Cortical volume alterations in the limbic network in adolescents with high reactive aggression

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Abstract

Previous studies show aggression-related structural alterations in frontal and limbic brain regions. Most studies have focused on overall aggression, instead of its subtypes, and on specific regions instead of networks. This study aims to identify both brain networks and regions that are associated with reactive and proactive subtypes of aggression. Structural MRI data were collected from 340 adolescents (125 F/215 M) with a mean age of 16.29 (SD = 1.20). Aggression symptomatology was indexed via the Reactive Proactive Aggression Questionnaire (RPQ). Freesurfer was used to estimate Cortical Volume (CV) from seven networks and regions within specific networks associated with aggression. Two multivariate analyses of covariance (MANCOVAs) were conducted on groups for low versus higher reactive and proactive RPQ scores. Our reactive aggression MANCOVA showed a main effect in CV \([F(14,321) = 1.935, p = 0.022, \eta^2_p = 0.078]\) across all the 7-Networks. Unpacking this main effect revealed significant volumetric differences in the right Limbic Network (LN) \((p = 0.029)\) and the Temporal Pole \((p = 0.011)\), where adolescents in the higher reactive aggression group showed higher cortical volumes. Such findings are consistent with region/voxel-specific analyses that have associated atypical structure within the LN and reactive aggression. Moreover, the temporal pole is highly interconnected with regions important in the regulation and initiation of reactive aggression.

Keywords: adolescence; aggression; limbic; MRI; network; reactive

(Received 16 February 2023; revised 12 March 2024; accepted 13 March 2024)

Introduction

High levels of aggression can have significant costs to society and are one of the leading causes for youth seeking referrals to mental health (Magalotti et al., 2019). While aggression is not atypical during childhood development, maladaptive levels of aggression (i.e., overly frequent and intense) can lead to impaired social relationships, incarceration, and even death (Hendricks & Liu, 2012). An increased risk for aggression is transdiagnostic with a variety of psychiatric diagnoses, including major depressive disorder (MDD), attention-deficit/hyperactivity disorder (ADHD), conduct disorder (CD), and oppositional defiant disorder (ODD) (Buchmann et al., 2014; Liu & Cole, 2021; Saylor & Amann, 2016). Given the poor prognosis for aggressive individuals, there is a considerable need to determine reliable trait variables that might aid in clinical decision-making.

Substantial neuroimaging work has pointed to an association between an increased risk for aggression and structural and functional disruptions within regions of the fronto-limbic-striatal systems (Blair, 2016; Ducharme et al., 2011; Sukhodolsky et al., 2021). However, it is important to note that acts of aggression are not homogenous and have different subtypes and etiologies. A commonly made distinction is drawn between reactive and proactive aggression. Reactive aggression is unplanned and made in response to threat or social provocation, whereas the less common proactive aggression is goal-oriented and is seen as more callous (Blair, 2018; Blair et al., 2021; Crick & Dodge, 1996).

There are a lack of studies distinguishing between these two subtypes of aggression, though there are indications that they can be differentiated at the neural level (Cima & Raine, 2009; Naajen et al., 2020). Most neuroimaging studies focus on frontal regions involved in response control and reinforcement-based decision-making as well as limbic structures, such as the amygdala and hippocampus. Overall, high aggression, especially reactive aggression, is associated with a decrease in activity in the ventral medial prefrontal cortex (vmPFC) and an increase in activity in the amygdala (Blair et al., 2021; Choe et al., 2015; Coccaro et al., 2007; Lee et al., 2008; Sukhodolsky et al., 2021). Structural and functional
connectivity between the amygdala and vmPFC and/or orbitofrontal cortex (OFC) has also been considered to be important in regulating aggression (Sukhodolsky et al., 2021; White et al., 2016). However, one DTI study in a healthy sample showed no structural differences within OFC-amygdala connectivity between participants with high and low physical aggressiveness (Beyer et al., 2014).

