Psychopathic traits modulate microstructural integrity of right uncinate fasciculus in a community population

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A B S T R A C T

Individuals with psychopathy possess emotional and behavioral abnormalities. Two neural regions, involved in behavioral control and emotion regulation, are often implicated: amygdala and ventromedial prefrontal cortex (VMPFC). Recently, in studies using adult criminal populations, reductions in microstructural integrity of the white matter connections (i.e., uncinate fasciculus (UF)) between these two neural regions have been discovered in criminals with psychopathy, supporting the notion of neural dysfunction in the amygdala–VMPFC circuit. Here, a young adult, community sample is used to assess whether psychopathic traits modulate microstructural integrity of UF, and whether this relationship is dependent upon levels of trait anxiety, which is sometimes used to distinguish subtypes of psychopathy. Results reveal a negative association between psychopathic traits and microstructural integrity of UF, supporting previous findings. However, no moderation of the relationship by trait anxiety was discovered. Findings provide further support for the notion of altered amygdala–VMPFC connectivity in association with higher psychopathic traits.

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1. Introduction

Psychopathy is a personality disorder in which some of the defining features include being manipulative, callous, and impulsive. Despite an abundance of research, the precise neural correlates and etiology of the disorder remain unknown. The disorder is costly to society, as individuals with psychopathy continuously rotate through the criminal justice system (Hare, 1999).

Individuals with psychopathy behave in some ways that are similar to ventromedial prefrontal cortex (VMPFC) and amygdala patients, such as having a lack of empathy, poor decision-making, failure to plan ahead (Koenigs et al., 2010), and deficits in fear conditioning (Birbaumer et al., 2005), leading researchers to theorize that these two neural regions may be plausible targets for dysfunction in psychopathy. Neuroimaging studies have provided evidence for functional and structural abnormalities in the amygdala–VMPFC circuit (Glenn et al., 2009; Yang et al., 2009), although the directionality of results often depends upon population types, psychopathy cut-offs, and research methodology (Koenigs et al., 2011).

Studies examining the association between psychopathic traits and the white matter tract that connects the VMPFC to the amygdala (uncinate fasciculus; UF) reveal a negative association (Craig et al., 2009; Motzkin et al., 2011). These studies, using populations of incarcerated adults with psychopathy (age means ~30 years) reveal decreased microstructural integrity of the UF in psychopathic groups, as compared to control groups. However, whether these findings can be extended to community populations has yet to be explored. Previous studies comparing incarcerated and community samples with antisocial personality disorder found no significant differences in prefrontal deficits in antisocial individuals (Yang and Raine, 2009). The current study importantly contributes a community sample to the literature to be similarly used in comparison to the incarcerated sample data.

Another issue that has been infrequently addressed is the possibility that subtypes of psychopathy may have different neurobiological profiles. The literature suggests that subtypes of psychopathy may be parsed using low and high levels of trait anxiety, and that these subtypes differ in behavior and physiology (Karpman, 1947; Lykken, 1957; Newman and Schmitt, 1998). Further, it is theorized that low-anxious individuals with psychopathy may have greater neural abnormalities, based on reports of no behavioral differences between this subtype and certain brain lesion patients (VMPFC) on some laboratory tasks, such as economic decision-making (Koenigs et al., 2010). Thus, the question of whether subtypes can be distinguished by neural
structure, and whether low-anxious psychopathic individuals have the greatest neural abnormalities arises. Motzkin et al., (2011) published the only study to examine microstructural integrity of UF in low-anxious and high-anxious male inmates with psychopathy, and found no significant differences between the two groups. However, this study is limited by its small sample size (n = 7) and it is possible that neurobiological differences may be found with increased numbers of subjects.

