Differential Relations Between Juvenile Psychopathic Traits and Resting State Network Connectivity

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Abstract: Traditionally, neurobiological research on psychopathy has focused on categorical differences in adults. However, there is evidence that psychopathy is best described by a set of relatively independent personality dimensions, that is, callous-unemotional, grandiose-manipulative, and impulsive-irresponsible traits, which can be reliably detected in juveniles, allowing investigation of the neural mechanisms leading to psychopathy. Furthermore, complex psychiatric disorders like psychopathy are increasingly being conceptualized as disorders of brain networks. The intrinsic organization of the brain in such networks is reflected by coherent fluctuations in resting state networks (RSNs), but these have not been studied in sufficient detail in relation to juvenile psychopathic traits yet. The current study investigated the distinct associations of juvenile psychopathic traits dimensions with RSN connectivity. Resting-state functional MRI and independent component analysis were used to assess RSN connectivity in a large sample of adolescents ($n = 130$, mean age 17.8 years) from a childhood arrestee cohort. Associations between scores on each of the three psychopathic traits dimensions and connectivity within and between relevant RSNs were investigated. Callous-unemotional traits were related to aberrant connectivity patterns of the default mode network, which has been implicated in self-

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referential and moral processes. Impulsive-irresponsible traits were associated with altered connectivity patterns in the frontoparietal cognitive control networks. Grandiose-manipulative traits were not associated with altered connectivity patterns. These findings confirm the association between psychopathic traits and brain network connectivity, and considerably add to emerging evidence supporting neurobiological heterogeneity in the processes leading to psychopathy. *Hum Brain Mapp* 36:2396–2405, 2015. © 2015 Wiley Periodicals, Inc.

Key words: resting state; psychopathy; personality disorders; functional MRI; functional connectivity; child psychiatry

INTRODUCTION

Psychopathy is characterized by severe antisocial behavior and pathological personality traits, such as emotional callousness and a narcissistic and manipulative interpersonal style [Hare and Neumann, 2009]. While the study of psychopathy has mainly focused on adult offenders in the past, this construct is increasingly being studied in juvenile offender and general population samples, resulting in its inclusion as a specifier to conduct disorder (CD) in the DSM-5 (limited prosocial emotions). The main reasons for the increased interest in juvenile psychopathy are its predictive validity for future antisocial behavior and its relevance to treatment [Frick and White, 2008], its potential for early and more successful intervention [Salekin et al., 2010], its high heritability [Viding et al., 2008], and its presumed neurobiological specificity [Viding et al., 2012]. These latter aspects, combined with evidence for a cross-diagnostic [Herpers et al., 2012] and dimensional [Edens et al., 2006] distribution of psychopathic traits in the population, converge with the NIMH Research Domain Criteria (RDoC) initiative to enhance psychiatry research translatability by focusing on “dimensions of observable behavior and neurobiological measures” [Cuthbert and Insel, 2013]. As such, investigating the neural correlates of juvenile psychopathic traits is likely to enhance our understanding of the pathophysiological processes underlying antisocial development and, ultimately, may aid in developing interventions aimed at these mechanisms.

A number of studies have investigated the neural correlates of juvenile precursors of psychopathy [Finger et al., 2008; Jones et al., 2009; Marsh et al., 2011, 2008]. Most of these neuroimaging studies investigated psychopathy as a categorical or unidimensional construct, or focused on callous-unemotional traits only. However, an increasing body of literature now supports the notion of psychopathy as a multidimensional construct, consisting of callous-unemotional, grandiose-manipulative, and impulsive-irresponsible traits that show differential associations with criterion variables in the behavioral [Patrick et al., 2005] and neurobiological [Patrick, 1994] domain. Subsequently, recent task-related functional magnetic resonance imaging (fMRI) studies in adults [Carré et al., 2013] and juveniles [Sebastian et al., 2012] have started to uncover the distinct

neural correlates of these dimensions. Callous-unemotional traits have been associated with hypoactivity of the amygdala, insula, anterior cingulate cortex (ACC), and posterior cingulate cortex (PCC) [Sebastian et al., 2012; White et al., 2012a,b, 2013]. Grandiose-manipulative traits have been associated with hypoactivity of the amygdala as well, whereas impulsive-irresponsible traits have been related to hyperactivity of the amygdala and ACC [Carré et al., 2013; Cohn et al., 2013].

