo-frontal network (Hoppenbrouwers *et al.*, 2013). Also in a large sample of incarcerated male offenders, a recent study reported a negative correlation between right UF FA and only the interpersonal facet, after adjusting for the other facet scores (Wolf *et al.*, 2015). Another study of a community sample of males found that an enriched, facet-unspecific measure of psychopathy was negatively correlated with right UF FA and that this association was not modified by trait anxiety (Sobhani *et al.*, 2015).

UF abnormalities have also been reported among adolescents presenting antisocial behavior. Results of comparisons of UF microstructure between antisocial and healthy adolescents, without examining the role of CU traits, are contradictory as to direction (increased or decreased FA) (Passamonti *et al.*, 2012; Haney-Caron *et al.*, 2014; Zhang *et al.*, 2014; Decety *et al.*, 2015) or presence of abnormalities (Finger *et al.*, 2012). Further, UF FA has been both positively (Sarkar *et al.*, 2013) and negatively (Breeden *et al.*, 2015) associated with callous-unemotional (CU) traits, the child measure of the affective facet. The integrity of a cluster covering the UF was positively correlated with interpersonal traits after adjusting for other trait scores, age and sex (Pape *et al.*, 2015).

The Dual Network Model of psychopathy proposes that UF abnormalities are associated with the lifestyle and antisocial facets and that cingulum abnormalities are associated with the interpersonal and affective facets (Sethi *et al.*, 2014). However, as described above, results of the associations of UF FA with psychopathic traits are inconsistent, as are results concerning the cingulum. Two studies of male offenders, differing in sample sizes, tract delineation techniques and analytic approaches, have examined the cingulum specifically, one reporting that relatively reduced integrity was associated with interpersonal and affective facets (Sethi *et al.*, 2014) and the other detecting no association (Wolf *et al.*, 2015). The dorsal cingulum connects the anterior and posterior medial nodes of the Default Mode Network (DMN), and plays a role in higher cognitive processes relating to introspection, social cognition and empathy (Whitfield-Gabrieli and Ford, 2012; Li *et al.*, 2014) known to be impaired in psychopathy (Bird and Viding, 2014). Several studies have observed DMN abnormalities among psychopathic offenders that were associated with the interpersonal and affective facets (Juárez *et al.*, 2013; Freeman *et al.*, 2014; Cohn *et al.*, 2015), suggesting that cingulum integrity may be indeed be attenuated.

In sum, evidence of associations of abnormalities of the UF and the cingulum with psychopathic traits is inconsistent and derived primarily from studies of male offenders. There are no well-powered studies of these associations in female only samples. Yet, some of the neural correlates of psychopathic traits may differ in females and males. Not only do females show lower levels of psychopathic traits (Cale and Lilienfeld, 2002; Vitale *et al.*, 2002; Berkout *et al.*, 2011), they also present a somewhat different phenotype that includes less direct aggressive behavior (Strand and Belfrage, 2005). Among adolescents with CD, males, but not females, displayed reduced FA of the UF compared with healthy peers (Zhang *et al.*, 2014). Among children, the association between reduced radial diffusivity of a cluster covering the left UF and more CD symptoms was stronger in girls than boys (Decety *et al.*, 2015). In a community sample of young adults, the lifestyle facet was positively associated with right amygdala reactivity to anger only in men, while a positive association between right ventral striatum reactivity and the affective facet was present only in women (Carré *et al.*, 2013). Additionally, in healthy individuals, there are important sex differences in white matter architecture and development (Asato *et al.*, 2010; Ingalhalikar *et al.*, 2014), and in the neural mechanisms underlying emotional processing and regulation (Whittle *et al.*, 2011).

The present study addresses several gaps in the literature by investigating white matter correlates of distinct psychopathic traits, measured dimensionally, in a sample of young adult women with a range of psychopathy scores not indicative of the syndrome of psychopathy. The study aimed to determine: (i) whether UF structural integrity was associated with any facet of psychopathy; (ii) whether the integrity of the cingulum was associated with the interpersonal and affective facets; and (iii) whether there were any other white matter correlates of distinct psychopathic traits across the brain.

Table 1. Sample characteristics

Measure	Participants (n=99)		
	M	SD	Range
Age	24.23	3.35	17.2–33.4
Verbal IQ	9	2.29	2–13
Performance IQ	10.06	2.79	2–17
PCL:SV facet 1	0.57	0.86	0–4
PCL:SV facet 2	0.69	1.15	0–5
PCL:SV facet 3	1.11	1.18	0–5
PCL:SV facet 4	0.96	1.41	0–6
PCL:SV total score	3.32	3.87	0–18
% PCL:SV score ≥13	3		
% Any recent aggressive behavior	23.2		
% Current alcohol dependence	0		
% Current drug dependence	2.0		
% Current anxiety disorder	15.2		
% Current depression disorder	4.0		

PCL:SV score ≥13 indicative of "possible psychopathy" (Cooke *et al.*, 1999). Verbal and performance IQ scores were missing for one participant.