In the current study, the relationship between psychopathic traits and microstructural integrity of the uncinate fasciculus, as measured with diffusion tensor imaging (DTI), was examined in a community sample of young adults with a wide range of psychopathic traits. This study contributes a novel population age range (18–21 years) to the literature, in contrast to the older adult criminal populations typically used in psychopathy research. Although much psychopathy research, particularly neuroimaging, has focused on adults with psychopathy, the construct has been validated in youth (Forth and Tobin, 1995; Brandt et al., 1997; Raine, 2002). Neuroimaging studies in youth with some psychopathic traits reveal altered microstructural integrity of UF (Passamonti et al., 2012; Sarkar et al., 2013), among functional differences in other regions (Finger et al., 2008; Marsh et al., 2008), however no clear picture has emerged of how neural differences in individuals with psychopathic traits are related in childhood, youth, or adulthood. The current study allows an examination of the time window during continued neural development in a non-incarcerated population. Additionally, we looked at neurobiological differences between sub-types of psychopathy (delineated by trait anxiety). Specifically, whether trait anxiety moderated the relationship between psychopathic traits and microstructural integrity of UF was examined. Based on previous findings, we predicted that if psychopathic traits were associated with microstructural integrity of UF, the association would be negative. Further, we predicted that if the relationship between psychopathic traits and microstructural integrity of UF were moderated by trait anxiety, then individuals with the highest scores on psychopathy, but the lowest scores on an anxiety measure would show the lowest microstructural integrity of the UF, indicating the greatest structural abnormality.

2. Methods

2.1. Participants

Twenty-four healthy males (18–21 years of age, mean ± SD = 18.9 ± 0.7) participated in the study. Only males were invited for participation, as a majority of studies have found psychopathy to be more prevalent in males than in females (Forth et al., 1990; Hamburger et al., 1996). Participants were recruited from the University of Southern California, a twin study of Risk Factors for Antisocial Behavior (RFAB). RFAB is a longitudinal study of the interplay of genetic, environmental, social, and biological factors on the development of antisocial and aggressive behavior from childhood to young adulthood. The RFAB twin study does not itself include neuroimaging of the entire sample as an assessment measure. Participating families were recruited from the Los Angeles community and the sample is representative of the ethnic and socio-economic diversity of the greater Los Angeles area (Baker et al., 2013). RFAB began assessment of twins from the general Los Angeles area in 2001, and has invited each twin pair to return every 2–3 years. The current investigation is a supplement to this larger study. This population was chosen because of available longitudinal psychopathy scores, allowing for participant selection based on previously measured psychopathic traits. Participants were invited in as singletons (i.e., only one twin per pair) in order to avoid the statistical dependency issue that exists between twins.

Invitations to participate in the study were mailed to potential participants, and a follow-up call was made 2 weeks following the mailing. Participants were told that the study was investigating the relationship between personality traits and brain function and structure. In order to ensure a wide range of scores for psychopathic traits in the analysis, we recruited half of the participants (12 participants) from the bottom quartile (0th–25th percentiles) and half (12 participants) from the top quartile (75th–100th percentiles) of a composite psychopathy score. The composite score was computed from a combination of the standardized scores for three psychopathy measures previously collected during Wave 3 of RFAB when the twins were age 14–15 years old: (1) Childhood Psychopathy Scale (CPS, youth self-report; Lynam, 1997); (2) Antisocial Process Screening Device (APSD, self-youth report; Frick and Hare, 2001); and (3) the PCL-R youth version (PCL-YV; administered and scored by trained examiners, with collateral information obtained from participants’ caregivers and participants’ interviews) (Forth et al., 1990). For PCL-YV (total scale), interrater reliability was found to be strong (rP = 0.89) and internal consistency (Cronbach’s alpha) of CPS (total) and APSD (total) were α = 0.78 and α = 0.74 (see Tuvblad et al., 2014 for an in-depth report on the measures). The rationale for making the composite score was provided by moderate to high significant correlations among the three psychopathy measures (r(509) = 0.45–0.64, p < 0.01) (see Table 1), indicating concordance among the measures. Further, a recent publication has revealed one common latent factor of psychopathic personality underlying the 3 measures used in our composite score (Tuvblad et al., 2014). Given this finding, in conjunction with the fact that we did not have a clear justification for choosing one psychopathy measure over another and did not want to increase type I error rate by running all three measures, we used the composite score.