While some of these findings indicate dysfunction of specific regions, such as the amygdala [Jones et al., 2009; Marsh et al., 2008; Viding et al., 2012; White et al., 2012a] a different strand of studies provides evidence for more widespread neural abnormalities in youths and adults with psychopathic traits [Kiehl, 2006]. These latter findings converge with one of the primary RDoC assumptions, that is, that mental disorders are likely to be disorders of brain circuits rather than brain regions [Insel et al., 2010]. One way to investigate such network-accounts of psychopathology is the study of coherent spontaneous fluctuations in the resting brain (resting-state functional connectivity [RSFC]), which are organized in distinct Resting State Networks (RSNs). RSNs are relatively stable across participants and time [Damoiseaux et al., 2006] and show strong spatial overlap with well-known functional networks involved in specific cognitive functions [Laird et al., 2011; Smith et al., 2009]. Moreover, connectivity in RSNs is related to performance on cognitive tasks [Damoiseaux et al., 2008] and to the presence of psychiatric disorders [Greicius, 2008]. Studying RSFC in relation to psychopathic traits may not only reflect their associations with the intrinsic network organization but may also provide additional validity, as it is less sensitive to attentional and motivational fluctuations, which have been reported in antisocial populations [Bjork et al., 2010; Newman et al., 2010].

Certain RSNs may carry special relevance for psychopathy. First, the default mode network (DMN), which consists mainly of the PCC and precuneus, the inferior parietal cortices, and dorsal and ventral areas of the medial prefrontal cortex, has been linked to self-referential and moral processing [Harrison et al., 2008]. Second, the salience network (SN), which consists of the ACC, anterior insula, amygdala, and dorsolateral prefrontal cortex, is

involved in salience processing and emotional responsiveness [Seeley et al., 2007]. Notably, both theoretical models of psychopathy [Blair, 2008] and results of task-related fMRI studies in juveniles [Juarez et al., 2013] have suggested psychopathic traits-related dysfunctions in these RSNs. Third, given neuropsychological evidence for executive dysfunctions [De Brito et al., 2009] and atypical task-related frontoparietal network function [Juarez et al., 2013] in psychopathy, frontal networks involved in executive function may also be relevant to the study of juvenile psychopathic traits. As several RSNs have been implicated in psychopathy, and preliminary evidence suggests distinct relations between psychopathy dimensions and specific RSN functionalities (e.g., executive dysfunctions are most strongly associated with the impulsive-antisocial facet of psychopathy [Ross et al., 2007]), investigating the differential neurobiological mechanisms underlying these dimensions in the brain's intrinsic functional architecture is warranted.

Until now there have been two studies investigating RSFC in adult psychopaths versus healthy controls, showing atypical connectivity in regions implicated in the DMN and SN [Motzkin et al., 2011; Pujol et al., 2012]. However, these studies are not informative with respect to the relation between specific RSNs and distinct dimensions of psychopathic traits. Moreover, brain dysfunctions in adult psychopaths may be heavily influenced by chronic substance abuse [Blair, 2004] or other aspects of an antisocial lifestyle, warranting their investigation in juveniles. In this respect, Shannon et al. [2011] showed that, in a sample of incarcerated juveniles, impulsivity was related to increased RSFC between motor planning regions and the DMN, and to decreased RSFC between motor planning regions and the SN and a dorsal attention network (DAN). While this study provides an important contribution to the previously mentioned studies in adults, several additional issues need to be addressed. First, the generalizability of these results to psychopathic traits in typical antisocial or community samples is limited by the inclusion of incarcerated subjects only. Second, and more importantly, none of the previous RSFC studies have assessed connectivity within and between specific RSNs, in relation to psychopathic traits, complicating their interpretability in the context of RSN function. Independent Component Analysis (ICA) is increasingly applied to assess RSN functional connectivity, since it takes into account the influence of all other RSNs as well as noise due to movement and cardiorespiratory cycles, allowing RSN-specific interpretations of connectivity. Moreover, connectivity within and between ICA-derived networks can be used to investigate the integration and segregation of RSN function, which are both essential for complex network and brain function [Tononi et al., 1998]. While within-network connectivity indexes the extent to which brain regions are recruited in the context of a specific RSN, between-network connectivity is a measure of the integration/ segregation of different RSNs.

