An Amygdala Structural Abnormality Common to Two Subtypes of Conduct Disorder: A Neurodevelopmental Conundrum

A volume reduction in the amygdala appears to be common in two different groups of conduct-disordered adolescents. In the largest structural imaging study of conduct disorder to date, Fairchild et al. (1), in this issue of the *Journal*, compared 63 children with conduct disorder (early onset: N=36; adolescent onset: N=27) with 27 healthy comparison subjects on gray matter volumes in four regions of interest. Their primary finding was reduced amygdala volumes in *both* conduct disorder subgroups compared with volumes in healthy subjects. The adolescent-onset subgroup additionally demonstrated volume reductions in the right insula, left orbito-frontal cortex, and dorsomedial prefrontal cortex relative to comparison subjects. The early-onset subgroup, in contrast, only evidenced reduced dorsomedial gray matter volumes. Finally, within the conduct disorder group, higher scores on callous-unemotional traits were associated with a volumetric *increase* in the caudate nucleus; otherwise, no association was found with psychopathic-like personality. These new research findings in adolescents with conduct disorder converge with other findings in adolescents and adults that have shown both structural and functional abnormalities in the amygdala (2, 3). As such, they provide an important lifespan perspective to the adult literature on conduct disorder and add growing support for a neurodevelopmental perspective on the disorder.

"Where exactly are we to draw the developmental line…between early and late conduct disorder?"

Fairchild et al. (1) argue that the amygdala volume reduction they observe may well underlie the fear conditioning deficits previously found in children with conduct disorder. This makes theoretical sense in that the amygdala is critically important in the generation of fear conditioning. They also suggest that because the amygdala plays a role in initiating the hypothalamic-pituitary-adrenal response to stress, it could also account for prior findings of blunted stress reactivity in both conduct disorder subgroups. This perspective again dovetails with theoretical perspectives and empirical findings in both child and adult literatures on antisocial behavior, psychopathy, and violence (4–6).

These findings raise the developmentally provocative question of how early in life amygdala deficits are in place in children with conduct disorder. As the authors are careful to point out, their study is agnostic as to whether amygdala deficits are a cause or a consequence of conduct disorder. A neurodevelopmental theoretical perspective would nevertheless predict that early maldevelopment of the amygdala gives rise to later antisocial behavior. One proxy for amygdala functioning, autonomic fear conditioning, has recently been found to be impaired in 3-year-old children who grow up to become criminal offenders (7). These early childhood findings support the putative etiological significance of the amygdala in predisposing to conduct disorder and to adult antisocial behavior and underscore the salience of Fairchild et al.'s findings.

The theoretical challenge posed by this new study stems from the finding that structural amygdala impairments are found not just in conduct-disordered children with an early onset of their behavior problems but also in children whose antisocial behavior

emerges later or in adolescence. DSM-IV divides children with conduct disorder into either an early-onset subtype (starting before age 10 years) or an adolescent-onset subtype (starting at age 10 years or older). While this distinction has been questioned with respect to how reliably clinicians can assess age of onset (8), differential correlates of these developmental forms of conduct disorder have been documented at the psychosocial, genetic, personality, and neuropsychological levels of analysis (8, 9). Why then would both subgroups be found with a structural brain abnormality that is thought to have neurodevelopmental significance?

There is not an unequivocal answer, as there is a dearth of imaging studies on conduct disorder. Sample sizes have been small, and researchers have understandably targeted only the early-onset subgroup hypothesized to have a neurodevelopmental origin (8). These few studies document structural brain abnormalities in the early-onset subgroup, but it can reasonably be questioned, as done by Fairchild et al., whether such brain abnormalities are specific to this early-onset subgroup.

This is the important gap in our knowledge that Fairchild et al. adroitly fill with their study. Theirs is the first to test a developmental taxonomic theory of antisocial behavior using structural brain imaging. Their empirical findings clash with the prevailing model that emphasizes a pathophysiological basis to early-onset antisocial behavior—but not in those whose antisocial behavior develops in adolescent years when rebellious behavior is almost normative (8). If anything, Fairchild et al. find the adolescent-onset subgroup to show a somewhat larger volume reduction in the amygdala and more widespread gray matter reductions (the insula and dorsomedial prefrontal cortex) than that found in the early-onset subgroup.