There are few neuroimaging studies that have examined the differences in reactive and proactive aggression. Functional studies tend to agree on a few key findings regarding the two subtypes. The response to threat involves increased function within the amygdala, hypothalamus, and periaqueductal gray (Coker-Appiah et al., 2013; Haller, 2018). These regions are shown to be associated with reactive aggression, which is mediated by a threat response circuit involving these regions and the vmPFC (Blair, 2016). Proactive aggression has been shown to be associated with not only the amygdala but also regions implicated in goal setting and reward, such as the dorsolateral PFC and striatum (Belfry & Kolla, 2021; Blair, 2016).

Of the very few structural studies that have looked at the subtypes, there have been mixed results. There have been reports that increased anterior cingulate cortex volume (Farah et al., 2018) but decreased thickness (Romero-Martinez et al., 2022; Yang et al., 2017) is selectively associated with proactive aggression. One study using youth with conduct disorder saw significant decreases in gyrification in the bilateral superior parietal cortex within individuals with high proactive aggression scores (Jiang et al., 2022). Alternatively, though, there is at least one report that both proactive and reactive aggression were associated with increased right OFC volume and thickness of the left paracentral areas (Yang et al., 2017). Amygdala volumes have been reported to negatively correlate with proactive aggression (Naaijen et al., 2020) but positively with reactive aggression (Farah et al., 2018). Reactive aggression has also been reported to negatively correlate with insula volume (Naaijen et al., 2020).

Few studies have specifically looked at networks implicated in aggression severity. Studies have seen that alterations in connectivity within and/or between the default-mode network (DMN) and other networks/regions were predictive of aggression (Dailey et al., 2018; Ibrahim et al., 2022; Weathersby et al., 2019). Other studies have seen disruptions in activity and connectivity within the DMN in individuals who are prone to aggression (Brouilidakis et al., 2016; Dalwani et al., 2014; Sun et al., 2022; Tang et al., 2013; Zhou et al., 2016). Another network commonly seen in aggression literature is the limbic network (LN), where structural and connectivity alterations relative to typical developing participants have been reported in individuals presenting with higher aggression (Ducharme et al., 2011; Yang et al., 2017). The LN is comprised of the OFC and temporal pole (Yeo et al., 2011) and involved in important frontal-limbic connections commonly seen in those with aggression (Gan et al., 2016).

This present study will look at the differences in cortical volume (CV) between high and low aggression groups (both reactive and proactive aggression groups) within seven different networks: Visual Network, Somatomotor Network; Dorsal Attention Network, Ventral Attention Network, Limbic Network, Frontoparietal Network, and Default-Mode Network. Previous literature has shown alterations in regions within the DMN and LN in individuals at increased risk for aggression (De Brito et al., 2009; Ducharme et al., 2011; Yang et al., 2017). Because of these previous findings, we adopted an exploratory approach and hypothesized that proactive and reactive aggression would be associated with alterations in CV within these regions in these networks (specifically orbitofrontal cortices and superior temporal gyri).

**Methods**

**Participants**

Participants were recruited from a residential care facility in the Midwest and from the surrounding community. Participants recruited from the residential facility had been referred for behavioral and mental health problems, whereas participants from the community were recruited through flyers or social media. Structural MRI data were collected from 340 adolescents (125 F/215 M) with a mean age of 16.29 (SD = 1.20, 14–18 years), and IQ of 103.91 (SD = 10.73).

Exclusion criteria included braces, claustrophobia, active substance dependence, pervasive developmental disorder, Tourette’s syndrome, lifetime history of psychosis, neurological disorder, head trauma, non-English speaking, and presence of active safety concerns. Clinical characterization was done through psychiatric interviews by licensed and board-certified child and adolescent psychiatrists with the participants and their parents to adhere closely to common clinical practice. All participants and their parents provided written informed assent/consent prior to enrollment. The study protocol was approved by the Institutional Review Board at Boys Town National Research Hospital (BTNRH).

**Demographics characteristics**

Group differences in sex, age, IQ, intracranial volume (ICV) (Barnes et al., 2010), and RPQ scores were examined via chi square and independent sample t-tests. These variables were used as covariates in the following analyses.