Therefore, the aim of this study is to examine the associations of connectivity within and between ICA-derived RSNs with a multidimensional measure of psychopathic traits in a large representative at-risk sample of adolescents from a childhood arrestee cohort [Cohn et al., 2012; van Domburgh et al., 2009]. In contrast to most previous studies, this sample captures the entire distribution of psychopathic traits in the population, from healthy to severely impaired. We focus our analyses on the DMN and SN, since these have been most strongly implicated in previous task-related and RSFC studies, as well as in theories on the development of psychopathy. Additionally, as this is the first study in the field of psychopathy research using ICA in such a large sample of juveniles, we perform exploratory analyses on the associations between psychopathic traits dimensions and connectivity within and between other frontal RSNs, relevant to a range of executive functions, given preliminary evidence for such associations [Juarez et al., 2013; Shannon et al., 2011].

METHODS

Subjects and Procedure

A total of 150 participants (17.6 years, SD 1.7) were recruited from a cohort of 364 adolescents who were first arrested by the police before the age of 12 and had already participated in three previous waves of this longitudinal study: mean age at study entrance was 10.8 (SD 1.5) and at wave three 12.9 (SD 1.5) [van Domburgh et al., 2009]. The dimensional distribution of psychopathic traits, capturing its entire severity range, was ensured by recruiting low-risk (those without a Disruptive Behavior Disorder [DBD]; Oppositional Defiant Disorder [ODD], or CD) diagnosis on the three previous waves' Diagnostic Interview Schedule for Children version IV [DISC-IV], and all previous waves' aggression (Reactive Proactive Aggression Questionnaire [RPQ]) and callous-unemotional traits (Youth Psychopathic Traits Inventory [YPI], callous-unemotional subscale) scores below median, including 37 out of the original $n = 110$, medium-risk (those with above-median previous waves aggression [RPQ] and callous-unemotional traits [YPI] scores but no previous diagnosis of DBD [DISC-IV], including 57 out of the original $n = 174$) as well as high-risk participants (those with a previous DBD diagnosis on the DISC-IV; including 56 out of the original $n = 80$). See Table I for sociodemographic and clinical characteristics).

From the 150 subjects participating in the neuroimaging protocol, 20 were excluded because of missing data ($n = 3$) or excessive head motion ($n = 17$). Excessive head motion was defined as more than 6 mm total translational movement in any direction ($n = 15$), equal to the threshold used in the recent influential methodological RSFC study by Allen et al. [2011]. Moreover, because recent reports have stressed the negative influence of movement on the reliability of resting-state measurements [van Dijk et al., 2012]

TABLE I. Sample characteristics (n = 130)

Male gender, no. (%)	111 (85.4)
Low SES neighborhood, no. (%)	44 (33.6)
Non-Western ethnicity, no. (%)	35 (27.1)
Age, mean $\pm$ SD (range)	17.8 $\pm$ 1.41 (12–20)
IQ, mean $\pm$ SD (range)	91.7 $\pm$ 12.8 (59–128)
RPQ Aggression, mean $\pm$ SD (range)	8.48 $\pm$ 4.68 (0–20)
CBCL Internalizing, mean	50.8 $\pm$ 10.8 (33–77)
T-score $\pm$ SD (range)	
YSR Internalizing, mean	47.9 $\pm$ 10.3 (30–75)
T-score $\pm$ SD (range)	
CBCL Externalizing, mean	51.6 $\pm$ 11.3 (34–78)
T-score $\pm$ SD (range)	
YSR Externalizing, mean	52.6 $\pm$ 9.94 (34–77)
T-score $\pm$ SD (range)	
ADHD no. (%)	45 (30.0)
DBD no. (%)	38 (25.4)
PTSD no. (%)	2 (1.5)
YPI Callous-Unemotional, mean $\pm$ SD (range)	24.4 $\pm$ 7.15 (15–55)
YPI Grandiose-Manipulative, mean $\pm$ SD (range)	30.4 $\pm$ 8.77 (20–61)
YPI Impulsive-Irresponsible, mean $\pm$ SD (range)	28.3 $\pm$ 7.54 (13–47)
YPI total Psychopathic traits, mean $\pm$ SD (range)	83.1 $\pm$ 19.5 (50–157)

