**Supplementary Materials to Fairchild et al. *Neuroanatomical markers of familial risk in adolescents with Conduct Disorder and their unaffected relatives***

**Supplementary Table 1.** Cortical structure differences between the Conduct Disorder, unaffected relative and healthy control groups, *when including lifetime ADHD symptoms as a covariate of no interest*.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Group comparison** | **Brain region** | **Hemisphere** | **NVtxs** | **Size (mm^2)** | **X** | **Y** | **Z** | **Max** | **CWP** |
| Cortical Volume |  |  |  |  |  |  |  |  |  |
| No significant differences between groups |  |  |  |  |  |  |  |  |  |
| Cortical Thickness |  |  |  |  |  |  |  |  |  |
| CD > HC | Medial orbitofrontal cortex | L | 644 | 553.2 | -2 | 27 | -26 | 2.1 | 0.037 |
| CD > UR | Superior frontal gyrus | L | 852 | 682.0 | -13 | 1 | 72 | 3.3 | 0.029 |
| Cortical Surface Area |  |  |  |  |  |  |  |  |  |
| No significant differences between groups |  |  |  |  |  |  |  |  |  |
| Local Gyrification Index |  |  |  |  |  |  |  |  |  |
| HC > CD | Inferior parietal cortex | L | 2190 | 1586.5 | -39 | -80 | 32 | 2.1 | <0.001 |
| CD > HC | Entorhinal cortex | L | 2120 | 1330.1 | -21 | -7 | -27 | 1.8 | <0.001 |
|  | Parahippocampal gyrus | R | 4135 | 2981.6 | 19 | -20 | -24 | 2.9 | <0.001 |
| HC > UR | Inferior parietal cortex | L | 1497 | 1184.8 | -39 | -79 | 33 | 2.3 | 0.001 |
| UR > HC | Inferior temporal cortex | L | 1161 | 962.2 | -43 | -16 | -39 | 2.4 | 0.010 |
|  | Rostral anterior cingulate | R | 2107 | 1552.9 | 2 | 25 | -9 | 3.0 | <0.001 |
| UR > CD | Superior frontal cortex | L | 1563 | 1227.7 | -13 | 28 | 55 | 2.5 | 0.001 |
|  | Inferior parietal cortex | L | 1276 | 807.4 | -46 | -59 | 44 | 1.7 | 0.023 |
| CD > UR | Entorhinal cortex | R | 2149 | 1538.3 | 24 | -18 | -21 | 2.0 | <0.001 |

**Key:** ADHD, attention-deficit/hyperactivity disorder; CD, Conduct Disorder; CWP, cluster-wise-P value; HC, healthy control; L, left; NVtxs, number of vertices; Max, maximum -log10(p value) in the cluster; R, right; UR, unaffected relatives. Note: Only significant pairwise comparisons between the groups are reported.

**Factor structure and psychometric properties of the Inventory of Callous-Unemotional traits (ICU) and Youth Psychopathic traits Inventory (YPI)**

**Factor structure of the ICU:**

The self-report version of the Inventory of Callous-Unemotional traits (ICU; Essau, Sasagawa & Frick, 2006) contains 24 items scored on a 0-3 scale. The factor structure of the ICU remains debated with some studies reporting problems identifying factor models with adequate fit without modifications (e.g., item exclusions; Houghton , Hunter, & Crow, 2013). The majority of studies support a three-factor structure comprising the factors callousness, uncaring and unemotional (Essau *et al.*, 2006; Pechorro, Ray, Barroso, Maroco, & Gonçalves, 2016), with some indication that these load onto a first-order general callous-unemotional factor (Essau *et al.*, 2006; Kimonis *et al.*, 2008).

**Reliability of the ICU:**

Cronbach’s alphas for the ICU total score and individual subscales were acceptable to good (.78-.82; Peterson, 1994), except for the ICU unemotional subscale which showed questionable internal consistency (α = .63; see Supplementary Table 2). These reliabilities are broadly in line with previous studies (e.g., Colins, Andershed, Hawes, Bijtterbier, & Pardini, 2016; Pechorro *et al.*, 2016), including a recent meta-analysis (Cardinale & Marsh, 2020). Mean inter-item correlations can be considered good if they fall between 0.15 and 0.50 (Clark & Watson, 1995), which was the case for the total ICU score as well as all three subscales.

**Factor structure of the YPI:**

The Youth Psychopathic traits Inventory (YPI; Andershed, Kerr, Stattin, & Levander, 2002) contains 50 items scored on a 1-4 point scale, which form 10 subscales (each consisting of five items). Exploratory and confirmatory factor analyses in community, clinical and forensic samples from a range of different countries (Andershed *et al.*, 2002; Colins, Bijttebier, Broekaert, & Andershed, 2014; Declercq*,* Markey, Vandist, & Verhaeghe, 2009; Hillege, Das, & de Ruiter, 2010; Pechorro, Ribeiro da Silva, *et al.*, 2016; but see Muñoz, Abate, Sharp, & Venta*,* 2019) suggest that these subscales form a three-factor structure comprising a Grandiose-Manipulative dimension, a Callous-Unemotional dimension, and an Impulsive-Irresponsible dimension, reflecting interpersonal, affective and behavioral aspects of psychopathy, respectively. However, growing evidence also supports improved fit for a new bifactor model that includes a general psychopathy factor reflecting the shared variance between all items (Pihet, Suter, Meylan, & Schmid, 2014; Wang *et al.*, 2017; Yang *et al.*, 2019).