**Data collection**

**Neuroanatomical data**

High resolution structural MRI (T1-weighted) data were collected using a 3-Tesla Siemens MRI scanner located at BTNRH. Whole-brain anatomical data for each participant were acquired using a 3D magnetization-prepared rapid acquisition gradient echo sequence, which consisted of 176 axial slices (slice thickness = 1 mm, voxel resolution = 0.9 × 0.9 × 1 mm3, repetition time = 2200ms; echo time = 2.48 ms; matrix size = 256 × 208; field of view (FOV) = 230 mm, and flip angle = 80°).

**General intelligence (IQ)**

The Wechsler Abbreviated Scale of Intelligence II (WASI-II) (Wechsler, 2011) was used to estimate IQ in the domains of perceptual reasoning, verbal comprehension, and Full-Scale IQ (FSIQ). FSIQ scores have high reliability (α = 0.98) and strong correlations (r = 0.92) with scores on the full Wechsler Adult Intelligence Scale-III (Wechsler, 1997, 1999) and were used in the current context.

**Reactive-proactive aggression questionnaire**

The Reactive-Proactive Aggression Questionnaire (RPQ; Raine et al., 2006) is a 23-item questionnaire which has shown to be a validated measure of both proactive aggression (11 items; α = 0.87) and reactive (12 items; α = 0.83) aggression in youth (Cima et al., 2013).
Table 1. Demographics of sample

<table>
<thead>
<tr>
<th>Demographics</th>
<th>High Reactive Aggression N = 178</th>
<th>Low Reactive Aggression N = 162</th>
<th>Significance (χ²/t-value)</th>
<th>High Proactive Aggression N = 208</th>
<th>Low Proactive Aggression N = 132</th>
<th>Significance (χ²/t-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>66 F/112 M</td>
<td>59 F/103 M</td>
<td>0.02*</td>
<td>73 F/135 M</td>
<td>52 F/80 M</td>
<td>0.64*</td>
</tr>
<tr>
<td>Age (SD)</td>
<td>16.26 (1.13)</td>
<td>16.31 (1.27)</td>
<td>0.30*</td>
<td>16.22 (1.12)</td>
<td>16.39 (1.30)</td>
<td>1.23**</td>
</tr>
<tr>
<td>IQ (SD)</td>
<td>102.20 (9.15)</td>
<td>105.79 (11.98)</td>
<td>3.08**</td>
<td>102.79 (9.98)</td>
<td>105.68 (11.64)</td>
<td>2.36*</td>
</tr>
<tr>
<td>ICV (10⁶) in mm³ (SD)</td>
<td>1.50 (1.57)</td>
<td>1.53 (1.56)</td>
<td>1.45*</td>
<td>1.51 (1.50)</td>
<td>1.52 (1.66)</td>
<td>0.81*</td>
</tr>
<tr>
<td>Total (SD)</td>
<td>14.73 (6.80)</td>
<td>4.37 (2.36)</td>
<td>−19.29***</td>
<td>13.08 (7.40)</td>
<td>4.49 (2.88)</td>
<td>−15.04***</td>
</tr>
<tr>
<td>Reactive (SD)</td>
<td>11.12 (3.49)</td>
<td>3.59 (1.85)</td>
<td>−25.14***</td>
<td>9.46 (4.63)</td>
<td>4.49 (2.88)</td>
<td>−12.21***</td>
</tr>
<tr>
<td>Proactive (SD)</td>
<td>3.61 (4.12)</td>
<td>0.67 (1.17)</td>
<td>−9.13***</td>
<td>3.61 (3.74)</td>
<td>0.00 (0.0)</td>
<td>−13.94***</td>
</tr>
<tr>
<td>MDD (%)</td>
<td>33 (18.5)</td>
<td>12 (7.4)</td>
<td>−</td>
<td>31 (14.9)</td>
<td>14 (10.6)</td>
<td>−</td>
</tr>
<tr>
<td>SAD (%)</td>
<td>47 (26.4)</td>
<td>30 (18.5)</td>
<td>−</td>
<td>49 (23.6)</td>
<td>28 (21.2)</td>
<td>−</td>
</tr>
<tr>
<td>GAD (%)</td>
<td>56 (31.5)</td>
<td>30 (18.5)</td>
<td>−</td>
<td>58 (27.9)</td>
<td>28 (21.2)</td>
<td>−</td>
</tr>
<tr>
<td>PTSD (%)</td>
<td>27 (15.2)</td>
<td>11 (6.8)</td>
<td>−</td>
<td>30 (14.4)</td>
<td>8 (6.1)</td>
<td>−</td>
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<tr>
<td>CD (%)</td>
<td>102 (57.3)</td>
<td>43 (26.5)</td>
<td>−</td>
<td>111 (53.4)</td>
<td>34 (25.8)</td>
<td>−</td>
</tr>
<tr>
<td>ODD (%)</td>
<td>111 (62.4)</td>
<td>64 (39.5)</td>
<td>−</td>
<td>119 (57.2)</td>
<td>50 (37.9)</td>
<td>−</td>
</tr>
<tr>
<td>ADHD (%)</td>
<td>111 (62.4)</td>
<td>58 (35.8)</td>
<td>−</td>
<td>121 (58.2)</td>
<td>54 (40.9)</td>
<td>−</td>
</tr>
<tr>
<td>Antipsychotics (%)</td>
<td>13 (7.30)</td>
<td>7 (4.30)</td>
<td>−</td>
<td>16 (7.7)</td>
<td>4 (3.0)</td>
<td>−</td>
</tr>
<tr>
<td>SSRIs (%)</td>
<td>29 (16.30)</td>
<td>23 (14.2)</td>
<td>−</td>
<td>39 (18.8)</td>
<td>13 (9.8)</td>
<td>−</td>
</tr>
<tr>
<td>Stimulants (%)</td>
<td>31 (17.4)</td>
<td>21 (13.0)</td>
<td>−</td>
<td>35 (16.8)</td>
<td>17 (12.9)</td>
<td>−</td>
</tr>
</tbody>
</table>