Abbreviations: SES: Socioeconomic status, RPQ: Reactive Proactive aggression Questionnaire, ADHD: Attention Deficit/Hyperactivity Disorder, DBD: Disruptive Behavior Disorders, PTSD: Post-Traumatic Stress Disorder, CBCL: Child Behavior Checklist, YSR: Youth Self Report, YPI: Youth Psychopathic traits Inventory.

we additionally excluded all subjects with excessive rotation ($n = 3$; more than 10 degrees total rotation around any axis). This yielded a final sample of 130 participants, who did not differ from the excluded group on socioeconomic status, ethnicity, psychopathic traits, or aggression but were significantly older (mean age 17.8, SD 1.4 vs. 16.0, SD 2.2; $t_{21.5} = 3.7$, $P = 0.001$).

The study was approved by the VU University medical center Amsterdam Institutional Research Board. After recruitment, all participants (and their parents/custodians, if age of the participant was below 18) signed for informed consent and were visited at home for a structured psychiatric interview and questionnaires. On a separate occasion, participants completed an MRI protocol including a resting-state fMRI scan (average time until MRI 25, SD 21, range 0–135 days).

Clinical Assessments

The YPI is a valid and reliable 50-item self-report instrument that was developed to study personality traits associated with adult psychopathy in juvenile community samples [Andershed et al., 2007]. To ensure that all participants were able to understand the questions, the Dutch child version of the YPI was used [van Baardewijk et al., 2008]. In the current study, internal consistency (Cronbach's

α) of the total score and its constituting dimensions were excellent (all $\alpha > 0.88$). The three psychopathy dimensions were significantly correlated ($r = 0.48$ – 0.58). See Supporting Information for complete assessment details, including psychometric measures obtained for descriptive purposes.

Imaging Assessments and Statistical Analyses

FMRI data acquisition

Participants were scanned using a Philips 3T Intera MRI-scanner at the Academic Medical Center in Amsterdam. First, T1 weighted anatomical scans were acquired using an 8-channel SENSE head-coil and consisting of 180 sagittal 1 mm slices, with an in-plane resolution of 0.5×0.5 mm (FOV $256 \times 256 \times 180$ mm, TR 9.0 ms, TE 3.5 ms). Then, 204 T2* weighted echo-planar images were acquired during resting state, each volume consisting of 38 ascending slices of 3 mm and 2.29×2.29 in-plane resolution, parallel to the anterior–posterior commissure line (FOV $220 \times 220 \times 114$ mm, TR 2300 ms, TE 30 ms). Participants were instructed to lie still with eyes closed, not to fall asleep and not to think of anything in particular. Lights were dimmed during the resting-state scan.

FMRI preprocessing

FMRI data were processed using SPM8 for MATLAB (<http://www.fil.ion.ucl.ac.uk/spm>). Preprocessing included spatial realignment, unwarping, slice-time correction, spatial normalization into standard Montreal Neurological Institute (MNI) space based on the segmented anatomical scan, and spatially smoothing with an 8 mm full width half-maximum Gaussian kernel.

Independent component analyses

Spatial group-ICA was conducted for all participants using the GIFT software (<http://icab.sourceforge.net>, version 1.3i). Typical [Allen et al., 2011] preprocessing steps were performed (i.e., intensity normalization, dimensionality reduction using principal component analysis, component estimation using Infomax [Bell and Sejnowski, 1995], and back-reconstruction using GICA3 [Erhardt et al., 2011]; see Supporting Information for complete details).