**Reliability of the YPI:**

Cronbach’s alphas for the YPI total score and the Grandiose-Manipulative, Callous-Unemotional, and Impulsive-Irresponsible subscales were good to excellent (.80-.93; see Supplementary Table 2), in line with values reported in previous studies (e.g., Colins *et al.*, 2014; Neumann & Pardini, 2012). All mean inter-item correlations can be considered good (all between 0.15 and 0.50; Clark & Watson, 1995).

**Supplementary Table 2.** Callous-unemotional and psychopathic traits by group, as assessed using the self-report Inventory of Callous-Unemotional traits (ICU) and the self-report Youth Psychopathic traits Inventory (YPI)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | HC (*n* = 38) | UR (*n* = 24) | CD (*n* = 41) | *p-*value | post-hoc | α | MIC |
| ICU |  |  |  |  |  |  |  |
| Missing | 1 | 0 | 0 |  |  | 6 | 6 |
| Total | 22.46 (7.89) | 22.33 (7.66) | 31.80 (8.02) | **<.001** | HC, UR < CD | .82 | .17 |
| Unemotional | 7.68 (2.60) | 7.25 (2.59) | 9.17 (2.95) | **.012** | UR < CD | .63 | .26 |
| Callous | 6.30 (3.45) | 6.96 (3.74) | 11.80 (5.12) | **<.001** | HC, UR < CD | .79 | .26 |
| Uncaring | 8.49 (4.12) | 8.12 (3.78) | 11.07 (4.25) | **.005** | HC, UR < CD | .78 | .31 |
| YPI |  |  |  |  |  |  |  |
| Missing | 2 | 0 | 1\* |  |  | 8 | 8 |
| Total | 100.83 (16.26) | 99.88 (17.63) | 120.96 (21.41) | **<.001** | HC, UR < CD | .93 | .20 |
| Callous-Unemotional | 29.92 (6.34) | 31.83 (6.64) | 36.25 (7.28) | **<.001** | HC, UR < CD | .81 | .22 |
| Grandiose-Manipulative | 37.39 (7.91) | 33.71 (9.79) | 40.78 (11.12) | **.021** | UR < CD | .90 | .33 |
| Impulsive-Irresponsible | 33.53 (6.97) | 34.33 (5.58) | 44.70 (7.40) | **<.001** | HC, UR < CD | .87 | .29 |

*p*-values are based on one-way ANOVAs and post-hoc pairwise comparisons are based on Bonferroni corrected *t*-tests (equal variances not assumed). HC, healthy controls; UR, unaffected relatives; CD, conduct disorder; α, Cronbach’s alpha; MIC, mean inter-item correlation.

\*None missing for YPI total.

**Detailed results of the subcortical volume analyses**

Supplementary Table 3 presents the main effects of Group and the effect sizes for all pairwise group comparisons on subcortical volumes, adjusted for sex, age, total intracranial volume (orthogonalized to sex) and IQ. The displayed *p*-values are not corrected for multiple comparisons. Following the equations provided by Nakagawa and Cuthill (2007), we calculated Hedge’s *g* and its 95% confidence interval (CI) as the effect size for each comparison. Hedge’s *g* is preferable to Cohen’s *d* when group sizes are small (Hedges & Olkin, 1985) but can be interpreted in a similar manner with 0.2, 0.5, and 0.8 indicating a small, medium and large effect, respectively (Cohen, 1992).

While there were no significant group effects on volumes of the amygdala, hippocampus, caudate, pallidum, putamen, thalamus, or nucleus accumbens, there was a trend towards a group effect in the left thalamus, *F*(2,96) = 2.50, *p* = .088, ηp2 = 0.05. Post-hoc tests revealed significantly lower volume in the CD relative to the HC group (*p* = .028, Hedges’s *g* = -0.50), whereas the UR group had thalamus volumes that were intermediate between CD and control participants with no significant differences in comparison to either group (Hedges *g* = 0.26 and -0.25, respectively; see Supplementary Figure 1). The group effect in the left thalamus reached significance at the nominal significance level when IQ was not included as a covariate, *F*(2,98) = 4.04, *p* = .021, ηp2 = 0.08, but did not survive False Discovery Rate correction for multiple comparisons or adjustment for lifetime ADHD symptoms.