Key to table. ns: Non-Significant; *p < 0.05; **p < 0.01; ***p < 0.001; SD = Standard Deviation; IQ = Intelligent Quotient; ICV = Intracranial Volume; MDD = Major Depressive Disorder; SAD = Social Anxiety Disorder; GAD = Generalized Anxiety Disorder; PTSD = Post Traumatic Stress Disorder; CD = Conduct Disorder; ODD = Oppositional Defiant Disorder; ADHD = Attention Deficit Hyperactivity Disorder; SSRIs=Selective Serotonin Reuptake Inhibitors. There was a 43.5% overlap between the two high aggression groupings.

Image preprocessing

The “recon-all” pipeline from the FreeSurfer toolbox (Version 6.0; https://surfer.nmr.mgh.harvard.edu) was used to process the anatomical brain images (Dale et al., 1999; Fischl et al., 1999) and for estimating CV measures. Structural image processing included head motion-correction, brain extraction, automated transformation to the standard MNI template space, volumetric segmentation into cortical and sub-cortical matter, intensity correction, and parcellation of the cerebral cortex into gyral and sulcal matter (Desikan et al., 2006). See (Dale et al., 1999; Fischl, 2004; Fischl et al., 1999) for full details. Steps to ensure preprocessing accuracy included a careful visual inspection of raw structural images, skull-stripped brain volumes, and pial surfaces via FreeSurfer (Version 6.0; https://surfer.nmr.mgh.harvard.edu).

Data analysis

Behavioral analysis

A correlation between reactive and proactive aggression scores was conducted to look at a possible association between these subtypes of aggression.

Network volume analysis

FreeSurfer was used to parcellate the whole brain into seven networks using Yeo’s atlas (Yeo et al., 2011) (N1: Visual Network; N2: Somatomotor Network; N3: Dorsal Attention Network; N4: Ventral Attention Network; N5: Limbic Network; N6: Frontoparietal Network; and N7: Default-Mode Network). A network cortical volume analysis was conducted (sex, age, IQ, and intracranial volume [ICV] were used as covariates) using network-wise CV data to look at potential differences between high and low aggression groupings. Two multivariate analyses of covariance (MANCOVAs) were conducted on the seven bilateral networks (14 total) for each subscale RPQ score group (i.e., one examining groups with higher vs. lower reactive aggression and a second examining groups differing in proactive aggression levels).