This procedure yielded 26 components with high stability (all ICASSO [Himberg et al., 2004] values > 0.85), which were classified based on visual inspection of the mean component maps and their average power spectra. Twelve non-RSN components were discarded from further analyses, as they were dominated by relatively high frequencies, showed overlap with known white matter structures or ventricles, or reflected vascular, motion, or susceptibility artifacts. Of the remaining 14 components, we selected eight components of interest: (1) the main (anterior) DMN component (aDMN), (2) a posterior DMN component (pDMN), as well as (3) the SN through comparison with

Figure 1.

Within-network connectivity. Callous-unemotional traits were related to higher connectivity within the aDMN in a cluster of five voxels in the lateral frontopolar cortex ($x = -20$, $y = 62$, $z = 22$, $t_{128} = 5.54$, Cohen's $d = 0.98$, $p_{\text{FWE-SVC}} = 0.003$). (a) Spatial map of the aDMN and the location of the significant cluster

in blue (thresholded at $P < 0.001$ uncorrected for display purposes). (b) Scatterplot displaying the correlation between predicted response for the peak voxel in arbitrary units and callous-unemotional traits. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

spatial maps reported in other resting-state papers [Beckmann et al., 2005; Damoiseaux et al., 2006; Shannon et al., 2011]. We also selected other components with potential relevance for executive functioning (i.e., excluding sensory and somatomotor networks), including (4) the DAN, (5, 6) the right and left lateralized frontoparietal networks (rFPN, IFPN), (7) the inferior frontal network (IFN), and (8) a supplementary motor network (SMN). For a more detailed description of these components, see Supporting Information Figure S1 and Table S1.

Within-network connectivity

We performed three separate voxel-wise regression analyses on the spatial maps of each RSN to evaluate the relation between the three psychopathic traits dimensions (callous-unemotional, grandiose-manipulative, and impul-

sive-irresponsible) and the extent to which each voxel is correlated with the selected RSN. Analyses were thresholded using small volume correction (SVC) for multiple voxel-wise comparisons within the component mask (thresholded at Family Wise Error [FWE] corrected $p_{\text{FWE}} < 0.05$ at $p_{\text{FWE-SVC}} < 0.006$ ($=0.05/8$, i.e., using additional Bonferroni correction for the number of selected RSNs). Whole brain FWE-corrected analyses were performed to ensure that significant associations outside the mask would not be missed. For exploratory purposes, we also report results at the commonly used threshold of $p_{\text{FWE-SVC}} < 0.05$.

Between-network connectivity

In addition to within-network connectivity, we also examined functional relationships between different RSNs by calculating correlations between mean component time-

TABLE II. Within-network connectivity results ($n = 130$)

								Corrected for age, IQ and motion
RSN	Uncorrected							
	Region	t ₁₂₈ (p _{FWE})	k	x	y	z	t ₁₂₄ (p _{FWE})	
aDMN	CU	FPC	5.54 (0.003)**	87	−20	62	22	5.62 (0.002)**
rFPN	II	IFG	4.95 (0.021) ^a	121	−48	36	16	4.58 (0.079)
SN	II	Amy	4.74 (0.050) ^a	36	−20	6	−20	4.23 (0.270)

Summary of relations of within-RSN connectivity and callous-unemotional (CU), impulsive-irresponsible (II), and grandiose-manipulative (GM) traits. Both results corrected for IQ, age and motion and uncorrected results are shown. k: number of voxels in cluster, RSN: resting state network, aDMN: anterior default mode network, rFPN: right-lateralized frontoparietal network, SN: salience network, FPC: frontopolar cortex, IFG: inferior frontal gyrus, Amy: amygdala.