Materials and methods

Ethics

The study was approved by the Stockholm Regional Ethical Review Board (2012/698-32). Participants provided written informed consent and were compensated with gift certificates worth 1600 SEK.

Participants and procedure

The sample included 44 women recruited as adolescents in treatment for substance misuse (Hodgins *et al.*, 2014), 31 of their sisters who were also enrolled in the larger cohort study, and 24 newly recruited healthy women. This recruitment strategy was designed to obtain a wide variation of Psychopathy Checklist:Screening Version (PCL:SV) scores. Ex-clients and sisters were contacted by telephone and mail and invited to participate in another follow-up assessment. Healthy women, similar to the other participants on age, education, and verbal and performance IQ, were recruited from among women replying to advertisements. The three recruitment groups were pooled into one, large sample.

All participants completed the Structured Clinical Interview for DSM-IV Axis I Disorders to assess current depressive disorders, anxiety disorders, alcohol dependence and drug dependence (First *et al.*, 2002), the MacArthur Community Violence Instrument (Steadman *et al.*, 1998) to report on recent aggressive behavior, and underwent a Magnetic Resonance Imaging (MRI) brain scan on the same day. Verbal and performance IQ tests (Wechsler, 1997) were completed either 18 months earlier (ex-clients and sisters) or just prior to scan (healthy women). Additionally, on the day of the scan, a breathalyzer test and a saliva sample indicated no recent use of alcohol or drugs by any participant. Participant characteristics are presented in Table 1 (characteristics by recruitment groups are presented in Supplementary Table S2).

Psychopathy assessment

Psychopathy was assessed in the healthy women on the day of the scan, and in the others 18 months previously. As recommended (Hart *et al.*, 1995), the healthy women were assessed using the PCL:SV (Hart *et al.*, 1995) and the other women using the PCL-R. PCL-R scores were transformed to PCL:SV scores following a validated procedure (Cooke *et al.*, 1999) and scores for the four facets were calculated.

As presented in Table 1, PCL:SV total and facet scores were slightly elevated compared to those previously reported for community samples, yet below those obtained by offenders (Hart *et al.*, 1995). Only three participants obtained PCL:SV scores indicative of the syndrome of psychopathy (>13). As presented in Figure 3, the facet scores were correlated with each other.

Participants who reported recent aggressive behavior obtained higher scores on the affective facet (M = 1.17, SD = 1.40; M = 1.52, SD = 1.59; $F[1,97]$=5.64, P=0.02) and on the antisocial facet (M = 1.52, SD = 1.59; M = 0.79, SD = 1.32, $F[1,97]$=4.93, P=0.03) than those who did not.

Diffusion-weighted imaging

Scanning was performed using a 3-Tesla scanner (GE Healthcare, Milwaukee) with an eight-channel coil, with 60 diffusion-weighted directions ($B = 1000\,s/mm^2$), eight opening $B = 0$ directions and a $2mm^2$ resolution (echo time = 81.6 ms, repetition time = 7600 ms). Images were pre-processed using the automatic quality-control feature of DTIPrep (Oguz *et al.*, 2014) and were tensor-fitted using the FSL software package (Jenkinson *et al.*, 2012), generating FA, axial and radial diffusivity maps (AD and RD). AD and RD metrics are thought to represent different aspects of white matter microstructure (axonal structure and myelination, respectively), while FA is a scalar measure of apparent coherence of fiber orientation, considered a proxy measure of microstructural architecture. See Supplementary material for details.

Uncinate fasciculus tractography

Due to the shape and location of the UF (intersecting with the inferior fronto-occipital fasciculus in the OFC and the inferior longitudinal fasciculus in the temporal pole, with considerable tract intertwinement), ROI analyses of the UF based on normalized, voxelwise data are suboptimal. Therefore, tractography and manual, virtual dissection (Catani *et al.*, 2002) of the UF was performed and tract-average DTI metrics were extracted. Preprocessed diffusion-weighted images were tensor-fitted using Diffusion Toolkit, and tracts reconstructed using the interpolated streamline algorithm, an angle threshold of 34° and an FA interval of 0.2–1. Manual dissection of the left and the right UF was performed in Trackvis by a trained operator (P.L.), blind to all other participant variables, according to an anatomically validated procedure that included placing a ROI in the OFC extending into the external capsule, displaying all tracts passing through this ROI, and then placing a second ROI (AND-gated) in the temporal pole. This dissection method captured the two branches of the UF that diverge at the anterior floor of the external capsule: the ventro-lateral branch terminating in the lateral OFC, and the antero-medial branch that terminates in the medial frontal pole (Thiebaut de Schotten *et al.*, 2012). Size and location of ROIs were modified in all directions to ensure all tracts were covered. Non-anatomically correct tracts resulting from reconstruction artefacts where manually removed using additional ROIs (NOT-gated). Probabilistic maps of the left and the right UF were saved and used to extract tract-average FA, AD and RD values. In four subjects, the left UF could not be reliably reconstructed and delineated; these were omitted case-wise in analyses.