**Supplementary Table 3:** Main effects of group on subcortical volumes and effect sizes for the post-hoc group comparisons, adjusted for sex, age, IQ, and total intracranial volume (orthogonalized to sex)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Subcortical Region | Group effect |  | *g* | 95% CIl | 95% CIu | *p* |
| Left thalamus | *F*(2,96)=2.50, *p*=.088 | **HC > CD** | **-0.50** | **-0.95** | **-0.05** | **.028** |
|  |  | HC > UR | -0.25 | -0.76 | 0.26 | .335 |
|  |  | UR > CD | -0.26 | -0.77 | 0.24 | .300 |
| Right thalamus | *F*(2,96)=0.52, *p*=.594 | HC > CD | -0.23 | -0.67 | 0.22 | .310 |
|  |  | HC > UR | -0.14 | -0.65 | 0.37 | .593 |
|  |  | UR > CD | -0.10 | -0.60 | 0.41 | .704 |
| Left caudate | *F*(2,96)=0.77, *p*=.468 | HC < CD | 0.22 | -0.23 | 0.66 | .333 |
|  |  | HC > UR | -0.06 | -0.57 | 0.45 | .810 |
|  |  | UR < CD | 0.28 | -0.22 | 0.79 | .266 |
| Right caudate | *F*(2,96)=0.56, *p*=.572 | HC < CD | 0.16 | -0.28 | 0.61 | .466 |
|  |  | HC > UR | -0.09 | -0.60 | 0.42 | .725 |
|  |  | UR < CD | 0.26 | -0.25 | 0.76 | .313 |
| Left putamen | *F*(2,96)=0.22, *p*=.803 | HC > CD | -0.11 | -0.55 | 0.34 | .638 |
|  |  | HC < UR | 0.05 | -0.46 | 0.56 | .841 |
|  |  | UR > CD | -0.16 | -0.66 | 0.35 | .532 |
| Right putamen | *F*(2,96)=0.62, *p*=.539 | HC < CD | 0.02 | -0.42 | 0.46 | .936 |
|  |  | HC < UR | 0.26 | -0.25 | 0.78 | .306 |
|  |  | UR > CD | -0.24 | -0.75 | 0.26 | .340 |
| Left pallidum | *F*(2,96)=0.09, *p*=.917 | HC < CD | 0.09 | -0.35 | 0.53 | .679 |
|  |  | HC < UR | 0.04 | -0.47 | 0.55 | .870 |
|  |  | UR < CD | 0.05 | -0.45 | 0.56 | .835 |
| Right pallidum | F(2,96)=0.12, *p*=.884 | HC > CD | -0.10 | -0.54 | 0.34 | .645 |
|  |  | HC > UR | -0.01 | -0.52 | 0.50 | .962 |
|  |  | UR > CD | -0.09 | -0.60 | 0.41 | .713 |
| Left hippocampus | *F*(2,96)=0.67, *p*=.517 | HC < CD | 0.25 | -0.19 | 0.69 | .264 |
|  |  | HC < UR | 0.07 | -0.44 | 0.58 | .785 |
|  |  | UR < CD | 0.19 | -0.32 | 0.69 | .463 |
| Right hippocampus | *F*(2,96)=0.34, *p*=.716 | HC < CD | 0.03 | -0.41 | 0.48 | .878 |
|  |  | HC > UR | -0.17 | -0.68 | 0.35 | .519 |
|  |  | UR < CD | 0.20 | -0.30 | 0.71 | .433 |
| Left amygdala | *F*(2,96)=1.51, *p*=.227 | HC < CD | 0.07 | -0.37 | 0.51 | .763 |
|  |  | HC < UR | 0.43 | -0.09 | 0.94 | .100 |
|  |  | UR > CD | -0.35 | -0.86 | 0.15 | .166 |
| Right amygdala | *F*(2,96)=0.67, *p*=.516 | HC < CD | 0.07 | -0.37 | 0.51 | .743 |
|  |  | HC < UR | 0.29 | -0.22 | 0.81 | .259 |
|  |  | UR > CD | -0.21 | -0.72 | 0.29 | .401 |
| Left accumbens | *F*(2,96)=0.26, *p*=.774 | HC > CD | -0.16 | -0.60 | 0.28 | .477 |
|  |  | HC > UR | -0.10 | -0.61 | 0.41 | .698 |
|  |  | UR > CD | -0.06 | -0.57 | 0.44 | .801 |
| Right accumbens | *F*(2,96)=0.11, *p*=.896 | HC > CD | -0.08 | -0.52 | 0.37 | .736 |
|  |  | HC < UR | 0.04 | -0.48 | 0.55 | .892 |
|  |  | UR > CD | -0.11 | -0.62 | 0.39 | .660 |

*Note.* The greater than/less than symbol and the sign of the effect size indicate the direction of the effect. A positive effect size reflects that the respective region is larger in the second group (e.g. CD in the case of HC – CD) whereas a negative effect size indicates that the region is smaller in the second group. Significant differences are marked in bold. *p*-values are not corrected for multiple comparisons. Key: CD = Conduct Disorder; HC = healthy controls; UR = unaffected relatives; *g* = Hedge’s *g*; 95% CIl/CIu = lower and upper 95% confidence intervals of *g*.



*Supplementary Figure 1.* Post-hoc group comparisons for left thalamus volume (shown in red in the top panel which displays a coronal view of the brain). Error bars represent standard errors and *p*-values are uncorrected. HC = healthy controls; UR = unaffected relatives; CD = Conduct Disorder.

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