Region-based analysis

Our steps for region-based analysis are as follows: 1. Identify any significant networks (as described above). 2. If any significant networks were discovered using the above analysis, we then extracted regions from the networks. 3. We then looked at associations of CV of the extracted regions and aggression groups by performing a MANCOVA—again with sex, age, IQ, and ICV as covariates.

Follow-up analyses

Potential confounds: impact of other major psychopathologies and prescribed medications

Several of our participants were diagnosed with different psychiatric disorders including Major Depressive Disorder (N = 45), Social Anxiety Disorder (N = 77), Generalized Anxiety Disorder (N = 86), Post-Traumatic Stress Disorder (N = 38), Conduct Disorder (N = 145), Oppositional Defiant Disorder (N = 169), and Attention-Deficit/Hyperactivity Disorder (N = 175). In addition, several of our youth were on psychiatric medications (N = 124) during the time of the study, including SSRIs, stimulants, and antipsychotics. Table 1
shows demographic characteristics of both comorbidities and medications. Given the potential confounds, the MANCOVA described above (individual networks) was repeated, first, with the inclusion of psychiatric diagnoses and, second, with the inclusion of prescribed medications as covariates.

Potential confounds
In order to control for the effects of proactive aggression when looking at reactive aggression and vice versa, a follow-up MANCOVA with the other aggression subtype as a covariate will be run if either of the groups showed significant network cortical volume differences. Another follow-up MANCOVA will be run after removing participants that had high scores in both reactive and proactive aggression as well.

Results

Bivariate analysis
Reactive aggression scores and proactive aggression scores from the RPQ were significantly correlated across the entire sample ($r = 0.63, p < 0.001$).

Demographics characteristics
Table 1 shows the total number of participants in each group. There was some overlap ($n = 148, 43.5\%$) between groups (meaning these youth had high scores in both reactive and proactive aggression). There were no significant differences in sex ($\chi^2(1) = 0.016, p = 0.90$; $\chi^2(1) = 0.642, p = 0.42$) or age ($t(338) = 0.302, p = 0.76$; $t(248.52) = 1.23, p = 0.22$) between high/low reactive and high/low proactive aggression groups respectively. ICV was not significantly different between high/low reactive aggression groups, [$t(338) = 1.452, p = 0.15$], but was significantly different between high/low proactive aggression groups, [$t(338) = 0.81, p = 0.04$], where those with low proactive aggression had higher ICV. There were significant differences in IQ between high and low reactive [$t(300.378) = 3.081, p = 0.002$] and high and low proactive [$t(247.64) = 2.36, p = 0.019$] aggression groups, where lower aggression groups had higher IQ scores.

Group differences in CV
Our MANCOVAs showed a significant main effect across the 7 networks in CV for reactive aggression [$F(14,321) = 1.935, p = 0.022, \eta^2_p = 0.087$; Wilk’s lambda = 0.922] but no significant effects for the MANCOVA on proactive aggression [$F(14,321) = 0.666, p = 0.807, \eta^2_p = 0.028$; Wilk’s lambda = 0.972]. This particularly reflected group differences driven by the right Limbic Network [$F(1,334) = 4.802, p = 0.029, \eta^2_p = 0.014$], where adolescents in the higher reactive aggression group showed higher cortical volumes (Figures 1 and 2).

Follow-up exploratory analysis of the MANCOVA main effect
Our ROI-specific MANCOVA for the right Limbic Network showed significant group differences in ROI volume [$F(2,333) = 3.471, p = 0.032, \eta^2_p = 0.020$; Wilk’s lambda = 0.980]. Specifically, we saw significant difference in CV of the Temporal Pole [$F(1,334) = 6.466, p = 0.011, \eta^2_p = 0.019$], where adolescents in the higher reactive aggression group showed higher cortical volumes (Figure 3).

Follow-up to reactive aggression analysis
Diagnoses
Our follow-up MANCOVA analysis with the addition of seven psychiatric diagnoses (see Table 1 for full list) continued to show a significant equation that mirrored the results of the main analysis [$F(14,314) = 2.145, p = 0.010, \eta^2_p = 0.087$], still showing strongest significant differences in the right Limbic Network [$F(1,327) = 7.116, p = 0.008, \eta^2_p = 0.021$].