These are vexing findings. The etiology of late-onset antisocial behavior is thought to reside more in peer pressure than in brain deformation. Is the hypothesized neurodevelopmental basis to conduct disorder really specific to the early-onset form as many researchers suggest? Or does a neurodevelopmental perspective extend more broadly into generic antisocial behavior? One swallow does not make a summer. Some may point out that while Fairchild et al. break into new territory, perhaps these new findings are serendipitous. The counterpoint is that this productive group has also previously documented in *both* conduct disorder subgroups blunted cortisol and cardiovascular stress responsivity, impaired autonomic fear conditioning, reduced startle-blink reflex, reduced affective decision making, and poorer facial expression recognition (1). The evidence from their laboratory is mounting, with multiple clinical neuroscience measures converging on the conclusion that both subgroups have common neurobiological and neurocognitive risk factors for conduct disorder. The conundrum continues.

The future challenges posed to researchers by this neurodevelopmental quandary are multiple and profound. Where exactly are we to draw the developmental line—if indeed we draw it at all—between early and late conduct disorder? Do individuals with structural or functional impairments to the amygdala show a different clinical course, irrespective of their age of onset? And in the wake of the Supreme Court's decision not to execute individuals under the age of 18 years based on developmental grounds, are we to judicially treat conduct-disordered children with amygdala and prefrontal impairments differently from those adolescents with conduct disorder who are lacking such neuroanatomical deficits? Just as rule-breaking children under the age of 18 years may lack the *cognitive* capacity to appreciate the wrongfulness of their acts, do those with a compromised amygdala and poor fear conditioning lack the *affective* capacity to appreciate the harm they do to others? Are they also less sensitive to the deterrent effects of punishment meted out by the criminal justice system? Assuming that the amygdala finding is replicable, is in place early in life prior to conduct disorder onset, and can be reliably assessed and compared with normative values, should amygdala volume reduction receive greater judicial attention in the guilt phase of a capital case of an *adult* with a documented childhood history of conduct disorder? These are significant questions for forensic psychiatry and also the tense interface between neuroscience and the law.

In the final analysis, Fairchild et al. report results that at least make us rethink the specificity of a neurodevelopmental hypothesis for either an early-onset conduct disorder subgroup or a psychopathic-like subgroup. Their findings are inevitably by no means definitive, requiring independent replication and extension in other laboratories. While there will be disagreement on whether they cast significant doubt on Moffitt's (8) developmental taxonomic theory of antisocial behavior, there may be more agreement on the converging lines of neurobiological evidence that are supporting an amygdala abnormality as both a central risk factor for conduct disorder and a neural source of the social-emotional disturbances found in individuals with the disorder. Prospective longitudinal imaging research that teases out the temporal ordering of variables will help further test a neurodevelopmental hypothesis of conduct disorder.

References

1. Fairchild G, Passamonti L, Hurford G, Hagan CC, von dem Hagen EAH, van Goozen SHM, Goodyer IM, Calder AJ: Brain structure abnormalities in early-onset and adolescent-onset conduct disorder. Am J Psychiatry 2011; 168:624–633
2. Yang Y, Raine A, Narr KL, Colletti P, Toga A: Localization of deformations within the amygdala in individuals with psychopathy. Arch Gen Psychiatry 2009; 66:986–994
3. Glenn A, Raine A, Schug R: The neural correlates of moral decision-making in psychopathy. Mol Psychiatry 2009; 14:5–6
4. Blair RJ: The amygdala and ventromedial prefrontal cortex in morality and psychopathy. Trends Cogn Sci 2007; 11:387–392
5. Sterzer P, Stadler C, Poustka F, Kleinschmidt A: A structural neural deficit in adolescents with conduct disorder and its association with lack of empathy. Neuroimage 2007; 37:335–342
6. van Goozen SH, Fairchild G, Snoek H, Harold GT: The evidence for a neurobiological model of childhood antisocial behavior. Psychol Bull 2007; 133:149–182
7. Gao Y, Raine A, Venables PH, Dawson ME, Mednick SA: Association of poor childhood fear conditioning and adult crime. Am J Psychiatry 2010; 167:56–60
8. Moffitt TE: Adolescence-limited and life-course-persistent antisocial behavior: a developmental taxonomy. Psychol Rev 1993; 100:674–701
9. Moffitt TE, Arseneault L, Jaffee SR, Kim-Cohen J, Koenen KC, Odgers CL, Slutske WS, Viding E: Research review: DSM-V conduct disorder: research needs for an evidence base. J Child Psychol Psychiatry 2008; 49:3–33

ADRIAN RAINE, D.PHIL.

Address correspondence and reprint requests to Dr. Raine, Departments of Criminology, Psychiatry, and Psychology, University of Pennsylvania, 3809 Walnut St., Philadelphia, Pa. 19104; araine@sas.upenn.edu (e-mail).
Editorial accepted for publication March 2011 (doi: 10.1176/appi.ajp.2011.11030416).

The author reports no financial relationships with commercial interests.