Initially, bivariate correlations between the four facet scores and FA, AD and RD of the left and the right UF were calculated.

As was expected (Coid *et al.*, 2009), the facets were intercorrelated (see Figure 3). Therefore, in step two, significant associations were re-analyzed in separate multiple regression models that included all facet scores and the metric of interest as outcome. A second regression model included the facet score, and age, VIQ and PIQ. Finally, analyses were repeated using dichotomized facet variables (either a score of zero, or above) in order to control for the distribution of PCL:SV scores. For significant between-group contrasts, Cohen's *d* effect sizes with bootstrapped confidence intervals were calculated and interpreted according to standard guidelines (<0.3 small, <0.8 medium, >0.8 large).

Cingulum analyses

Tract-Based Spatial Statistics (TBSS) (Smith *et al.*, 2006) were used to extract tract-average measure for cingulum tract-of-interest analyses and to perform unrestricted whole-brain voxel-wise analyses. The TBSS standard lower FA threshold of 0.2 was used, with alignment into FMRIB58 standard space. Cingulum analyses were restricted to the dorsal part of the cingulum, connecting the medial prefrontal cortex to the posterior cingulate cortex, consistent with previous findings that the integrity of only this section was associated with interpersonal-affective facets scores (Sethi *et al.*, 2014). The dorsal cingulum was defined according to an established anatomical protocol (Budisavljevic *et al.*, 2015) to include cingulum tracts anterior to the vertical midline of the corpus callosum splenium (see Figure 2A). The dorsal cingulum is successfully reconstructed after the TBSS skeletonization procedure and can be reliably delineated since it does not intertwine with other tracts. Cingulum ROI analyses were performed by manually selecting voxels on the co-registered and normalized TBSS skeleton. Since previous research has shown similar correlations to personality psychopathic traits with FA of both the left ($r = -0.61$) and right ($r = -0.62$) dorsal cingulum (Sethi *et al.*, 2014), our mask included the cingulum bundle of both hemispheres. Tract-average FA, AD and RD values were extracted and used in statistical analyses as with UF data.

Whole-brain voxel-wise analyses

Whole-brain voxel-wise analyses using TBSS were performed, in two stages. First, correlations among FA, AD and RD values and each, zero-centered PCL:SV facet score were investigated using permutation statistics (the randomize tool, 5000 permutations), threshold-free cluster enhancement and a statistical threshold of $P < 0.05$, fully corrected for multiple comparisons using family-wise error correction (FWE). Second, significant clusters in each correlation contrast were thresholded, binarized and used as masks to extract cluster-average FA, AD or RD values for further calculation, as with tracts-of-interest data.