Medication
Our follow-up MANCOVA analysis with the addition of the three medications (Antipsychotics, stimulants, and SSRIs) continued to
Figure 2. Limbic network: identified cortical network, limbic network (a), and identified region of significance, temporal pole (b). Cortical volume of the right limbic network was significantly different between those with high and low reactive aggression (high reactive aggression > low reactive aggression). $^* = p < 0.05$.

Figure 3. Temporal pole. Within the right limbic network, cortical volume of the temporal pole was also significantly different between those with high and low reactive aggression (high reactive aggression > low reactive aggression) $^* = p < 0.05$. 

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show a significant equation that mirrored the results of the main analysis \[F(14,318) = 2.023, p = 0.016, \eta^2 = 0.082\], again showing strongest significant differences in the right Limbic Network \[F(1,331) = 5.126, p = 0.024, \eta^2 = 0.015\].

**Subtype**

Our follow-up MANCOVA analysis with the addition of proactive aggression as a covariate in our regression analysis, continued to show a significant equation that mirrored the results of the main analysis \[F(14, 320) = 1.805, p = 0.037, \eta^2 = 0.073\], again showing strongest significant differences in the right Limbic Network \[F(1,333) = 5.557, p = 0.019, \eta^2 = 0.016\]. When adding reactive aggression as a covariate to our MANCOVA looking at proactive aggression, we still saw a non-significant result \(p = 0.879\).

**Removal of participants in both high score groups**

Our next follow-up MANCOVA was the same as the main analysis (7 Network), however, with the removal of individuals that had both high reactive aggression scores and high proactive aggression scores \(43.5\% who had both\). The removal of these participants made our results no longer significant within the reactive aggression groupings \[F(14,173) = 1.423, p = 0.147, \eta^2 = 0.103\].

**Discussion**

The goal of this study was to examine differences in cortical volumes (CV) in brain networks within high and low aggression groups (both reactive and proactive aggression). We found that CV of the right Limbic Network (LN) was significantly greater in those with higher vs. lower reactive aggression scores. In addition, region-specific analysis showed that within the right LN, CV of the temporal pole was significantly increased in the higher reactive aggression score group. Contrary to our hypothesis, we did not see any significant differences in CV within networks in proactive aggression groups.

Previous work has typically taken a region/voxel-focused approach to analysis and not focused on network-level structural alterations in individuals prone to higher levels of aggression (Chester et al., 2017; Jiang et al., 2022; Naajien et al., 2020). However, and consistent with the current findings, there are several previous results which indicate atypical LN function/structure relating to increased aggression risk. Indeed, accounts of reactive aggression have stressed the importance of dysfunction in components of this system for some time (Bertsch et al., 2020; Blair, 2004). Individuals at increased risk of reactive aggression frequently show poor emotion regulation (Nikolic et al., 2022). Notably, the role of OFC in emotion regulation has long been recognized (Blair, 2004; Christiansen et al., 2019; Zheng et al., 2018). Empirical work has associated atypical connectivity between the amygdala/temporal cortex and OFC with an increased risk for aggression, particularly reactive aggression (Sukhodolsky et al., 2021; White et al., 2016). These regions have also been implicated in mediating reactive aggression (Coccaro et al., 2007; Gan et al., 2016). Moreover, atypical structure of OFC and amygdala volumes have been associated with an increased risk of reactive aggression (Farah et al., 2018; Yang et al., 2017), and lesions within the LN can lead to increased impulsivity and aggression (Berlin et al., 2004; Kunishi et al., 2016; Potegal, 2012; Shiba et al., 2015).

