Atypical Neural Responses During Face Processing in Female Adolescents With Conduct Disorder

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Objective: Conduct disorder (CD) in females is associated with negative adult outcomes including mental health problems and personality disorders. Although recent neuroimaging studies have reported changes in neural activity during facial emotion processing in males with CD or callous-unemotional (CU) traits, there have been no neuroimaging studies specifically assessing females with CD. We addressed this gap by investigating whether female adolescents with CD show atypical neural activation when processing emotional or neutral faces. **Method:** We acquired functional magnetic resonance imaging (fMRI) data from 20 female adolescents with CD and 20 female control participants while they viewed angry, sad, and neutral faces. **Results:** An omnibus group (CD, control) by facial emotion (angry, sad, neutral) analysis of variance (ANOVA) revealed main effects of facial emotion in superior temporal cortex, fusiform gyrus, ventrolateral prefrontal cortex and insula, and main effects of group in medial orbitofrontal cortex (OFC) and right anterior insula. Female participants with CD showed reduced medial OFC and increased anterior insula responses relative to healthy controls. There were no significant group × facial emotion interactions. Lifetime CD symptoms were negatively correlated with amygdala, superior temporal cortex, fusiform gyrus, and dorsolateral prefrontal cortex activity for the contrast "all-faces versus fixation." CU traits were negatively correlated with fusiform gyrus activity for the contrast sad versus neutral faces. **Conclusion:** Females with CD showed atypical neural activation during the processing of all facial expressions, irrespective of valence. Our results demonstrate that severity of CD symptoms and CU traits is important in explaining abnormal patterns of neural activity. J. Am. Acad. Child Adolesc. Psychiatry, 2014;53(6):677–687. **Key Words:** CD, CU traits, females, face processing, fMRI

Conduct disorder (CD) is characterized by a pervasive pattern of antisocial and violent behavior in which the rights of others are violated.[1] CD is one of the most common disorders in adolescent females[2] and is associated with an increased risk of developing antisocial or borderline personality disorder, substance dependence, depression, and physical health problems in adulthood.[3-6] Despite this negative prognosis, we know relatively little about the neurobiological mechanisms underlying CD in females, as there have been few neuropsychological studies of this group, and as functional magnetic resonance imaging (fMRI) studies of CD have been largely restricted to males. Of the previous 26 fMRI studies of CD, 17 have included only males, and the remaining 9 studies recruited mixed samples containing only a small number of females, resulting in an underrepresentation of females with CD (442 males versus 41 females pooled across 26 studies; Table S1, available online, provides references). Critically, none of these studies investigated brain activity in females with CD specifically.

To address this gap in the literature, we investigated neural responses to emotional and neutral facial expressions in female adolescents with CD relative to healthy controls. An earlier behavioral study found impaired recognition of facial expressions of anger and disgust in female adolescents with CD, and an additional impairment in sadness (but not fear) recognition

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in females with CD and psychopathic traits.[7] Similar deficits in anger and disgust recognition were observed in males with CD, [8] indicating that CD in both sexes is associated with difficulties in processing these emotions. In contrast, psychopathic traits were associated with deficits in both sadness and fear recognition in males with CD.[8] To follow up these behavioral findings and characterize the underlying neural processes, we previously conducted an fMRI study and observed reduced amygdala, anterior insula, orbitofrontal cortex (OFC), and anterior superior temporal cortex responses to emotional versus neutral faces in male adolescents with CD.[9]

On the basis of these earlier results, we predicted that female adolescents with CD would show atypical neural responses when processing angry or sad relative to neutral facial expressions. Specifically, we predicted that females with CD would show reduced activity in regions involved in social cognition and emotion processing, such as the amygdala, anterior insula, OFC and superior temporal cortex, during the processing of negative facial expressions.[10,11] This would be demonstrated by significant interactions between group and facial emotion in these regions, in which healthy controls would show greater neural responses to angry and sad faces than neutral faces. Meanwhile, participants with CD would show weaker differentiation between these facial expressions. However, it was also possible that females with CD would show increased neural responses to neutral faces, as we previously found that male adolescents with CD showed increased amygdala and insula responses to neutral faces.[9]

Our second aim was to examine relationships between brain activity and severity of CD, as quantified by number of CD symptoms. We predicted that CD symptoms would be negatively correlated with amygdala, anterior insula, OFC and superior temporal cortex activity, given previous research in males showing negative relationships between activity in these regions and CD symptoms[9] or aggressive behavior.[12]

The presence of CU traits (such as emotional detachment) is thought to delineate a particularly severe and persistent form of CD.[13] Given the importance of callous-unemotional (CU) traits for understanding heterogeneity within antisocial behavior,[14] our final aim was to investigate whether CU traits would modulate neural activity during facial emotion processing. The Integrated Emotion Systems (IES) model[15] proposes that distress cues, such as sad or fearful facial expressions, play a critical role in the socialization process. According to this model, typically developing children find distress cues aversive, so they learn to stop engaging in aggressive behaviors that elicit such cues. Individuals with CU traits are proposed to be insensitive to distress cues, which disrupts their socialization, rendering them at increased risk for instrumental aggression. The IES model therefore predicts that CU traits would be associated with impaired recognition of sad and fearful expressions, along with reduced neural responses to these facial expressions. Previous research has provided evidence for selective or disproportionate impairments in sadness and fear recognition in individuals with CU traits[8,16,17] (although see Dawel *et al.*[18] for a meta-analysis showing pervasive emotion recognition deficits in psychopathy). However, with the exception of 1 study showing impaired sadness recognition in female adolescents with CD and CU traits[7] and a study reporting deficits in sadness recognition in female psychopaths,[19] most previous studies of CU traits or psychopathy have either focused on males alone or have included small numbers of females.[16-18] fMRI studies have shown reduced amygdala responses to fearful facial expressions in male children with conduct problems and CU traits[20] and in a group of adolescents with CU traits and disruptive behavior disorder diagnoses who were predominantly male.[21] Studies in adults have shown reduced amygdala or fusiform gyrus responses to fearful faces in males with psychopathy.[22,23] However, no comparable data exist on the effects of CU traits on neural activation in females. To further investigate the IES model, we assessed whether CU traits were associated with reduced brain activation during the processing of sad facial expressions. Sadness, rather than fear, was selected, given previous behavioral results showing that CU or psychopathic traits were associated with impaired recognition of sadness but not fear in females,[7,19] and on the basis of a meta-analysis showing that CU traits are most strongly linked with deficits in sadness recognition.[18] We predicted that CU traits would be negatively correlated with amygdala, anterior insula, OFC and fusiform gyrus responses to sad versus neutral expressions.

METHOD

Participants

Twenty-two female adolescents with CD were recruited from schools, pupil referral units, and the Cambridge

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