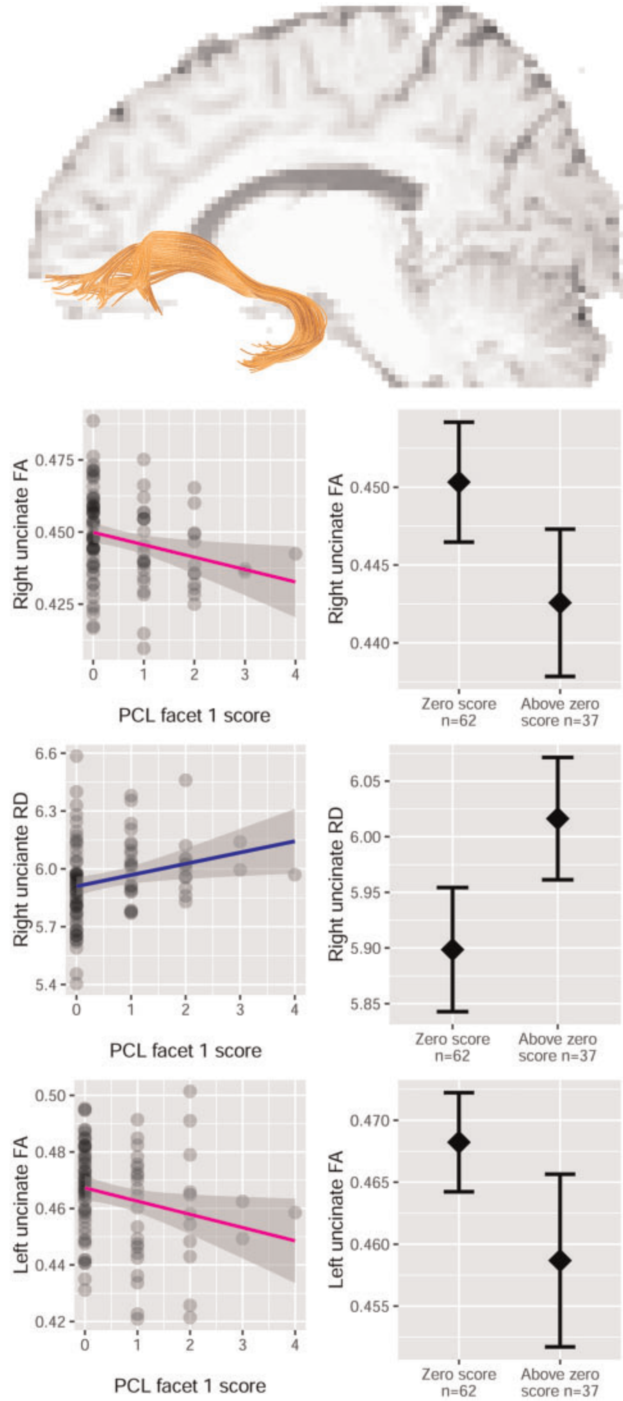

Fig. 1. Correlations between facet scores and uncinate fasciculus structural measures. *Top*: example uncinate fasciculus dissection. *Bottom*: linear (left) and group-wise (right) associations between PCL facet 1 scores and structural integrity proxy measures.

Results

Uncinate fasciculus ROI analyses

Facet 1: interpersonal. Facet 1 scores correlated negatively with FA ($r = -0.24$, $P = 0.0156$) of the right UF. The corresponding between group difference was medium-sized ($d = 0.52$, 95% CI: 0.94–0.09). Facet 1 scores were also positively correlated with RD in the right UF ($r = 0.24$, $P = 0.016$). The corresponding between group difference was medium-sized ($d = 0.59$, 95% CI: 0.18–1.00).

The correlations and group differences remained significant after adjusting for other facet scores, and age, VIQ and PIQ. See Figure 1, Table 2 and Supplementary Table S3.

Facet 1 scores also correlated negatively with FA ($r = -0.22$, $P = 0.03$) of the left UF and the corresponding between group effect size was medium-sized ($d = 0.53$, 95% CI: 0.99–0.07). Facet 1 scores remained a significant predictor when entered into a multiple regression model that adjusted for age, VIQ and PIQ,

Table 2. Results of multiple regression models associating PCL:SV facet scores with fractional anisotropy, radial diffusivity, and axial diffusivity of the uncinate fasciculus, and fornix and fusiform gyrus clusters

	Linear predictor						Binarized predictor (facet score zero or above)					
	Covarying for other facet scores			Covarying for age, VIQ and PIQ			Covarying for other facet scores			Covarying for age, VIQ and PIQ		
Model	B	t	P	B	t	P	B	t	P	B	t	P
Right uncinate FA ~ Interpersonal Facet 1	−0.006	−2.55	0.012	−0.005	−2.56	0.012	−0.009	−2.57	0.012	−0.009	−2.59	0.011
Right uncinate RD ~ Interpersonal Facet 1	0.08	2.42	0.017	0.07	2.74	0.007	0.14	2.99	0.004	0.13	3.04	0.003
Left uncinate FA ~ Interpersonal Facet 1	−0.004	−1.52	0.133	−0.005	−2.04	0.045	−0.011	−2.53	0.013	−0.009	−2.31	0.023
Fornix AD ~ Interpersonal facet 1	−1.45	−2.03	0.046	−1.27	−2.18	0.032	−2.21	−2.07	0.041	−2.04	−2	0.048
Fusiform gyrus AD ~ Affective facet 2	−0.65	−2.5	0.014	−0.77	−4.37	<.001	−1.07	−2.05	0.043	−1.28	−2.87	0.005
Fusiform gyrus FA ~ Affective facet 2	−0.019	−2.84	0.006	−0.021	−4.54	<.001	−0.042	−3.16	0.002	−0.047	−4.07	<.001
Fusiform gyrus FA ~ Lifestyle facet 3	−0.015	−2.12	0.036	−0.021	−4.03	<.001	−0.012	−0.83	0.41	−0.035	−2.66	0.009

but not one that included the other facet scores. Binarized scores remained significantly associated in both models. On the left, there were no significant correlations with AD (*P*=0.372) or RD (*P*=0.152).

Facet 2: affective. There were no linear bivariate correlations among AD, FA or RD of the left or the right UF and facet 2 scores, nor were there any group differences.

Facet 3: lifestyle. There were no linear bivariate correlations among AD, FA or RD of the left or the right UF and facet 3 scores, nor were there any group differences.

Facet 4: antisocial. There were no linear bivariate correlations among AD, FA or RD of the left or the right UF and facet 4 scores, nor were there any group differences.

Cingulum ROI analyses

There were no significant correlations between any facet score and any DTI measure of the cingulum, nor were then any group differences. See Figure 2 for scatter plots.

Whole-brain analyses using TBSS

Correlations between measures of white matter microstructure and psychopathy facets are presented in Figure 3 and Table 2 and Table S4.