It should be noted that within the LN, it was particularly atypical temporal pole structure that was associated with increased risk for reactive aggression. The temporal pole is a dominant hub in the processing of semantic and socioemotional information (Guo et al., 2022; Pehrs et al., 2017) and is considerably interconnected with other regions very important in the regulation and initiation of reactive aggression: the amygdala (Li et al., 2016), as well as OFC (Novitskaya et al., 2020; Olson et al., 2007). It could be speculated that larger volumes are associated with strong emotional reactions and disruptions in the perception of provocations, leading to outbursts or disrupted emotional processing. Previous work has tended to report reductions in thickness and volume in the temporal pole (rather than the increased volume seen here) in groups of aggressive individuals (Cope et al., 2014; Ermer et al., 2012; Gregory et al., 2012; Ly et al., 2012). However, most of that work has been conducted in individuals with psychopathy which was not a predominant feature of the sample with higher reactive aggression studied here. It is notable that one previous finding, in a slightly more similar study, also observed increased temporal pole volumes in those exhibiting higher reactive aggression (Breitschuh et al., 2018).

In contrast to predictions, there was no association of CV within the DMN and either reactive or proactive aggression. Previous work has reported alterations in connectivity within and/or between the DMN and other networks/regions were predictive of aggression (Dailey et al., 2018; Ibrahim et al., 2022; Weathersby et al., 2019), disruptions in activity and connectivity within the DMN in individuals who are prone to aggression (Broudlakids et al., 2016; Dalwani et al., 2014; Sun et al., 2022; Tang et al., 2013; Zhou et al., 2016) and structural alterations within the DMN in individuals at increased risk for aggression (De Brito et al., 2009; Ducharme et al., 2011; Yang et al., 2017). The reason for the absence of comparable findings in the current cohort are unclear but it is possible that it represents a Type II error.

Also, in contrast to predictions, we found no networks showing atypical structural in the group of participants showing higher levels of proactive aggression. Relatively little previous work has focused on individuals showing higher levels of proactive aggression as opposed to focusing on samples who are at increased for proactive aggression (but also reactive aggression), such as individuals with psychopathy (Blair, 2010; Garofalo et al., 2021; Hofhansel et al., 2020). It has been argued that proactive aggression is a chosen behavior reflecting the individual’s decision-making (Blair, 2019). This may result in socially undesirable choices because of the economic realities of the individual or because the individual’s representations of potential costs (e.g., the distress of others) is disrupted (Blair, 2019). As such, it is possible that structural differences may be less commonly seen in those at increased risk for proactive rather than reactive aggression.

Despite the strengths of our study, including large sample size and diverse range of clinical symptomatology, there were some caveats. First, 72% of the adolescents in our sample had at least one psychiatric diagnosis, and it could be argued that we are seeing results from specific disorders instead of aggression severity. Our follow-up analysis with diagnoses as covariates showed results approximate to the main analysis, with the LN still showing highest significance. Second, multiple adolescents were on medications including SSRIs, stimulants, and antipsychotics. Our follow-up analysis with the inclusion of the medications as covariates also revealed LN showing significant differences between the two groups. Third, our reactive aggression group was not matched in IQ scores; those in the lower reactive aggression group had higher IQ scores than those with higher reactive aggression. However, we did use IQ as a covariate in our analysis (in addition to age, sex, and ICV). As such, it is unlikely that our findings can be considered to
reflect group differences in IQ. Fourth, multiple participants were in both the high proactive aggression group as well as the high reactive aggression group. A post hoc analysis was ran removing individuals in both groups, which made our results no longer significant (see Table 1 for breakdown of groups). Fifth, the group-based analysis approach chosen here due to test-retest reliability concerns runs the risk of data loss by dichotomizing the variable of interest (Dawson & Weiss, 2012) Our goal would be to extend the current study in future work where the test-retest reliability of core measures is known and satisfactory.

In conclusion, our study revealed that CV of the right LN, particularly the temporal pole region within the LN, was significantly greater in those with higher reactive aggression scores. These findings broaden our knowledge of the neurobiology of reactive aggression and can inform future imaging work.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0954579424000750.

Data availability statement. The data that support the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to IRB restrictions.

Funding statement. This research was in part supported by the National Institute of Mental Health under award number K22-MH109558 (RJB). We would like to thank Ron Copsey, Kim VanHorn, Michael Wright, Mark Timm, Michelle Kelly, and Sarah Johnson for their contributions to data collection.

Competing interests. None.

References