^a $P < 0.05$, ** $P < 0.006$.

courses (see Supporting Information) and examining their (i.e., between-network correlations) relationships with distinct psychopathic traits dimensions. Separate linear regression analyses were conducted for all between-network correlations significant at the whole-group level with the three psychopathy dimensions as independent variables and correlation values as dependent variables. To correct for multiple comparisons, results were thresholded at $P < 0.0035$ ($= 0.05/24^{(1-0.16)} = \alpha/k^{(1-r)}$, where k is the number of outcome variables and r their mean correlation, that is, adjusted Bonferroni-correction, taking into account their mean correlation) to control the overall false-positive rate at $\alpha = 0.05$ for each analysis [Li et al., 2014]. Again, results meeting the commonly used $P < 0.05$, but not the Bonferroni-adjusted $P < 0.0035$ threshold are also reported for exploratory purposes.

Post hoc analyses

We performed post hoc analyses for both within- and between-network connectivity to control for the effects of age, IQ (block-design and vocabulary subtests of the Wechsler Intelligence Scale for Children) [Wechsler, 1974] and motion, by adding four covariates to the models (age, IQ, log-transformed root-mean-squared translation, and rotation parameters). As sex did not interact with psychopathic traits in the prediction of within and between-network connectivity, main effects of psychopathic traits for the total sample will be reported.

RESULTS

Sample Characteristics

Table I shows that our sample was characterized by low socioeconomic status and a lower than average IQ. Thirty percent of the sample met criteria for a DSM-IV diagnosis of ADHD, and 25% for either ODD or CD. Consistent with the sample's broad range of conduct problem severity, mean YPI scores were moderately high, and ranged from almost zero to severe (157 of 192).

Within-Network Connectivity

Psychopathy-related intensity differences of the spatial maps, representing the extent to which regions' connectivity within an RSN are associated with psychopathic traits, are depicted in Figure 1 and Table II. Only one finding survived stringent correction at a Bonferroni-corrected threshold of $\alpha_{FWE} = 0.006$: callous-unemotional traits were positively associated with connectivity within the anterior DMN (aDMN), in the lateral frontopolar cortex.

At a less conservative threshold (at a typical $\alpha_{FWE} = 0.05$), impulsive-irresponsible traits were related to higher connectivity in the left inferior frontal gyrus within the right frontoparietal network (rFPN). Furthermore, in the

Figure 2.

Between-network connectivity. Connectivity between the left frontoparietal network (IFPN) and the inferior frontal network (IFN) was positively associated with impulsive irresponsible traits. **(a)** Correlation matrix depicting mean between-network connectivity values (Pearson's r ; $n = 130$). **(b)** Spatial maps of the IFPN and IFN and their average correlation (r_{avg}), thresholded at $T > 20$ and overlaid on a standard anatomical template. **(c)** Scatterplot displaying the correlation between functional network connectivity (FNC) of the IFPN and IFN and impulsive-irresponsible traits (Pearson's r). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE III. Between-network connectivity results

RSN-combination		Uncorrected		Corrected for age, IQ and motion	
		Pearson's <i>r</i>	<i>P</i> -value	Partial <i>r</i>	<i>P</i> -value
pDMN-SMN	CU	-0.198	0.024 ^a	-0.180	0.044 ^a
IFPN-IFN	II	0.280	0.001**	0.270	0.002**
aDMN-rFPN	II	0.183	0.037 ^a	0.151	0.091
SMN-IFPN	II	0.197	0.025 ^a	0.164	0.067
pDMN-rFPN	GM	0.222	0.011 ^a	0.258	0.004 ^a

Summary of correlations between RSNs and callous-unemotional (CU), impulsive-irresponsible (II) and grandiose-manipulative (GM) traits. Both results corrected for IQ, age and motion and uncorrected results are shown. pDMN: posterior default mode network, SMN: supplementary motor network, IFPN: left frontoparietal network, IFN: inferior frontal network, aDMN: anterior default mode network, rFPN: right frontoparietal network.

^a*P*-value < uncorrected α , ***P*-value < adjusted α , corrected for multiple comparisons.

SN, impulsive-irresponsible traits were related to lower connectivity in the left amygdala.