Although the psychopathy measures were obtained during an earlier time frame, they were considered a reliable indicator of psychopathic traits in adulthood, as these traits are known to emerge early in life and remain stable through adulthood (Hare and Neumann, 2008). The distribution of the composite score for males in the entire initial RFAB sample can be seen in Fig. 1, with the final range for the current study of the 0th–25th percentiles (cut-off: z = −0.62; range: z = −0.62 to −1.51, mean ± SD = −1.02 ± 28) and the 75th–100th percentiles (cut-off: z = 0.47; range: z = 0.53–1.63, mean ± SD = .91 ± 0.35) marked by red circles.

As expected, the mean psychopathy composite differed significantly between the selected high and low groups, t(23) = −14.93, p < 0.001. All participants had at least two of the psychopathy measures completed (14 participants had all 3 measures completed). The missing scores came solely from the PCL-YV. A chi-square test determined that individuals in the lower quartile were more likely to have completed only two psychopathy measures (i.e., were missing the PCL-YV rating): χ2(2, n = 24) = 9.88, p = 0.002. Therefore, in order to ensure that group differences in total composite psychopathy scores were not being driven by the PCL-YV scores, it was tested whether differences in overall psychopathy scores remained significant after excluding PCL-YV from the analysis. A t-test between the two quartiles’ new composite scores, comprised of only APSD and CPS, revealed that composite scores of the low quartile remained significantly lower than those in the high quartile, t(23) = −6.56, p = 0.001. The two quartiles were also race-matched, and there were no significant group differences for age, gender, or socioeconomic status.

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Table 1

| Measure          | CPS-youth | APSD-youth | PCL-YV |
|------------------|-----------|------------|--------|
| CPS-youth        | 0.64†     | –          | 0.45†  |
| APSD-youth       | 0.64†     | 0.49*      | –      |
| PCL-YV           | 0.45†     |            | 0.49*  |

Notes. CPS-youth − Child Psychopathy Scale, youth report; APSD-youth = Anti-social Process Screening Device, youth report; PCL-YV = Hare Psychopathy Checklist Revised, Youth Version † p < 0.01.
t(23) = −0.74, p > 0.05, IQ (WAS-I), t(23) = 1.16, p > 0.05, or socioeconomic status, t(23) = 1.53, p > 0.05. All ethnicities were included in recruitment, except for African-Americans. This ethnic group was excluded due to the fact that the participants of the current study also participated in a separate fear conditioning study that examined skin conductance responses, and it has been reliably shown that this ethnic group exhibits lower basal skin conductance levels (higher skin resistance; Johnson and Corah, 1963; Korol and Kane, 1978), and could thus make determination of fear conditioning (from skin conductance responses) difficult in these participants. Age, SES, and composite psychopathy scores of both groups of MRI participants were comparable to those of the two quartiles in the larger RFAB potential participant pool, indicating good representation of the RFAB community-based sample (see Table 2).

All the participants were right-handed, had normal or corrected-to-normal vision, and had no neurological or psychiatric history, as assessed by a pre-experiment screening interview with all potential participants. The participants were compensated for their time. Written informed consent was obtained from all participants before inclusion in the study. The study was approved by the Institutional Review Board of the University of Southern California.

Twins do not differ from singletons on psychopathy (including Opposition Defiant Disorder, and Conduct Disorder, and antisocial behavior in general), personality, cognitive ability, academic performance, or brain development (Christensen et al., 2006; Hjern et al., 2012; Barnes and Boutwell, 2013a, 2013b; Moilanen et al., 1999; Ordaz et al., 2010; Simonoff et al., 1997; van den Oord et al., 1995). This suggests that findings from the twin samples may be generalized to the general population.

### 2.2. Behavioral procedure

In order to determine the stability of psychopathic traits over time, and to ensure the levels of high and low psychopathy in the recruited participants, the Psychopathic Personality Inventory, Revised (Lilienfeld and Andrews, 1996), a 154-item, adult self-report psychopathy measure, was administered to the scanned participants.

Similar to other studies on psychopathy subtypes the Welsh Anxiety Scale (WAS; Welsh, 1956) (Newman and Kosson, 1986; Newman et al., 1990; Kosson et al., 1990) was used to assess trait anxiety. The WAS is a 39-item, self-report scale that is derived from the MMPI (Hathaway et al., 2000). Statistical analysis of all questionnaire data was performed using Statistical Package for the Social Sciences (SPSS; version 19, SPSS, Inc., Chicago).