Facet 1: interpersonal. Facet 1 scores were negatively correlated with AD in a 134-voxel large cluster covering the body and bilateral pillars of the fornix. At this imaging resolution, the fornix is indistinguishable from the stria terminalis, running inferior to the fornix along a similar C-shaped path, although the larger volume of the fornix makes this the more likely contributor to the observed finding. Women with a facet score of zero showed higher AD in the cluster than those with higher scores (Cohen's $d = 0.47$ (95% CI: 0.88–0.05). Both the correlation and the group difference survived correction for the other facet scores, and for age, VIQ and PIQ. TBSS revealed no correlations with FA or RD.

Facet 2: affective. Facet 2 scores were negatively correlated with FA values in a 154-voxel large cluster adjacent to the left posterior fusiform gyrus, with a corresponding between group effect size of $d = 0.89$ (95% CI: 1.35–0.45). Facet 2 scores were also negatively correlated with AD in a small cluster (six voxels) located more laterally, adjacent to the left posterior inferior temporal gyrus. The between-group effect size was $d = 0.69$ (95% CI: 1.14–0.26). Both the AD and FA associations (both linear and between-group) survived correction for other facet scores, and age, VIQ and PIQ. TBSS revealed no correlations with RD.

Facet 3: lifestyle. Facet 3 scores were negatively correlated with FA in a 116-voxel large cluster also located adjacent to the left posterior fusiform gyrus, with a between-group effect size of $d = 0.51$ (95% CI: 0.95–0.07). The linear association survived correction for other facet scores, and age, VIQ and PIQ, but only survived correction for age, VIQ and PIQ in group comparisons. TBSS revealed no correlations with AD or RD.

Facet 4: antisocial. TBSS revealed no significant ($p_{FWE}<0.05$) correlations between facet four scores and AD, FA or RD of any voxel.

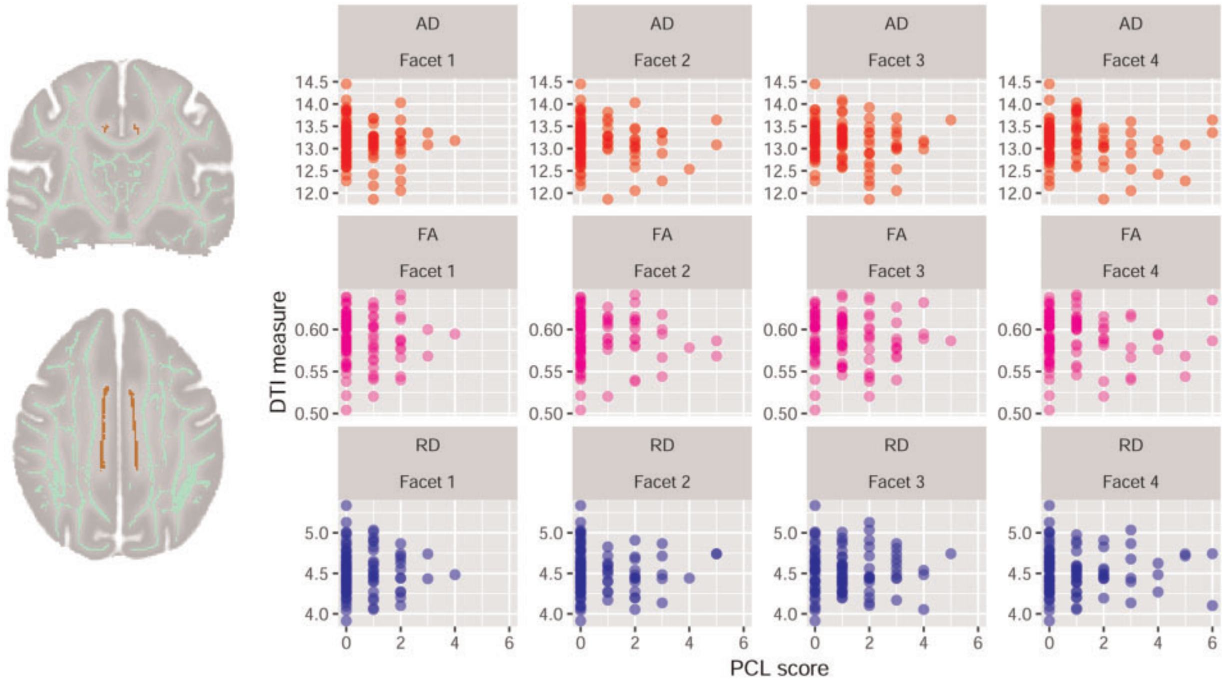

Fig. 2. No associations between cingulum structural measures and any facet score *Left*: mask of the dorsal cingulum used to extract tract-average measures. *Right*: scatterplots revealing no correlations between structural measures and any facet score. Organized as facets (columns) by measures (rows, colors).

Discussion

This is the first well-powered study of white matter correlates of specific psychopathic traits among females. The interpersonal facet of psychopathy was negatively associated with UF and fornix integrity, cingulum integrity was not correlated with any psychopathy facet score, and both the affective and lifestyle facet scores were negatively correlated with white matter integrity adjacent to the fusiform gyrus.