Post hoc correction for age, IQ, and motion did not change the significance of the aDMN finding, but lowered the significance of the rFPN ($p_{\text{FWE-SVC}} = 0.079$) and SN findings ($p_{\text{FWE-SVC}} = 0.30$). Grandiose-manipulative traits were not related to within-RSN connectivity.

Between-Network Connectivity

Mean correlations between component time-courses, representing the connectivity between the selected RSNs, were computed (Fig. 2). Subsequently, the correlation between psychopathic traits dimensions and connectivity between each component-pair was calculated. Again, only one finding survived correction for multiple comparison at a Bonferroni-corrected threshold of $\alpha = 0.0035$: impulsive-irresponsible traits were associated with higher connectivity between the left frontoparietal network (IFPN) and the IFN ($r = 0.28$, $P = 0.001$).

At a less conservative threshold ($\alpha = 0.05$), impulsive-irresponsible traits were also related to higher connectivity between rFPN and aDMN ($r = 0.18$), as well as between IFPN and SMN ($r = 0.20$). Grandiose-manipulative traits were associated with higher connectivity between rFPN and posterior DMN (pDMN; $r = 0.22$), while callous-unemotional traits were associated with lower connectivity between pDMN and SMN; ($r = -0.20$).

Post hoc correction for age, IQ and motion lowered the significance of the relations between impulsive-irresponsible traits and higher connectivity between the rFPN and aDMN (partial $r = 0.15$, $P = 0.091$) and IFPN and SMN (partial $r = 0.16$, $P = 0.067$; see Table III).

DISCUSSION

This study investigated the association between dimensions of psychopathic traits and RSFC within and between RSNs in a representative at-risk sample of adolescents

from a cohort of childhood arrestees. First, our results showed that callous-unemotional traits were related to higher within-network connectivity in the DMN in the frontopolar cortex, whereas impulsive-irresponsible traits were related to higher connectivity between the IFPN and IFN. At a more liberal threshold, we found evidence for more widespread differences in connectivity in both the DMN in relation to callous-unemotional traits, as well as in the lateralized frontoparietal networks in relation to impulsive-irresponsible traits. These findings suggest that, first, psychopathic traits are associated with the level of connectivity within and between RSNs, thus reflecting specifically intrinsic functional organizations of the brain. Second, although there were substantial correlations between the three dimensions, our findings suggest that psychopathic traits dimensions represent neurobiologically distinct processes, consistent with multiple-process accounts of psychopathy [Fowles and Dindo, 2009].

Although our results are consistent with previous studies in suggesting a relation between psychopathic traits and connectivity in the DMN [Motzkin et al., 2011; Pujol et al., 2012; Shannon et al., 2011], our overall pattern of results is somewhat different. Whereas previous studies have reported *decreased* connectivity between the anterior and posterior regions within the DMN in psychopathy [Motzkin et al., 2011; Pujol et al., 2012], we found a positive correlation between within-network connectivity of the lateral frontopolar cortex in the DMN and callous-unemotional traits. However, post hoc analyses provided preliminary evidence that our hyperconnectivity finding was mainly due to local hyperconnectivity within the anterior part of the DMN (see Supporting Information)—as opposed to anterior-posterior long-range connectivity—and is, therefore, not necessarily incompatible with the results of previous studies. Differences in study outcomes may also be due to differences in the method used to assess RSN connectivity (ICA in our study vs. seed-based correlations in previous studies). Alternatively, these findings may represent age-specific manifestations of psychopathic traits, similar to

previous studies in antisocial youths showing effects opposite to those identified in their adult counterparts, both with respect to structural connectivity [Passamonti et al., 2012; Sarkar et al., 2013], and brain volume [De Brito et al., 2009]. One may speculate that differences in the functional organization of the DMN carry relevance for the supposed moral reasoning impairments in psychopaths [Pujol et al., 2012]. The frontopolar cortex and DMN have both been implicated in moral reasoning [Harrison et al., 2008] while higher recruitment of the lateral frontopolar region could be interpreted as conveying higher cognitive control [Gilbert et al., 2006], facilitating impersonal moral judgments. However, the exact cognitive interpretation of this finding remains elusive due to its inherent task-free nature and warrants further research.