### 2.3. Scanning procedure

The participants were scanned at the Dana and David Dornsife Cognitive Neuroscience Imaging Center at the University of Southern California in a 3 T Siemens MAGNETOM Trio MRI scanner. All images were collected using a 32-channel head coil. A high resolution T1-weighted anatomical scan was performed on all participants’ MPRAGE; TR = 2530 ms; TE = 3.37 ms; flip angle = 7°; 256 mm FOV; 256 × 256 voxel matrix; 208 coronal slices; 1 mm isotropic voxels.

### 2.4. DTI acquisition

A 64-direction diffusion tensor imaging sequence was implemented using parallel imaging acceleration (GRAPPA), factor = 2. A total of 64 diffusion-weighted images were acquired (axial slices = 60; TR/TE = 10,000/88 ms; FOV = 256 mm; b-value = 1000 s/mm²; in-plane resolution = 2 × 2 mm²; slice thickness = 2 mm).

### 2.5. DTI analysis

Preprocessing of diffusion data was performed using FSL (FMRI’s Software Library, http://www.fmrib.ox.ac.uk/fsl). Preprocessing included: skull-stripping to remove non-brain tissue, eddy current correction, head movement correction, and realignment of diffusion-weighted data using the mean of the b0 volumes as a reference. Diffusion tensor calculation and tracking were performed with Diffusion Toolkit 0.6.1 and TrackVis 0.5.1 (http://trackvis.org). Tracts were reconstructed by using a fiber assignment by continuous tracking (FACT) algorithm and an angular threshold of 35°. A DWI (diffusion-weighted image) mask was used to remove CSF, and an FA threshold of 0.02 was used for tract reconstruction. Tracts were isolated in all subjects by a research assistant who was blind to the psychopathy score. The manual “obligatory passage” two-ROI approach (Catani and Thiebaut de Schotten, 2008) was used to isolate the fibers of the UF. With this method, one ROI was drawn in the anterior temporal lobe, with the other being defined around the white matter of the anterior floor of the external/ extreme capsule. Each resulting set of tracts was edited by exclusion ROIs to ensure that tracts reliably represented the characteristic “c” shape of UF fibers, see Fig. 2 (Wakana et al., 2007).

To isolate the inferior longitudinal fasciculus (ILF) as a control tract, a third ROI was drawn in the occipital lobes according to a previously detailed procedure (Catani, 2008). Briefly, an ROI was drawn in the occipital lobes on 13–15 axial slices, and ILF was defined as tracts that only pass through both the occipital and temporal ROIs, see Fig. 3.
ROIs were drawn on the participant’s high resolution T1 anatomical scan for more precise accuracy. The T1-weighted scan was manually virtually aligned with the participant’s b0 image using FSL’s Nudge. After virtual alignment, FSL’s FLIRT (Jenkinson et al., 2002) was used to register the T1 image to diffusion space using an affine registration with 12 degrees of freedom. Using the tracts derived from the ROI masking, FA values for the UF from both hemispheres were calculated by averaging the FA values of all voxels of the tract.

The relationship between psychopathic traits (composite psychopathy score, PPI) and UF values was first assessed using correlation analyses. To test whether trait anxiety moderated the relationship between amygdala–VMPFC microstructural integrity and psychopathic traits, the FA values were used as the dependent variable in multiple regression analyses in SPSS (Release Version 18.0, SPSS®., Inc., 2009, Chicago, IL, http://www.spss.com). In the multiple regression model, psychopathic traits (composite psychopathy score, PPI), trait anxiety (WAS), and an interaction term of psychopathic trait scores and trait anxiety scores were used as predictors. The interaction term investigates whether the correlation between psychopathic trait scores and FA values of the UF is dependent upon trait anxiety levels. We note that a recent fMRI study showed that fMRI between-group studies that included less than 10 individuals per group were susceptible to false positive results due to high levels of intersubject variability in fMRI results (Bhaumik et al., 2009). Given that dividing our sample into 4 groups would yield 4–8 subjects per group, we chose to run a correlation analysis rather than a group design.