The negative association among the interpersonal facet scores, indexing glibness, grandiosity, and manipulation, and UF structural integrity observed in this sample of young women replicates a previous finding among male offenders (Wolf *et al.*, 2015). This is noteworthy given the dramatic difference in the behavioral phenotypes examined in the two studies: young women with low-to-medium psychopathy scores and middle-aged incarcerated male offenders with medium-to-high scores. While FA is an unspecific marker of white matter structural integrity, the additional, positive association with right UF RD suggests abnormalities of myelination. Although inferences should be made with caution (Wheeler-Kingshott and Cercignani, 2009), increased RD has been shown to be a proxy measure of decreased myelination (Song *et al.*, 2005). Changes in myelination as a result of repeatedly engaging in specific behaviors are well-documented (Zatorre *et al.*, 2013). This suggests, perhaps, that the increased RD of UF associated with psychopathy scores may result from less frequent, or less intense, amygdala-OFC functional coupling (Motzkin *et al.*, 2011) consistent with observed amygdala abnormalities (Carré *et al.*, 2012; Sebastian *et al.*, 2012; Viding *et al.*, 2012; Harenski *et al.*, 2014; Hyde *et al.*, 2014; Lozier *et al.*, 2014).

We speculate that this UF abnormality may be associated with the failure to learn from punishment (Olson *et al.*, 2015), characteristic of psychopathy (De Brito *et al.*, 2013), that in turn leads to developing traits such as glibness and grandiosity, and pathological lying. Adults with the syndrome of psychopathy learn associations that are rewarded, have difficulty changing behavior as reinforcement contingencies change (Budhani *et al.*, 2006; De Brito *et al.*, 2013), and fail to use prospective signals of regret to guide their behavior (Baskin-Sommers *et al.*, 2016). Similarly, children with high CU traits learn when rewarded and not when punished (Hawes and Dadds, 2005). These findings suggest difficulty in creating and updating contingencies, and in turn dysfunction of the OFC that is involved in encoding and representing outcome expectancies (Blair, 2008). A behavior that leads to punishment, for example aggressive behavior that is typical of most toddlers (Broidy *et al.*, 2003), may also to lead to a reward, for example, social dominance, that in turn, and with repetition, could lead to glibness, grandiosity. Similarly, among such children, punishment would not lead to reductions in lying and manipulation of others. This speculation highlights the need for prospective, longitudinal studies beginning in toddlerhood that examine both behavior and neural structure and function. Regardless, the lack of association between the microstructure of the UF and the affective facet found both in the present study and the study of male offenders (Wolf *et al.*, 2015) is surprising, given the multitude of studies associating amygdala hypo-reactivity with the affective component of psychopathy (Carré *et al.*, 2012; Sebastian *et al.*, 2012; Viding *et al.*, 2012; Harenski *et al.*, 2014; Hyde *et al.*, 2014; Lozier *et al.*, 2014), and a recent finding associating UF integrity with CU traits (Breeden *et al.*, 2015).

Our finding that the structural integrity of the UF was not associated with the PCL:SV antisocial and lifestyle facets is also consistent with previous evidence of intact UF among teenage girls with CD (Zhang *et al.*, 2014). In a sample that partially overlaps with the sample in the present study, we too reported that young women with a history of CD did not display abnormalities of the UF after adjusting for comorbid disorders (Lindner *et al.*, 2016). Thus, the lack of association between the structural integrity of the UF and any of the behavioral facets of the