In the current study, we also report a positive association between impulsive-irresponsible traits and connectivity between the IFPN—implicated in adaptive executive control [Dosenbach et al., 2007]—and the IFN—implicated in behavioral inhibition [Aron et al., 2004]. Furthermore, there was a marginally significant positive association with within-network connectivity in the contralateral prefrontal cortex of the rFPN. While aberrant connectivity of executive control networks is not surprising in relation to impulsive-irresponsible traits [Fowles and Dindo, 2009], the latter finding suggests a specific mechanism in the context of increased interhemispheric connectivity [Raine et al., 2003] and deficient interhemispheric segregation. As mentioned in the introduction, segregation is essential for complex brain network function [Tononi et al., 1998], while lateralization is a key characteristic of the neuroanatomy of several cognitive functions [Zaidel and Iacoboni, 2003]. Of note, differences in interhemispheric asymmetry have previously been reported in ADHD [Hoepfner et al., 2008], human aggressive behavior [Hofman and Schutter, 2009] and in adult psychopathy [Hoppenbrouwers et al., 2014]. Our findings are consistent with those of Hoppenbrouwers et al. [2014] who showed higher Transcranial Magnetic Stimulation (TMS) induced Interhemispheric Signal Propagation from the right to the left dorsolateral prefrontal cortex (dlPFC) in psychopathy. This finding may be interpreted as indicating reduced local inhibition of the interhemispheric input signal by interneurons relying on γ -aminobutyric acid (GABA) as their primary neurotransmitter within the left dlPFC. This is consistent with a second study by Hoppenbrouwers et al. [2013], using paired pulse TMS to show reduced cortical inhibition—mediated by GABA_B-dependent interneurons—in the left dlPFC of psychopaths, when compared to healthy controls. Although the number of comparisons and trend-level significance of the rFPN finding in the current study warrant replication, we speculate that these findings—indicating deficient contrahemispheric inhibition and segregation—may relate to the inability to switch from approach to avoidance oriented behavior [Harmon-Jones, 2003], as observed in psychopathic individuals [Arnett et al., 1997].

Finally, we found a marginally significant negative association between within-network connectivity in the SN in a cluster of voxels in the amygdala and impulsive-irresponsible traits. Although this finding is interesting given the amygdala's prominent role in theories on antisocial and psychopathic development [Blair, 2013], it should be replicated before suggestions on its implications can be made.

In summary, this study provides evidence for RSN connectivity as a robust and specific correlate of juvenile psychopathic traits dimensions. While this study has several important strengths, including its large representative sample of adolescents from a childhood arrestee cohort, the multidimensional approach of psychopathy and a focus on multiple ICA-derived measures of RSFC, its results should be interpreted in light of several limitations. First, we used a self-report measure of psychopathic traits and as such some response bias may have been present. Although this questionnaire is widely used in juvenile psychopathy research [Skeem and Cauffman, 2003], we recommend that future studies also use informant measures of psychopathic traits. Second, given the novelty of some of our findings and the exploratory nature of some analyses, replication is warranted. Finally, our study population is relevant with respect to cross-diagnostic dimensional approaches to psychopathic traits, but its uniqueness does not allow generalization of the results to all antisocial populations. Nonetheless, this study provides clear indications for trait-specific associations with RSN connectivity in at-risk adolescents.

CONCLUSIONS

We conclude that psychopathic traits are related to distinct and plausible RSN correlates: callous-unemotional traits were related to connectivity in the DMN, whereas impulsive-irresponsible traits were predominantly related to connectivity differences in frontoparietal circuits. Based on our findings as well as previous studies, it is clear that psychopathic traits can be conceptualized in the context of neural network connectivity, and that psychopathy is not a unitary construct, but consists of several correlated but distinct dimensions that show overlap but also clear dissociations in underlying neural substrates. Separating these dimensions may greatly enhance specificity of research findings, as well as clinical diagnoses and treatment.

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