Lastly, correlation analyses were performed to investigate whether any one of the youth psychopathy measures that comprised the composite score could better predict the FA values of UF.

**3. Results**

**3.1. Sample characteristics**

Means, standard deviations, and correlations between trait anxiety and total psychopathy measures for the sample are shown in Table 3. Total PPI scores (mean ± SD = 286.72 ± 34.3; α = 0.89) were comparable to the total PPI scores for males aged 18–24 years from the community/college samples (Lilienfeld; mean = 301.06). Means for the WAS scores (mean ± SD = 11.38 ± 8.72) were comparable to those previously reported for non-clinical samples of adult males (Mean = 10.5; Colligan and Offord, 1988).

The PPI and the composite psychopathy score were moderately correlated (r(22) = 0.35), with a trend toward significance (p = 0.09). However, a closer inspection of the scores revealed that two individuals had switched their pattern of psychopathic traits: one person switched from a low to high score, and one person switched from a high to low score. When these individuals were removed from the correlation analysis, PPI and the composite psychopathy scores were strongly significantly correlated (r(20) = 0.68, p < 0.001). The two individuals were included in all subsequent analyses as they were not deemed outliers in their respective measures. Importantly, neither of the psychopathy measures was correlated with trait anxiety.

**3.2. DTI results**

Left and right UF ROIs were used to extract mean FA values to assess whether they are modulated by psychopathic traits in the community sample. Parallel correlation analyses were used for the two psychopathy measures (composite psychopathy scale, PPI) with the left and right FA values of the UF. The composite psychopathy score was found to be negatively correlated with FA values of the right UF, r(23) = −0.52, p < 0.01 (see Fig. 4). No significant correlations were found for the PPI.

Given that the composite psychopathy score and total PPI score are more strongly correlated when the two individuals who switched levels of psychopathy are removed, a second exploratory correlation was run between the right UF values and total PPI score after removing these two subjects. In this case, the total PPI score and right UF also showed a significantly negative correlation, r(21) = −0.43, p < 0.05 (Fig. 5), while the original correlation between composite psychopathy score and right UF remained significant, r(21) = −0.40, p < 0.05.

Psychopathic traits were not correlated with FA values from the left or right IL (with or without the two individuals who switched psychopathy levels), indicating that differences in microstructural integrity associated with psychopathic traits do not extend to all white matter tracts of the brain.

In order to assess whether trait anxiety would moderate the relationship between FA values of the UF and psychopathic traits, multiple regression models were conducted. The FA values of the left and right UF were used as dependent variables in separate multiple regression analyses, with psychopathic traits (composite psychopathy score, PPI) and trait anxiety (WAS) as predictors. None of the regression models were significant.

| Table 3 | Descriptive statistics and correlations for trait anxiety and psychopathy measures. |
|---------|---------------------------------------------------------|
| n       | Mean | SD | Correlations
| PPI     | Comp-P | WAS |
| PPI     | 24    | 287.5 | 34.8 | − .35 | −0.08 |
| Comp-P  | 24    | −0.05 | 1     | −     | −0.01 |
| WAS     | 24    | 11.38 | 8.72  | −     | −     |

Fig. 2. Example of a reconstructed uncinate fasciculus (UF) tract using diffusion tensor imaging.

Fig. 3. Example of a reconstructed inferior longitudinal fasciculus (ILF).
4. Discussion

In accordance with psychopathy literature, a negative correlation was observed between psychopathic traits and microstructural integrity (indexed by the FA value) of the right uncinate fasciculus (UF), the white matter tract connecting the amygdala and ventromedial prefrontal cortex. Furthermore, the possible anatomical specificity of the finding was supported by the fact that psychopathic traits did not modulate the control tract (inferior longitudinal fasciculus).

As mentioned previously, the current study contributes a novel age range of participants (18–21 years) to the literature on psychopathy. This provides the opportunity to examine the unique window of neural development, which has been identified as a period of continued prefrontal growth and pruning (Bourgeois et al., 1994; Gogtay et al., 2004; Huttenlocher, 1979; Zecovic and Rakic, 2001). Results indicate that with increases in psychopathic traits, the microstructural integrity profiles of young adults resemble that of adults with psychopathy. The best way to assess the neural development in relation to psychopathic traits would be, of course, to use a longitudinal experimental design, which future studies can address.