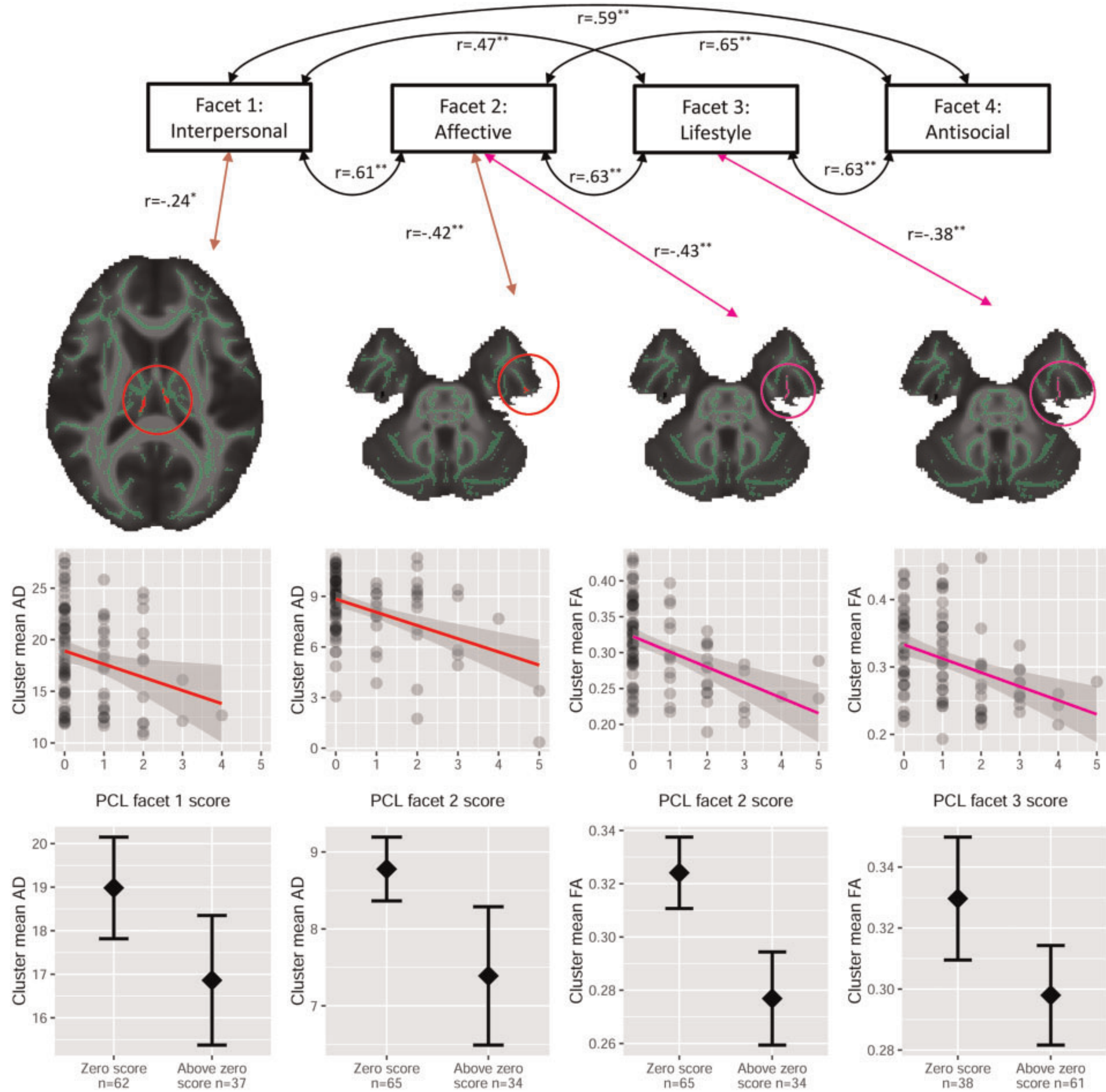

Fig. 3. Significant associations between psychopathy facet scores and measures of white matter integrity revealed by whole-brain TBSS. *Top*: inter-correlation between facets. *Middle*: bivariate correlations between facet scores (black arrows). Red arrows and clusters indicate correlations between axial diffusivity (AD) and facet scores. Magenta arrows and clusters indicate correlations between fractional anisotropy (FA) and facet scores. $^{*}P<0.05$, $^{**}P<0.01$. *Bottom*: scatterplots and bar plots display unadjusted significant ($P<0.05$) associations between implicated cluster-average metric and facet, both linear (upper row) and group-wise (lower row; 95% confidence intervals) associations.

PCL:SV may also reflect a sex difference in some of the neural correlates of antisocial behavior, consistent with sex differences in brain maturation and architecture (Asato *et al.*, 2010; Ingalhalikar *et al.*, 2014), structures underlying emotional processing (Whittle *et al.*, 2011), and the antisocial phenotype (Cale and Lilienfeld, 2002; Strand and Belfrage, 2005; Berkout *et al.*, 2011).

In this sample of young women, whole-brain analyses revealed novel white matter associations with psychopathy. Scores for the affective and lifestyle facets were inversely associated with proxy measures of the structural integrity of white matter adjacent to the fusiform gyrus, and the interpersonal facet score was associated with the integrity of the fornix. These findings are consistent with previous reports of gray matter abnormalities and neuropsychological deficits associated with psychopathy traits. Changes in white matter integrity (as detected by DTI metrics), even rapid ones, are believed to reflect plasticity processes such as myelination, synaptogenesis, dendritic branching and glial remodeling (Ding *et al.*, 2013; Zatorre *et al.*, 2013). The present findings of associations between the structural integrity of the fornix and fusiform gyrus and psychopathy facets 1, 2 and 3 suggest that functional abnormalities in the grey matter regions connected by these tracts may be related to psychopathy.