The current study differs from previous studies in that a community sample is utilized, rather than offender samples. Our results extend previous findings by demonstrating a negative relationship between psychopathic traits and microstructural integrity of UF in a non-incarcerated population. They suggest, once more, that to understand the neurobiological underpinnings of psychopathy, it is important to investigate both incarcerated and non-incarcerated populations, as they are qualitatively different and can provide unique insights to the development of this personality disorder (Raine, 1993).

The current study also adds to previous knowledge by demonstrating that psychopathy scores in younger subjects can be used to predict microstructural integrity of UF in young adulthood, and that some psychopathy measures are better than others at this type of prediction. Some amount of variation in scores should be expected over time, and was observed in the current sample in the two individuals who switched levels of psychopathic traits between adolescent and adult psychopathy assessments. However, when the two individuals are removed from the analysis, the negative relationship between total adult psychopathy score (indexed by the total PPI score) and microstructural integrity of UF is maintained. We note that this latter analysis is strictly exploratory, however, and more research is needed to explore the relationship between adult psychopathy scores and UF microstructural integrity, especially with much larger sample sizes.

4.1. Role of trait anxiety

The relationship between psychopathic traits and microstructural integrity of UF was not moderated by trait anxiety in the current study, counter to our predictions. Motzkin et al. (2011) also investigated differences in microstructural integrity of UF between subtypes of psychopathy in offenders based on trait anxiety, but did not find significant differences between low-anxious and high-anxious offenders with psychopathy. Thus, although trait anxiety has been demonstrated to interact with psychopathic traits to predict amygdala–VMPFC function (Sobhani et al., in submission) and functional connectivity (Motzkin et al., 2011), it is possible that trait anxiety does not moderate the relationship between amygdala–VMPFC structural connectivity and psychopathic traits. However, it should also be noted that the offender study (Motzkin et al., 2011) utilized a small sample size of only 7 individuals per group, and that the current study is limited by both a small sample size and not including individuals with extremely high scores of psychopathy. Thus, the interpretation of results for both studies is limited. It is possible that larger sample sizes and the inclusion of subjects with higher psychopathy scores may reveal the moderating effect of trait anxiety on psychopathic traits and neural structure. Alternatively, it may be that other neural structures and pathways, not explored in the current study, are more strongly predictive of psychopathic subtypes.

The normal developmental trajectory of the uncinate fasciculus begins with increasing fractional anisotropy (FA) values in early childhood and continues through adolescence and young adulthood (Lebel et al., 2008; Mabbott et al., 2009; Mukherjee and McKinstry, 2006), and declines after young adulthood (Lebel et al., 2010). Factors such as premature birth (Constable et al., 2008) and early socio-emotional deprivation have been shown to be associated with reduced FA values of UF (Eluvathingal et al., 2006). Given the role of the amygdala–VMPFC connections in emotion regulation and behavioral control, it is plausible that disruption of this pathway early in life results in increased antisocial behavior and affective deficits. Future studies that examine differences in upbringing and early childhood experience could help explain microstructural integrity differences in the UF, and parse how these relate to psychopathic traits.

A few limitations of the present study should be noted. The FA values are determined by multiple neuronal properties and should be considered an indirect measure of "microstructural integrity". Multiple factors contribute to the FA value, such as degree of myelination and cellular arrangement around axons (Assaf and Pasternak, 2008), thus it is difficult to say for certain what the specific cause of a difference in FA value is. However, while the underlying cellular mechanisms may remain

Fig. 4. Psychopathy scores from ages 14–16 negatively correlate with right uncinate fasciculus fractional anisotropy (FA) values. PsychoComp = composite psychopathy score. \( r(23) = -0.52, p < 0.01 \).

Fig. 5. Adult psychopathy scores negatively correlate with the right uncinate fasciculus fractional anisotropy (FA) values when psychopathy score switchers are removed. PPI = psychopathic personality inventory. \( r(21) = -0.43, p < 0.05 \).
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