The fusiform gyrus lies directly adjacent to the parahippocampal gyrus, connected by short association fibers (Powell *et al.*, 2004). The parahippocampal gyrus forms part of the Papez circuit (Catani *et al.*, 2013; Mori and Aggarwal, 2014) connecting the hippocampus via the fornix to the mammillary body (which is also connected to the amygdala via the stria terminalis), onwards to the anterior thalamic nucleus via the mammillothalamic tract and from there, closing the circuit through cingulum projections back to the hippocampus (Shah *et al.*, 2012). A recent meta-analysis reported increased grey matter volumes of the fusiform gyrus in antisocial populations, but did not distinguish between participants with and without interpersonal-affective psychopathy traits (Aoki *et al.*, 2014). Abnormal activity in this region while viewing emotional faces, as found in females with CD (Fairchild *et al.*, 2014) and adult male offenders with psychopathy (Deeley *et al.*, 2006), may reflect impairments in the encoding of semantic information from faces (Schultz *et al.*, 2003), manifesting as reduced facial emotion recognition that is associated with CU traits in both males and females (Fairchild *et al.*, 2010). Reduced gray matter volumes of the hippocampus observed in adult males with the syndrome of psychopathy (Boccardi *et al.*, 2010) suggests that the disrupted processing is carried forward to the hippocampus (and likely back again), resulting in abnormal affective autobiographical memory encoding and retrieval (Rubin *et al.*, 2014), a key aspect of social cognition (Spreng, 2013). Further, an intact amygdala–hippocampal complex is crucial for aversive conditioning, known to be impaired in antisocial populations, including females with CD (Fairchild *et al.*, 2010). A hippocampal processing abnormality may manifest as lower structural integrity of the fornix, as observed in the present study, and further along the Papez circuit, potentially also of the cingulum, as observed by others (Sethi *et al.*, 2014) but not in the current study. In support of the involvement of the Papez circuitry in psychopathy, a recent study of adolescents with disruptive behavior disorders and either high or low CU traits and healthy peers reported abnormal functional connectivity of the amygdala with parahippocampal and fusiform gyri when responding to provocation (White *et al.*, 2016). In sum, evidence supports the involvement of fornix and fusiform gyrus white matter in the presentation of psychopathic traits. Future studies using both high-resolution neuroimaging and well-delineated behavioral paradigms are needed to further understanding of the associations between psychological processes and mechanisms, functional brain correlates, and how the relatively reduced integrity of white matter structures promote different psychopathic traits.

Strengths and limitations

Strengths of the study include a large, community sample of females, presenting a range of PCL:SV facet scores but not the syndrome of psychopathy, allowing for study of the neural correlates of psychopathy traits as dimensional constructs (Walters *et al.*, 2015). Positive associations of the affective and antisocial PCL:SV facets with recent aggressive behavior confirmed previous results showing the importance of these traits for real-world functioning. Importantly, psychopathy was assessed by trained clinicians. In addition to tract-of-interest analyses of the UF using tractography and manual dissection and of the cingulum, voxel-wise whole-brain analyses were also performed. The associations revealed by the UF tractography analyses were not detected in the TBSS analyses, highlighting the importance of accurate delineation the UF that does not rely on voxel-wise, normalization-derived methods to make inferences about this tract. Prior to the scan, participants completed a diagnostic interview that detected low levels of current mental disorders, including substance dependence, and breathalyzer and saliva tests indicated no recent use of alcohol or drugs.

The primary limitation of the current study is the absence of precise neuropsychological measures (e.g. reinforcement learning) to test the hypothesis suggested by the neuroimaging findings. A second limitation of the present study was that psychopathy among some participants was assessed 2 years prior to the scan. However, evidence shows stability of scores from mid-adolescence to adulthood (McMahon *et al.*, 2010; Hemphälä and Hodgins, 2014; Hemphälä *et al.*, 2015). At the imaging resolution used in the present study, abnormalities of the fornix and stria terminalis may not have been distinguishable. However, the fornix is the larger structure and is fully reconstructed after skeletonization. Even if we interpret our finding as an association between facet 1 scores and structural abnormalities of the stria terminalis, rather than the fornix, this would implicate the same neural circuit. The ventral regions of the anterior temporal lobes often contain susceptibility artifacts that can lead to spurious results in TBSS analysis. However, this may not have biased results as the extent of the artefacts is unlikely to be associated with psychopathy facet scores. The tensor model used for TBSS and tractography is vulnerable to intravoxel crossing fibers. While High Angular Resolution Diffusion Imaging (HARDI) acquisition protocols and more advanced mapping techniques such as spherical deconvolution (Dell'acqua *et al.*, 2010) would have been preferable, the tensor model succeeded in accurately reconstructing the white matter skeleton (in TBSS) and the UF (for tractography). Finally, inter-rater assessment of UF dissections was not possible; however, dissections were carried out on blinded data and according to a strict protocol.

Conclusions

We report for the first time that in young adult women, both affective and lifestyle psychopathy facet scores were negatively associated with the structural integrity of white matter adjacent to the fusiform gyrus, and that interpersonal facet scores were negatively associated with integrity of the fornix and the uncinate fasciculus. Taken together, these findings are consistent with evidence of abnormalities of gray matter and functioning within limbic and paralimbic networks associated with psychopathic traits, and suggest that these findings may also apply to females.

Supplementary data

Supplementary data are available at *SCAN* online.

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